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Biliary Anastomotic Complications in 400 Living Related Liver Transplantations

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Abstract. The purpose of this study was to evaluate the cause and outcome of biliary anastomotic complications occurring after living related liver transplantation (LRLT). A database of 391 patients undergoing 400 LRLT from June 1990 to August 1998 was reviewed. The overall incidence of biliary anastomotic complications was 18.2% (71 patients). There were 45 bile leaks, 35 anastomotic strictures, and the bile duct was ligated inadvertently in 3 cases. Univariative analysis revealed that the manner of stent usage, intrapulmonary shunting, and gender of recipients were significant risk factors for leakage. Anastomotic leaks, cytomegalovirus infection, hepatic artery complications, and gender of recipients were significant risk factors for stricture. In pediatric patients older than 2 years old, ABO blood type compatibility was another risk factor for leakage and stricture. Choice of stent usage and earlier transplantation for patients with intrapulmonary shunting should reduce the rate of biliary leaks, and prophylaxis of leaks for patients with intrapulmonary shunting, and minimizing hepatic artery complications should reduce the rate of biliary stricture after LRLT. Avoidance of ABO-incompatible donors or innovative immunosuppression in ABO-incompatible transplantation should be considered in children.

In spite of great technological and immunological advances in the field of liver transplantation, biliary complications remain an Achilles heel with an incidence 10% to 30% [1–7]. Prolonged cold ischemia, arterial thrombosis, and chronic rejection were shown to be significant etiologic factors in biliary complications after transplantation.

In pediatric liver transplantation, the application of reduced-size and split liver transplantation has been a major advance in expanding the donor pool. The development of living related liver transplantation (LRLT), recent usage of the right lobe graft in LRLT, and split transplantation further increased donor availability for adult patients [8, 9]. In LRLT, cold ischemia may be kept to the minimum, human leucocyte antigen(HLA) matching is usually haploidentical [10], and the length of the extra-hepatic bile duct is kept short. With microvascular arterial reconstruction [10], one might expect biliary complications to occur less frequently than in cadaveric transplantation. Heffron et al. reported a higher incidence of biliary complications in their initial experience with LRLT (38%) compared to cadaveric reduced-size (12%) and split (13%) liver transplantation [4]. Cronin et al. also reported comparative incidence [11]. Although the incidence of biliary complications was 13.9% in our initial 208 pediatric cases [6], recent increase of adult patients, patients with severe intrapulmonary shunting, and critically ill patients waiting in intensive care units might have some impact on the incidence and risk factors of biliary complications. We reviewed our database of 400 LRLTs followed beyond 3 months posttransplant to analyze the etiology and outcome of biliary anastomotic complications after LRLT.

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Materials and Methods

From June 1990 to August 1998, 391 patients (139 males and 252 females) underwent 400 LRLTs at Kyoto University Hospital, Japan. The median age of recipients was 44 months (range 2 months to 66 years). The age of 159 patients was younger than 24 months; 177 patients were between 24 months and 18 years; and 55 patients were 18 years or older. The median body weight was 14.4 kg (range 3.1 kg to 77.8 kg). At the time of transplantation, 153 patients weighed less than 10 kg. Demographic data are shown in Table 1.

The main indications for LRLT were biliary atresia ($n = 272$); metabolic diseases ($n = 32$); fulminant hepatic failure ($n = 28$); primary biliary cirrhosis ($n = 11$); Allagille syndrome ($n = 10$); intrahepatic cholestasis ($n = 6$); liver tumor ($n = 5$); primary sclerosing cholangitis ($n = 4$); Budd-Chiari syndrome ($n = 3$); cryptogenic liver cirrhosis ($n = 18$); and graft failure ($n = 9$).

Seventy percent (279 patients) received ABO-identical grafts, 17% (68) received ABO-compatible grafts, and 13% (53) received ABO-incompatible grafts. For ABO-incompatible combinations, blood exchange for children less than 10 kg or plasmapheresis for children weighing more than 10 kg was performed preoperatively until donor-specific IgM titer was below 8 times dilution. OKT3, azathioprine, or cyclophosphamide was administered, and splenectomy was performed in selected patients. Antidonor blood

Table 1. Demographic characteristics in 400 consecutive living related liver transplants.

