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ORIGINAL ARTICLE

Vascular Reconstruction and Complications in Living Donor Liver Transplantation in Infants Weighing Less Than 6 Kilograms: The Kyoto Experience

Yasumasa Shirouzu, Mureo Kasahara, Daisuke Morioka, Seisuke Sakamoto, Kaoru Taira, Kenji Uryuhara, Kohei Ogawa, Yasutsugu Takada, Hiroto Egawa, and Koichi Tanaka
Departments of Transplant Surgery, Kyoto University Hospital, Kyoto, Japan

Smaller-size infants undergoing living-donor liver transplantation (LDLT) are at increased risks of vascular complications because of their smaller vascular structures in addition to vascular pedicles of insufficient length for reconstruction. Out of 585 child patients transplanted between June 1990 and March 2005, 64 (10%) weighing less than 6 kg underwent 65 LDLTs. Median age and weight were 6.9 months (range: 1-16 months) and 5 kg (range: 2.8-5.9 kg), respectively. Forty-five lateral segment, 12 monosegment, and 8 reduced monosegment grafts were adopted, and median graft-to-recipient weight ratio was 4.4% (range: 2.3-9.7). Outflow obstruction occurred in only 1 patient (1.5%). Portal vein complication occurred in 9 (14%) including 5 with portal vein thrombosis. Hepatic artery thrombosis (HAT) occurred in 5 (7.7%). Patient and graft survivals were 73% and 72% at 1 yr, and 69% and 68% at 5 yr after LDLT, respectively. Thirteen of 22 grafts (58%) lost during the follow-up period occurred within the first 3 months posttransplantation. Overall graft survival in patients with and without portal vein complication was 67% and 65%, respectively ($P = 0.54$). Overall graft survival in patients with and without HAT was 40% and 67%, respectively. HAT significantly affected graft survival ($P = 0.04$). In conclusion, our surgical technique for smaller-size recipients resulted in an acceptable rate of vascular complications. Overcoming early posttransplantation complications will further improve outcomes in infantile LDLT. ***Liver Transpl 12:1224-1232, 2006.*** © **2006 AASLD.**

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Liver transplantation (LT) is an established curative therapy for children with end-stage chronic liver disease or acute liver failure. Outcomes following LT in children have significantly improved over the past 2 decades, because of advances in surgical procedures, preservation technology, immunosuppressive management, and perioperative care.[1] Shortage of full-size grafts from pediatric donors once produced high waiting-list mortality in the pediatric population, especially in children younger than 5 yr old, and prompted the identification of alternative graft sources for pediatric patients.[2,3] To increase the supply of appropriate-sized organs for pediatric recipients, the techniques of reduced, split, and living-donor liver transplantation (LDLT) was developed. This technological innovation expanded the potential donor pool, and led to a significant decrease in waiting-list mortality for children.[4-6]

Although LT in small infants provides similar results as those in older groups.[7,8] it is more challenging technically because of the smaller vascular structures. Additionally, pediatric LT from living donors faces problems of size mismatch of vessels between adult donors and pediatric recipients, accompanied by technical difficulties arising from insufficient vascular pedicles for reconstruction. More importantly, LDLT in infants is often limited by the large-for-size graft, even when using a left-lateral segment graft. This is attributed to the small size of the infantile abdominal cavity and insufficient blood supply to the graft.[9] Consequently, small infants undergoing LDLT are indeed at increased risks

Abbreviations: LT, liver transplantation; LDLT, living-donor liver transplantation; HAT, hepatic artery thrombosis; IVC, inferior vena cava.

Address reprint requests to Yasumasa Shirouzu, M.D., Departments of Transplant Surgery, Kyoto University Hospital, 54 Kawara-cho, Shogoin, Sakyo-ku, Kyoto 606-8507, Japan. Telephone: 81-75-751-4323; FAX: 81-75-751-4877; E-mail: yasumasa@indigo.plala.or.jp

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TABLE 1. Demographic Data of Recipients and Grafts

Gender	
Male	24 (37%)
Female	41 (63%)
Body weight (kg)	5 (2.8-5.9)
Age (months)	6.9 (1-16)
Diagnosis	
Biliary atresia	44 (68%)
FHF	7 (11%)
Tyrosinemia	4 (6%)
Cryptogenic cirrhosis	3 (5%)
Alagille syndrome	2 (3%)
Other*	5 (8%)
Graft weight (gm)	217.6 (105-365)
GRWR (%)	4.4 (2.3-9.7)
Graft type (segment)	
II and III	45 (69%)
III	12 (19%)
Reduced III	8 (12%)
Blood combination	
Identical	42 (65%)
Compatible	13 (20%)
Incompatible	10 (15%)

Abbreviations: FHF, fulminant hepatic failure; GRWR, graft-to-recipient weight ratio.

*Hepatoblastoma (n = 1), infantile hepatic hemangioendothelioma (n = 1), congenital biliary dilation (n = 1), congenital absence of the portal vein (n = 1) and chronic rejection (n = 1).

of surgical complications such as vascular stricture or thrombosis.

Acceptable results of LT in small infants have already been reported.[7,8,10,11] However, previous studies reported that the incidence of vascular complications was higher in smaller-size recipients.[12,13] LDLT requires high surgical skills in the reconstruction of the portal and hepatic veins.[14,15] Moreover, reconstruction of the hepatic artery of a smaller caliber is considered to present risks of hepatic artery thrombosis (HAT).[16]

We present a retrospective analysis of our experience with orthotopic LT from living donors in recipients weighing less than 6 kg. Special attention was given to analysis of the surgical pattern for vascular reconstruction, and to vascular complications in a series of 64 small infantile recipients.

