Surgical Techniques and Innovations in Living Related Liver Transplantation

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The authors successfully performed a series of 33 living related liver transplantations (LRLT) on children (15 males and 18 females, ranging from 7 months to 15 years of age) from June 1990 to May 1992, with the informed consent of their parents and the approval of the Ethics Committee of Kyoto University. Before operation, six of the children required intensive care, another 14 were hospitalized, and 13 were homebound. Donors (12 paternal and 21 maternal) were selected solely from the parents of the recipients on the basis of ABO blood group and graft/recipient size matching determined by computed tomography scanning. Procurement of graft was performed using ultrasonic aspirator and bipolar electrocautery without blood vessel clamping and without graft manipulation. All donors subsequently had normal liver function and returned to normal life. The left lateral segment (16 cases), left lobe (16 cases), or right lobe (one case) were used as grafts. The partial liver graft was transplanted into the recipient who underwent total hepatectomy with preservation of the inferior vena cava using a vascular side clamp. Twenty-seven of 33 recipients are alive and well with the original graft and have normal liver function. The patient survival rate was 89% (24/27) in elective cases and 50% (3/6) in emergent cases. The other six recipients had functioning grafts but died of extrahepatic complications. Complications of the graft were minimal in all cases. Hepatic vein stenosis, which occurred three times in two cases, was successfully treated by balloon dilatation. In cases with sclerotic portal vein, the authors anastomosed the portal vein of the graft to the confluence of the splenic vein and the superior mesenteric vein without a vascular graft, after experiencing a case of vascular graft thrombosis. After hepatic artery thrombosis occurred in one of the initial seven recipients whose arterial anastomosis was done with surgical loupe, microsurgery was introduced for hepatic artery reconstruction. There has been no occurrence of thrombosis since then. The current results with LRLT suggested that the meticulous management of surgical factors at each stage of the LRLT procedure is crucial for successful outcome. Living related liver transplantation is a promising option for resolving the graft shortage in pediatric liver transplantation and may be regarded as an independent modality to supplement cadaver donation.

Among the several therapeutic modalities that have been introduced to deal with the graft shortage in pediatric liver transplantation, living related liver transplantation (LRLT) is the latest modality for children with end-stage liver disease, and in terms of the technical, medical, and ethical aspects of the procedure, can be said to repre-

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sent a significant advance when compared with reduced liver transplantation or the split liver technique.[1-3] When the LRLT program was started in our department, we anticipated that it would have the following potential advantages: (1) improved preservation of graft viability due to minimal cold ischemic time; (2) accurate graft/recipient size matching based on computed tomography done before operation; and (3) better histocompatibility as a result of tissue type matching based on ABO blood group, human leukocyte antigen (HLA) serologic and HLA-DNA analyses.[4] Besides these advantages, we also anticipated a number of difficulties in the surgical procedures of LRLT. Several surgical complications experienced in early cases in our series have led us to realize the importance of certain surgical factors of LRLT. In this study, we reviewed all 33 cases of LRLT performed by our department in terms of surgical techniques and factors affecting the outcome of LRLT.

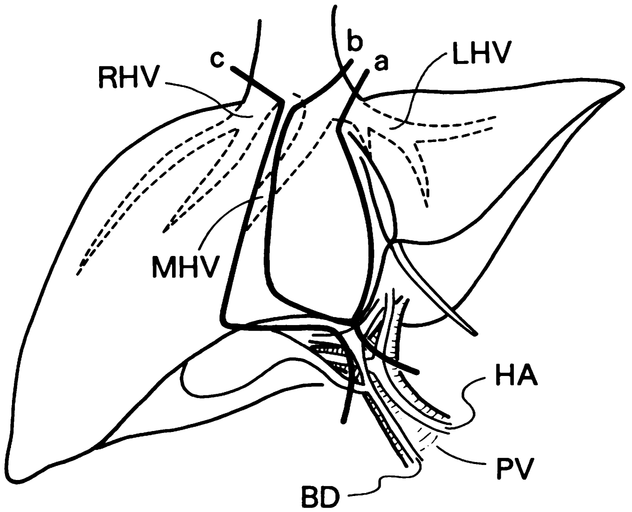

Figure 1. Schematic representation of the graft-harvesting operation. Lines indicate the cutting planes for (A, top left) left lateral segmentectomy, (B, top right) left lobectomy, and (C, bottom) right lobectomy.

