

ORIGINAL ARTICLE

Biliary complications in right lateral sector graft live donor liver transplantation

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Summary

Biliary complications remain the most challenging issue in adult living donor liver transplantation (LDLT) and to the best of our knowledge, no study has focused on the biliary complications in LDLT with right lateral sector graft (RLSG), a graft consisting of segments VI and VII according to Couinaud's nomenclature for liver segmentation. Between January 1996 and October 2006, 310 LDLTs were performed for adult recipients at our institution. Among them, 20 patients received RLSG. The incidence of biliary complications during follow-up in these patients with RLSG was retrospectively analyzed. Follow-up period after transplantation ranged from 1 to 87 months (median 58 months). The 3-year and 5-year graft survival rates following the use of RLSGs in LDLT were 90% and 90%, respectively. Biliary complications were encountered in altogether nine patients. Two patients (10%) were complicated with bile leakage requiring surgical intervention. Seven patients (35%) were complicated with bile duct stenosis, which occurred with a median interval of 26 months (range: 6–51 months) after LDLT. Four were treated surgically and the other three were treated by endoscopic approach. Outcomes of the interventions were satisfactory in all cases. The incidence and severity of biliary complications after LDLT using RLSG was within an acceptable range with excellent graft survival. Accordingly, it is concluded that RLSG is a technically feasible option that may effectively expand the donor pool. Further application of RLSG is warranted.

Introduction

The first successful adult-to-adult living donor liver transplantation (LDLT) was performed in 1994 using a left liver graft [1]. Since then, the procedure has evolved and become widespread. Currently, LDLT in adults is accepted as one of the most effective resolutions in regions where shortage of cadaveric donor organs is critical, such as in many countries in the Far East.

In LDLT, the size of the available graft is a major concern because the resectable liver volume from a live donor is limited. A left liver graft obtained from a living donor might not always satisfy the recipient's metabolic demand, resulting in small-for-size syndrome,

which increases the risk of fatal complications [2]. The use of a right liver graft was devised to overcome this problem [3–6]. Increasing the extent of the donor hepatectomy leaving behind less remnant liver volume, however, carries a higher risk. Fan *et al.* [3] concluded that safe donation was possible only when the estimated residual liver volume was over 30%. Clearly, the procurement of a right liver graft is not possible in all potential donors.

Earlier, we reported the use of right lateral sector graft (RLSG); a graft consisting of segments VI and VII according to Couinaud's nomenclature for liver segmentation, as a novel option [7]. The indications for harvesting this type of graft includes a right liver estimated to be over 70% of the total liver volume and an estimated volume of

the RLSG is greater than that of the left liver. In addition, the graft should be more than 40% (35% for low-risk patients) of the recipient's standard liver volume. Although RLSG has become accepted as a feasible option [7–9], its procurement is considered to be associated with some technical difficulties originating from the wider plane of parenchymal transection and complicated intra-hepatic anatomic variations of the bile duct and vasculature.

Many previous studies have reported the rate and severity of biliary complications after LDLT using right liver graft [6,10–15]. Little information, however, is available regarding the biliary complications after LDLT using an RLSG. To clarify the nature and incidence of biliary complications encountered in RLSG, we retrospectively analyzed our series of patients.

Patients and methods

From January 1996 to October 2006, 310 adult patients underwent LDLT at Tokyo University Hospital. LDLT using RLSG was performed in 20 patients. Among these recipients, eight were men and 12 were women, ranging in age from 23 to 58 years (median 44 years). Primary biliary cirrhosis was the most common indication for LDLT ($n = 6$; 30%), followed by hepatitis B virus-related liver disease ($n = 2$; 10%), hepatitis C-related liver disease ($n = 2$; 10%), liver failure in post-Kasai biliary atresia ($n = 2$; 10%), hepatolithiasis ($n = 2$; 10%), autoimmune hepatitis ($n = 2$; 10%), primary sclerosing cholangitis ($n = 1$), fulminant hepatitis of unidentified cause ($n = 1$), hypercitrullinemia ($n = 1$), and cryptogenic cirrhosis ($n = 1$). Model for end-stage liver disease (MELD) score ranged from 9 to 27 (median 16). Follow-up period after transplantation ranged from 1 to 87 months (median 58 months). Post-transplant immunosuppression consisted of steroid induction followed by the combined use of tacrolimus and steroids, as in the other graft types at our institution [16].