Characteristics	Mean ± SD	Range	Median
Age (months)	106.7 ± 149.3	1–797	44
Weight (kgs)	21.8 ± 18.0	3.1–77.8	14.4

	Number (%)
Recipient gender	
Male	144 (36%)
Female	256 (84%)
Status	
ICU	73 (18.25%)
Hospitalized	176 (44%)
At home	151 (37.75%)
Intrapulmonary shunt > 40%	
Yes	47 (11.75%)
No	353 (88.25%)
Disease	
Cholestatic liver disease	297
Metabolic liver disease	32
Cryptogenic cirrhosis	18
Fulminant liver failure	28
Liver tumor	5
Graft failure	9
Budd-Chiari syndrome	3
ABO blood type compatibility	
Identical	279 (69.75%)
Compatible	68 (17%)
Incompatible	53 (13.25%)
Hepatic artery reconstruction	
Complete	308 (77%)
Partial	92 (23%)
Operation	
Lateral segment	248 (62%)
Extended lateral segment	35 (8.75%)
Left lobe	75 (18.75%)
APOLT	25 (6.25%)
Right lobe	17 (4.25%)
Cytomegalovirus disease	
Yes	103 (25.75%)
No	297 (74.25%)
Hepatic artery complication	
Yes	47 (11.75%)
No	353 (88.25%)
Number of graft bile ducts and anastomoses	
1 duct/1 anastomosis	356 (89%)
2 ducts/1 anastomosis	26 (6.5%)
2 ducts/2 anastomoses	14 (3.5%)
3 ducts/1 anastomosis	3 (0.75%)
3 ducts/2 anastomoses	1 (0.25%)
Stent for biliary reconstruction	
No stent	258 (64.5%)
1 internal stent	57 (14.25%)
1 external stent	77 (19.25%)
2 internal stents	3 (0.75%)
1 internal & 1 external stents	3 (0.75%)
1 internal & 2 external stents	1 (0.25%)
2 internal & 1 external stents	1 (0.25%)

APOLT: auxiliary partial orthotopic liver transplantation.

type titers were measured serially before and after transplantation by a microhemagglutination assay.

Our donor evaluation and donor surgery protocols have been reported elsewhere [12]. In brief, after a rigorous work-up to identify a suitable donor (usually parental), preoperative evaluation with high resolution duplex ultrasound is carried out to map donor vascular anatomy. This is followed by spiral computerized tomography (CT) with intravenous contrast to determine graft volume, fat content, and hepatic venous and portal anatomy. Where concerns exist, 3-dimensional reconstruction by CT is performed to optimally define the vascular anatomy. We do not routinely subject donors to mesenteric or celiac angiography, and we do not advocate pre-operative donor liver biopsy. Our experience in donor evaluation suggests that these investigations are redundant, and may subject a healthy donor to added risk. Rather, a detailed intraoperative cholangiogram is obtained early in the course of the hilar dissection in the donor to better define aberrations in biliary anatomy. Donor cholangiography was not part of our routine practice until after our 106th case in which the left hepatic duct was ligated. Prior to cholangiography, two small vascular clips are placed on either side of the left hepatic duct 3 mm to 5 mm from the bifurcation, which aids in definition of the optimal level of transection of the left hepatic duct. When two large branches run parallel and it is difficult to identify the bifurcation, bi-planar cholangiography is performed. Contast media is injected through a small intravenous catheter (24G) inserted into the common bile duct in the setting of a lateral segmentectomy and through a plastic tube (5Fr) inserted into the cystic duct in the setting of a left lobectomy or right lobectomy combined with cholecystectomy. The median hepatic artery to segment IV is preserved with the graft, maintaining maximal length when it is found to arise from the right hepatic artery. The aberrant left hepatic artery was also preserved. After systemic heparinization with 1000 units of heparin, the graft was flushed via the portal vein with 2 to 3 times of graft weight (g) of University of Wisconsin (UW) solution or histidine-tryptophan-ketoglutarate (HTK) [13] at 4°C. To prevent intimal injury from cannulation, the artery was not flushed. The bile duct was flushed. The cold ischemia ranged from 28 to 300 minutes. Left lateral segment grafts were implanted in 63.25% (253) patients, extended lateral segment grafts in 9.25% (37) patients, left lobe grafts in 24.25% (93) patients, and right lobe grafts in 4.25% (17) patients.

Surgical techniques and the perioperative management of our recipients have been reported elsewhere [10, 14]. Arterial reconstruction was carried out using microvascular techniques as described previously [10]. When an accessory artery supplied the left lobe or lateral segment, either a double arterial reconstruction was performed under microscope or as in the majority of cases, when arterial backflow through the second artery was deemed adequate after reflow through the major artery, a second reconstruction was not done. These are designated complete or partial reconstruction, respectively.