PATIENTS AND METHODS

Selection of Donors and Recipients

From June 1990 to May 1992, we performed a series of 33 LRLT on children (15 males and 18 females, ranging from 7 months to 15 years of age) with end-stage liver disease, with the informed consent of their parents and the approval of the Ethics Committee of Kyoto University. After obtaining the informed consent of the donor and the family's agreement to proceed with the operation, thorough medical examinations were done on the parents to determine their suitability as donors. Donors were selected from among the parents of the recipients on the basis of liver function tests, ABO blood group, and graft/recipient size matching as described previously.[4] Preoperative immunologic evaluation included lymphocyte cross-matching, serologic HLA typing, mixed lymphocyte culture reaction, and HLA-DNA typing in all recipients and their parents.[5,6]

Donor Operation

The surgical techniques used for harvesting the graft from a living related donor have been reported previously in detail.[7,8] Briefly, the plane of liver resection was determined before operation on the basis of donor liver volumetry using CT scan and the anatomic analysis of the vascular structure of the hepatic vein, portal vein, and hepatic artery using ultrasonography (US) and magnetic resonance imaging.[4] Graft/recipient size matching produced the following; (1) left lateral segmentectomy (16 cases), (2) left lobectomy (16 cases), (3) right lobectomy (one case) (Fig. 1). After performing an intraoperative US scan with linear array electronic scanner (Aloka SSD-650; Aloka, Tokyo, Japan) to confirm the hepatic vein anatomy, the hepatic parenchyma was transected using an ultrasonic aspirator (CUSA; Cavitron, Stanford, CA) and bipolar electric cautery without blood vessel clamping and without graft manipulation. The triangular and hepatogastric ligaments then were dissected from the liver, and the hepatic veins were isolated. Although the left portal vein and left hepatic artery were isolated from Glisson's sheath, the sheath around the bile duct was left undisturbed as much as possible to maintain the blood flow to the biliary system. After transection of the left hepatic artery and left hepatic vein, the isolated graft was perfused *in situ* through the left portal vein, first with 4 C lactated Ringer's solution (200 mL), and then with 4 C UW solution (600 to 1000 mL). The hepatic veins of the graft were prepared on the back table for smooth and prompt venous anastomosis. Fibrin glue was sprayed on the cut surface of the liver for secure hemostasis.

Recipient Operation

After isolation of the hepatic artery and portal vein at the hepatic hilum, the liver was dissected from the inferior vena cava (IVC) by ligation and dissection of the short hepatic veins without IVC clamping. After dissection and closure of the right hepatic vein, total hepatectomy was completed after side-clamping the IVC to maintain caval blood flow. The liver graft was implanted into the hepatic cavity after the trimming of the hepatic vein orifice (Fig. 2).[9] The vascular and biliary reconstruction procedures actually used varied according to the case, and the surgical techniques are described in

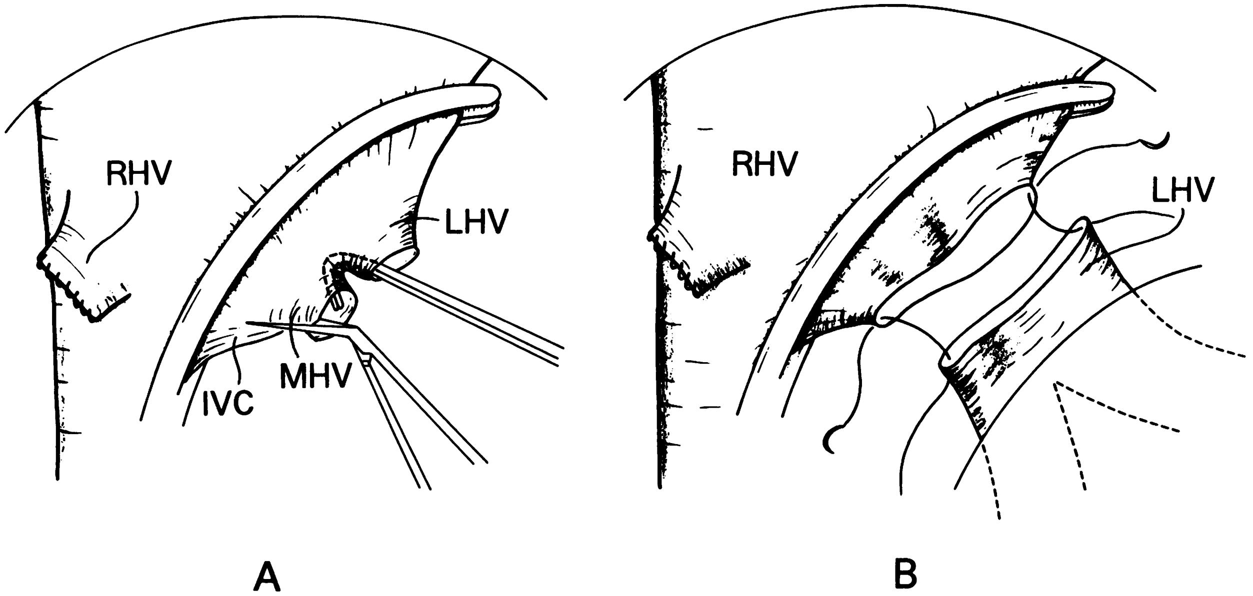

Figure 2. Reconstruction of the graft hepatic vein. (A, left) After side-clamping the recipient vena cava, the septum between the middle and left hepatic vein was incised to create a common anastomotic orifice. The vena cava wall was incised as needed to widen the orifice according to the size of graft hepatic vein. (B, right) Anastomosis of the hepatic vein was performed between the left hepatic vein of the graft and the common anastomotic orifice.

detail in Results. Basically, vascular reconstruction was performed in end-to-end fashion in the left hepatic vein with 5–0 polypropylene (Prolene) and in the portal vein with 7–0 polyglyconate (Maxon). The left hepatic artery or the arteries to segments 2, 3, or 4 of the graft were anastomosed to the proper hepatic artery of the recipient. The hepatic artery anastomosis was accomplished with surgical loupe (3×) and 7–0 polybutester (Novafil) suture in the first seven cases and with surgical microscope (10 to 20×, Contravus AG, Zurich, Switzerland) and 8–0 or 9–0 Prolene sutures in the remaining 26 cases.[10] Biliary reconstruction was performed with a Roux-en-Y limb or interposed jejunal conduit previously existing in patients treated for biliary atresia. Hepatic jejunostomy with Roux-en-Y anastomosis was performed in the remaining patients (Fig. 3).

