Multiple bile duct anastomoses without stent in living-donor liver transplant

Aims: It is unclear whether the presence of multiple bile ducts in the graft increases the risk of biliary complications after living-donor liver transplant. In this study, we present our results to identify risk factors for the development of biliary complications and to determine the effect of multiple bile ducts in the incidence of biliary complications after living-donor liver transplant. **Materials & methods:** A total of 106 living-donor liver transplants were performed since 2006 and were divided into two groups: those with a single bile duct (n = 70) and those with multiple bile ducts (n = 36). Duct-to-duct biliary anastomosis was used in 79 (75.5%) living-donor liver transplants and a Roux-en-Y-hepaticojejunostomy was used in the remaining 27 (24.5%). **Results:** The overall biliary complications rate was 12.2% (four leaks, seven stenoses, two leaks plus stenoses). All biliary complications were treated using interventional radiologic techniques. Only hepatic arterial complications were a significant risk factor for the development of biliary complications. During the mean follow-up, 11.1 ± 4.2 months (range: 1–28 months), 16 recipients died (15%) and the remaining 89 recipients (85%) are alive with normal liver function. **Conclusions:** We found that only hepatic arterial complications were associated with a higher rate of biliary complications. Although our follow-up period was short, the presence of more than one bile duct in the graft does not appear to increase the risk of biliary complications after living-donor liver transplant.

KEYWORDS: biliary complication ▪ biliary reconstruction technique ▪ living-donor liver transplant ▪ multiple bile ducts

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Liver transplant is the definitive treatment for end-stage liver disease. Technical complications lead to significant morbidity and mortality during the post-operative period following liver transplant. Despite advances in immunosuppression, organ preservation, intraoperative management and various refinements in surgical technique, 10–25% of recipients who undergo deceased-donor liver transplant develop biliary complications [1]. The corresponding range for living-donor liver transplant (LDLT) complications is 15–64% [2–8]. These high complication rates fuel continued debate about the optimal type of biliary anastomosis, and whether stents or T tubes should be used in the reconstruction process. Prolonged cold-ischemia, hepatic arterial thrombosis (HAT), cytomegalovirus infection and chronic rejection have been linked to an increased incidence of biliary complications [9–11]. However, the presence of multiple bile ducts in the graft has rarely been studied as a risk factor. In this study, we present our results to identify risk factors for the development of biliary complications and to determine the effect of multiple bile ducts in the incidence of biliary complications after LDLT.

Materials & methods

Between September 2001 and March 2009, 216 LDLTs were performed for 213 recipients at Baskent University Hospital in Ankara, Turkey. Before December 2006, 110 LDLTs were performed, for which we used different drainage techniques for biliary reconstruction, including T tubes, straight feeding tubes and transhepatic catheters [12]. Since December 2006, we have been performing biliary reconstruction for liver transplant without a drainage catheter [13]. After this time, we performed 106 LDLTs on 105 recipients, which were analyzed retrospectively. The number of bile ducts was defined as the number of biliary anastomoses that were performed for biliary reconstruction. According to the reconstruction described in the operating note, recipients were subsequently divided into two groups: those with single bile duct grafts (single bile duct group; n = 70) and those with multiple bile duct grafts (multiple bile ducts group; n = 36).

The surgical technique used in the living donors has been described previously [14]. In addition, the technical details of the hepatic vein, portal vein and hepatic arterial anastomosis have been previously described [15,16].