In biliary reconstruction, all patients except one underwent Roux-en-Y hepaticojejunostomy; a choledocho-choledochostomy with an internal stent was carried out on a single occasion. For Roux-en-Y hepaticojejunostomy, an internal stent (2 cm of 18 G silicone vascular catheter) was placed in the first 28 recipients, after which stents were not used routinely unless the bile duct was of very small caliber (<2 mm). From our 235th patient and remaining patients of ABO-incompatible transplant, we began to use external stents (4 Fr pancreatic duct tube, Sumitmo Bakelite, Tokyo) to make an early diagnosis of biliary complication by postoperative cholangiogram. Afterward, as for ABO-incompatible cases and severe intrapulmonary shunting which had been shown as risk factors for biliary complications in our previous report [6], we routinely use the external stent for patients follow-

ing the 300th patient except for patients receiving right lobe graft or left/lateral segment grafts with the bile ducts easily reconstructed. The anastomosis was made using 7-0 Polydioxanone absorbable monofilament interrupted suture (PDS, Ethicon, Somerville, New Jersey). When a graft had two or three bile ducts, we basically tried to make an anastomosis between the bile ducts with ductoplasty and one hole in the jejunum. When it was impossible because of the distance, we made separate anastomoses.

In order to determine the adequacy of the transplanted hepatic mass, we applied the value of graft volume (as measured by CT volumetry and confirmed subsequently by weighing the graft at the time of explanation) to the recipient weight ratio (graft volume [mls]/recipient body weight [Kg] $\times$ 100%). It ranged from 0.61% to 10.1%.

Immunosuppression consisted of tacrolimus with low-dose steroids [10]. Target tacrolimus levels were 15 ng/ml to 20 ng/ml (IMX, whole blood) in the first week, and reduced to 5 ng/ml to 15 ng/ml over the first month. Methylprednisolone (20 mg/kg IV) was administered during the anhepatic phase, followed by 1 mg/kg IV b.i.d for the first 3 days, and reduced to 1 mg/kg q.d. for 3 days, and to 0.5 mg/kg/day (prednisone). Steroids were tapered and discontinued routinely by 6 months posttransplant.

Acute or chronic rejection was diagnosed in the presence of biochemical and consistent histological abnormalities, with the exclusion of other causes of graft dysfunction, and required treatment with steroid pulse or OKT3 [15, 16].

Cytomegalovirus (CMV) surveillance was not carried out routinely in the postoperative period, but when clinical, biochemical, or biopsy findings raised our suspicions that CMV disease was implicated, serology, CMV PCR, and CMV antigenemia were sent. Ganciclovir (5 mg/kg/day IV for 14 days) was begun when CMV antigenemia was documented or CMV PCR was positive in the fluid. Tacrolimus and steroids were also decreased with close monitoring of tacrolimus trough levels and hepatic chemistries. Prophylaxis against CMV was not used routinely.

Hepatic blood flow was assessed by Doppler ultrasound every day during the first 2 weeks. When the peak height of arterial wave decreased within 7 days after transplant, we began or increased dopamine and started IV urokinase (2000 units/kg/day) under meticulous ultrasound study. When the patients did not improve or in cases of loss of artery signals accompanied by abnormal liver function test, they were treated by surgery, such as evacuation of hematoma around the artery, thrombectomy, and reanastomosis. When patients with transient loss of artery signals did not have abnormal liver function tests or after the surgeries for the artery complications mentioned above, they were treated by administration of IV urokinase (2000 units/kg/day for 3 to 5 days) and then with PO anticoagulants (dipyridamole 4 mg/kg/day; or coumadin, targeting between 20% to 30% on the thrombotest).

Biliary complications were diagnosed clinically (bile in drain, cholangitis, peritonitis, sepsis), biochemically (elevated bilirubin or alkaline phosphatase), or radiologically. Ultrasonography was the initial radiological investigation, followed by cholangiography, CT, or biliary scintigraphy as indicated. Regarding leaks, we keep a drain in the right subphrenic space for at least 7 days. In the setting of high-risk recipients, the drain is left in situ for at least 14 days. In most instances, this permits a timely diagnosis of bile leak even without cholangiography. When yellowish discharge was found from a drain or the wound, we measured the levels of amylase and bilirubin in it. When the level of amylase was high or the patient's condition was critical, we proceeded to laparotomy. Because, in the setting, the anastomosis was too fragile for revision, we placed multiple drains and made an enterostomy to isolate the anastomosis from intestinal juice. The enterostomy was taken down after the leak was successfully treated. When the level of amylase was low, we continued to followed-up on the patient even if the level of bilirubin was high. These patients sometimes required fasting and antibiotics. When patients continued to develop fever, abdominal pain, or increase of discharge, we did a laparotomy. Otherwise, we would follow them conservatively.

Regarding stricture, when ultrasonography and/or CT scan revealed a dilated bile duct, percutaneous transhepatic cholangiography followed with balloon dilatation. If the balloon dilatation was impossible because of complete obstruction or the stricture recurred after several treatments within 2 to 3 weeks, revision was scheduled. Usually revision was done by an anastomosis between the Roux-en-Y limb and the opened bile duct. If the bile duct was not reached at the hilum, an anastomosis was made between the intrahepatic bile duct and the available intestine [6].

Data were expressed as mean $\pm$ standard deviation. Univariative analysis were performed on the entire patient sample to test the statistical strength of independent association between selected independent variables and biliary complications.

