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ORIGINAL ARTICLE

Biliary Complication in Pediatric Liver Transplantation: a Single-Center 15-Year Experience

Chih-Yang Hsiao[1,2] · Cheng-Maw Ho[3] · Yao-Ming Wu[3,4] · Ming-Chih Ho[3,4,5] · Rey-Heng Hu[3,4] · Po-Huang Lee[3,4]

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Abstract

Background The incidence and several risk factors of biliary complication (BC) following pediatric liver transplantation (LT) are widely known, but data on long-term outcomes and management is limited. This retrospective study aimed to investigate the incidence, associated risk factors, management, and outcomes of early and late BC in pediatric LT.

Methods This study enrolled 134 pediatric patients (< 18 years old) who underwent LT at a tertiary care center in Taiwan between January 2001 and December 2015. Diagnosis of BC was based on clinical, biochemical, and radiologic examinations. Clinical data and chart records were reviewed and compared between the groups.

Results Among the 134 children, 21 children (15.7%) had BC after LT. Nine children had early complications, including leakage plus stricture ($n = 2$), stricture only ($n = 2$), and leakage only ($n = 5$). Twelve children had late BC; all of whom had anastomotic stricture. Of the 21 patients with BC, 11 patients (52.4%) were treated without surgery. The median time of first treatment for BC was 6.5 months (range, 11 days to 6.2 years). Five of the 9 patients with early complications and two of the 12 patients with late complications died of biliary tract infection. The major risk factors of BC in pediatric LT were (1) recipient age > 2 years, (2) Kasai portoenterostomy revision, and (3) hepatic artery thrombosis.

Conclusions Several risk factors of BC in pediatric LT were identified. Children with early BC appeared to have relatively unfavorable outcomes. However, late BC treated by either radiological or surgical methods appeared to have a relatively good long-term prognosis.

Keywords Biliary complications · Pediatric liver transplantation · Risk factors

Introduction

Liver transplantation (LT) is the only effective treatment for children with end-stage liver disease.[1] Although there has been a significant improvement in the long-term outcomes of patient and graft survival in recent decades, the occurrence of biliary complications (BC) has been shown to increase morbidity, prolong hospital stay, and result in increased costs.[2] A single-center study reported that BC in pediatric LT patients decreased graft survival and had an incidence of 10% to 45%.[3] The variation in the reported incidence of BC between centers might be due to the different criteria for diagnosis of BC. Bile leakage and biliary strictures are the most frequent types of BC. Bile leakage, which usually presents in the initial period after LT, may be a risk factor of long-term anastomotic stricture because bile acid irritates the anastomotic site and results in inflammation and fibrosis. Anastomotic and non-anastomotic biliary stricture could develop in the early or late period after LT. Anastomotic stricture in the early period after LT could be surgery-related. However, anastomotic and non-anastomotic late-developed strictures are thought to be related with any etiology that causes chronic inflammation and fibrosis, including the recipient's

✉ Ming-Chih Ho
mcho1215@ntu.edu.tw

[1] Department of Surgery, National Taiwan University Hospital Yun-Lin Branch, Douliou City of Yun-Lin County, Taiwan

[2] Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan

[3] Department of Surgery, National Taiwan University Hospital, Taipei, Taiwan

[4] College of Medicine, National Taiwan University, Taipei, Taiwan

[5] Department of Surgery, National Taiwan University Hospital, No. 7, Chung-Shan South Road, Taipei, Taiwan

native liver disease, graft quality (donor age, ischemic time), stretching or kinking of anastomosis[4] after liver regeneration,[5] and ischemia of the biliary system.