The donors were 13 men and seven women, ranging in age from 22 to 65 years (median 38 years). Their relationship to the patients was child ($n = 4$; 20%), sibling ($n = 8$; 40%), spouse ($n = 3$; 15%), parent ($n = 2$; 10%), nephew ($n = 1$; 5%), and others ($n = 2$; 10%).

Determination of graft type and donor surgery

The medical evaluation of live liver donors at our institution was previously described in detail [17]. Donation must be absolutely voluntary and must be either ABO blood-type compatible or identical. No blood type – incompatible donor recipient combination was accepted in our series.

During the medical work-up, volumetric study of an available graft size was meticulously performed to secure donor safety. In brief, a computed tomography (CT) scan for preliminary volumetry was obtained and estimation of the available graft size was evaluated [18]. For the recipient, the standard liver volume was calculated as previously described using Urata's equation [19]. Appropriate graft type was determined according to the algorithm previously described [20]. For precise understanding of the anatomy and estimation of graft volume, triple-phase abdominal CT scan with contrast medium was acquired to obtain a three-dimensional reconstruction image [21]. The digital data were further processed to obtain the segmental volume drained by each tributary of the middle hepatic veins and portal veins, estimated with virtual hepatectomy simulation software (Hitachi Image Processing System, Version 0.7a, Patent no. 283191) [22], using a region-growing technique [23]. When planning to obtain an RLSG, drip infusion cholangiography CT (DIC CT) was added to the routine preoperative donor evaluation to determine the biliary anatomy in detail.

Our surgical technique for RLSG retrieval was previously described in detail [7,20,24–26]. The donor was placed in the supine position. Occlusion of the right paramedian and left branches of the portal veins and hepatic arteries was performed to reveal the demarcation line on the liver surface. The dissection plane for an RLSG was planned 5 mm to the left of the right portal fissure. An ultrasonic dissector with electrocautery (SONOP 5000, Aloka Inc., Tokyo, Japan) was used for the parenchymal dissection in most of the donors. Pringle's maneuver (10-min preconditioning, 5-min reperfusion, and several cycles of 15 min of clamping and 5-min release) were applied during the parenchymal transection [27]. The Belghiti liver-hanging maneuver [28], modified as the sling suspension technique [29], was applied to facilitate liver parenchymal division.

The right lateral bile duct was identified using intra-operative cholangiography ahead of liver transection. Following cholecystectomy, a Phycon Cholangiocatheter (Fuji Systems Corp., Tokyo, Japan) was inserted through the cystic duct stump to the common bile duct. Contrast medium was injected after occluding the proximal end of the common bile duct by inflating the occlusion balloon at the tip of the catheter. Intra-operative cholangiography was then obtained under manipulation of C-arm mobile fluoroscopy to verify the transection point of the hepatic duct from several different angles. The hepatic duct was sharply severed near the confluence and the remnant stump was carefully sutured and closed with 4-0 Vicryl (Ethicon, Inc., Somerville, NJ, USA). Following graft removal and stump closure, completion cholangiography

was performed to confirm that there was no bile juice leakage or biliary stricture.

Donor morbidity was assessed by modified Clavien's classification for surgical complications [30]. Overall morbidity and mortality of our living liver donor series are described elsewhere [31]. No donor deaths occurred.

Recipient surgery and biliary reconstruction

In total hepatectomy of the patients, the hilar plate was dissected sharply at or distal to the second-order branch of the bile ducts. In dissection, careful attention was paid to preserve as much as possible of the surrounding tissues with an adequate blood supply to the bile duct. To maintain the blood supply from the right hepatic artery to the bile duct, dissection between the right hepatic artery and the bile duct was avoided.