Whenever possible, our first choice was to perform a direct anastomosis between the bile duct of the graft and the common bile duct of recipients. When multiple ducts were present and in proximity to one another, we performed a single anastomosis including all possible orifices joined by a ductoplasty. When a direct biliary anastomosis was not possible because the ducts were distant from each other, a Roux-en-Y hepaticojejunostomy (RYHJ) or an anastomosis with the cystic duct was performed. A total of 27 LDLTs (24.5%) underwent RYHJ, and 79 underwent direct duct-to-duct (DD) anastomosis (75.5%). In all recipients, bile duct reconstruction was performed by the same surgeon with a surgical loop (2.5×). A biliary reconstruction is usually performed with a 6–0 monofilament absorbable suture. Surgical details of bile duct anastomosis have been previously described [13]. External drains were kept in the right subphrenic space and below the biliary anastomosis. In the single bile duct group, in 18 LDLTs (22.7%) we performed a RYHJ; in the remaining 52 LDLTs (77.3%), we performed a direct DD anastomosis. In the multiple bile duct group, 31 of the 36 grafts had two bile ducts, four had three bile ducts, and one had four bile ducts. RYHJs were performed in nine LDLTs (25%), and a DD anastomosis was performed in the remaining 27 (75%). In seven grafts with two bile ducts, two separate anastomoses were performed using the recipient's common bile duct and the cystic duct. In three grafts with two bile ducts, two separate anastomoses were performed using a RYHJ. In the remaining 21 grafts with two bile ducts, we created a single bile duct opening with a ductoplasty. After creation of a single orifice, a DD anastomosis was performed in 17 LDLTs and a RHYJ was performed in the remaining four. In one graft with three bile ducts, two neighboring ducts were sutured together, and anastomosed to a common bile duct; other bile ducts were anastomosed to the cystic duct separately. In one graft with three bile ducts, two neighboring ducts were sutured together, and two separate anastomoses were performed using a RYHJ. In two grafts with three bile ducts, a single orifice was created at the back table, and anastomosed to the common bile duct. In one graft with four bile ducts, two neighboring ducts were sutured together; this single orifice and the remaining two bile ducts were anastomosed using RYHJs separately. Biliary anatomy and type of anastomosis are summarized in Table 1 for multiple bile duct groups.

Immunosuppression consisted of a calcineurin inhibitor (usually tacrolimus), and steroids for all recipients. Doppler ultrasound was used to confirm flow in the portal vein and hepatic artery during the first 7 days after transplant twice daily. Biliary complications were defined as leaks or stenoses, which required a surgical or interventional radiologic treatment. Leaks were confirmed by the presence of bile staining in the external drains, or by radiologic methods. Strictures were diagnosed first by ultrasound or computed tomography and confirmed by percutaneous transhepatic cholangiogram. Potential risk factors for biliary complications that were reviewed in our analysis included recipient sex, age, preoperative Child–Pugh scores, length of surgery, cold ischemia time, type of graft used, type of biliary reconstruction (RHYJ vs DD anastomosis), presence of multiple bile duct, relative amount of intraoperative transfused blood, presence of hepatic arterial complications (hepatic arterial stenosis and hepatic arterial thrombosis), presence of cytomegalovirus infection, presence of acute rejection, and number of bile ducts.

Table 1. Biliary anatomy and type of anastomosis.

No. of patients	No. of ducts	No. of anastomoses	Type of anastomoses
4	2	1	Ductoplasty and RYHJ
17	2	1	Ductoplasty and duct-to-duct
3	2	2	RYHJ, separately
7	2	2	Duct-to-duct (RABD + CBD, RPBD + CyD)
1	3	2	Ductoplasty and duct-to-duct, AcD + CyD
2	3	1	Ductoplasty and duct-to-duct
1	3	2	Ductoplasty and RYHJ, AcD + RYHJ
1	4	3	Ductoplasty and RYHJ, AcD + RYHJ, AcD + RYHJ

AcD: Accessory duct; CBD: Common bile duct; CyD: Cystic duct; RABD: Right anterior bile duct; RPBD: Right posterior bile duct; RYHJ: Roux-en-Y hepaticojejunostomy.

The significance of differences between groups was determined by the *t*-test and Mann–Whitney test, and p-values less than 0.05 were considered statistically significant.