Risk factors associated with BC in pediatric LT include duct-to-duct bile reconstruction,[3,4,6,7] acute rejection,[8] prolonged surgical time,[7], and hepatic artery thrombosis (HAT).[4,7] Although duct-to-duct reconstruction has a theoretically physiological benefit, previous studies have failed to show that it has a consistent benefit compared with the Roux-en-Y hepaticojejunostomy (HJ). Indeed, a number of studies reported that the Roux-en-Y hepaticojejunostomy was superior to duct-to-duct reconstruction at minimizing BC.[3,4,6,7] The management of BC after pediatric LT also varies between centers depending on treatment policies and availability of radiological modalities. Many centers have initially tried percutaneous or endoscopic intervention by the radiologist, with a PTC success rate ranging from 83 to 100%.[9–12] However, some data suggests that surgical re-anastomosis should be the first line of treatment.[8]

The aim of this study was to analyze the incidence, associated risk factors and long-term outcomes of BC in pediatric LT patients in a tertiary center in Asia.

Materials and Methods

Patients

This study was approved by the Ethics Committee of National Taiwan University Hospital, and the study was carried out in accordance with the approved guidelines. This study enrolled a total of 139 children who underwent LT at our center between January 2001 and December 2015. Two children with re-transplantation and three children with ABO-incompatible transplantation were excluded during analysis. All 134 patients were followed until December 2016 or death. Medical records were reviewed to retrospectively collect patients' demographic data.

The median age of donors was 33 years, and the median size of the grafts was 300 g. There were 9 deceased donor grafts (6 whole livers, and 3 left lobes) and 125 living donor grafts (99 lateral segments, 21 left lobes, and 5 right lobes). Histidine-tryptophan-ketoglutarate solution was used as allograft infusate in all patients. The median size of the reconstructed bile ducts was 5 mm. Most of grafts used in this study had a single hepatic duct, or, at least, had a common orifice of hepatic ducts. Only three patients (who used lateral segment grafts) in this study underwent two separate bile ducts reconstructions; one of them had double duct-to-duct anastomosis (B3 to common hepatic duct and B2 to cystic duct of recipient) and the other two had Roux-en-Y hepaticojejunostomy.

Bile Duct Reconstruction

Bile duct reconstruction was performed during LT based on the recipient's underlying disease and clinical condition. We regard duct-to-duct anastomosis as the standard method, however, in patients who had underlying biliary atresia, primary biliary cirrhosis, or any other clinical condition where duct-to-duct anastomosis was not feasible (such as poor integrity of native common bile duct), we chose to perform Roux-en-Y reconstruction. Among patients undergoing different types of bile duct reconstruction, there was no age difference in donors nor graft size differences. Donor ductoplasty was sometimes performed when there were two orifices of the bile ducts in the partial graft according to the distance between them. If the two bile ducts were close to each other with a common septum, we anastomosed them as a single orifice. If they were separate but acceptably close (less than 3 mm), we unified both ducts (ductoplasty) into a single orifice before reconstruction by joining the medial wall (the newly created septum was divided vertically and sutured transversely to create a large opening). If they were widely separated, we anastomosed them independently. Duct-to-duct anastomosis with a silicon stent across the anastomosis was the preferred method. Before 2011, a straight biliary stent was used in a partial graft and a T-tube stent was used in a whole liver graft. After 2012, a straight biliary stent was used in all type of grafts. Roux-en-Y hepaticojejunostomy (partial graft) or choledochojejunostomy (whole graft) was performed in patients who had underlying biliary atresia, primary biliary cirrhosis, or any other clinical condition where duct-to-duct anastomosis was not feasible. Both duct-to-duct anastomosis and hepaticojejunostomy/choledochojejunostomy were done by interrupted sutures with the biliary stent through the anastomosis site. Before 2011, interrupted monofilament absorbable sutures (Maxon® and PDS®) were used in bile duct reconstruction. To improve durability, interrupted non-absorbable sutures (Prolene®) were used after 2012.