Hepaticojejunostomy was preferred until 1999. Anastomosis was performed using an interrupted 4–0 Vicryl suture and internal stent tube. Since 2000, we have altered our strategy and applied duct-to-duct anastomosis. Technical details regarding duct-to-duct anastomosis were previously described [25]. In summary, an end-to-end anastomosis between the graft and patient bile duct was performed using an interrupted 4–0 Vicryl suture. On the patient's hilar plate, an external stent tube was inserted into the bile duct from the orifice situated opposite to the duct for which anastomosis was planned. When there were multiple bile duct orifices in the graft, stent tubes were used separately for each of them. When two bile ducts in the graft were located close to each other, they were joined into one. If they were widely separated, they were anastomosed independently. The knots were always located outside of the bile duct.

Definition of biliary complications

Biliary complications were classified into two categories: bile juice leakage and bile duct stenosis. Bile juice leakage was diagnosed when the bilirubin level of the discharge collected from drainage tubes draining the proximity of the dissection plane of the graft was significantly higher than expected, requiring additional surgical intervention. Bile duct stenosis was suspected on the basis of abnormal liver function tests, especially including a significant (two- to threefold) increase in γ -glutamyl transpeptidase and alkaline phosphatase levels. When suspected, further radiologic studies with CT and ultrasound evaluation with Doppler studies to rule out vascular complications were performed, and finally confirmed by endoscopic retrograde cholangiography or percutaneous transhepatic cholangiography.

Statistics

Differences in categorical variables were assessed using the Fisher's exact or chi-squared test, when applicable. Paired continuous data were evaluated by Mann–Whitney *U*-test. Graft survival curves were generated by the Kaplan–Meier method. Differences were considered significant at a *P*-value of <0.05.

Results

Overall outcomes after LDLT with RLSG

Surgical factors of RLSG grafting are summarized in Table 1. Three patients died after liver transplantation. One patient died of simultaneous portal vein and arterial obstruction on the 6th postoperative day. Another patient died of uncontrollable esophageal variceal rupture in the midst of severe acute cellular rejection on the 49th postoperative day. These two cases were considered mortality on account of graft failure. One other patient died of *de novo* occurrence and systemic dissemination of metastatic squamous cell carcinoma originating from the buccal region 79 months after transplantation. Other recipients were alive with normal liver function at the median follow-up period of 55 months. Re-transplantation was not performed in any case. The 1-, 3-, and 5-year graft survival rates were 90%, 90%, and 90%, respectively (Fig. 1).

Table 1. Surgical factors of right lateral sector graft engraftment.

GW/SLV (%)	44 (35–55)
Cold ischemic time (min)	113 (40–182)
Warm ischemic time (min)	75 (35–237)
Operation time (min)	970 (740–1345)
EBL/Body weight (ml/kg)	81 (15–389)

GW, graft weight; SLV, standard liver volume; EBL, estimated blood loss.

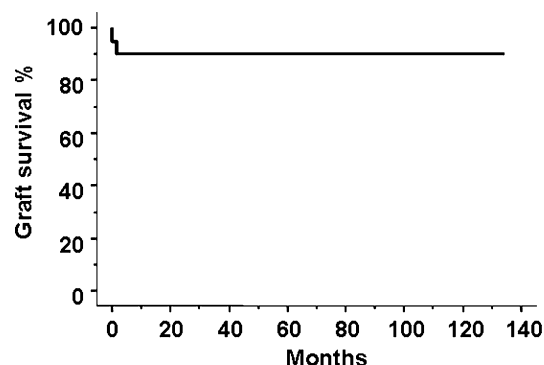


Figure 1 Graft survival in living donor liver transplantation with right lateral sector graft.

Retrospective study of the donor's chart revealed seven donors (35%) with complications. There were 3 (15%) patients with grade I, one (5%) with grade II, and 3 (15%) with grade IIIa complications according to Clavien's system [30,31]. The donor classified as having grade II complication was complicated by a mild episode of pneumonia treated by medication and physical therapy. The two donors classified as having grade IIIa complication suffered from bile leakage which required prolonged placement of drainage tubes. One other donor classified as having grade IIIa complication suffered from pleural effusion treated by thoracentesis under local anesthesia under ultrasound guidance. All donors have returned to normal social life after discharge without any disability. Overall rates and degrees of complications found in the entire series of adult-to-adult LDLT donors during the overlapping period at our institution according to Clavien's system were, grade I in 15%, II in 4%, IIIa in 5%, IIIb in 4%, IV in 0% [31].