PATIENTS AND METHODS

Patient Characteristics

Between June 1990 and March 2005, 585 children (under 15 yr old) underwent 615 LDLTs at Kyoto University Hospital. Sixty-four of these patients (10%) were less than 6 kg in weight at transplantation, and underwent 65 LDLTs; this number included 1 patient who weighed less than 6 kg at the first transplantation and at a subsequent retransplantation for chronic rejection. Demographic data for the recipients are listed in Table 1. These 64 patients were followed until June 2005, with a median follow-up period of 6.3 yr (range: 0.5-13.5 yr). Potential donors were evaluated by liver function tests, blood type, human leukocyte antigen typing, anatomical variation, and graft size. All patients received grafts from either their mother or father. The left-lateral segment was used as the graft in principle although monosegmental LDLT was introduced to our institution in September 2000.[17] Reduction of the left-lateral segment graft was considered when a graft-to-recipient weight ratio estimated by preoperative computed tomography volumetry was as large as over 5%. The actual employed grafts consisted of 45 lateral segments, 12 of monosegments, and 8 reduced monosegments.

Operation

The operative procedure has already been described.[17,18]

Donor Hepatectomy

The plane of the liver resection was determined on the basis of preoperative computed tomography volumetry and anatomic analysis of the vascular structure of the hepatic vein, portal vein, and hepatic artery using preoperative Doppler ultrasonography and computed tomography. An ultrasonic dissector and bipolar electrical cautery were used for parenchymal transection during donor left-lateral segmentectomy. If the occasion arose, the left-lateral segments of the donors were reduced to monosegment grafts by cutting between segments II and III, or reduced monosegment grafts were obtained by further in situ resection of monosegments. The choice of procedures was made according to the graft-to-recipient weight ratio estimation. The graft liver was removed after vascular clamping, followed by ex vivo perfusion through the left portal vein. The perfusate was either chilled in University of Wisconsin solution (ViaSpan; Bristol-Myers Squibb, New York, NY) or in histidine-tryptophan-ketoglutarate solution (CUSTODIOL; Odyssey Pharmaceuticals, East Hanover, NJ).

Anastomosis of the Hepatic Vein

When possible, the hepatic veins on the graft were prepared on the back table. The liver graft was implanted in an orthotopic manner following total hepatectomy, preserving the inferior vena cava (IVC) in the recipient. Depending on the size and number of hepatic veins on the graft and on the graft shape, either the cuff of the native single hepatic vein, the single orifice reformed from 2 or 3 hepatic veins, or the new orifice created on the IVC was prepared in the recipient for a single reconstruction. When 2 independent reconstructions were necessary, 2 separate orifices created from 3 hepatic veins were prepared in the recipient. Types of orifices prepared in the recipients for hepatic vein anastomosis are shown in Figure 1. Type 1 represented a new single orifice created by incision of the IVC wall between the right hepatic vein and the common truncal

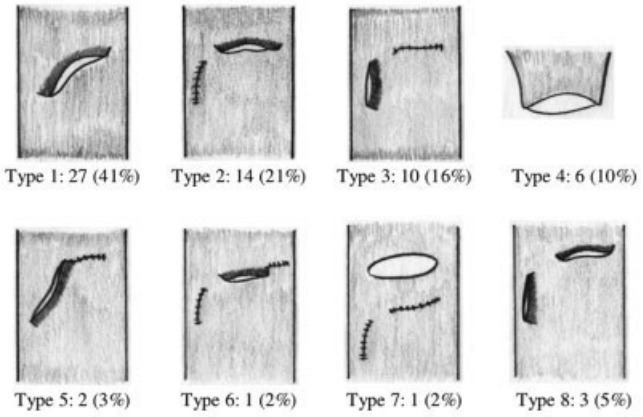

Figure 1. Types of orifices prepared in recipients for hepatic vein anastomosis. Type 1: a new single orifice created by the incision of the IVC wall between the right hepatic vein and the common truncal vein of the middle and left hepatic veins (n = 27); Type 2: a common truncal stump created by incising the septum between the middle and left hepatic veins (n = 14); Type 3: an orifice created using the native cuff of the right hepatic vein (n = 10); Type 4: the dissected stump of the suprahepatic IVC (n = 7); Type 5: an orifice created by dividing the wall of the IVC between the right and middle hepatic veins (n = 2); Type 6: an orifice created using the native cuff of the middle hepatic vein (n = 1); Type 7: a new orifice created on the front surface of the suprahepatic IVC (n = 1); and Type 8: 2 separate orifices using respective cuffs of the right hepatic vein and the common truncal vein of the middle and left hepatic veins (n = 3).

vein of the middle and left hepatic veins. Type 2 corresponded to a common truncal stump created by incising the septum between the middle and left hepatic veins. Type 3 involved the native cuff of the right hepatic vein. Type 4 referred to the dissected stump of the suprahepatic IVC. Type 5 was created from the right and middle hepatic veins, dividing the wall of IVC between these 2 veins. Type 6 represented the native cuff of the middle hepatic vein. Type 7 was a new orifice created on the front surface of the suprahepatic IVC. Type 8 corresponded to 2 separate orifices using respective cuffs of the right hepatic vein and the common truncal vein of the middle and left hepatic veins for 2 independent anastomoses. Hepatic vein anastomosis was performed in an end-to-end or end-to-side fashion by means of a running suture with 5-0 or 6-0 polypropylene monofilament (Prolene; Ethicon, Somerville, NJ).