Follow-up and Biliary Complications

Patients received regular monthly or bimonthly follow-up at the outpatient clinic after discharge. Routine blood tests for liver function and immunosuppressant levels were checked at each visit. Abdominal sonography was performed every year. Additional imaging studies such as computed tomography (CT) or magnetic resonance imaging (MRI) were recommended for patients with specific complaints or abnormal blood tests. Biliary complications were classified as early (< 3 months) or late (> 3 months) according to the time of development after LT. The diagnosis of bile leakage was made if there was evidence of bile content drainage from the intraabdominal drainage tubes persistent after 1 week, or if there was a significant amount of biloma formation on imaging exams. A diagnosis of biliary

stricture was made if the patient had obstructive type hyperbilirubinemia accompanied with dilated intrahepatic duct on abdominal CT or MRI. Radiological intervention was our first choice in treatment of anastomotic biliary stricture. Surgical intervention was performed when radiological intervention had been thought to be ineffective, such as no contrast medium passing through the obstruction site being observed, or the attempts of percutaneous transluminal dilatation failing too many times. Successful treatment was defined as no evidence of residual stenosis on CT or MRI, and no obstructive type hyperbilirubinemia exceeding 2 mg/dL.

Immunosuppression

The immunosuppression protocol after LT consisted of a calcineurin inhibitor (cyclosporine or tacrolimus), mycophenolate mofetil (MMF), and steroid therapy. The calcineurin inhibitor was given orally beginning on the first postoperative day after LT, and was continued with dose adjustments to maintain blood levels within the therapeutic range. Calcineurin inhibitor was rapidly tapered to trough level < 5 ng/ml in 3 months after LT in pediatric patients < 2 years old, in order to reduce the risk of incidence of posttransplant lymphoproliferative disorder, since January 2005. Basiliximab was not administered for these pediatric patients. MMF was not given routinely, and was only prescribed for patients with more than one episode of acute rejection. Steroid therapy was tapered off in 6 months for most of the patients.

Statistical Analysis

Data were expressed as mean ± standard deviation, median [interquartile range (IQR) or range], or number (percentage) when appropriate. Categorical variables were compared using the Fisher exact tests and Pearson χ^2 tests. Continuous variables were compared using the Student's *t* test and Mann–Whitney *U* test, as appropriate. Survival curves were estimated using the Kaplan–Meier method, and compared with the log-rank test. Variables were put into multiple logistic regression analysis to determine the independent risk factor for BC. A *P* value < 0.05 was considered significant. Statistical analyses were performed using SPSS 18.0 for Windows (SPSS Inc., Chicago, IL).

Results

Patient Demographic Characteristics and Biliary Complications

The demographic data and clinical characteristics of the 134 pediatric study patients are summarized in Table 1. The study population comprised 55 males (41%) and 79 females (59%), and the median age at transplantation was 1.331 [IQR 0.896–3.94] years (range, 82 days to 17.411 years). The median duration of follow-up was 83.86 [IQR: 33.4–142.6] months (range, 2 days to 192 months). Of the 134 patients, 125 underwent living donor transplants (93.3%) and 9 underwent deceased donor transplants (6.7%). The major indications for LT were biliary atresia (68.7%), followed by metabolic disease (13.4%).

Incidence, Management, and Outcome of Biliary Complications

Of the 134 children, 21 children (15.7%) had BC after LT (Fig. 1). Nine children had early biliary complications, including 2 children who had leakage plus stricture (both children died of infection), 2 children who had stricture only (one died of HAT and bleeding at 48 days after LT), and 5 children who had leakage only (3 children developed biliary stricture during follow-up, and 2 of the 3 died of infection). All complications were biliary anastomosis related, and no major leakage from the liver cut surface or intrahepatic biliary stricture was observed. All 12 children who had late BC suffered from anastomotic stricture (2 children died of biliary tract infection). The analysis, treatment, and outcome of 21 patients with BC after LT are shown in Table 2. The detailed analysis, treatment, and outcomes of 7 patients with bile leakage and 19 patients with bile duct anastomosis stricture after LT are shown in Tables 3 and 4. Of the 21 patients with BC, 11 patients (52.4%) were treated without surgery; and 10 patients (47.6%) eventually underwent surgical management for their biliary complications. The median time of first treatment for BC was 6.5 months (range, 11 days to 6.2 years). Of the 21 patients with BC, 5 of the 9 patients with early complications died of biliary tract infection, while 2 of the 12 patients with late complications died of biliary tract infection.