Methods of bile duct reconstruction in RLSG

The majority of grafts had a single duct (80%, $n = 16$). Four grafts (20%) presented with two bile duct orifices. Ductoplasty was performed in two cases to create a single anastomotic orifice, and in the other two cases, reconstruction was performed separately. Duct-to-duct biliary reconstruction was performed in 12 grafts (60%) and hepaticojejunostomy was performed in eight (40%). Single duct-to-duct anastomosis was performed in 11 of the 12 cases (92%) and double duct-to-duct anastomosis was performed in one case (8%). An external stent was used in 10 cases and no stent was placed in the remaining two cases. A standard hepaticojejunostomy was performed in seven of the eight remaining cases (87%), and double choledochojejunostomy was performed in one case (13%). An internal stent tube was placed in seven cases and no stent in the remaining case.

Table 2. Biliary reconstruction and complications in right lateral sector graft.

	Cases	No. of complications	
		Leakage (%)	Stenosis (%)
Bile duct orifice and anastomosis			
1 duct, 1 anastomosis	16	2 (13)	5 (31)
2 ducts, 1 anastomosis	2	None	1 (50)
2 ducts, 2 anastomoses	2	None	1 (50)
Type of reconstruction			
Choledochojejunostomy	8	2 (25)	2 (25)
Duct-to-duct	12	0 (0)	5 (42)
Use of stent tube			
No stent	3	None	1 (33)
Internal stent	7	2 (29)	1 (14)
External stent	10	0 (0)	5 (50)

Biliary complications in RLSG and treatment

Of 20 patients that underwent LDLT with RLSGs, nine patients (45%) experienced biliary complications (biliary leakage in 2, and anastomotic stenosis in 7). Specifics of the biliary complications encountered are depicted according to the technique and methods of biliary reconstruction in Table 2.

The onset of biliary leakage was observed on 7 and 53 days after LDLT, respectively. Both required surgical intervention. In one case, revision of the choledochojejunostomy was required. In the other, laparotomy followed by additional drainage tube placement was performed. Biliary stenosis occurred with a median interval of 26 months (range: 6–51 months) after LDLT. Among these cases, three required major surgical intervention; conversion surgery from duct-to-duct to hepaticojejunostomy was performed in one, and re-anastomosis of hepaticojejunostomy was performed in two. In one other case, transhepatic biliary drainage with external tube placement was performed under small laparotomy. This particular patient suffered from *de novo*

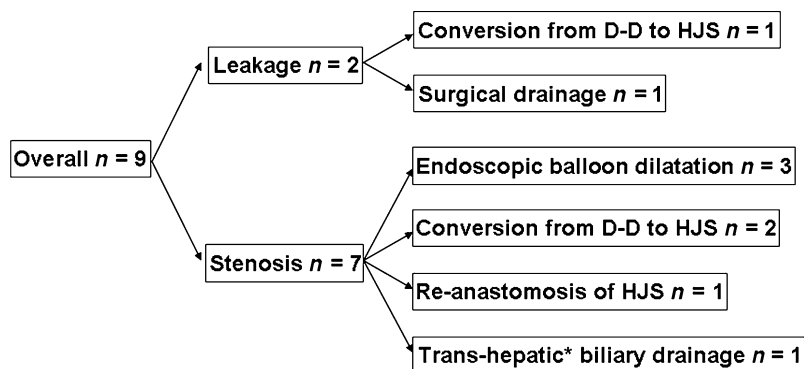


Figure 2 Biliary complications and treatments in living donor liver transplantation using a right lateral sector graft. D-D, duct-to-duct bile duct anastomosis; HJS, hepaticojejunostomy. *Performed under laparotomy.