Anastomosis of the Portal Vein

Following hepatic venous reconstruction, the portal vein was reconstructed using 5 different modalities (Fig. 2). Type A involved standard end-to-end anastomosis between the graft portal vein and the trunk of the recipient's portal vein. Type B corresponded to anastomosis of the graft portal vein to the bifurcation of the right and left branches of the recipient's portal vein. Type C involved direct suture of the graft portal vein to the confluence of the superior mesenteric vein and the splenic vein of the recipient. In Type D, the vein graft was interposed between the graft portal vein and the

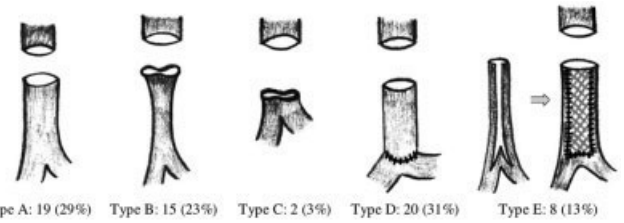

Figure 2. Reconstructive types for portal vein anastomosis. Type A: standard end-to-end anastomosis between the graft portal vein and the trunk of the recipient's portal vein (n = 19); Type B: anastomosis of the graft portal vein to the bifurcation of the right and left branches of the recipient's portal vein (n = 15); Type C: direct suture of the graft portal vein to the confluence of the superior mesenteric vein and the splenic vein of the recipient (n = 2); Type D: interposing vein graft between the graft portal vein and the confluence of the recipient's superior mesenteric vein and splenic vein (n = 20); and Type E: suturing the graft portal vein to the orifice of the recipient's portal vein widened by patching the space on the anterior wall incised in a Y-shaped fashion with the vein graft (n = 8).

confluence of the recipient's superior mesenteric vein and splenic vein. The vein used as graft was usually either the left ovarian vein from a maternal donor or the inferior mesenteric vein from a paternal donor. Type E involved suturing the graft portal vein to the orifice of the recipient's portal vein widened by patching the space on the anterior wall incised in a Y-shaped fashion with the vein graft. The vein used as for the patch was either the donor's ovarian or inferior mesenteric vein, or a part of the recipient's own portal vein. Exceptionally, portal venous flow was reconstructed between the graft portal vein and the recipient's superior mesenteric vein in the case of a patient with congenital absence of the portal vein, in which case the superior mesenteric vein was connected directly with the azygous vein. The portal vein was anastomosed using running and interrupting sutures with 6-0 or 7-0 polypropylene monofilament or polyglyconate absorbable monofilament (Maxon; Davis and Geck Inc., Danbury, CT) without using the growth factor technique. The graft was reperfused following completion of portal vein anastomosis.

Anastomosis of the Hepatic Artery

The hepatic artery was anastomosed under a surgical microscope. A single or 2 independent arterial anastomoses were performed in an end-to-end fashion. Two independent arterial anastomoses were performed when there was no backward flow from the smaller artery following reconstruction of the larger artery in the graft with 2 separate arteries. Sites of the recipient's hepatic arteries prepared for reconstruction consisted of the right hepatic, middle hepatic, left hepatic, proper hepatic, common hepatic, gastroduodenal, left gastric, and splenic arteries. End-to-end anastomosis was completed with interrupted sutures using 8-0 or 9-0 polypropylene monofilament.

Immunosuppression

Immunosuppression was performed using tacrolimus and low-dose steroids. The target whole-blood tacrolimus level was 10-12 ng/mL for the first 2 weeks, approximately 10 ng/mL for the next 2 weeks, and 5-10 ng/mL thereafter. Steroid treatment was initiated at the time of graft reperfusion at a dose of 10 mg/kg, and then tapered from 1 mg/kg per day to 0.3 mg/kg per day during the first month.[19]

Postoperative management and evaluation of hepatic blood flow

Heparin or fresh-frozen plasma was used after LDLT to maintain both prothrombin time and activated coagulation time at around 15-20 seconds and 150-200 seconds, respectively. In addition, dipyridamole (4 mg/kg/day) was given orally instead of heparin from postoperative day 8 onward, for 3 months. Blood flow in the graft was strictly followed by Doppler ultrasonography every day for the first week after surgery and as the need arose after that. Patients suspected of having vascular complications by Doppler ultrasonography with or without computed tomography were confirmed by angiography or surgery.

Outcome Parameters

Operational records of the 65 transplantations in the 64 patients of less than 6 kg of weight at transplantation were reviewed, especially with regard to surgical patterns for vascular reconstruction. Incidence of vascular complications was assessed as patient and graft survivals.

Statistics

Data are expressed as means ± standard deviation. The method of Kaplan-Meier was used to calculate actuarial survival. Fisher's exact and unpaired *t*-tests were used for statistical analysis. *P* values less than 0.05 were regarded as significant.