Table 2. Results of chi-square tests for biliary complications (only significant variables are shown) in all patients.

Variables	Incidence (%)	p value
Leakage		
Stent for biliary reconstruction		0.0002
No stent	10.1	
1 internal stent	8.8	
1 external stent	15.6	
2 internal stents	100	
1 internal & 1 external stents	66.6	
1 internal & 2 external stents	0	
2 internal & 1 external stents	0	
Intrapulmonary shunt $>$ 40%		
Yes vs. no	36.4 vs. 12.4	0.0101
Gender		
Male vs. female	6.3 vs. 14.8	0.0104
Stricture		
Anastomotic leak		
Yes vs. no	31.9 vs. 5.7	$<$ 0.0001
Cytomegalovirus disease		
Yes vs. no	4.3 vs. 12.8	0.0003
Hepatic artery complication		
Yes vs. no	31.3 vs. 7.8	0.0012
Gender		
Male vs. female	4.1 vs. 12.8	0.0150

Results

The actuarial graft and 5-year survival of these 391 patients was 76.9% and 76.1%, respectively. The overall incidence of biliary anastomotic complications was 18.2% (71 patients). There were 45 bile leaks, 35 anastomotic strictures, and the bile duct was ligated inadvertently in 3 cases. The impact of demographic characteristics on biliary complications shown in 1 was assessed and summarized in Table 2. The patients with choledoco-choledoco anastomosis did not have leaks or strictures.

Table 3. Management and outcome of patients after leak.

Management	Outcome				
	Healed	Stenosis	IHBC	Follow-up	Dead
Drainage (n = 25)	48% (12)	32% (8)	—	4% (1)	16% (4)
Revision (n = 8)	37.5% (3)	25% (2)	25% (2)	—	12.5% (1)
Laparotomy and drainage (n = 5)	57.1% (4)	14.3% (1)	14.3% (1)	—	14.3% (1)
Laparotomy, drainage, and enterostomy of Roux-en-Y (n = 5)	40% (2)	20% (1)	—	40% (2)	—

IHBC: intrahepatic bile duct; ( ) number of patients.

Bile Leaks

Onset of anastomotic leaks ranged from postoperative day (POD) 5 to POD 32. Manner of stent usage for biliary reconstruction, severe intrapulmonary shunting, and gender had significant impact on bile leaks (Table 2). There was no significant difference among the no-stent group, the one internal stent group, and the one external stent group. Patients with biliary reconstruction associated with two internal stents or one internal stent combined with one external stent had a higher incidence of leaks. The onset of leaks in patients with severe shunting appeared on POD 6, 14, 20, and 21. There was no significant risk factors for development of stricture in patients with bile leaks. The management and outcome of bile leaks is summarized in Table 3. Six patients with bile leaks died. The causes of death were pneumonia in one patient, portal vein thrombosis in one, rupture of portal vein aneurysm in one, and sepsis in three patients, one of which developed the sepsis due to uncontrollable leaks.

Anastomotic Strictures

In this study, transient intrahepatic bile duct dilatation in two patients 2 weeks after transplantation were included in biliary stricture. The possible etiology of anastomotic strictures and onset are shown in Figure 1. The episode of anastomotic leaks, CMV disease, hepatic artery complication, and gender were significant risk factors as shown in Table 2. One patient developed cholangitis leading to complete obstruction at the anastomosis without any possible etiology and underwent revision. The lateral segment graft grew and rotated anticlockwise and the hilum moved to the right subphrenic space. The Roux-en-Y limb was stretched too much and the anastomosis was closed.

Transient intrahepatic bile duct dilatation was observed in the two patients 2 weeks after transplantation and was spontaneously improved. In both patients, no stent was used at the biliary anastomosis. Inadvertent bile duct ligation was diagnosed by development of jaundice and dilatation of the intrahepatic bile ducts shown by ultrasound. A new anastomosis between the ligated bile duct and the jejunum was made. After we began the intraoperative cholangiography, another patient had the same complication.

The outcome and management of anastomotic strictures is summarized in Figure 2. Anastomotic strictures were managed by percutaneous transhepatic cholangiography and drainage (PTCD). Thirteen patients with complete obstruction required surgical treatment. Ten underwent successful revision, two intrahepatic hepaticojejunostomy, and one intrahepatic hepaticogastrostomy. Balloon dilatation was attempted in all patients but was technically possible in 21 cases. Ten patients were successfully treated by balloon dilatation. Eleven patients had recurrence and five of them underwent revision. One patient had atrophy of segment 2. Seven patients were followed with PTCD.

The incidence and the risk factors of biliary complications were further analyzed to determine the difference among patients younger than 2 years, between 2 years and 18 years, and 18 years or older. The results are shown in Table 4. Incidence of bile leaks in female patients was significantly higher than leaks in male patients when patients were younger than 2 years old. Risk factors for stricture were the same as those in overall patients. In patients between 2 years old and 18 years old, ABO blood type compatibility was added as a risk factor for leaks and stricture. CMV disease was a common risk factor for stricture for patients of all age.