		Occurrence of biliary complications		<i>P</i>
		Yes (<i>n</i> = 9)	No (<i>n</i> = 11)	
Age of recipient (years)		46 (25–57)	49 (23–58)	0.76
MELD score		16 (10–27)	16 (9–29)	0.85
Age of donor (years)		30 (22–65)	45 (28–62)	0.04
GW/SLV (%)		42 (35–55)	46 (37–53)	0.67
CIT (min)		98 (46–182)	117 (40–146)	0.57
WIT (min)		66 (35–91)	75 (55–237)	0.66
Operation time (min)		965 (750–1150)	975 (740–1345)	0.62
EBL/BW (g/kg)		80 (26–120)	111 (15–389)	0.31
F/u period (month)		69 (16–87)	49 (1–85)	0.16
Anastomotic orifice	Single	8	10	0.99
	Double	1	1	
Stent use	Yes	8	9	0.99
	No	1	2	
Duct-to-duct	Yes	5	7	0.99
	No	4	4	
First 10 cases	Yes	6	4	0.37
	No	3	7	
HAT	Yes	2	1	0.57
	No	7	10	
CMV	Yes	3	3	0.99
	No	6	8	
ACR	Yes	5	2	0.16
	No	4	9	

MELD score, Model for end stage liver disease score; GW, graft weight; SLV, standard liver volume; CIT, cold ischemic time; WIT, warm ischemic time; EBL, estimated blood loss; BW, body weight; f/u, follow-up; mo, months; Duct-to-duct, duct-to-duct biliary reconstruction; HAT, hepatic artery thrombosis; CMV, cytomegalovirus infection; ACR, acute cellular rejection.

Continuous data are depicted as median (range), excluding the follow-up period.

occurrence of squamous cell carcinoma of the buccal region, and died despite aggressive surgical removal of the lesion and radiation therapy hindering further therapeutic manipulation of the biliary system. In the other three cases, endoscopic modalities were selected with satisfactory results (Fig. 2).

Risk factors for biliary complications in RLSG

To study the risk factors for the occurrence of biliary complications in RLSG, various clinical factors were evaluated by univariate analysis (Table 3). Recipient's age, severity of the pre-operative condition by MELD score, condition or size of the graft, and duration of surgery did not seem to be related. Surgical factors such as bile duct reconstruction method, as well as post-transplantation complications such as rejection, cytomegalovirus infection, or arterial complication also did not seem to affect the occurrence of biliary complications. Among the analyzed factors, only the age of the donor presented with statistical significance. It must be noted, however, that on account of the small sample size, these outcomes are prone to type II error.

Discussion

Various refinements in surgical technique, organ preservation, and immunosuppressive management have reduced the overall complications following liver transplantation. Biliary tract complications, however, continue to be a significant cause of morbidity after LDLT [10,11]. Recent studies reported the occurrence of biliary tract complications to be 21–41% following LDLT with right liver grafts [Table 4; references 10,12,15,32–36]. Liu and colleagues, comparing the outcomes of right liver graft LDLT and deceased donor liver transplantation, described a higher incidence of biliary complications in LDLT [14]. Other reports also indicate that rates of biliary complication after LDLT are rather high, with incidence rates of leakage between 4% and 29% and stricture of 5–29% [10,12,15,32–36]. The need for further refinement of the biliary reconstruction techniques has been recognized in centers experienced in both LDLT and DDLT [11,14]. Although we have frequently taken recourse to the use of external stent tube in RLSG, its benefits were not clearly demonstrated in the current series (Table 2). Its advantages and disadvantages require further evaluation.

Table 3. Biliary complications and clinical factors.

Table 4. Literature review of biliary complications in adult-to-adult live donor liver transplantation using the right liver and right lateral sector grafts.

Refs	Center	Year	No. of living donor liver transplantation	Rate of biliary complications (%)
10	Hong Kong, China	2002	74	26
32	New York, USA	2004	96	41
36	Seoul, Korea	2005	65*	32
15	Kyoto, Japan	2006	321	24
33	Seoul, Korea	2006	225*	21
34	Bologna, Italy	2006	27	26
35	Milan, Italy	2006	23	35
12	Toronto, Canada	2007	130	26
Present study	Tokyo, Japan	2007	20	45

*Right liver graft.

Precise understanding of the biliary tree is mandatory in each single case. Some centers including ourselves favor the use of intra-operative cholangiography [34,36], on the other hand, recent studies suggest the possible beneficial effect of adding preoperative cholangiography by CT or magnetic resonance imaging [35–38].

