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ORIGINAL ARTICLE

Impact of biliary complications in right lobe living donor liver transplantation

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Summary

Biliary reconstruction is one of the most challenging parts of right lobe living donor liver transplantation (RL LDLT), and biliary complications have been reported as the first source of surgical complications of this procedure. We reviewed biliary reconstruction and complications in 27 consecutive RL LDLTs. We compared the first 14 procedures (group 1) to the last 13 (group 2). Seven patients (25.9%) experienced a biliary complication (five leaks and two strictures). The incidence of biliary complications was 11.1% in RL grafts with a single duct and 55.5% in graft presenting multiple bile ducts ($P = 0.03$). Four of the 18 patients with a duct-to-duct reconstruction (22.2%) and three of the 11 patients with a Roux-en-Y reconstruction (27.3%) developed a biliary complication ($P =$ ns). The incidence of biliary complications significantly decreased from 42.9% ($n = 6$) in the first group to 7.6% ($n = 1$) in the second group ($P = 0.05$). The overall 1-year graft and patient survival were 57.1% and 64.3% in group 1 versus 100.0% and 100% in group 2 ($P = 0.01$; $P = 0.006$). Biliary complications remain one of the most important technical complications affecting RL LDLT. Nevertheless, attention and surgical refinement can lead to a significant reduction of the biliary complication rate, improving graft and patient survival.

Introduction

Living donor liver transplantation (LDLT) using right lobe (RL) grafts has become an accepted therapeutic option for adult patients with end-stage liver diseases in both Western and Eastern countries [1–3]. However, indications for this procedure remain controversial and recommended for selected patient population [4].

One of the most debated technical aspects of RL LDLT is the biliary reconstruction, which has long been reported as the Achilles' heel of this procedure [5].

Different variables such as arterial blood supply, multiple biliary ducts, prolonged cold ischemia time, chronic rejection and cytomegalovirus infection have been advocated as associated with biliary complications [6]. Moreover, although both the Roux-en-Y hepato-jejunostomy or the duct-to-duct anastomosis have been proposed as routine reconstruction, the most appropriate procedure of biliary reconstruction remains to be established [7,8].

The aim of the study was to assess the impact of biliary complications on our series of 27 consecutive RL LDLT procedures, analyzing incidence, time of onset, risk factors, treatment and outcome.

Methods

From November 2001 to July 2003, 27 consecutive RL LDLTs were performed in adult patients suffering from end-stage liver disease at the Liver and Multivisceral Transplant Unit, University of Modena, Italy.

There were 16 males (59.2%) and 11 females (40.8%). Mean age was 52.3 ± 13.5 years and mean weight was

67.7 ± 9.3 kg. The primary indications for transplantation were Hepatitis C (HCV)-related cirrhosis in 15 cases, Hepato cellular carcinoma (HCC) in seven cases, cholestatic diseases in two and other causes in three patients. The United Network for Organ Sharing (UNOS) status was 2A in three cases (11.1%), 2B in 19 cases (70.4%), and 3 in five cases (18.5%).

Only AB0 identical donations were considered. All donors were studied according to an imaging protocol including chest X-ray, abdominal ultrasound-Doppler scan and abdominal multislice computed tomography with hepatic vascular reconstructions. Estimated graft-to-recipient weight ratio (GRWR) was >0.8% in all cases.

Biliary complications were defined as leaks or stenoses, which required a surgical or interventional radiology treatment.

We retrospectively reviewed the following variables as possible risk factors for biliary complications: recipients' gender, age, primary diagnosis, UNOS status, graft weight, GRWR, number of bile ducts to be reconstructed, type of biliary reconstruction, type of drainage, total ischemia time, operative time and occurrence of arterial complications. Length of stay in hospital, graft and patient survival rates were also analyzed.

Finally, to evaluate the impact of the learning curve on the rate of biliary complications, we compared the results obtained in the first 14 procedures (group 1) with those achieved in the last 13 of this series (group 2).

Univariate analysis for quantitative variables was calculated using the Student's *t*-test and using the chi-square test for qualitative variables. Significance was defined as $P < 0.05$. Graft and patient survival rates were analyzed using Kaplan–Meier test; the differences between curves were assessed by log-rank test. The Software Package for Social Sciences (SPSS for Windows 10.0; SPSS Inc., Chicago, IL, USA) was used for statistical analysis.