Eleven grafts had three hepatic arteries, 106 grafts had two hepatic arteries, and 283 grafts had a single hepatic artery. The incidence of anastomotic leaks of grafts with two or three hepatic arteries reconstructed in the partial fashion was 16.5%, and 3.8% for those reconstructed in the complete fashion, although there was no significant difference. The incidence of leaks of grafts with single artery reconstruction was 10.2%. The incidence of stricture of grafts with two or three hepatic arteries reconstructed in the partial fashion was 4.4%, and 7.7% for those reconstructed in the complete fashion. The incidence of stricture of grafts with single artery reconstruction was 10.2%.

The relation between the number of bile ducts and the manner of stent usage and outcome are shown in Table 5. The grafts with one bile duct and one external stent had a higher incidence of leaks (16.6%) than other grafts with one bile duct and no stent or one internal stent, but the difference was not statistically significant. The incidence of stricture was similar among groups in grafts with one bile duct. In patients with grafts with two bile ducts and one anastomosis, 100% of patients (3/3) with two internal stents developed leaks and 33% (1/3) of them developed stricture. Patients with grafts with two bile ducts and two anastomoses had a lower incidence of leaks (21.4%) than patients with two bile ducts and one anastomosis (36.4%), and none of these patients developed stricture. In patients with three bile ducts, no patients developed stenosis or stricture.

In the 400 donors, one had pulmonary embolism which was successfully treated, three developed bile collection requiring puncture for drainage, one developed adhesion ileus requiring laparotomy, and four had duodenal ulcers requiring medication.

Discussion

Heffron et al. reported a high incidence of biliary complications (38%, 5/13) in their early series of LRLT. Five years later, the incidence remained unchanged at 38% (35/91) in LRLT versus 14% (14/98) in cadaveric reduced-size transplantation in their recent update [17]. Reichert et al. reported similar results in their reduced-size liver transplantation [11]. Arterial thrombosis, prolonged cold ischemia, chronic rejection, and CMV disease have all been recognized as important etiologic factors in posttransplant biliary complications [3–7, 18]. Our current series confirms the

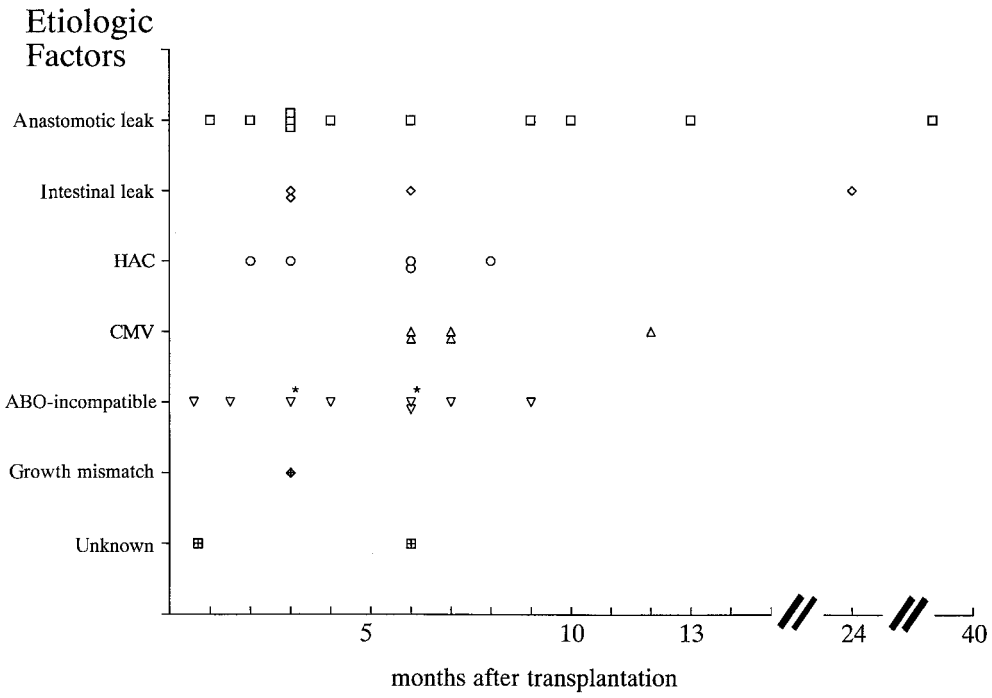

Fig. 1. Onset of biliary anastomotic leaks and possible etiology. HAC: hepatic artery complication; CMV: cytomegalovirus; ∗: cases combined with intestinal leaks.

