Table 2. Detail of Vein Grafts

Technique	Cryopreserved Vein					Autograft
	IVC	SVC	IV	F	PV	
Double VC (n = 16)	14	2	1*	2*	0	0
Using rectangular shaped vein patch (n = 14)**	0	2	2	5	0	6
Using diamond shaped vein patch (n = 10)	0	0	1	0	1	8

Abbreviations: F, femoral vein; IV, iliac vein; IVC, inferior vena cava; PV, portal vein; SVC, superior vena cava; VC, vena cava.
*Used for middle hepatic vein reconstruction.
**In one patient, cryopreserved femoral vein graft was used for middle hepatic vein reconstruction and auto left portal vein was used for patching.

Aspartate aminotransferase peaked on the first postoperative day, and then decreased gradually thereafter (Fig. 4). The total bilirubin level decreased rapidly after LDLT.

Two patients died 99 and 117 days after LDLT due to multiple graft abscesses after hepatic arterial thrombosis and bleeding from the ileum, respectively. The remaining patients survived the operation and stayed in the hospital for 16–123 (median, 35) days. All but the two patients are alive with a median follow-up of 9 months. There was no evidence of anastomotic stricture or thrombosis in the hepatic vein in any of the patients.

Discussion

Although the appropriate length of the outflow reconstruction is controversial in LDLT using a right liver graft,[14] short and direct anastomosis is generally performed in RHV reconstruction for RLG implantation. Marcos and colleagues created an elliptical defect of approximately 1.5–2.0 times the diameter of the donor RHV in the right side of the IVC.[15] The IVC and the RHV were then anastomosed side-to-end. A recent report presented a similar technique.[16] The stump of the recipient RHV was excised along a portion of the IVC, creating an oval cavotomy. Marcos and colleagues reported no outflow stenosis in their 48 LDLT recipients.[15] In the series by Kinkhabwala and associates, there was only a 2% incidence of outflow complications.[16] There seems to be no evidence to contraindicate these simple and short anastomoses.

The implanted graft is always smaller than the recipient standard volume in adults, however, and will regenerate in the postoperative course. The graft will grow toward the left and ventral sides because the right subphrenic cavity is not large enough to accommodate the regeneration (Fig. 5). When a short anastomosis is performed, the dissection plane of liver graft faces the IVC. The enlarged graft might push on the IVC on the dorsal side. The resulting outflow obstruction could congest the graft, leading the patient to a malignant cycle of further graft expansion and dysfunction. In our technique, the anastomosis is lengthened by adding a venous patch. Long preservation of recipient hepatic veins allowed formation of a reservoir between the liver graft and recipient IVC. With this concept, we have previously presented venous patching at the anastomotic site of RHV[12] and double VC method for ERLG.[11] In the present paper we have a newly devised rectangular-shaped vein graft technique and have formulated our strategy in MHV and RHV reconstruction for right liver graft.

Fan and colleagues analyzed the results of ERLG in 11 patients.[17] Originally, they reconstructed the RHV and MHV separately. For RHV anastomosis, the recipient IVC was incised longitudinally to make the RHV anastomosis as short as possible. The MHV of the graft was anastomosed to the MHV or left hepatic vein of the recipient end-to-end. Using this technique, MHV reconstruction is technically demanding. The MHV position in the graft should not always be constant in relation to the position of the recipient MHV. Addi-

Table 3. Time for Outflow Reconstruction (min)

Technique	On Bench	After Out of Ice
Double VC (n = 16)	62–142 (89)	12–24 (18)
Using rectangular shaped vein patch (n = 14)	33–117 (67)	35–62 (45)
Using diamond shaped vein patch (n = 10)	12–21 (16)	21–42 (30)

Abbreviation: VC, vena cava.
Numbers in parenthesis indicates a median value.

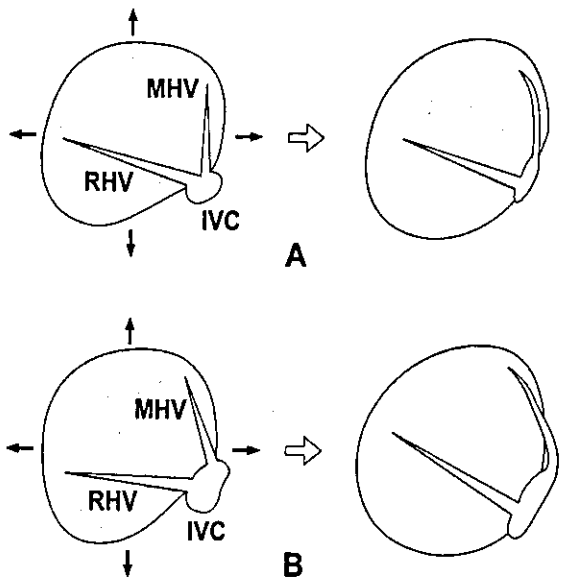

Figure 5. The graft will regenerate (arrows) and rotate toward left and dorsal side because the right subphrenic cavity is not large enough to accommodate the regeneration. (A) Short outflow reconstruction of middle and/or right hepatic vein (MHV or RHV) places the graft riding on the inferior vena cava (IVC). The regenerated graft might push the IVC. (B) Long outflow reconstruction can set the graft in a more natural position. The anastomosis could be maintained wider after graft regeneration.