Immunosuppression

Immunosuppressant regimen consisted of FK 506 and low-dose steroids as described elsewhere.[11] Intravenous administration of FK 506 initially at doses of 0.030 to 0.075 mg/kg every 12 hours was followed by oral administration of FK 506 every 12 hours. The period of overlapped administration was 1 to 2 days. FK 506 dose was adjusted according to 12-hour plasma trough levels. Methylprednisolone (10 mg/kg) was given in the operating room, with steroid administration being tapered from 2 mg/kg/day to 0.5 mg/kg/day over a 7-day period. Steroid administration was discontinued 3 to 6 months after LRLT, unless the patient developed signs of rejection. Graft viability was determined by serial measure-

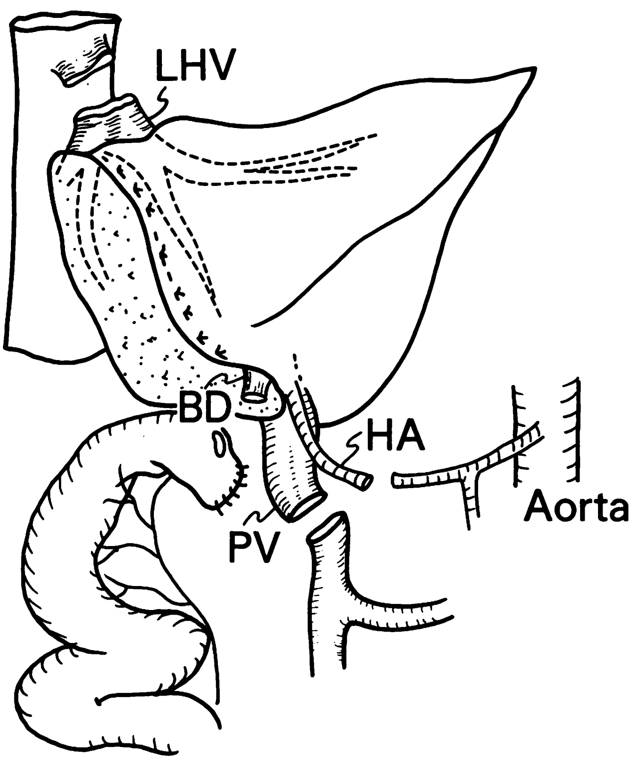

Figure 3. Schematic representation of the graft implantation of the recipient. LHV, left hepatic vein; BD, bile duct; HA, hepatic artery.

ment of arterial ketone body ratio during and after surgery.[12,13]

Analysis of Surgical Risk Factors

Surgical risk factors for the LRLT recipient were investigated at each stage of the surgical procedure, including reconstruction of the hepatic vein, portal vein, hepatic artery, and bile duct. All results were expressed as mean ± standard error of the mean. Surgical curves were analyzed by the Kaplan-Meier method. Statistical significance was determined by the chi square test. P values < 0.05 were regarded as significant.

RESULTS

Donor Survival and Complications

All donors had normal liver function and no history of liver disease. Table 1 summarizes the profiles of the donors and grafts for the 33 LRLT cases. The donors consisted of 12 fathers and 21 mothers, with an average age of 33 ± 1.1 years and an average body weight of 57.5 ± 1.5 kg. All donors were discharged from the hospital at 10 to 17 (mean, 11.6) days after surgery without any complications that needed surgical intervention, and were able to return to normal life.[7] Only one donor who underwent right lobectomy had transient hyperbilirubinemia up to 4.4 mg/dL.

Recipient Survival

Patient profiles and diagnostic indications for LRLT are summarized in Table 2. Donor to recipient body weight ratio ranged from 1.4:1.0 to 11.0:1.0 (mean, 5.0), showing a negative correlation ($r = 0.79$, $p < 0.001$) with recipient body weight (Figure 4). Twenty-seven of the 33 recipients are alive and well with the original graft and have normal liver function with follow-up between 1 and 23 (mean, 11) months. The survival rates were 89% (24/27) in elective cases and 50% (3/6) in emergency cases (Fig. 5). The other six patients had functioning grafts but died of extrahepatic complications including aspiration asphyxia (one case), cardiac insufficiency (one), pulmonary and renal insufficiency (one), candida infection (one), multiple organ failure (one), and lymphoproliferative disorder (one). None of the deaths was caused by surgical failure or mortality associated with graft dysfunction. Graft complications included hepatic vein stenosis, portal vein thrombosis, hepatic artery thrombosis, and biliary stenosis (Table 3). Twenty-one cases were ABO blood group identical, nine cases were ABO compatible, and three cases were ABO incompatible. Three compatible cases and one incompatible case developed liver dysfunction suspected to be liver allograft rejection, whereas no definite hepatic dysfunction due to rejection occurred in the ABO identical cases.