RESULTS

Hepatic Vein Reconstruction

A total of 62 transplantations (95%) were single anastomosis, and the remaining 3 (5%) were 2 independent anastomoses. The recipient's orifice used for single anastomosis consisted of 7 patterns (Fig. 1). Types 1 and 2 were used in 27 (41%) and 14 (21%) transplantations, respectively, and were adopted as our standard methods for hepatic vein reconstruction in infants who had smaller hepatic veins and IVC. Type 3, which was used prior to the introduction of the technique for graft reduction, was used in 10 transplantations (16%) in the earlier era. Use of the recipient's right hepatic vein as the anastomotic site allowed the graft to be placed in the most comfortable position when the shape of the harvested graft was flatter and longer. In 6 transplantations (10%) in patients with no infrahepatic IVC, including 1 patient with another patent IVC, Type 4 was used to anastomose to the graft hepatic vein. Types 5 and 6 were used in 2 (3%) and 1 (2%) transplantations, respectively; both involved anastomotic sites chosen uncommonly in the earlier era to produce a more stable outflow. In a case (2%) of retransplantation for chronic rejection, Type 7 was used for the anastomotic site. Five (8%) of 62 grafts with a single orifice had a single common anastomotic cuff reformed from 2 independent veins using back table procedures, and the 57 others (87%) involved a genuine single stump without major plasty. Type 8 was used in 3 transplantations (5%) that needed 2 independent outflow reconstructions.

Anastomotic diameter is restricted by the number and the caliber of the stump of the hepatic vein on the cut surface of the graft, and the recipient's orifice is then prepared adjusting by cutting or suturing the corner of the cuff. Accordingly, both Types 1 and 2, which were our standard methods, allowed smaller recipients to supply similar anastomotic calibers sufficient to accept the larger hepatic vein of the graft (20.0 ± 3.4 mm, and 19.5 ± 3.9 mm, respectively, $P = 0.70$).

Incidence of Hepatic Vein Complications

Outflow obstruction developed in only 1 patient (1.5%). The graft implanted in this patient had a single orifice created from 2 adjacent veins, which drained segments II and III into the middle hepatic vein. This patient's new anastomotic site on IVC was of Type 1, with an anastomotic caliber of 20 mm. This patient had a pulsatile wave form on Doppler ultrasonography during hospital stay for transplantation, and has repeatedly undergone percutaneous balloon dilation for recurrent stenosis in the 9 months since LDLT.

Portal Vein Reconstruction

Five different types of portal vein reconstructions were used in the present study (Fig. 2). Type A was used in 19 transplantations (29%), Type B in 15 (23%), Type C in 2 (3%), Type D in 20 (31%), and Type E in 8 (13%). The vein graft harvested for interposition was usually either the ovarian vein from a maternal donor (n = 12) or the inferior mesenteric vein from a paternal donor (n = 6). In 1 case, the external iliac vein was used, and in another the new conduit was produced by sewing together the inferior mesenteric vein and the ovarian vein, divided into 2 equal parts and slit lengthwise, which was then anastomosed to the new orifice of the recipient's portal vein widen by the patch technique using the vein graft. The graft used as patch was from the ovarian vein (n = 2) or the inferior mesenteric vein (n = 5) of the donor, or the part of the recipient's own portal vein (n = 1).

Incidence of Portal Vein Complications

Portal vein complications developed in 9 patients (14%). The incidences of portal vein complications in each of the reconstructive types are shown in Table 2. Although Type A had the highest incidence, differences among the 5 different types were not significant ($P = 0.10$). The

TABLE 2. Portal Vein Complications Related to Reconstructive Types

Type	Number (n = 64)	Complication
A	19	6 (32%)
B	15	1 (7%)
C	2	0 (0)
D	20	2 (10%)
E	8	0 (0)

NOTE: A case of congenital absence of the portal vein is excluded from this list. The incidence of portal vein complications did not significantly differ among groups (P = 0.10).

main clinical features of patients with portal vein complications are given in Table 3. Patients with portal vein stenosis were all successfully treated by percutaneous transhepatic balloon dilation, but those with portal vein thrombosis showed poor responses to surgical and/or interventional treatments. Although cases 3, 4, and 9 all currently maintain their intrahepatic patent portal vein with the help of cavernous transformation and stable liver function, they all suffer from refractory ascites and/or gastrointestinal bleeding caused by portal hypertension.

Hepatic Artery Reconstruction

Single arterial anastomosis without interposition graft was performed in an end-to-end fashion in 61 of 65 transplantations. The sites of the recipient's hepatic arteries prepared for this reconstruction consisted of the right hepatic (n = 21), left hepatic (n = 16), proper hepatic (n = 15), common hepatic (n = 4), gastroduodenal (n = 2), left gastric (n = 1), middle hepatic (n = 1), and splenic (n = 1) arteries. Arterial reconstruction with the interposition graft was performed in just 1 transplantation because of poor quality of the native hepatic artery. In this patient, hepatic arterial flow was reconstructed by interposing her own superior rectal artery between the graft hepatic artery and the recipient's splenic artery. Three cases required 2 independent arterial anastomoses to supply sufficient arterial blood flow to the graft. Their 2 independent anastomotic sites included left and middle hepatic arteries, left and right hepatic arteries, and right hepatic artery and the artery to segment III, respectively. Average diameters of the stump of the graft and recipient's arteries were 2.5 ± 0.5 and 2.5 ± 0.6 mm, respectively, and the average of these caliber differences was 0.3 ± 0.5 mm.

Incidence of Hepatic Artery Complications

HAT developed 2 to 6 days (mean 4.8 days) after LDLT in 5 patients (7.7%). Their clinical features are shown in Table 4. Both the diameter of the hepatic artery stump and the caliber difference were not significantly different between patients with and without HAT.