Risk Factors of Biliary Complication After Pediatric LT

Univariate logistic regression analysis was performed to identify the risk factors associated with BC in pediatric LT patients (Table 5). The major risk factors associated with post-LT BC included age > 2 years old at the time of transplantation (odds ratio [OR] = 4.18, 95% CI 1.528–11.042), Kasai portoenterostomy revision before transplantation (OR = 5.573, 95% CI 1.522–20.406), and hepatic artery thrombosis (OR = 9.25, 95% CI 1.444–59.254). Variables with *P* values < 0.1 in univariate analysis were included into the multivariate analysis. Multivariate logistic regression analysis showed that age > 2 years old at the time of transplantation (OR = 4.087, 95% CI 1.376–12.141),

Table 1 Demographics and clinical characteristics of patients with and without biliary complications after pediatric liver transplantations

	All patients ($n = 134$)	With BC ($n = 21$)	Without BC ($n = 113$)	P value
Age (years) at LT	1.33 (0.90–3.94)	4.15 (1.48–12.8)	1.24 (0.82–3.09)	< 0.001
Male sex	55 (41.0)	8 (38.1)	47 (41.6)	0.481
Indication for LT				
Biliary atresia	92	11	81	
PSC	3	2	1	
PFIC	5	2	3	
Alagille syndrome	3	1	2	
Cryptogenic cirrhosis	2	0	2	
Caroli disease	2	0	2	
Metabolic disease	18	1	17	
Fulminant hepatitis	4	2	2	
Neonatal hepatitis	1	0	1	
Hepatoblastoma	4	1	3	
Follow-up period (month)	83.9 (33.4–143)	41.1 (20.5–144)	99.7 (36.6–142)	0.179
Surgical history				0.011
Without Kasai portoenterostomy	47	8	39	
Kasai portoenterostomy without revision	76	8	68	
Kasai portoenterostomy with revision	11	5	6	
Graft type				0.109
Deceased donor	9	2	7	
Whole liver	6	2	4	
Left lobe	3	0	3	
Living donor	125	19	106	
Lateral segment	99	10	89	
Left lobe	21	7	14	
Right lobe	5	2	3	
Bile duct reconstruction type				0.178
Duct-to-duct	20	5	15	
Hepaticojejunostomy	114	16	98	
HAT	5	3	2	0.027

Data are reported as median (IQR) or number (percentage)

BC, biliary complication; *HAT*, hepatic artery thrombosis; *LT*, liver transplantation; *PFIC*, progressive familial intrahepatic cholestasis; *PSC*, primary sclerosing cholangitis

Kasai portoenterostomy revision before transplantation (OR = 6.624, 95% CI 1.556–28.196), and hepatic artery thrombosis (OR = 9.814, 95% CI 1.306–73.743) were independent risk factors of post-LT BC (Table 6).

Impact of Biliary Complication on Survival

Kaplan-Meier curves were used to analyze overall survival of pediatric LT recipients with and without BC (Fig. 2). Seven patients with BC and 19 patients without BC died after LT during follow-up. Children with BC after LT had higher mortality rates (33.3%, 7/21) compared to children without BC after LT (16.8%, 19/113). Although there was a trend, there was no significant difference in survival time between patients with and without post-LT BC (log rank (Mantel-Cox) $P = 0.079$) (Fig. 2).

Discussion

Our present study showed that transplant age > 2 years old, previous Kasai portoenterostomy revision, and HAT after LT were risk factors of BC in pediatric LT patients.