Table 1. DESCRIPTION OF DONORS AND GRAFTS OBTAINED

Description	Mean (Range)
Donors	
Relation to recipient	
Father	n = 12
Mother	n = 21
Age (yr)	33 (24–43)
Weight (kg)	57.5 (44–80)
Donor weight/recipient	5.0 (1.4–11.0)
Graft	
Graft weight (g)	
Left lateral segment (n = 16)	232 (174–275)
Left lobe (n = 16)	301 (230–440)
Right lobe (n = 1)	630
Graft weight/recipient (%)	2.4 (0.75–4.2)

Table 2. PATIENT PROFILES AND DIAGNOSTIC INDICATIONS

Category	No.
Sex	
M	15
F	18
Age (yr)	4.9 (range, 7 mo–15 yr)
Weight (kg)	16.4 kg (5.5–45.0)
Diagnostic indication	
Biliary atresia	24 (73%)
Budd-Chiari syndrome	2 (6%)
Liver cirrhosis	2 (6%)
Progressive intrahepatic cholestasis	2 (6%)
Protoporphyria	1 (3%)
Wilson's disease	1 (3%)
Fulminant hepatitis	1 (3%)
Preoperative status	
Intensive care	6 (18%)
Hospitalized	14 (42%)
Home bound	13 (40%)

Surgical Factors in Hepatic Vein Reconstruction

The site of hepatic vein transection varied depending on both the anatomic variation of the hepatic vein and the number of segments required for the graft. Anatomy and shape of the graft hepatic veins and the hepatic vein

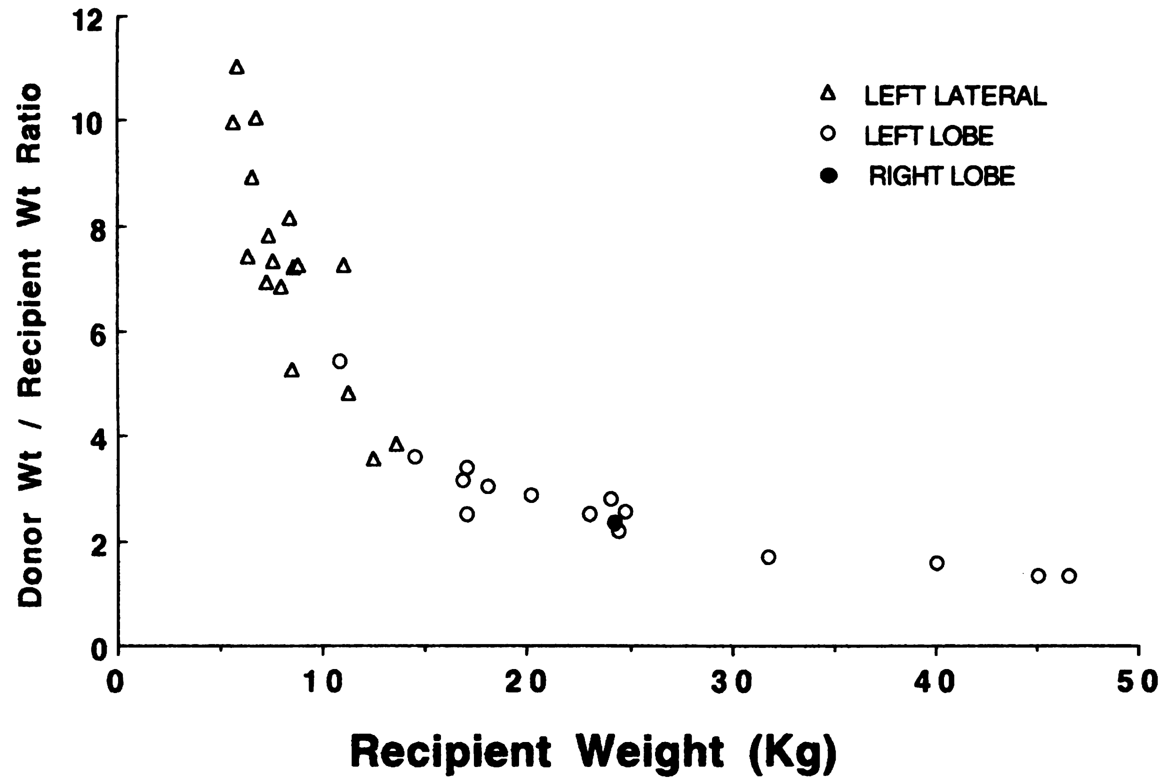

Figure 4. Relationship between donor to recipient body weight ratio and recipient body weight.

orifice of the recipients are shown in Figure 6. As shown in the figure, 25 of 33 (76%) grafts had a single anastomotic stump of the left hepatic vein. Four of 33 (12%) grafts had a single truncal stump proximal to the middle and left hepatic vein. Two of 33 (6%) grafts had a single common anastomotic stump created from two adjacent veins by back table procedure. Only one graft had two independent hepatic veins anastomose when the distance between the veins (>10 mm) did not allow for the creation of a common anastomotic stump (Fig. 6). Of the 32 of 33 (97%) recipients who had a single anastomotic orifice, 26 were created from a common truncal vein of the middle and left hepatic veins, four from a new opening in the vena cava, and two from the right hepatic vein. The one remaining recipient had two independent orifices (Fig. 7).