Impact of Vascular Complications on Survival

Overall graft survival rate was 65% (Fig. 3). Furthermore, patient and graft survivals were 73% and 72% at 1 yr, and 69% and 68% at 5 years, respectively, after LDLT. A total of 22 grafts were lost during the follow-up period in the present series. The causes of the graft loss are shown in Table 5. Eighteen of the 22 grafts (82%) were lost within the first year posttransplantation, and 13 (58%) were lost within the first 3 months posttransplantation when surgical factors might have strongly affected the demise of the implanted graft. None of these patients was able to undergo retransplantations because of the meagerness of the donor pool in Japan; just 1 patient was an exception. This infant underwent the second LDLT for chronic rejection 5 months after the first LDLT for biliary atresia, but died of refractory acute cellular rejection 2 months after the retransplantation. Graft survival related to vascular complications is shown in Figure 4. Graft survival in patients with and without portal vein complication was 67% and 65%, respectively. Portal vein complications had no impact on graft survival (P = 0.54). Graft survival in patients without HAT was 67%, while HAT lowered graft survival to 40% (P = 0.04).

DISCUSSION

This retrospective study analyzed the technique of vascular reconstruction, incidence of vascular complications, and graft survival in 64 infants weighing less than 6 kg. There is no doubt that surgical innovations have improved utilization of LT and overall survival in children with end-stage liver disease. However, despite these advances, vascular complications still remain a serious cause of graft loss. These complications are more frequently found in smaller-size recipients.[12,13] LDLT is more challenging, particularly with regard to insufficient vascular pedicles, compared to whole liver implantation, and also is limited in respect to vascular structure size mismatches between adults and infants. In this series, we reviewed our experiences of LDLT in smaller-size infants, focusing on the technique of vascular reconstruction. Since the first LDLT at Kyoto University Hospital, the surgical technique in infantile LDLT, especially in vascular reconstruction, has evolved by trial and error. In hepatic vein reconstruction, we previously employed various anastomotic sites on the recipient's IVC to comfortably place the larger graft; subsequently, our policy has changed from devising an anastomotic site to ensuring a wider orifice in addition to fixing the reduced graft to the abdominal wall. Our early strategy to reconstruct portal venous flow was aimed at creating a sufficient caliber, in order to anastomose and to prevent a kink of the reconstructed portal tract. This strategy remains in place, whether with or without vein graft. Our principle in hepatic artery reconstruction has, from the early days of this procedure, been to ensure the precise handling of the needle under a surgical microscope.[20]

Transplanting a reduced liver from a living donor necessitates a technical device for achieving successful

TABLE 3. Clinical Features of Patients with Portal Vein Complications

Case	Indication	Graft type (segment)	GRWR (%)	Type of portal vein reconstruction	Type of portal vein complications	Onset of porta vein complications (months after LDLT)	Manifestations	Treatment	Result	Outcome
1	Biliary atresia	II and III	3.9	D	Stenosis	51	Splenomegary	PTBD	Successful	Alive at 72 months
2	Biliary atresia	II and III	4.7	A	Thrombosis	0.2	Acute liver failure	Operation	Failed	Died after 10 days of graft failure
3	Biliary atresia	II and III	5.6	B	Thrombosis	27	None	PTBD	Failed	Alive at 62 months
4	Biliary atresia	III	4.7	D	Thrombosis	9	None	PTBD	Failed	Alive at 57 months
5	Infantile hepatic hemangioendothelioma	III	3.9	A	Stenosis	9	None	PTBD	Successful	Died after 53 months of heart failure
6	Biliary atresia	III	4.3	A	Thrombosis	6 and 14	Ascites	PTBD	Successful	Alive at 47 months
7	Biliary atresia	II and III	4.1	A	Stenosis	26	Melena due to esophageal varices	PTBD	Successful	Alive at 37 months
8	Alagille syndrome	II and III	3.5	A	Stenosis	7 and 20	Splenomegary	PTBD	Successful	Alive at 33 months
9	Congenital biliary dilation	Reduced III	2.3	A	Thrombosis	3	Ascites	PTBD and operation	Failed	Alive at 18 months

Abbreviations: GRWR, graft-to-recipient weight ratio; LDLT, living-donor liver transplantation; PTBD, percutaneous transhepatic balloon dilation.

TABLE 4. Clinical Features of Patients with Hepatic Artery Thrombosis

Case	Indication	ABO matching	Graft type (segment)	GRWR (%)	Hepatic artery reconstruction	Onset of HAT (days after LDLT)	Outcome
1	Biliary atresia	Identical	II and III	5.6	Single anastomoses between the graft LHA and the recipient RHA	5	Died after 9 days of graft failure
2	Biliary atresia	Incompatible	II and III	3.9	Single anastomoses between the graft LHA and the recipient LHA	5	Alive at 106 months
3	Biliary atresia	Identical	II and III	4.1	Single anastomoses between the graft LHA and the recipient MHA	6	Alive at 103 months
4	Biliary atresia	Identical	II and III	3.6	Interposition graft between the graft LHA and the recipient splenic artery	2	Died after 18 days of graft failure
5	Biliary atresia	Compatible	II and III	4.7	Single anastomoses between the graft LHA and the recipient RHA	6	Died after 10 days of graft failure

Abbreviations: GRWR, graft-to-recipient weight ratio; HAT, hepatic artery thrombosis; LDLT, living-donor liver transplantation; LHA, left hepatic artery; RHA, right hepatic artery; MHA, middle hepatic artery.