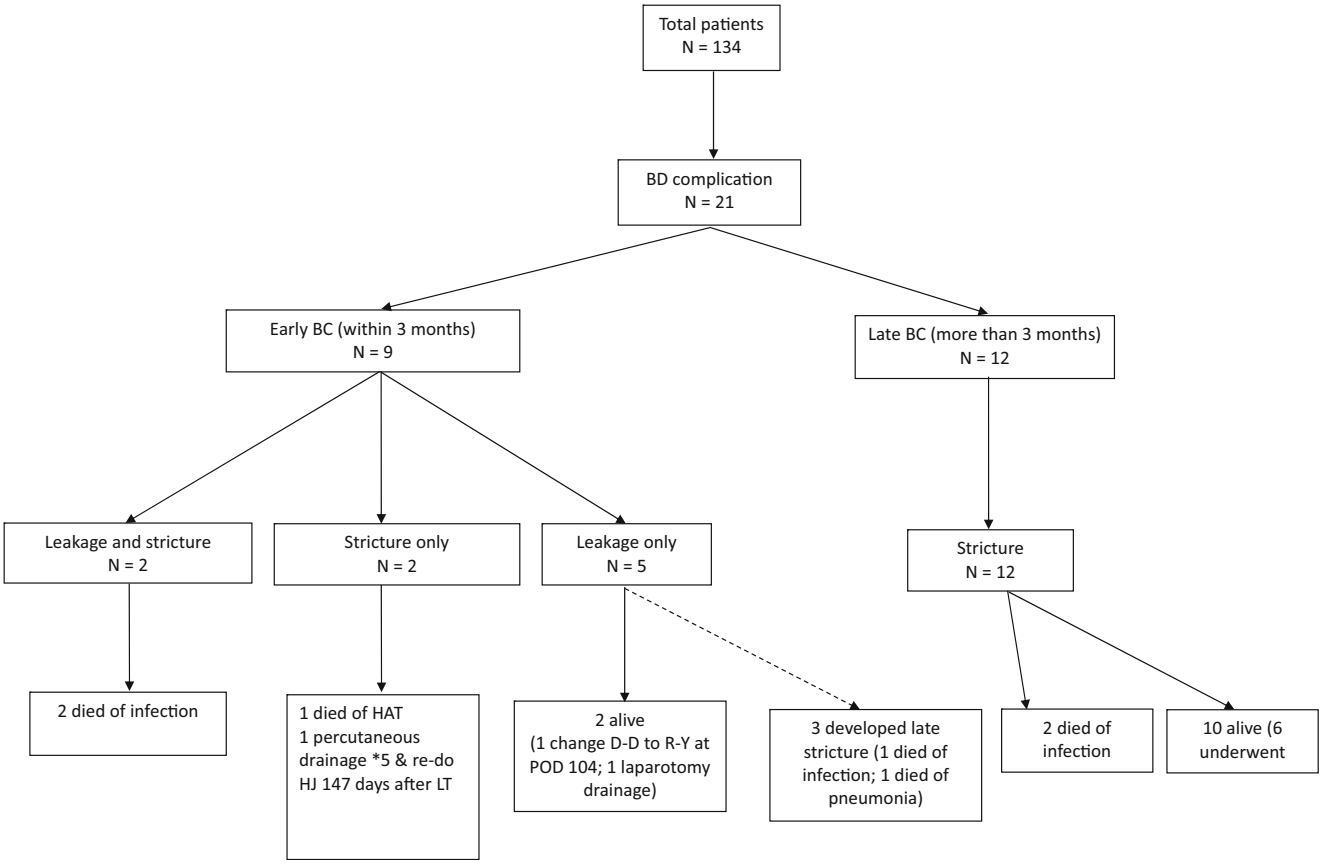


Fig. 1 Clinical outcomes of 21 patients who experienced biliary complications after liver transplantations (BC, biliary complication; BD, bile duct; D-D, duct-to-duct anastomosis; HJ, hepaticojujunostomy; HAT, hepatic artery thrombosis; LT, liver transplantation; POD, postoperative day; R-Y, Roux-en-Y reconstruction)

Age > 2 years old at LT may refer to a longer time on the waiting list and a prolonged treatment course of complicated underlying liver disease in patients with relatively poor physical condition. A recent study[13] reported that older children (6–17 years old) with BA post Kasai portoenterostomy had a significantly higher incidence of BC in the case of living donor LT. Children with early failed Kasai portoenterostomy and a late diagnosis of BA usually undergo LT before the age of

Table 2 Analysis, treatment, and outcome of 21 pediatric patients with biliary complications (BC) after liver transplantation