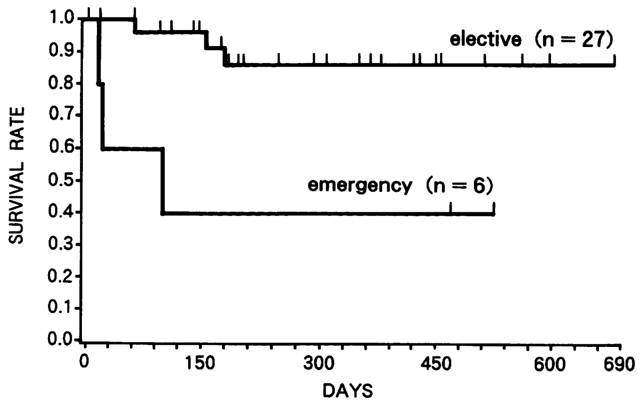

Figure 5. Patient survival curves of living related liver transplantation (Kaplan-Meier method).

Stenosis of the reconstructed hepatic vein occurred three times in two cases at 95, 108, and 250 postoperative days. In one case, it occurred where the graft hepatic vein was anastomosed to the common truncal vein of the recipient, and in another case where the graft hepatic vein was anastomosed to a new aperture in the recipient IVC. In each case, the stenosis was completely repaired by percutaneous transhepatic venoangioplasty using a balloon dilator (inflated diameter: 10 mm). There has been no incidence of stenosis in either of these patients or in any of the patients since then.

Surgical Factors in Portal Vein Reconstruction

Graft portal veins were 7.1 ± 0.3 mm wide and 20.3 ± 1.6 mm long, and were of sufficient length for the reconstruction. In 20 of 33 recipients, the portal vein was > 4 mm in diameter and could be anastomosed to the graft portal vein in end-to-end fashion. The portal vein was at least mm in diameter in the other 13 recipients. In 10 of these recipients, the graft portal vein was anasto-

Table 3. POSTOPERATIVE COMPLICATIONS IN THE GRAFT AND THE RECIPIENT

Complication	No.
Graft	
Hepatic vein stenosis	2 (6%)
Portal vein thrombosis	1 (3%)
Hepatic artery thrombosis	1 (3%)
Biliary stenosis	2 (6%)
Recipient	
Intraperitoneal bleeding	5 (15%)
Biliary leakage	4 (12%)
Intestinal perforation	1 (3%)

mosed to the confluence of the splenic vein and the superior mesenteric vein of the recipient instead of the portal vein trunk. In the remaining three recipients, a vascular graft was obtained from the donor ovarian vein, the donor inferior mesenteric vein, or the recipient infrarenal vena cava, and introduced between the donor portal vein and the confluence of the recipient (Table 4).

Portal vein thrombosis requiring thrombectomy occurred in one of the vascular graft cases, whereas no thrombosis has occurred in any of the other cases since then (Table 4). Intraoperative Doppler US showed hepatopedal blood flow in the portal vein trunk of 25 recipients, to and fro blood flow in four recipients, and hepatofugal blood flow in four recipients. When intraoperative US showed to and fro blood flow or hepatofugal blood flow in the portal system of the recipient, we closed the spontaneous portosystemic shunts, which produced hepatopedal blood flow in almost all recipients.

Surgical Factors in Hepatic Artery Reconstruction

The left hepatic arteries of the donors were classified into four types (Fig. 8). In 26 cases, the left (25/26) or right hepatic artery (1/26) of the graft was anastomosed to the proper hepatic artery of the recipient in end-to-end fashion. In the other seven cases, the arteries to segments 2, 3, and 4 were independently anastomosed to the right and left hepatic arteries of the recipient (Table 5). Hepatic artery reconstruction was carried out using surgical loupe in the first seven cases and surgical microscope in the remaining 26 cases. This change in procedure was made after we experienced episodes of decreased arterial blood flow detected after operation by Doppler US and after thrombosis of the artery occurred because of the small caliber of the artery in one of our earlier cases in which surgical loupe was used (Table 6). We have experienced no episodes of thrombosis after operation, since the introduction of the surgical microscope.