Donor operation

The procedure started with cholecystectomy followed by intraoperative cholangiography to evaluate the biliary anatomy and plan the transaction line of the right bile duct. After mobilization of the right lobe, attention was paid to the hilar structures, isolating the right hepatic artery and the right portal vein. To preserve the vascularization of the donor biliary system, the right bile duct or ducts were isolated and transected sharply, leaving the peribiliary plexus intact as much as possible. The retrohepatic vena cava was then isolated, preserving any significant large (diameter >5 mm) short hepatic vein for reimplantation. The parenchymal transection plane was maintained just to the right of the middle hepatic vein, allowing for identification and preservation of any significant segment 5 and 8 tributary veins. Parenchymal transection was performed under intermittent inflow occlusions (cycles of 10–15 min occlusion and 6 min reperfusion), using ultrasound aspirator, harmonic scalpel, or electrocautery [9]. After removal from the operative field, all the RL grafts were flushed *ex situ* with Celsior solution.

Recipient operation

Recipient hepatectomy was performed preserving the inferior vena cava. After anastomosis of the right hepatic vein, significant large accessory veins were reimplanted on the vena cava directly or by a graft interposition. The donor portal vein was anastomosed to the recipient's main or right portal vein. After reperfusion of the graft, attention was paid to the arterial anastomosis that was performed between the donor's right hepatic artery and the recipient's right or proper hepatic artery.

Before biliary reconstruction, in order to guarantee an adequate blood supply both the donor and recipient bile ducts were shortened until significant arterial bleeding was obtained from the cut surface of both ducts. The recipient's gastroduodenal artery was always preserved.

The type of reconstruction was strictly dependent on the number of bile ducts to be reconstructed and by their orientation as regards the recipient bile duct, preferring whenever possible a duct-to-duct anastomosis.

In nine cases (33.3%) we performed a Roux-en-Y hepato-jejunostomy, four of which had two ducts to be reconstructed. In 16 patients (64.0%) we performed a duct-to-duct anastomosis, three with two ducts to anastomose. In two of these cases we performed a ductoplasty to create a single anastomosis to the recipient's common hepatic duct. In a third case we performed two separate anastomoses, using the recipient's common bile duct and cystic duct. Finally, in two cases with two bile ducts so distant from each other that ductoplasty was not feasible, we combined both duct-to-duct and Roux-en-Y reconstructions.

In the first group of patients we performed the biliary anastomosis using a standard running suture, while in the second group we adopted a parachute technique [10] both in duct-to-duct and in Roux-en-Y reconstructions. The parachute technique is performed by putting the first stitch at the corner of the posterior wall of the two stumps of the anastomosis and leaving a few excess centimeters at each end of the stitch. After the last stitch of the posterior wall the two ends of the suture are pulled till the stumps are brought together; a running suture of the anterior wall completes the anastomosis.

All biliary anastomoses were performed using 6-0 polydioxanone (PDS; Ethicon, Somerville, NJ, USA). In the case of Roux-en-Y reconstruction, transanastomotic biliary stents were used in five cases while four biliary

anastomoses were not drained. In all cases of duct-to-duct reconstruction a T-tube was placed.

Results

Mean follow-up time was 15.4 months (range 3–34.8 months). Neither biliary complications nor liver failure occurred in donors after hepatectomy. Seven of the 27 recipients (25.9%) experienced a biliary complication. Five (18.5%) patients had bile leaks and two (7.4%) patients had biliary strictures. The mean time of onset of the biliary complications was 25.0 ± 16.2 days (range 6–52 days).

Of the 18 patients with a duct-to-duct reconstruction (two of them with an associated Roux-en-Y), four (22.2%) had a biliary complication (two leaks and two strictures). Otherwise, of the 11 patients with a Roux-en-Y reconstruction (two of them with an associated duct-to-duct), three (27.3%) developed a biliary complication (three leaks) (P = ns).

The incidence of biliary complications was 11.1% in patients who received grafts with a single duct and 55.5% in patients with graft presenting multiple bile ducts (P = 0.03). Otherwise, recipients' gender, age, primary diagnosis, UNOS status, graft weight, GRWR, type of biliary reconstruction, type of drainage, total ischemia time, operative time and occurrence of arterial complications were not associated with biliary complications.