The preferred technique, since its introduction in adult LDLT, has recently shifted from hepaticojejunostomy to duct-to-duct anastomosis on account of the long-term physiologic advantage of duct-to-duct anastomosis [13,25]. Kasahara and colleagues analyzed their large series of cases of right liver LDLT, and reported a significantly lower incidence of leakage (5%), and a higher incidence of stricture (27%), in duct-to-duct anastomosis [15].

In our institution, hepaticojejunostomy was preferred for RLSG until 1999 on account of the technical challenges originating from the theoretically thinner and smaller bile duct orifice, and further difficulties faced with the rather limited length of the donor's bile duct compared with that found in the conventional right liver graft. Over time, however, it has come to be recognized that size and length are not critical restrictive factors. Since 2000, we have altered our strategy and applied duct-to-duct anastomosis primarily for the sake of its physiologic advantage.

The obtained results in the current study should be considered within acceptable range when compared with the findings reported in the previous series of adult LDLT consisted mostly of conventional right liver liver grafts. With a wider liver parenchymal plane to transect, which increases the risk of insufficiently dealt minute hepatic ducts, and with a smaller duct orifice to reconstruct, which increases the risk of anastomotic complications, it might be speculated that biliary complications

occur more frequently in RLSG than in right liver liver graft. In our institution, the overall rate of biliary complications following LDLT during the same period among the 310 patients was 28%. Left liver without the caudate lobe was used in 19 recipients, left liver grafts with the caudate lobe in another 105 patients, right liver graft without the middle hepatic vein in 120, and right liver graft with the middle hepatic vein in 44 recipients. Overall rates of biliary complications in each groups were, 16%, 32%, 25% and 32%. Thus, our series suggests that RLSG is an acceptable option in LDLT, despite its theoretical anatomic challenges.

Following its occurrence, the proper treatment strategy for biliary complications is an important matter. As described above, surgical intervention was required in two cases with bile leakage. Both conversions from duct-to-duct to hepaticojejunostomy and drainage procedures were successfully performed. Although the necessity for prophylactic drains in hepatic resection has been questioned [39], we continue to find it useful as a source of information at an early stage of biliary leakage in our LDLT series. This was no exception in the two cases with biliary leakage in RLSGs, providing useful information for the timing of surgical intervention and preventing the spread of biliary peritonitis.

We experienced seven cases of biliary stenosis. Four were treated surgically and three were treated by nonsurgical approach, all with satisfactory outcomes resulting in excellent recovery of graft function. Until recently, surgical intervention by conversion from duct-to-duct to hepaticojejunostomy was the strategy of choice [11,13,40,41]. More recent studies suggest the effectiveness of an initial endoscopic approach in adult LDLT recipients [42–44]. Although there was initially a concern regarding successful cannulation of the posterior hepatic duct of RLSG after enlargement and rotation on account of graft regeneration, an endoscopic maneuver seems feasible without much difficulty. At this point, the numbers are too small to draw any definite conclusions as to which approach, surgical or endoscopic, should be taken as the first-line in case of biliary stenosis in RLSG. Further experience is necessary for discussion.

Finally, it must be emphasized that RLSG was an imperative option in 13 of the present cases. In all 20 of the cases presented here, the volume of the donor's left liver was <35% of the recipient's standard liver volume, obligating the choice of conventional right liver graft. In 13 cases, however, the right liver exceeded 70% of the total liver volume of the donor. The option to obtain an RLSG has successfully circumvented the difficult question of making the choice between using an extremely small-for-size left liver graft, or placing the recipient on a near hopeless waiting list for a deceased donor liver transplan-

tation in a region where deceased donor organs remain extremely scarce. RLSG, therefore, definitely offers an option to expand the donor pool.

Conclusion

Right lateral sector graft provides a satisfactory outcome with regard to the incidence and severity of biliary complications. RLSG is a technically feasible option that effectively expands the donor pool. Its further application is warranted.

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Authorship

YS and MM designed the study; YK, ST, YS, NA, YM, JT, JK, and MM performed the study; YK, ST and YS collected and analyzed the data, and wrote the paper.

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