Surgical Factors in Bile Duct Reconstruction

In all cases but two, a single bile duct of the left lobe or left lateral lobe of the donor was anastomosed to the

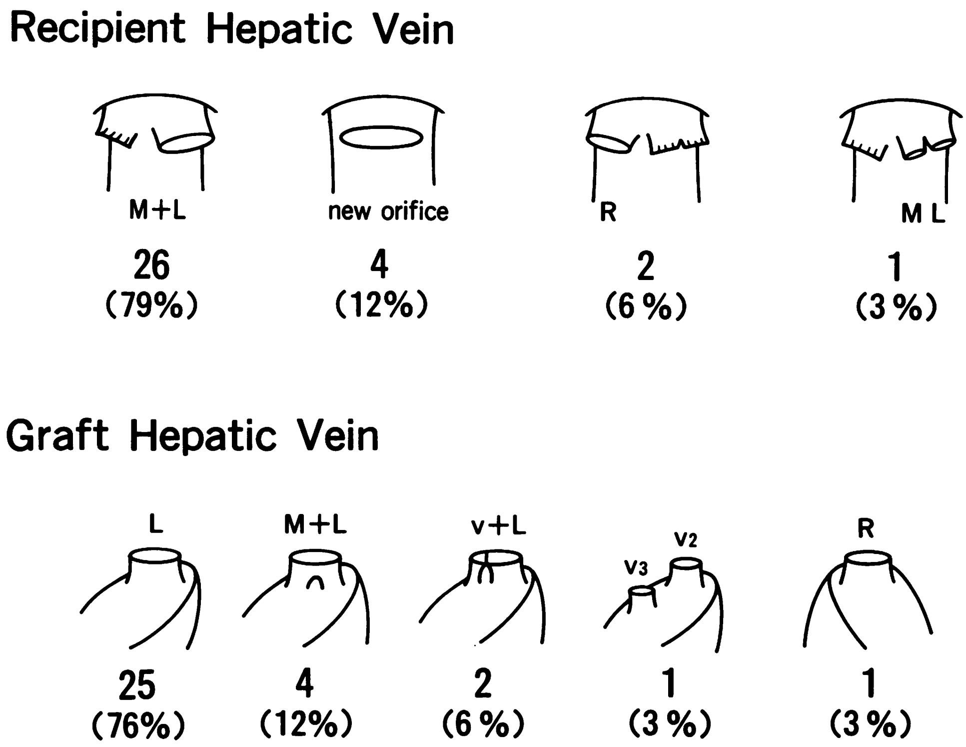

Figure 6. Schematic representation of the anatomic variations of hepatic vein reconstruction. A variety of modalities for hepatic vein reconstruction was employed. The left hepatic vein of the graft was anastomosed to a single anastomotic orifice created from a common truncal vein of the middle and left hepatic veins in most cases (>75%). One graft required two independent hepatic vein anastomoses when the distance between the veins (>10 mm) did not allow for the creation of a common truncal anastomotic stump. In another case, a right lobe graft was anastomosed to the recipient right hepatic vein. M, middle hepatic vein; L, left hepatic vein; R, right hepatic vein; v, segmental hepatic vein.

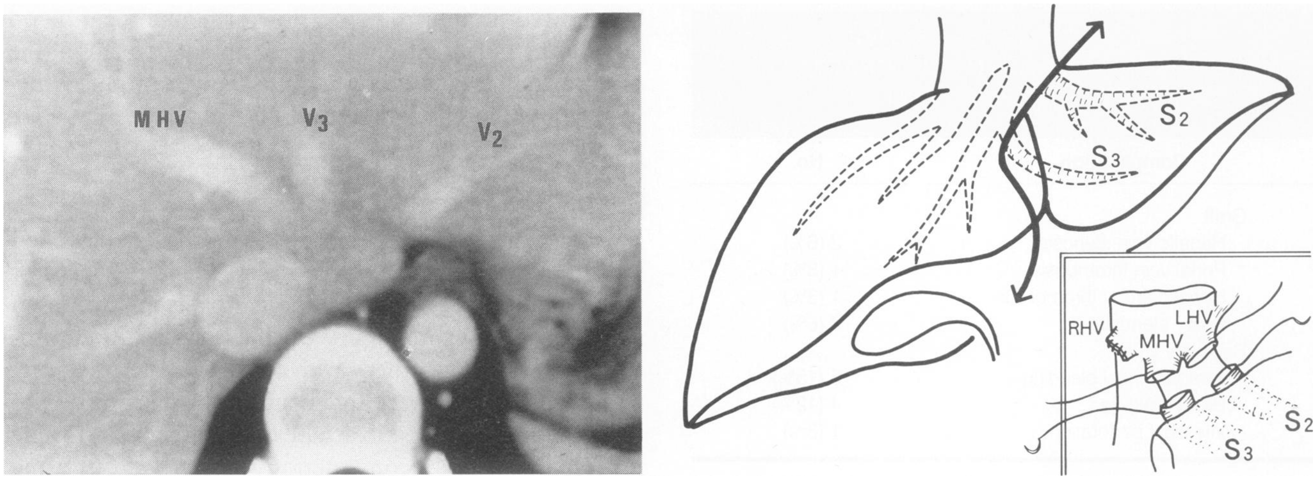

Figure 7. In one case, two independent veins from segments 2 and 3 were anastomosed to the recipient middle hepatic and left hepatic veins, respectively. (A, left) Computed tomography scan showed that the two independent hepatic veins (v2, v3) drained into the vena cava. MHV, middle hepatic vein. (B, right) Schematic description of the hepatic vein anastomosis of this case.

interposed jejunal conduit or jejunal Roux-en-Y limb. Both bile ducts from segments 2 + 3 and segment 4 were independently anastomosed to the jejunal conduit in two cases. Four of 33 (12%) recipients developed biliary leakage, occurring in most cases from pin-hole perforations at the closed jejunal stump used previously for jejunostomy, rather than from the biliary LRLT anastomosis. Two of these four recipients with biliary leakage had stenosis at the biliary anastomosis, requiring surgical intervention, including transhepatic balloon dilatation.