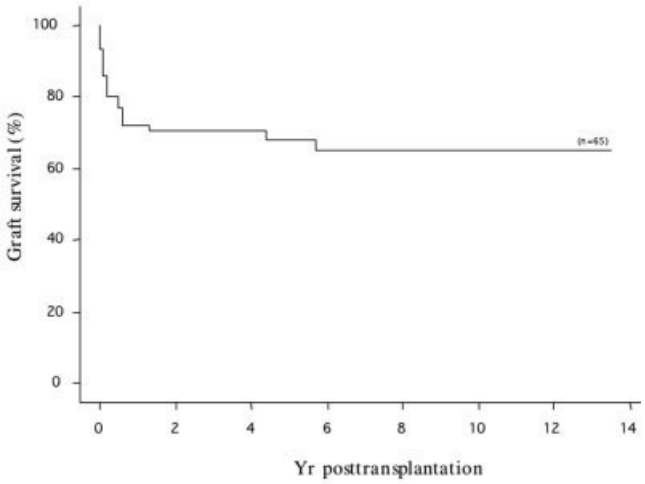

Figure 3. Overall graft survival.

TABLE 5. Causes of Death

Causes	Number (n = 22)	Timing of death posttransplantation
Sepsis	4	16, 18, 28, 41 days
Rejection	4	1, 2, 2, 6 months
Viral infection	3	6, 7, 68 months
Abdominal bleeding	2	9, 20 days
Recurrent disease*	2	3, 7 months
PTLD	1	2 months
GVHD	1	1 month
Portal vein thrombosis	1	10 days
Hepatitis B	1	16 months
Heart failure	1	53 months
Traffic accident	1	19 months
Choking	1	5 months

Abbreviations: PTLD, posttransplant lymphoproliferative disease; GVHD, graft-versus-host disease.
*Recurrent disease: hepatoblastoma and fulminant hepatic failure.

outcomes for hepatic vein reconstruction.[21] However, the incidence of the hepatic vein complications is relatively low, and Buell et al.[22] has reported that it was 4% in reduced-size or split, and 2% in living-related grafts. Similarly, only 1 patient had a hepatic vein complication in the present small infantile series. Previous studies reported early outflow obstruction caused by graft dislocation into the right subphrenic cavity.[15,23] There was no incidence of acute outflow obstruction in the present series. This might be explained by the limited space in an infantile abdominal cavity, which would not allow an implanted graft to twist. Furthermore, fixing the graft to the abdominal wall by using the falciform and round ligaments was expected to contribute to retaining venous outflow and preventing a kink in the hepatic vein. Nevertheless, late-onset outflow obstruction developed in 1 patient who underwent monosegmental LDLT, with a venogram showing a funnel-shaped stenosis, suggesting a stricture caused by gradually increasing torsion of the hepatic vein following regeneration of the graft.

The reported incidence of portal vein complications varies from 1.2 to 16.5% in pediatric LT.[12,13,24] It is reported that portal vein complications more frequently develop in smaller-size recipients.[12,13] There are 2 major problems in portal vein reconstruction in pediatric LT. One is the quality of the recipient's portal vein. The vascular structure of a patient with biliary atresia is often impaired by previous surgery and recurrent cholangitis. Another problem is the differences between

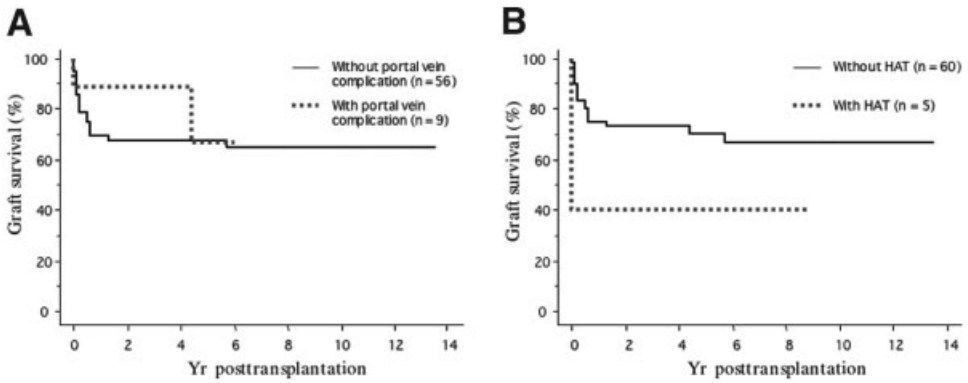

Figure 4. Graft survival related to vascular complications. (A) Graft survival in patients with and without portal vein complication ($P = 0.54$). (B) Graft survival in patients with and without hepatic artery thrombosis (HAT) ($P = 0.04$).