Table 1 shows the type, time of onset, treatment and outcome of the seven cases with biliary complications.

No patients with biliary complications required Retransplantation (ReLT). Four of 7 (57.1%) patients with biliary complications died, two of whom (28.6%) from sepsis related to biliary complications after the surgical treatment (both with a Roux-en-Y reconstruction), one due to recurrence of the primary disease and one due to cardiac failure. Among 20 patients with no biliary complications, one underwent ReLT for hepatic artery thrombosis and four (20.0%) died (two from hepatic artery thrombosis, one due to rupture of an aneurysm of the splenic artery and one from sepsis). Overall, the 1-year graft and patient survival rates of the 27 patients were 77.1% and 80.1%, respectively. The actuarial 1-year graft and patient survival rates of patients with biliary complications were 71.4% and 71.4%, respectively, versus 78.9% and 84.0% for patients with no biliary complications (P = ns).

Group 1 versus group 2

As shown in Table 2, the demographic characteristics of the two groups were homogeneous. Table 3 reports the incidence of the clinical data of the two groups. The incidence of biliary complications significantly decreased from 42.9% (n = 6) in the first group to 7.6% (n = 1) in the second group (P = 0.05).

Two of six patients (33.3%) in group 1 died from sepsis related to biliary complications, while no patient in group 2 died from biliary complications. The overall 1-year graft survival was 57.1% in the first group versus 100.0% in the second group (P = 0.006) (Fig. 1). The

Table 2. Demographic data of group 1 and group 2 patients.

Parameters	Group 1 (no. 1–14)	Group 2 (no. 15–27)	*P*-value
Gender			
Male	6 (42.8)	10 (76.9)	0.08
Female	8 (57.2)	3 (23.1)	
Mean age (years)	51.5 ± 16.4	53.1 ± 10.1	0.78
Mean weight (kg)	66.4 ± 9.5	70.3 ± 7.8	0.22
UNOS status			
2A	2 (14.3)	1 (7.7)	0.27
2B	11 (78.5)	8 (61.5)	
3	1 (7.2)	4 (30.8)	
Diagnosis			
Cirrhosis HCV+	7 (50.0)	8 (61.5)	0.51
HCC	4 (28.5)	3 (23.1)	
Cholestatic	1 (7.2)	1 (7.7)	
Other	2 (14.3)	1 (7.7)	

Values within parenthesis are expressed as percentage. UNOS, United Network for Organ Sharing; HCV, Hepatitis C; HCC, Hepto cellular carcinoma.

Table 1. Summary of patient biliary complications, time of onset, treatments and outcome.

Patient no.	Biliary reconstruction	Complication	Time of onset	Treatment	Outcome/days of follow-up
3	Roux-en-Y	Anastomotic leak	28	Surgical revision	Died from leak-related sepsis/163
4	Duct-to-duct	Anastomotic stricture	20	Conversion to Roux-en-Y	Died from HCV recurrence/761
5	Combined	Anastomotic leak (from Roux)	33	Surgical revision	Recovered/871
7	Duct-to-duct	Anastomotic stricture	6	Conversion to Roux-en-Y	Died from cardiac failure/468
11	Roux-en-Y	Anastomotic leak + cut liver surface	40	Surgical revision	Died from leak-related sepsis/69
13	Duct-to-duct	Anastomotic leak	52	Conversion to Roux-en-Y	Recovered/731
19	Duct-to-duct	Anastomotic leak	13	Conversion to Roux-en-Y	Recovered/475

HCV, Hepatitis C.

Table 3. Clinical data of group 1 and group 2 patients.