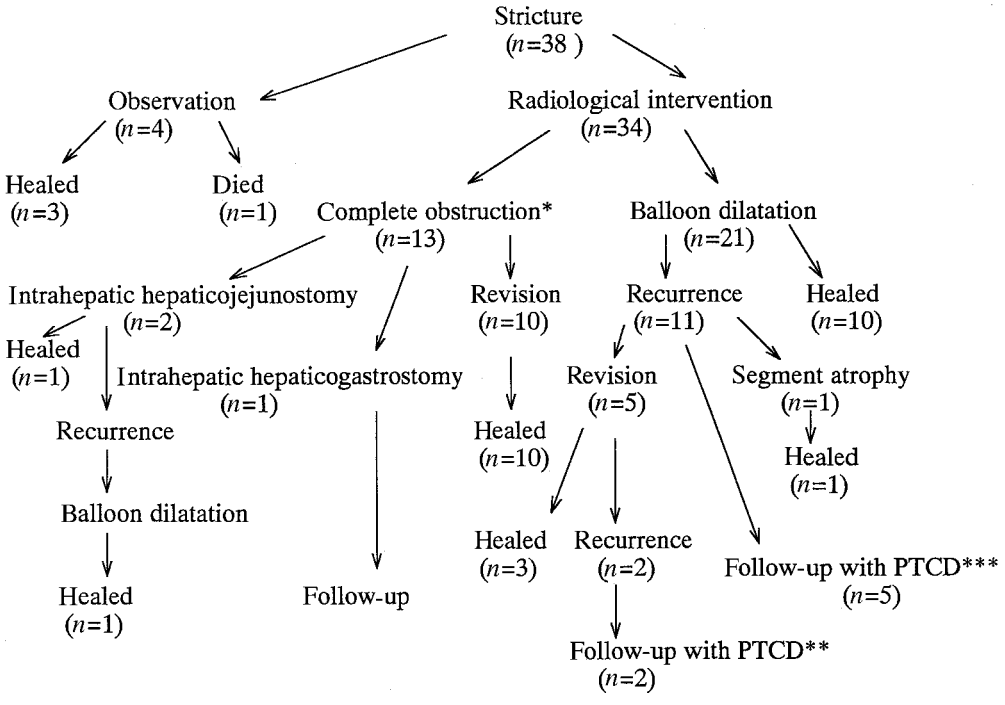

Fig. 2. Summary of clinical outcome after anastomotic stricture. *: including three cases of inadvertent bile duct ligation; **: one case of hepatic artery complication, one case of auxiliary partial liver transplantation, and three unknown etiology; ***PTCD: percutaneous transhepatic cholangiography and drainage.

significance of arterial complications, severe intrapulmonary shunt, CMV disease, and stent usage as significant and important etiologic variables. In terms of age less than or over 2 years, ABO-compatibility, stent usage, and shunt are significant factors in pediatric patients older than 2 years, and hepatic artery complication and gender are significant in patients younger than 2 years old. CMV disease is a common risk factor for patients of all age.

The two principal etiologic factors associated with biliary complication after transplantation are ischemia and technical failures [5]. Hepatic artery thrombosis (HAT) is a well described cause of ischemic biliary complications [3–5, 7]. All patients surviving HAT had biliary complications in our series, although the introduction of microvascular arterial reconstruction reduced the incidence of HAT after LRLT in our institution [10]. It has been proposed that ischemia from marked tissue hypoxemia in the hepatopulmonary

Table 4. Risk factors of biliary complications in infants, children, and adults.

Variables	Incidence (%)	*p* value
Age < 24 months		
Leakage		
Gender		0.0293
Male vs female	1.8 vs 11.5	
Stricture		
Biliary leakage		< 0.0006
Yes vs no	38.5 vs 8.1	
Hepatic artery complication		0.0039
Yes vs no	36.4 vs 8.7	
Cytomegalovirus disease		0.0228
Yes vs no	19.9 vs 7.0	
24 months ≤ Age < 18 years		
Leakage		
Intrapulmonary shunt >40%		0.0036
Yes vs no	21.1 vs 4.3	
Stent for biliary reconstruction		0.0044
No stent	7.0	
1 internal stent	6.7	
1 external stent	21.1	
2 internal stents	100 (1/1)	
1 internal & 1 external stents	0 (0/1)	
ABO blood type compatibility		0.0427
Identical	10.3	
Compatible	2.8	
Incompatible	23.4	
Stricture		
Biliary leakage		< 0.0001
Yes vs no	42.1 vs 2.9	
Stent for biliary reconstruction		0.0048
No stent	6.2	
1 internal stent	3.3	
1 external stent	7.9	
2 internal stents	100 (1/1)	
1 internal & 1 external stents	0 (0/1)	
Cytomegalovirus disease		0.0345
Yes vs no	13.3 vs 4.3	
ABO blood type compatibility		0.0409
Identical	5.6	
Compatible	1.8	
Incompatible	19.0	
Age ≥ 18 years old		
Leakage		
Preoperative status		0.0381
ICU	31.3	
Hospitalized at home	9.1	44.4
Stricture		
Cytomegalovirus disease		0.0476
Yes vs no	27.3 vs 6.7	

Table 5. Relation among number of bile ducts and anastomoses and stent usage and complications.