	Early BC < 3 months ($n = 9$)	Late BC > 3 months ($n = 12$)
Type of complication		
Leakage	2	0
Anastomosis stricture	2	12 (100)
Leakage with stricture	2	0
Leakage with late anastomosis stricture	3	0
Treatment		
Without surgical re-anastomosis bile duct	5	6 (50)
Surgical re-anastomosis bile duct	4	6 (50)
Outcome		
Mortality	5	2 (16.6)
Survive with functional graft	4	10 (83.3)
Follow-up/survival period (month) (median, range)	36.8 (1.6–187)	75.3 (14.5–163)

Data are reported as median (range) or number (percentage)

Table 3 Analysis, treatment, and outcome of 7 pediatric patients with bile leakage after liver transplantation

	Bile leak ($n = 7$)
Days post-LT when complication occurred (median, range)	24 (4–84)
During LT hospitalization (< 3 months)	7 (100)
After LT discharge (≥ 3 months)	0
Vascular complications during LT	0
Other complications during LT	
Bowel perforation	1 (14.3)
Biliary stricture at initial	2 (28.6)
Treatment for bile leakage	
Surgical re-anastomosis	1 (14.3)
Surgical drainage	3 (42.9)
Percutaneous drainage	4 (57.1)
Outcome	
Development of biliary stricture (≥ 3 months)	3 (42.9)
Mortality	4 (57.1)
Mortality during LT hospitalization	2 (28.6)
Mortality (late biliary stricture related)	1 (14.3)
Mortality (pneumonia related during treat biliary stricture)	1 (14.3)
Follow-up/survival period (month) (median, range)	36.8 (2.4–187.3)

Data are reported as median (range) or number (percentage)

Five patients had both leakage and stricture

Table 4 Analysis, treatment, and outcome of 19 pediatric patients with bile duct anastomosis stricture after liver transplantation

	Early (< 3 months) bile duct anastomosis stricture ($n = 4$)	Late (≥ 3 months) bile duct anastomosis stricture ($n = 15$)
Days post-LT when complications occurred (median, range)	17 (11–24)	301 (140–2264)
Vascular complications during LT		
HAT	1 (25)	2 (13.3)
PVT	0	0
HVT	0	0
Other complications during LT		
Bowel perforation	0	2 (13.3)
Bile leakage	2 (50)	3 (20)
Bleeding	1 (25)	0
Treatment for biliary stricture		
Percutaneous drainage	4 (100)	15 (100)
Percutaneous dilatation	0	14 (93.3)
Surgical re-anastomosis	1 (25)	8 (53.3)
Outcome		
Graft failure or mortality	3 (75)	4 (26.7)
Mortality (BC related)	2 (50)	3 (20)
Mortality (non-BC related)	1 (25)	1 (6.7)
Survive with functional graft	1 (25)	11 (73.3)
Follow-up/survival period (month) (median, range)	2 (1.6–183)	44.1 (14.5–163)
Post Kasai portoenterostomy revision	2 (50)	1 (6.7)

Data are reported as median (range) or number (percentage)

Table 5 Univariate logistic regression analysis to identify risk factors associated with biliary complications in pediatric liver transplantation

Variable	OR (95% CI)	*P* value
Age (> 2 years)	4.108 (1.528–11.042)	0.005
Male sex	0.864 (0.332–2.250)	0.765
Biliary atresia as LT indication	0.435 (0.168–1.123)	0.085
Metabolic disease as LT indication	0.282 (0.036–2.246)	0.232
Kasai portoenterostomy before LT	0.856 (0.327–2.242)	0.752
Kasai portoenterostomy revision before LT	5.573 (1.522–20.406)	0.009
Living donor graft	0.627 (0.121–3.252)	0.579
Partial graft	0.349 (0.060–2.038)	0.242
D2D bile duct reconstruction	2.042 (0.652–6.395)	0.220
HAT	9.25 (1.444–59.254)	0.019

D2D, duct-to-duct; *HAT*, hepatic artery thrombosis

two. Children with initial successful Kasai portoenterostomy but who progress to liver failure and eventually undergo LT at age > 2-years old were a distinct group. These children tolerated chronic liver diseases for a long time and suffered from the cumulative negative effects of long-term liver dysfunction, i.e., malnutrition, cholestasis, recurrent cholangitis, portal hypertension, and coagulopathy. These are important factors associated with surgical complications, including BC. Analysis of our cohort appears to support the above opinion, among 19 children with failed Kasai who underwent early liver transplantation before age of two, only one child had BC.