Results

A total of 71 recipients were female and 34 were male; the mean age was 23.4 ± 22.1 years (range: 6 months to 63 years). A total of 51 of the 105 recipients were children, and 54 were adults. The mean body weight and graft-to-body weight ratio were 44.3 ± 28.7 kg (range: 4.5–92 kg), and 2.1 ± 1.7 (range: 0.8–5.5), respectively. Indications for liver transplant were acute liver failure (11 recipients), biliary atresia (14 recipients), hepatic tumor (25 recipients), viral hepatitis (19 recipients), cholestatic liver disease (13 recipients), Wilson's disease (eight recipients), and other (15 recipients). All grafts were obtained from ABO-compatible living-related donors or spouses, and most of them were recipients' parents (42.4%). A total of 53 right lobes, 21 left lobes and 32 left lateral segments were transplanted. Retransplant was performed in one patient owing to chronic rejection of the graft 7 months after her first transplant. The mean operative time, and the mean cold ischemia time of the graft were 8.2 ± 1.9 h (range: 6–12 h), and 71 ± 17.9 min (range: 44–104 min), respectively. All recipients except four received a blood transfusion (2.4 ± 2 U; range: 1–13 U) of erythrocyte suspensions. Mean post-operative stay in the intensive care unit was 2.4 ± 2.2 days (range: 1–18 days), and the mean post-operative stay in the general surgery ward of the hospital was 14.3 ± 7.8 days (range: 7–42 days).

The overall biliary complication rate was 12.2% in this series. Biliary leakage occurred in four recipients (3.7%); these were treated with percutaneous transhepatic biliary drainage. Biliary stenosis was diagnosed in seven recipients (6.6%) during the mean follow-up of 11.1 ± 4.2 months (range: 1–28 months). All biliary stenoses were treated by percutaneous transhepatic biliary drainage and repeated balloon dilatations. Two recipients (1.8%) experienced biliary leak in the early post-operative period and a subsequent biliary stenosis. Also, biliary leaks were treated by percutaneous drainage and stenoses were treated by balloon dilatations. Details of biliary complications and their treatment for each patient are summarized in Table 2. According to the types of biliary reconstruction, the difference in biliary complications rates of 11.3% in those with DD anastomosis and 14.8% in those with RYHJ were not significantly different (p = 0.769). When we evaluated the number of bile duct anastomoses, bile duct complications occurred in five recipients (13.8%) who had multiple bile duct grafts (n = 36), and in eight recipients (10.1%) who had single bile duct grafts (n = 70). The presence of multiple bile ducts was not a risk factor for the development of bile duct complications (p = 0.353). By univariate analysis (Table 3), only hepatic arterial complications (six hepatic arterial thrombosis, ten hepatic arterial stenosis) (p = 0.042) were significant risk factors for the development of biliary complications.

During the study, 16 recipients (15%) died of acute respiratory distress syndrome (n = 2), sepsis (n = 6), pulmonary emboli (n = 2), drug

Table 2. Biliary complications and their treatment.

No	Complication	Time (post-LT day)	Treatment	Post-treatment follow-up (month)	Outcome
1	BS	39	BD	6	Died*
2	BS	150	BD	25	Alive
3	BS	133	BD	13	Alive
4	BS	115	BD	14	Alive
5	BL + BS	2	PD + BD	18	Alive
6	BS	164	BD	10	Alive
7	BL + BS	7	PD + BD	14	Alive
8	BS	167	BD	17	Alive
9	BL	6	PD	12	Alive
10	BL	2	PD	12	Alive
11	BS	89	BD	5	Alive
12	BS	62	BD	1	Alive
13	BL	23	PD	6	Alive
14	BL	39	PD	11	Alive

*Retransplantation was needed 7 months after the first living-donor liver transplant and she died 1 month later.
BD: Balloon dilatation; BL: Biliary leak; BS: Biliary stenosis; LDLT: Living-donor liver transplant; LT: Liver transplantation; PD: Percutaneous drainage.