DISCUSSION

One of the key issues our LRLT series has raised is with regard to the donor/recipient body weight ratio and the graft size. Broelsch et al.[1] have limited the indication of LRLT using the left lateral segment graft to children younger than 2 years of age and smaller than 15 kg in body weight in their early series.[1] They also classified the application of reduced-size liver graft according to the following donor/recipient weight ratios; left lateral lobe graft, ratio greater than 4 and up to 10; left lobe graft, ratio of 2 to 4; and right lobe graft, ratio less than 2.[14] Although a variety of harvesting modalities are needed to adjust the graft size in LRLT to the recipient size, using the techniques described above we performed our LRLT series with a donor/recipient ratio ranging from 1.4 to 11.0, thus broadening the present boundaries on donor/recipient size limitation proposed by the Chicago group and others.[1,2,14]

Another key issue is that of the surgical factors, especially the vascular reconstruction technique, which is crucial for graft blood supply and graft drainage. Because the hepatic vein, portal vein, and hepatic artery vary widely anatomically,[15-17] an understanding of the anatomic landmarks of these structures is essential for successful outcome in LRLT. Various harvesting modalities are required for proper reconstruction of the hepatic vein without stenosis. Venous congestion, even in a limited region, can seriously damage the newly implanted graft. Conversely, postoperative complications in the adjacent segment can be prevented if at least one of the main trunks of the hepatic vein is patent in the residual donor liver.[18] Therefore, as long as one segment of the hepatic vein shared between the donor liver and the graft liver is patent, this provides the corresponding drainage vein needed for the graft. Stenosis of the hepatic vein occurred 3 times in two cases. Because the patency of their hepatic veins was well maintained for 3 months or longer, it is speculated that the stenosis was partially due to fibrotic adhesion around the anastomosis resulting

Table 4. SURGICAL PROCEDURES OF PORTAL VEIN RECONSTRUCTION

Portal Vein Diameter	Anastomosis	No.	Complication
>4 mm	Portal to portal	19 (58%)	—
	Portal to confluence	1 (3%)	—
≤4 mm	Portal to portal	0 (0%)	—
	Portal to confluence	10 (30%)	—
	Vascular graft	3 (9%)	
	Donor ovarian vein	1	—
	Donor inf mesentric vein	1	Thrombosis
	Recipient infrarenal cava	1	—

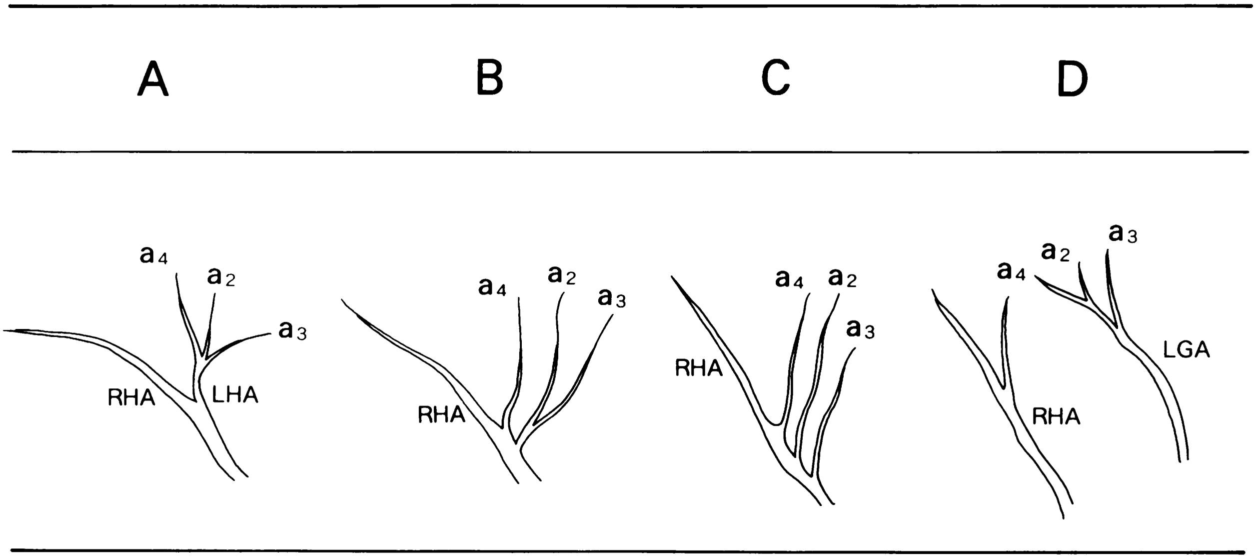

Figure 8. Schematic description of the left hepatic artery of the donor.

from bleeding and partially due to twisting of the extrahepatic segment of the hepatic vein associated with rotation of the regenerating graft. The stenoses were dilated successfully by balloon dilatation.[19] This incident suggested that the extrahepatic segment of the hepatic vein should be as short as sound anastomosis will allow. The Chicago group prefers a wide venous anastomosis with rotation of the graft to the right.[1] As they proposed, we recently widened the anastomotic orifice by making an incision in the IVC wall according to the size of the graft vein (Fig. 2).