		Incidence of complications	
Stent	Number	Leakage	Stricture
1 duct/1 anastomosis (n = 357)			
No stent	242	9.9%	9.5%
1 internal stent	42	9.5%	7.2%
1 external stent	72	16.6%	8.3%
2 ducts/1 anastomosis (n = 26)			
No stent	11	9.1%	9.1%
1 internal stent	8	0%	12.5%
1 external stent	3	0%	0%
2 internal stents	3	100%	33%
1 internal & 1 external stents	1	0%	0%
2 ducts/2 anastomoses (n = 14)			
No stent	5	20%	0%
1 internal stent	6	16.7%	0%
1 external stent	1	0%	0%
1 internal & 1 external stents	2	50%	0%
3 ducts/1 anastomosis (n = 3)			
1 internal & 1 external stents	1	0%	0%
2 internal & 1 external stents	1	0%	0%
3 ducts/2 anastomoses (n = 1)			
1 internal & 2 external stents	1	0%	0%

syndrome may be an important etiologic variable in posttransplant biliary complication [19]. Poor tissue healing may have contributed to biliary complications in these cases [20]. Partial arterial reconstruction was also recognized as a significant risk factor of bile leaks when a graft has multiple hepatic arteries, although there was no statistical significance. In a partial arterial reconstruction, it has been our practice to ligate rather than reconstruct the second artery, where backflow through the small artery is deemed adequate after reconstruction of the larger artery. However, although there was no significant difference, the current data suggests that a double reconstruction may have merit in reducing the risk of biliary complications.

Internal stents were used routinely in our initial 28 cases. Thereafter, no stent became standard for the next 230 cases and internal stents were used eventually. After the 260th patient, we began to perform LRLT for patients with severe intrapulmonary shunting or ABO-incompatible transplantation. External stents were used for those patients until the 300th case. After the 300th case, external stents were used routinely. In our current policy, no stent is used when a graft has a single large bile duct and a recipient has none of the risk factors mentioned above. External stents are used routinely for usual cases. When recipients have risk factors for biliary complications, external stents are mandatory for early diagnosis. This could be a reason why the incidence of leaks was higher in cases with external stents than others. An internal stent is used when the diameter is too small for the external stent. In right lobe graft transplantation, we basically do not use any stents.

In patients with single anastomosis for two bile ducts, all patients with two internal stents (3/3) had leaks. Although the double stents could be one of the etiologic factors, the reason why the double stents were required (i.e., double small bile ducts) might be the real etiology. In these difficult situations, innovation for timely diagnosis and appropriate intervention for biliary complications is crucial. Regarding leaks, in the setting of high-risk recipients, the drain is left in situ for at least 14 days. In most instances this permits a timely diagnosis of bile leaks, even though cholangiography is not available. Keeping a drain for 1 week longer should be much cheaper and less invasive than planned reexplorations. It has not been our policy to perform "second look" laparotomies in LRLT, believing that the majority of serious complications may be diagnosed by careful postoperative surveillance. When the leak is major and the level of amylase in the drain is high, the laparotomy for drainage combined with enterostomy of the Roux-en-Y limb is effective to avoid serious complications. All patients with this procedure survived this complication and underwent successful reconstruction of the Roux-en-Y limb.

When a patient slowly develops anastomotic stenosis, clinical cholangitis develops first. The episode of fever and liver function tests derangement may be transient and a liver biopsy may not always provide a definitive answer. We, therefore, have a low threshold for obtaining a postoperative cholangiogram (via stent or by PTC as indicated). Biliary stricture may result from fibrosis after bile leakage, may be related to prolonged cold ischemia, or ABO-incompatible transplantation as reported previously [3–7, 21]. Fibrosis formation after leaks could be the etiologic mechanism in patients managed conservatively with bile leaks. In LRLT, in which donor and recipient surgeries are conducted simultaneously, cold ischemic insult is minimized, compared with cadaveric transplantation. The maximum time was 300 minutes in our series. ABO-incompatible combination led to multiple stenosis of the intrahepatic bile ducts, and possibly was one of the etiologic factors of anastomotic stenosis, presumably due to injury to small arteries supplying the biliary epithelium [22]. Balloon dilatation after PTCD for anastomotic stricture management was possible in 21 of 34 patients, but long-term success was achieved in 10. When conservative therapy failed, revisional hepaticojejunostomy and further intrahepatic hepaticojejunostomy was associated with a good outcome [22].