Table 3. Results of univariate analysis of the risk factors for the overall number of biliary complications.

Variables	Incidence	p-value
Age (pediatric vs adult)	49 vs 51%	0.092
Age (years)	23.4 ± 22.1	0.096
Sex (female vs male)	34 vs 71	0.096
Weight (kg)	44.3 ± 28.7	0.169
Graft:recipient weight ratio (%)	2.1 ± 1.7	0.169
Child–Pugh score	9.2 ± 1.8	0.419
MELD score	18.3 ± 5.5	0.618
PELD score	24.1 ± 10.6	0.476
Type of the biliary reconstruction (DD vs RYHJ)	79 vs 27	0.769
Blood transfusion (unit)	2.4 ± 2	0.169
Length of the surgery (hours)	8.2 ± 1.9	0.146
Cold ischemia time (min)	71 ± 17.9	0.146
Albumin level, g/dl (pre-LT)	3.2 ± 0.7	0.850
Bilirubin level, mg/dl (pre-LT)	19.2 ± 18.7	0.515
Prothrombin time (seconds)	22.6 ± 6.4	0.105
Previous surgery (yes vs no)	23 vs 82	0.365
Type of graft		
Right lobe	53	0.115
Left lobe	21	
Left lateral segment	32	
No of the biliary anastomosis (1 vs ≥2)	70 vs 36	0.353
Hepatic artery complications (HAT and HAS) (yes vs no)	16 vs 90	0.042*
Cytomegalovirus infection (yes vs no)	9 vs 97	0.465
Acute rejection episodes (yes vs no)	20 vs 86	0.260

*$p < 0.05$

DD: Duct-to-duct; HAS: Hepatic artery stenosis; HAT: Hepatic artery thrombosis; LT: Liver transplantation; MELD: Model for End-Stage Liver Disease (≥18 years old); PELD: Pediatric End-Stage Liver Disease score (<18 years old); RYHJ: Roux-en-Y hepaticojejunostomy.

overdose (n = 1), hepatic failure (n = 2), recurrence of hepatoblastoma (n = 1) and cardiac arrest (n = 2). We did not encounter any complications resulting in mortality. At the time of this writing, the remaining 89 recipients (85%) are alive and are experiencing good graft function.

Discussion

Even with the recent advances in immunosuppression, organ preservation, patient management and surgical techniques, biliary complications remain a significant cause of morbidity after liver transplant. Today, there is no consensus on the best way to restore biliary continuity during this operation. Despite advances in surgical technique and diagnostic modalities, 15–65% of recipients undergoing LDLT experience biliary complications [1–8,17,18]. The incidence of bile duct complications is lower in recipients who have deceased-donor liver transplants (15%) than they are in recipients who undergo LDLTs (30–60%) [12]. The drainage catheter accounts for 60% of all post-operative biliary complications [19].

Biliary tract reconstruction is the final step of liver transplant and can be performed using two major techniques. The first, an end-to-end DD anastomosis, is rapid, simple and physiologic. The second, a RHYJ, is used when the former is not feasible for anatomic reasons or reasons related to the underlying hepatobiliary disease. RHYJ is preferable for the reconstruction of bile ducts in children and in grafts with multiple bile ducts than DD anastomosis, due to the suitability of multiple anastomosis [20]. At our center, our first choice for biliary reconstruction for both deceased-donor liver transplant and LDLT in pediatric and adult recipients is a DD anastomosis [21]. DD anastomoses were successfully performed in 27 grafts (75%) with multiple bile ducts. Separate anastomoses were carried out in the DD fashion in eight of these 27 grafts. Additionally, our series consists of 52 LDLTs in children, and DD anastomoses were used in 27 of these (52%). In our study group, 27 RYHJs (24.5%) were used for biliary reconstruction; all of which had extrahepatic biliary system problems such as biliary atresia or primary sclerosing cholangitis. The type of bile duct reconstruction had no effect on the biliary complication rate in our series in adult and pediatric recipients. Our data demonstrate that DD biliary reconstruction can be used safely in LDLT, including children and grafts with multiple bile ducts.