adults and the infants in the diameter of the portal vein. We used 5 different methods for portal vein reconstruction to overcome these problems. When the recipient's portal vein was of good quality, either Type A or Type B was chosen according to differences in diameter of the portal vein between the graft and the recipient. When the recipient's portal vein was impaired, either Type C or Type D was chosen according to the length of the graft portal vein. Moreover, Type E was used to widen the caliber when the recipient's portal vein was smaller than the graft portal vein. We experienced only 1 patient with acute portal vein thrombosis under this criterion, although Lin et al.[25] reported 7 patients with acute portal vein thromboses requiring immediate thrombectomy in a group of 30 small infants. Abdominal closure may result in insufficient portal flow caused by pressure on the graft when the left-lateral segment graft is too large for the pediatric recipient. Therefore, reduction of the left-lateral segment graft was expected to mitigate this problem. Indeed, no early portal vein thrombosis developed in patients who underwent monosegmental LDLT. However, late-onset portal vein complications developed in 8 patients. Venoplasty with a graft patch to create a sufficient caliber for anastomosis appeared to be a useful technique for smaller infantile LDLT because no hazardous complications occurred. Millis et al.[26] reported that the use of a venous conduit, particularly from cryopreserved vessels, resulted in a significantly higher stenosis rate in pediatric LDLT. Although we used only fresh venous conduits, there was no significant difference in the incidence of portal vein complications between patients with and without the vein graft. This result may support the usefulness of fresh vein grafts when venous extension is preferably desired to obtain sufficient inflow. Percutaneous transhepatic balloon dilation is a safe and effective treatment of portal vein stenosis after LDLT.[27] However, this procedure resulted in failure due to preclusion of access to the mesenteric vein side by complete thrombotic occlusion in 3 of 4 patients with late-onset portal vein thrombosis. Long-term periodical examination by Doppler ultrasonography is mandatory for early detection of perturbation of portal venous flow before completion of thrombotic occlusion, even if the children are well with satisfactory liver function tests.

HAT remains a significant cause of graft loss after pediatric LT.[13,28] However, the incidence of HAT has steadily been lowered with technological advances. The latest reported incidence ranges from 7 to 10% in large pediatric liver transplant programs.[13,29] Although anastomoses of hepatic arteries with smaller caliber are considered as risks for HAT,[16] our microsurgical technique also produced acceptable results in smaller-size recipients. Furthermore, simple end-to-end anastomosis without an interposing graft appears to have contributed to the low incidence of HAT in the present study.[16] However, HAT significantly affected graft survival, as it did in previous studies.[13,28]

Reports focusing on vascular complications in infantile not pediatric LDLT are less common. Noujaim et al.[8] reported no incidences of hepatic vein complications, but they reported 1 portal vein thrombosis (7%) and 1 HAT (7%) in 15 infants weighing less than 5 kg; although most of these patients underwent LT under highly urgent conditions. Van der Wert et al.[30] reported that incidences of portal vein thrombosis and HAT were 9.5 and 19%, respectively. The current series represents the largest experience from a single center in infantile LDLT; however, it also includes a learning curve. Several surgical factors might contribute to prevention of vascular complications in smaller-size recipients. Our review indicates the relevance of the following suggestions: 1) even on smaller IVCs, undertake venoplasty to ensure a sufficient outflow in addition to fixing the graft to the abdominal wall; 2) do not hesitate to trim the native portal vein if it is of low quality and to employ a vein graft; and 3) if possible, complete hepatic artery reconstruction with simple end-to-end anastomosis without an interposing graft. Moreover, technical refinements due to increasing operational experience are indispensable for improving outcomes in the smaller-size infant group.

Technical complications remain the most significant factors contributing to graft loss after pediatric LT.[31] Most deaths within the first 3 months posttransplantation are more significantly related to surgical factors. Jain et al.[32] reported that 55.4% of 258 deaths in 808 pediatric recip-

ients occurred within the first 3 months of the follow-up period after LT. Similarly, in our infantile series 58% of deaths in 22 patients occurred within the same period. Deaths of 7 patients (4 with sepsis, 2 with abdominal bleeding, and 1 with portal vein thrombosis) were undoubtedly attributable in some part to surgical factors. Overcoming early complications would improve outcomes in infantile LDLT.

In conclusion, smaller-size infants who undergo LDLT require the implementation of unique devices to connect their smaller vascular structures with the larger vascular pedicles from adult donors. The surgical technique we have developed has produced an acceptable incidence of vascular complications. Overcoming earlier posttransplantation complications is expected to improve outcomes in infantile LDLT.