Parameters	Group 1 (no. 1–14)	Group 2 (no. 15–27)	*P*-value
Graft weight (kg)	748.5 ± 191.9	765.7 ± 182.7	0.81
GRWR	1.21 ± 0.40	1.08 ± 0.17	0.27
No. ducts			
1	9 (64.3)	9 (69.2)	0.55
2	5 (35.7)	4 (30.8)	
Reconstruction type			
Roux-en-Y	5 (35.8)	4 (30.8)	0.96
Duct-to-duct	8 (57.0)	8 (61.6)	
Combined	1 (7.2)	1 (7.6)	
Stents			
No stent	2 (14.3)	2 (15.4)	0.91
Internal	2 (14.3)	2 (15.4)	
External	1 (7.2)	0 (0.0)	
Kehr	9 (64.2)	9 (69.2)	
Ischemia time (min)	74.28 ± 21.8	86.1 ± 47.0	0.29
Operative time (min)	521.4 ± 64.1	608.0 ± 113.7	0.02
Arterial thrombosis	3 (21.4)	0 (0)	0.22
Biliary complications	6 (42.9)	1 (7.6)	0.05
Biliary leaks	4 (28.6)	1 (7.6)	0.32
Biliary stenosis	2 (14.3)	0 (0)	0.48

Values within parenthesis are expressed as percentage. GRWR, graft-to-recipient weight ratio.

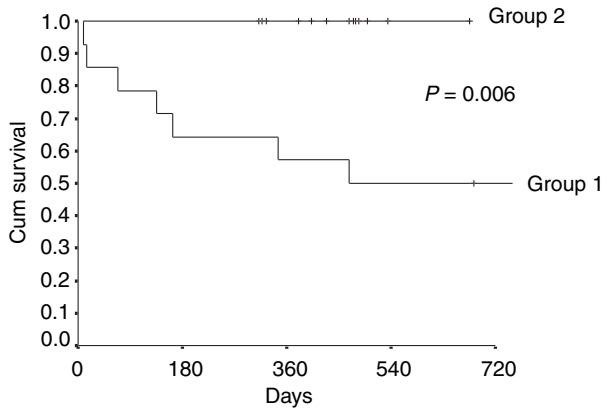

Figure 1 Kaplan–Meier 2-year graft survival curves of group 1 and group 2 patients.

overall 1-year patient survival was 64.3% in the first group versus 100.0% in the second group ($P = 0.01$) (Fig. 2).

Discussion

Although historically defined as the 'Achilles' heel of the procedure' [11], the incidence of biliary complications in orthotopic whole liver transplantation has now dropped below 10% [12].

Conversely, the first reports of the main centers performing RL LDLT show a greater incidence of biliary

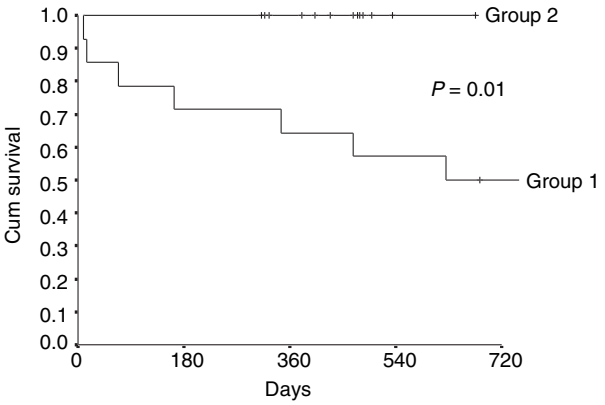

Figure 2 Kaplan–Meier 2-year patient survival curves of group 1 and group 2 patients.

complications ranging from 15% to 40% [13–18]. In addition to the greater technical challenge, the high incidence of multiple ducts represents one of the main reasons that could explain the variable impact of biliary complications between whole and RL grafts. Because the anatomical variations of the biliary tree are very common, around half of the RL grafts have more than one duct to reconstruct, which is an independent risk factor of biliary complications as confirmed by our results [19,20].

A second reason for the higher rate of biliary complications is the possible failure of the periductal arterial blood supply of the hepatic ducts during donor operation. The common bile duct and the confluence receive arterial blood supply from the periductal plexus that is fed mainly from branches of the posterior-superior pancreaticoduodenal artery (arising from the gastroduodenal artery) and secondarily from a net of collateral vessels that can arise from the left and right hepatic, cystic, gastroduodenal, celiac and right gastric arteries [21].

In RL grafts, part of this net of vessels is inevitably sacrificed and the blood supply to the right hepatic duct is maintained by only the right hepatic artery. In some cases, this may lead to local or extended areas of ischemia of the bile duct, with the possible risk of developing a secondary biliary stenosis [22].