Our study showed that Kasai portoenterostomy revision was a risk factor of BC, while previous Kasai portoenterostomy was not. The effect of previous Kasai portoenterostomy on the outcome of LT remains controversial.[14–23] Some studies have suggested that previous Kasai portoenterostomy increased the risk of bowel perforations and BC from LT, whereas other studies showed that operation time, blood loss, and LT complications were not significantly associated with the length of intensive care unit or hospital stay.[14–23] Pediatric patients require a more meticulous surgical technique for bile duct reconstruction compared to adults because of the relatively small size of structures. Additionally, rapid growth of the body trunks during the follow-up period after LT can result in kinking or stretching of the reconstructed biliary system. Although younger-age and previous Kasai portoenterostomy can theoretically make LT technically more challenging, the transplant age of children having a previous history of Kasai portoenterostomy was generally higher compared to BA children who underwent LT directly, inasmuch that these were confounding factors. The impact of Kasai portoenterostomy revision to LT is also controversial.[16,24] However, it is reasonable to expect that Kasai portoenterostomy revision is a risk factor of BC in pediatric LT patients because of the difficulties and challenges in biliary reconstruction. First, repeated abdominal and hepatobiliary surgery results in severe adhesions, thereby increasing blood loss and surgical time. Second, the Y-limb of the jejunum, which often needs to be cut short during Kasai portoenterostomy revision, is even shorter during LT. The benefits of hepaticojejunostomy revision after failed Kasai portoenterostomy and LT should be carefully evaluated. The success rate of a Kasai portoenterostomy revision is low.

It is not surprising that HAT was a risk factor of BC after pediatric LT. HAT is a serious complication after LT which is often associated with not only BC, but also early graft loss and patient death.[25–27] Late biliary stricture is often caused by impaired blood supply of the biliary system mainly from arterial system. Development of HAT is usually followed by ischemia of the anastomotic site, which affects the healing process and could result in anastomotic leakage and consequent stricture associated with irritation of leakage bile juice.

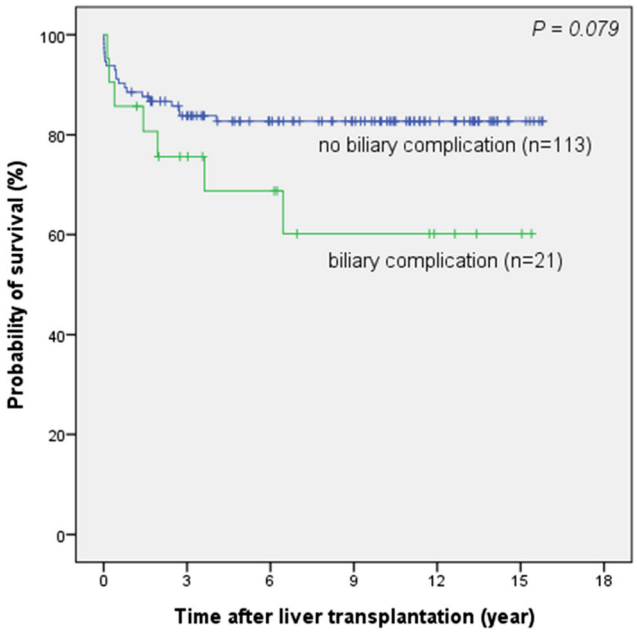
A number of studies reported that hepaticojejunostomy is the preferred method for bile duct reconstruction in pediatric LT patients.[3,4,6,7] However, our present study showed that duct-to-duct anastomosis was not a risk factor of BC. From our limited experience, we believe that duct-to-duct anastomosis is a safe and feasible method of biliary reconstruction in selected pediatric LT patients.