REFERENCES

1. Ferreira CT, Vieira SM, Silveira TR. Liver transplantation. J Pediatr 2000;76:S198-S208.
2. McDiarmid SV. Current status of liver transplantation in children. Pediatr Clin North Am 2003;50:1335-1374.
3. Magee JC, Bucuvalas JC, Farmer DG, Harmon WE, Hulbert-Shearon TE, Mendeloff EN. Pediatric transplantation. Am J Transplant 2004;4:54-71.
4. Kiuchi T, Kasahara M, Uryuhara K, Inomata Y, Uemoto S, Asonuma K, et al. Impact of graft size mismatching on graft prognosis in liver transplantation from living donors. Transplantation 1999;67:321-327.
5. Otte JB, de Ville de Goyet J, Sokal E, Alberti D, Moulin D, et al. Size reduction of the donor liver is a safe way to alleviate the shortage of size-matched organs in pediatric liver transplantation. Ann Surg 1990;211:146-157.
6. Rogiers X, Malago M, Gawad K, Jauch KW, Olausson M, Knoefel WT, et al. In situ splitting of cadaveric livers. The ultimate expansion of a limited donor pool. Ann Surg 1996;224:331-339.
7. Broelsch CE, Whitington PF, Emond JC, Heffron TG, Thistlethwaite JR, Stevens L, et al. Liver transplantation in children from living related donors: surgical techniques and results. Ann Surg 1991;214:428-437.
8. Noujaim HM, Mayer DA, Buckles JA, Beath SV, Kelly DA, McKiernan PJ, et al. Techniques for and outcome of liver transplantation in neonates and infants weighing up to 5 kilograms. J Pediatr Surg 2002;37:159-164.
9. Grabhorn E, Schulz A, Helmke K, Hinrichs B, Rogiers X, Broering DC, et al. Short- and long-term results of liver transplantation in infants aged less than 6 months. Transplantation 2004;78:235-241.
10. Iglesias J, Lopez JA, Ortega J, Roqueta J, Asensio M, Margarit C. Liver transplantation in infants weighing under 7 kilograms: management and outcome of PICU. Pediatr Transplant 2004;8:228-232.
11. Woodle ES, Millis JM, So SK, McDiarmid SV, Busuttil RW, Esquivel CO, et al. Liver transplantation in the first three months of life. Transplantation 1998;66:606-609.
12. Chardot C, Herrera JM, Debray D, Branchereau S, DeDreuzy O, Devictor D, et al. Portal vein complications after liver transplantation for biliary atresia. Liver Transplant Surg 1997;3:351-358.
13. Sieders E, Peeters PMJG, Ten Vergert EM, De Jong KP, Porte RJ, Zwaveling JH, et al. Early vascular complications after pediatric liver transplantation. Liver Transpl 2000;6:326-332.
14. Saad S, Tanaka K, Inomata Y, Uemoto S, Ozaki N, Okajima H, et al. Portal vein reconstruction in pediatric liver transplantation from living donors. Ann Surg 1998;227:275-281.
15. Egawa H, Inomata Y, Uemoto S, Asonuma K, Kiuchi T, Okajima H, et al. Hepatic vein reconstruction in 152 living-related donor liver transplantation patients. Surgery 1997;121:250-257.
16. Mazzaferro V, Esquivel CO, Makowka L, Belle S, Kahn D, Koneru B, et al. Hepatic artery thrombosis after pediatric liver transplantation-a medical or surgical event? Transplantation 1989;47:971-977.
17. Kasahara M, Kaihara S, Oike F, Ito T, Fujimoto Y, Ogura Y, et al. Living-donor liver transplantation with monosegments. Transplantation 2003;76:694-696.
18. Tanaka K, Uemoto S, Tokunaga Y, Fujita S, Sano K, Nishizawa T, et al. Surgical techniques and innovations in living related liver transplantation. Ann Surg 1993;217:82-91.
19. Inomata Y, Tanaka K, Egawa H, Uemoto S, Ozaki N, Okajima H, et al. The evolution of immunosuppression with FK506 in pediatric living related liver transplantation. Transplantation 1996;61:247-252.
20. Inomoto T, Nishizawa F, Sasaki H, Terajima H, Shirakata Y, Miyamoto S, et al. Experiences of 120 microsurgical reconstructions of hepatic artery in living related liver transplantation. Surgery 1996;119:20-26.
21. Kubota K, Makuuchi M, Takayama T, Harihara Y, Watanabe M, Sano K, et al. Successful hepatic vein reconstruction in 42 consecutive living related liver transplantations. Surgery 2000;128:48-53.
22. Buell JF, Funaki B, Cronin DC, Yoshida A, Perlman MK, Lorenz J, et al. Long-term venous complications after full-size and segmental pediatric liver transplantation. Ann Surg 2002;236:658-666.
23. Emond JC, Heffron TG, Whitington PF, Broelsch CE. Reconstruction of the hepatic vein in reduced size hepatic transplantation. Surg Gynecol Obstet 1993;176:11-17.
24. Deshpande RR, Bowles MJ, Vilca-Melendez H, Srinivasan P, Girlanda R, Dhawan A, et al. Results of split liver transplantation in children. Ann Surg 2002;236:248-253.
25. Lin CC, Chuang FR, Wang CC, Chen YS, Chen CL, Liu YW, et al. Early postoperative complications in recipients of living donor liver transplantation. Transplant Proc 2004;36:2338-2341.
26. Millis JM, Seaman DS, Piper JB, Alonso EM, Kelly S, Hackworth CA, et al. Portal vein thrombosis and stenosis in pediatric liver transplantation. Transplantation 1996;62:748-754.
27. Shibata T, Itoh K, Kubo T, Maetani Y, Shibata T, Togashi K, Tanaka K. Percutaneous transhepatic balloon dilation of portal venous stenosis in patients with living donor liver transplantation. Radiology 2005;235:1078-1083.
28. Shackleton CR, Goss JA, Swenson K, Colquhoun SD, Seu P, Kinkhabwala MM, et al. The impact of microsurgical hepatic artery reconstruction on the outcome of liver transplantation for congenital biliary atresia. Am J Surg 1997;173:431-435.
29. Stringer MD, Marshall MM, Muiesan P, Karani JB, Kane PA, Mieli-Vergani G, et al. Survival and outcome after hepatic artery thrombosis complicating pediatric liver transplantation. J Pediatr Surg 2001;36:888-891.
30. Van der Wert WJ, D'Alessandro AM, Knechtle SJ, Pilli G, Hoffmann RM, Judd RH, et al. Infant pediatric liver transplantation results equal those for older pediatric patients. J Pediatr Surg 1998;33:20-23.
31. McDiarmid SV. Management of the pediatric liver transplant patient. Liver Transpl 2001;7:S77-S86.
32. Jain A, Mazariegos G, Kashyap R, Kosmach-Park B, Starzl TE, Fung J, Reyes J. Pediatric liver transplantation. A single center experience spanning 20 years. Transplantation 2002;73:941-947.