When the recipient portal vein was so sclerotic and small such as in the biliary atresia cases due to cholangitis or previous multiple laparotomies, the portal vein of the graft was anastomosed to the confluence of the splenic vein and superior mesenteric vein of the recipient because we thought that performing an anastomosis at this point would enable maximal blood flow. We also were concerned about thrombosis resulting from the slightest stretching of the portal vein due to inadequate length of the graft vein, as pointed out by the Chicago group,[1] although, this has not occurred in our series thus far. Instead, the graft portal vein maximized the blood flow by totally supplementing the sclerotic portal vein in the recipient. Furthermore, we refrained from using a vascular graft in the portal system between the donor liver and the recipient portal vein after experiencing thrombosis in a vein graft obtained from the donor inferior mesenteric vein. Intraoperative Doppler US was found to be helpful for real-time evaluation of graft blood supply at each stage of the surgical procedure. We closed the spontaneous splenosystemic shunts according to the findings of intraoperative Doppler flowmetry of

Table 5. SURGICAL PROCEDURES FOR HEPATIC ARTERY RECONSTRUCTION

Graft Hepatic Artery	Diameter (mm)	No. Loupe	No. Microscope
Single left hepatic artery	<2		1
	2–3	4*	15
	>3	3*	3
Separate arteries to segments 2, 3 & 4	<2		5
	2–3		1
	>3		1

* Initial seven cases in which the hepatic artery anastomosis was done with surgical loupe.

Table 6. COMPARISON OF THE RESULTS IN HEPATIC ARTERY ANASTOMOSIS WITH LOUPES AND MICROSCOPES

Criteria of Comparison	Loupe	Microscope
No. of times for each reconstruction in the primary operation		
1	5	25
2	1	1
3	1	0
Episodes of postoperative decrease in arterial flow*	4/7 arteries	1/26
Hepatic artery thrombosis	2 times/1 case	0

* $p < 0.05$.

the portal vein, resulting in the correction of portal flow direction or increase in the afferent portal flow to the liver.

Reconstruction of the hepatic artery has been the most problematic procedure we have faced, because only the left hepatic artery is available as the graft artery. There were two episodes of hepatic artery thrombosis out of the initial seven LRLTs with surgical loupe.[10] Moreover, in a donor who had unusual branching of the three left hepatic arteries that arose completely independent from one another, with each branching feeding separately into segments 2, 3, and 4, we were forced to switch from the left lobe to the right lobe for a graft, because the small caliber of the arteries would have made thrombosis highly likely. To overcome this problem, we later introduced microvascular surgery. To the best of our knowledge, microvascular surgery has never before been applied to arterial reconstruction in pediatric liver transplant, probably because it seemed time consuming and complicated, despite its ultimate suitability in dealing with pediatric patients, whose arterial caliber is usually much smaller than that of adults, and who have a higher incidence of hepatic arterial thrombosis compared with adults.[20–22] As it turned out, the time required for microscopic anastomosis procedures is comparable to the conventional method with loupe. Furthermore, there have been no postoperative arterial complications, including thrombosis, detected after microscopic reconstruction. The technique has also enabled us to successfully use the left liver graft from a donor with two arteries supplying the left lobe of the liver, although the criteria of the Chicago group would warn against using such donors because of high risk of arterial thrombosis.[1] The initial success with the microscopic procedure has encouraged us to discontinue preoperative donor angiography, which helps to further reduce donor risk.[10]

Biliary complications occurred at a rate comparable to those reported by the Chicago group.[1,23] Blood supply to the biliary system is provided entirely by arterial flow, which we spared by preserving the Glisson's sheath as much as possible during graft harvesting.[8] There has been no biliary complication in the late postoperative period. Several recipients developed biliary leakage resulting from pin-hole perforations in the closed jejunal limb stump previously used for extraperitoneal biliary drainage, rather than from the biliary anastomosis. Moreover, because this jejunal limb has caused extensive peritoneal adhesions that resulted in increased blood loss and time loss required for its dissection, we stand in full agreement with a proposal made by others[24] that jejunostomy for extraperitoneal biliary drainage in Kasai's procedure should be discontinued in children with biliary atresia.

In conclusion, our initial experience with LRLT suggests that thorough consideration and meticulous management of surgical factors at each stage of the procedure is required for successful outcome. Living related liver transplantation is a promising option for resolving the graft shortage in pediatric liver transplantation and should be regarded as an independent modality, rather than an alternate to cadaver donation.

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