Usually, a DD anastomosis is performed over a drainage catheter. Use of this stent allows monitoring of bile flow and color, and ease when performing cholangiography. Moreover, presence of a stent may protect against anastomotic stenoses [22]. However, presence of a stent may also lead to specific complications, which account for 30–60% of the overall biliary complications [13,22–24]. These complications include bile leakage around the stent, cholangitis after cholangiography, displacement of the stent and biliary peritonitis after stent removal. The disadvantages associated with the use of a stent has led several authors to perform biliary reconstruction without a stent [13,17,25,26]. In 2007, Li and colleagues reported their results with biliary reconstruction with or without stenting in 84 recipients. Overall biliary complications developed in 19% of recipients. The rate of early biliary complications was 30.3% in the stent group and 11.8% in the group without stents. Biliary complications that were directly caused by drainage stent placement occurred in 12.1% of the recipients. The authors concluded that development of early biliary complications in recipients of liver transplant was significantly related to the use of a drainage catheter [27]. Before December 2006, 110 LDLTs were performed, for which we used different drainage techniques for biliary reconstruction, including T tubes, straight feeding tubes and transhepatic catheters. During this time, our overall biliary complications rate was 28.8%, and 35% of these complications were directly related to the drainage catheter. In the present study, we performed 106 LDLTs without a drainage catheter, and the biliary complications rate was assessed as 12.2%. This result supports the literature that recommends that LDLTs should preferably be performed without a catheter.

Multiple bile ducts in a LDLT are an added challenge to liver transplant. These make biliary reconstruction more difficult, and are thus associated with a higher risk of biliary complications. It is also unclear whether the presence of multiple bile ducts in the graft increases the risk of biliary complications after LDLT. The Kyoto group has reported their experience in the management of biliary complications with LDLT. Although they have observed a higher rate of biliary complication with the presence of stents for biliary reconstruction, no difference was observed with the presence of single or multiple biliary anastomoses [28]. Salvalaggio and colleagues reported their results of biliary complication in 101 recipients. Overall biliary complications developed in 26.7%. The rate of biliary complications was 42% in the presence of multiple bile ducts group, and 22%% in the single bile duct group. The authors concluded that the presence of multiple bile ducts in the liver graft was an independent risk factor for the development of biliary complication [20]. In our series, the biliary complication rate was similar between single and multiple bile ducts groups (10.1 vs 13.8%).

Hepatic arterial complications were associated with a very high incidence of biliary complications in our series. However, other potential risk factors that have previously been associated with an increased likelihood of biliary complications, such as prolonged cold ischemia time, ABO blood type incompatibility, cytomegalovirus infection, length of surgery, blood transfusion, graft type, the method of biliary reconstruction, drainage catheter, number of bile duct, number of acute rejections, age and body weight were not found to be risk factors in our series [23–30]. In addition, we tested the effect of preoperative liver functioning tests (serum bilirubin level, serum albumin level and prothrombin time) on the development of biliary complications. Contrary to the results of Qian and colleagues [31], we demonstrated that the preoperative liver functions tests were not a risk factor for biliary complications.

In conclusion, we have reviewed several risk factors for the development of biliary complications after LDLT. We found that only hepatic arterial complications were associated with a higher rate of biliary complications. The presence of multiple bile ducts did not increase the relative occurrence of biliary complications. In addition, biliary reconstruction without a stent is safe for LDLT, even in a pediatric population. Although our follow-up period is relatively short, and long-term follow-up should be performed at a later date, the results of this study support biliary reconstruction without stenting as a preferred method of biliary reconstruction following LDLT, including grafts with multiple bile ducts.

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The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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