In Japan, 90% of adults are CMV positive, and the donors are restricted to relatives. Therefore, the CMV issue is not a significant factor for donor selection compared to ABO compatibility, size matching, and disease transmission. However, CMV disease is shown to be a significant risk factor in this study. It has been reported previously that CMV infection is associated with extrahepatic biliary strictures [16]. A possible explanation of the link between CMV infection and biliary complication may be related to occlusion of small arteries leading to biliary complications through ischemic insult [23]. In our current policy, we do not do prophylactic administration of gancyclovir. However, the results of this study underlined the importance of the prophylaxis.

Four of the patients with cholangitis developed portal vein thrombosis. In three of them, the portal vein was found to be completely occupied by thrombi. One patient died because of sepsis. The other two patients have been followed-up in an outpatient clinic. In the other patient, the partial thrombus and diminishing portal flow were found when she developed cholangitis due to anastomotic stricture 2 years after transplantation. After her successful balloon dilatation, portal flow improved. Not only evaluation of the bile ducts but also evaluation of hepatic blood flow are important in long-term follow-up.

We encountered difficulties with inadvertent ligation of the main left hepatic duct on two occasions, mistaking it for the duct to B4. We believe that intraoperative cholangiography (biplanar if the initial films are difficult to interpret) is an essential adjunct, offering additional safety to the donor and to the recipient. It is especially valuable when there are aberrations in donor biliary anatomy, such as aberrant drainage of B6 or a left-sided gallbladder.

Biliary complications remain an Achilles' heel of liver transplantation despite major advances in immunosuppression and technical advances in surgery and interventional management. The overall risk of biliary complications in LRLT in this series is no different from that reported by other centers for cadaveric whole liver transplantation. It is clear that our biliary complication rate may be further improved by taking the above factors into account.

Résumé

Objectifs: Le but de cette étude a été d'évaluer les causes et l'évolution des complications biliaires anastomotiques après transplantation du fole par donneur vivant familial (TFDVF). Patients et méthodes: On a revu les données provenant d'une banque de données de 391 patients ayant eu 400 TFDVF entre juin 1990 et août 1998. Résultats: L'incidence globale des complications biliaires anastomotiques a été de 18,2% (71 patients). II y avait 45 fistules biliaires, 35 sténoses anastomotiques alors que la voie biliaire a été liée par inadvertance chez trois patients. Par analyse univariée, les facteurs prédictifs significatifs de fuite ont été la manière d'utiliser le stent, la présence d'un shunt intrapulmonaire et le sexe. Les facteurs prédictifs significatifs de sténose ont été la fuite anastomotique, une infection à cytomégalovirus (CMV), une complication portant sur l'artère hépatique et le sexe du receveur. Chez le patient pédiatrique âgé de plus de deux ans, la compatibilité ABO était également un facteur de fistule anastomotique et de sténose. Conclusions Le choix du stent, et la transplantation précoce des patients ayant un shunt intrapulmonaire, devrait réduire le risque de fistule biliaire alors que la prophylaxie de la fistule pour les patients ayant un shunt intrapulmonaire et la minimisation des complications artérielles hépatiques devraient réduire le risque de sténose après transplantation par donneur vivant. Chez l'enfant, il faut éviter une incompatibilité ABO ou en cas de transplantation ABO incompatible, une immunodépression innovatrice doit être prise en considération.

Resumen

Propósito: evaluar las causas y efectos de las complicaciones anastomóticas de la vía biliar que ocurren luego del trasplante intrafamiliar de higado vivo (TIHV). Pacientes y métodos: se revisó la base de datos de 391 pacientes sometidos a 400 transplantes entre junio de 1990 y agosto de 1998. Resultados: la tasa global de complicaciones anastomóticas de la vía biliar fue 18.2% (71 pacientes). Se registraron 45 fugas, 35 estenosis anastomóticas y la vía biliar fue accidentalmente ligada en 3 casos. El análisis univariable reveló que el método de uso de "stents", el shunt intrapulmonar y el género de los receptores fueron factores de riesgo en cuanto a fuga anastomótica. La fuga anastomótica, la infección por citomegalovirus, las complicaciones de la arteria hepática y el género del receptor, aparecieron como factores de riesgo significativo de estenosis. En los pacientes pediátricos mayores de dos años, el tipo de sangre ABO también fue factor de riesgo tanto para fuga como para estenosis. Conclusiones: la escogencia del uso del "stent" y un transplante más precoz deben resultar en reducción de la tasa de fuga biliar en pacientes con shunt intrapulmonar, y la minimización de las complicaciones de la arteria hepática debe disminuir la tasa de estenosis biliar en el TIHV. Evitar la incompatibilidad ABO en el donante o una innovativa inmunosupresión en un trasplante ABO incompatible, deben ser consideradas en el caso de los pacientes pediátricos.

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