There were no recipients with intrahepatic biliary stricture in this study. Intrahepatic stricture was previously shown to be

Table 6 Multivariate logistic regression analysis to identify risk factors associated with biliary complications in pediatric liver transplantation

Variable	OR (95% CI)	*P* value
Age (> 2 years)	4.087 (1.376–12.141)	0.011
Biliary atresia as LT indication	0.441 (0.150–1.295)	0.136
Kasai portoenterostomy revision before LT	6.624 (1.556–28.196)	0.011
HAT	9.814 (1.306–73.743)	0.026

HAT, hepatic artery thrombosis



Number of patients at risk

No BC	113	85	66	51	27	6
BC	21	13	10	6	4	2

Fig. 2 Kaplan-Meier curves to analyze overall survival of pediatric liver transplant recipients with and without biliary complications (BC)

associated with older age of the donor.[7,28] The occurrence of intrahepatic strictures could be associated with liver grafts from older donors prone to develop fibrosis.[29] In our study, most donors were living donors (parents of recipients) aged between 25 and 39, which could explain our findings.

Another finding of this study was that patients with early BC appeared to have relatively unfavorable outcomes. Late BC, treated by either radiological or surgical methods, appeared to have a relatively good long-term prognosis. Of the nine patients with early BC, five (55.6%) eventually died. Three of four patients with early biliary stricture died within 6 months postoperatively (including one who died of bleeding and two who died of biliary infection). The one survivor underwent surgical revision of Roux-en-Y hepaticojejunostomy 146 days after LT, with a long-term survival of 15.04 years without any further BC. Of the five patients with purely early bile leakage, three patients developed late biliary stricture, of whom two died of infection. The only survivor of these three patients underwent surgical revision of Roux-en-Y hepaticojejunostomy 682 days after LT with a survival of 3.02 years. Our present study suggested that patients who develop early biliary stricture after LT should be recommended aggressive management such as surgery if their cholestasis does not resolve properly in a short period. Of the 12 patients with late BC, six eventually underwent surgical re-anastomosis, all without mortality. The other six patients underwent radiological intervention without surgery. Two patients died of infection during their treatment course. Our data suggested that surgical intervention may be a better option for biliary stricture in pediatric patients.

The management of biliary stricture differs between institutions. Although some data indicated that surgery is the best therapeutic choice,[8] rapid advances in interventional radiology in recent years have resulted in the adoption of radiological intervention as the gold standard for first-line management of biliary stricture.[30–32] We prefer percutaneous transluminal bile duct dilatation rather than the endoscopic dilatation approach, regardless of Roux-Y or duct-to-duct reconstruction. There are several advantages in the percutaneous transluminal approach over endoscopic dilatation approach. First, it is technically much easier. We perform percutaneous transluminal biliary drainage from an evident dilated intrahepatic duct, followed by an easy and direct route to approach the anastomotic site, and then we perform balloon dilatation. After balloon dilatation, we can leave a percutaneous transluminal tube in the bile duct which passes through the anastomosis to protect its patency.

Interventional radiology in treating pediatric biliary stricture depends on the modality of hospital, and the success rate is highly dependent on the experience of the radiologist. It is important to investigate larger samples in order to determine whether surgical re-anastomosis or radiological intervention provide better long-term outcomes.

Some important limitations of this study were that (1) it was a single-center retrospective analysis, and spanned a long time period, and (2) the improvements in transplant surgery and advances in radiological intervention may have influenced the incidence, treatment policy, and outcome in this study.

Conclusions

This study demonstrated that recipient age > 2 years old, Kasai portoenterostomy revision, and HAT were the most important risk factors of BC in pediatric LT patients. However, duct-to-duct reconstruction was not a risk factor of BC in pediatric LT. Children with early BC appeared to have relatively unfavorable outcomes, and late BC treated by either radiological or surgical methods appears to have better long-term prognoses. Surgical intervention for early BC seems warranted for a better outcome.

Author Contributions Hsiao CY and Ho MC contributed to data collection, interpretation of data, and drafted the manuscript; Ho MC and Hu RH contributed to study concept and design; Hsiao CY, Ho CM, Wu YM, Ho MC, Hu RH, and Lee PH contributed to critical revision of the manuscript.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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