Although Roux-en-Y reconstruction was adopted first, most of the main centers performing RL LDLTs have recently introduced the duct-to-duct reconstruction which is now considered the first choice technique for many groups [15,17,18,22,23]. The advantages advocated in favor of the duct-to-duct reconstruction are that it is easier, faster, and more physiologic, as it preserves the sphincter of Oddi, reducing the incidence of reflux cholagitis and allowing easy access for postoperative endoscopic maneuvers. Moreover, as shown in our report, the duct-to-duct proves feasible not only for single

reconstructions. In the case of double ducts, we performed a ductoplasty or used the recipient's right hepatic and cystic duct contemporarily. Other techniques such as an end-to-side anastomosis, or using both the recipient's left and right hepatic ducts, or performing a ductoplasty of three separate ducts have been proposed by other authors [13,24,25].

The Mount Sinai group has recently published a series of 96 RL LDLTs [13]; they have showed no significant risks of complications between the two types of reconstruction, but a trend of a higher number of leaks using the Roux-en-Y and conversely a higher risk of stenosis using a duct-to-duct reconstruction. They also reported a higher morbidity and mortality in patients who developed biliary leaks. These findings seem to reflect our results; both patient groups that developed a stenosis had a duct-to-duct reconstruction but they were successfully surgically treated.

Vice versa, three of five cases of leaks were from a Roux-en-Y anastomosis, and two of them died from related sepsis. Thus, although we found no significant differences of complications between the two types of biliary anastomosis, we favor duct-to-duct reconstruction which we consider safer because of the lower risk of leaks that in some cases proves difficult to manage, often requires multiple treatments with a high risk of developing infections and related sepsis, clearly comprising patient survival.

When we compared the first group of patients with the second group we found significant improvements in terms of the incidence of biliary complications as well as of graft and patient survivals.

The high rate of complications (42.9%) which occurred in the first period probably represents the price paid in the approach to a new surgical procedure like RL LDLT, where biliary reconstruction is one of the most challenging aspects. Progressive surgical experience and technical refinements have made it possible to achieve a considerable reduction of complications. In fact, all three HAT and two biliary leaks leading to patient death occurred in the first period, showing an overall improvement of results linked to a learning curve.

One of the main modifications in surgical technique between the two periods included the adoption of the parachute technique in both duct-to-duct and Roux biliary anastomosis. When performing a standard running suture, the first stitch is made at the corner of the anastomosis and sometimes there is not enough space to correctly insert the needle for the subsequent stitches.

To overcome this inconvenience, different methods of anastomosis have been reported [26]. As described by Yoshimi *et al.* [10], the parachute technique is usually used to anastomose small blood vessels but can be useful for reconstruction of small bile ducts with a diameter of a few millimeters.

We found this technique very helpful because it leaves more space between the two stumps and allows a clear view of the posterior wall of the anastomosis, proving easier and faster to insert the needle and to make stitches correctly. Although other factors may have contributed to the decrease in biliary complications over time (e.g. reduction of HAT), the above-mentioned technical modification could have played a role.

The management of biliary complications in RL LDLT is difficult [17]. To avoid further operative interventions, some authors have suggested an early and aggressive use of percutaneous radiologic treatments [6,13,27]. Nevertheless, in most of the cases percutaneous treatment may be particularly difficult and it is necessary that interventional radiologists be highly skilled and experienced. Recently, some groups have emphasized the use of endoscopy to diagnose and manage biliary complications [6,28]. We agree that conservative treatments should be attempted initially, and that is our current policy in whole liver transplantation. Nevertheless, because of our initial experience, we felt safer and effective initially to adopt a direct surgical approach to manage either leaks or the strictures diagnosed early in our RL LDLT patients.

In conclusion, our results confirm biliary complications as one of the most important technical complications affecting RL LDLT. Also, because of the small number of cases, we found no significant difference between Roux-en-Y and duct-to-duct reconstruction. Nevertheless, we consider this latter technique to be feasible also for multiple reconstructions, quicker and safer because of the trend of a lower risk of leaks, which can affect patient survival.

As a result of a fast learning curve, attention and surgical refinement as well adoption of the parachute technique led to a significant reduction of the biliary complication rate, improving graft and patient survival. Further randomized studies with a longer follow-up are necessary to better define our findings.

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