tionally, expansion of the right liver graft might displace the MHV anastomosis to the left side, provoking stenosis. Recently, Fan et al have revised their technique.[18] In the bench surgery, the adjacent walls of the graft MHV and RHV orifices were sutured. In the recipient, the RHV orifice was enlarged with a transverse incision across the anterior wall of the IVC. In this method, the position of the graft is determined by the triangle-shaped hole in the ventral plane of the IVC. The dissection plane of the graft faces the IVC. Excellent results were achieved after adopting the technique. The possibility remains, however, that the expanded graft will compress the IVC.

There is no consensus regarding the optional strategy for MHV reconstruction in RLG. It would be ideal to reconstruct every significant MHV tributary in RLG. The most likely background in routine MHV deprivation in some institutions is that these veins cannot drain into the IVC without the aid of a jump graft, which necessitates a complex reconstruction strategy. Marcos and associates[15] pointed out some concerns related to MHV reconstruction: 1) that the donor liver cannot be separated safely if the MHV tributaries are not ligated; 2) that construction of jump grafts will prolong the warm ischemic time and increase the risk of bleeding; and 3)that the intrahepatic collaterals will be adequate for acute decompression of right paramedian sector. Some transplant teams have performed reconstruction of the MHV tributaries overcoming these proposed difficulties and obtained satisfactory results. A previous report revealed that in LDLT, venous flow of the ligated MHV tributaries drained into the right hepatic vein by way of the venous collaterals that developed rapidly approximately 1 week after transplantation, which was confirmed by Doppler ultrasonography.[19] There is no evidence that the prompt formation of such collaterals can be generally expected. Cattral and associates reported a case of reconstruction using the recipient's left portal branch.[20] Ghobrial and colleagues reported a venous variant type of the small RHV and large MHV branch and proposed that MHV reconstruction should be performed in such cases.[14] We have reconstructed the MHV tributaries if the congested area was dominant by the clamping test or ultrasonography as proposed by Sano and associates.[13] The reconstructed MHV might be easily compressed by regeneration of the liver graft. The rectangular-shaped vein patch between the reconstructed MHV and the graft RHV is optimal for preventing the displacement of the anastomosis.

The major concern in venous reconstruction using cryopreserved vein grafts is vein graft obstruction or the possibility of narrowing in the long-term observation period. Kuang and associates used cyropreserved grafts for portal vein interposition (iliac vein or saphenous vein, n=7) and hepatic artery interposition (saphenous vein, n=2) in LDLT.[21] The patients were five children and two small adults. Complications of the vein grafts were recognized in eight of the nine grafts including aneurysm (n=4), thrombosis (n=3), and stricture (n=1). Mills and associates reported that incidence of late portal vein stenosis or thrombosis was 51% when cryopreserved vein was used as an interposition graft.[22] The previous discouraging results indicate that long-term follow-up are necessary to confirm the feasibility of the present technique.

In summary, the present techniques seem to be feasible for outflow reconstruction in a right liver graft although there was no evidence that they were advantageous over the conventional simple reconstruction. There remain some problems in our techniques in its complexity and long-term patency of cryopreserved vein grafts.

References

1. Brown RS Jr, Russo MW, Lai M, Shiffman ML, Richardson MC, Everhart JE, et al. A survey of liver transplantation from living adult donors in the United States. N Engl J Med 2003; 348:818–825.
2. Wachs ME, Bak TE, Karrer FM, Everson GT, Shrestha R, Trouillot TE, et al. Adult living donor liver transplantation using a right hepatic lobe. Transplantation 1998;66:1313–1316.
3. Lo CM, Fan ST, Liu CL, Wei WI, Lo RJ, Lai CL, et al. Adult-to-adult living donor liver transplantation using extended right lobe grafts. Ann Surg 1997;226:261–269.
4. Lo CM, Fan ST, Liu CL, Lo RJ, Lau GK, Wei WI, et al. Extending the limit on the size of adult recipient in living donor liver transplantation using extended right lobe graft. Transplantation 1997;63:1524–1528.
5. Gyu Lee S, Min Park K, Hwang S, Hun Kim K, Nak Choi D, Hyung Joo S, et al. Modified right liver graft from a living donor to prevent congestion. Transplantation 2002;74:54–59.
6. Sugawara Y, Makuuchi M, Sano K, Imamura H, Kaneko J, Ohkubo T, et al. Vein reconstruction in modified right liver graft for living donor liver transplantation. Ann Surg 2003;237:180–185.
7. Lee S, Park K, Hwang S, Lee Y, Choi D, Kim K, et al. Congestion of right liver graft in living donor liver transplantation. Transplantation 2001;71:812–814.
8. Urata K, Kawasaki S, Matsunami H, Hashikura Y, Ikegami T, Ishizone S, et al. Calculation of child and adult standard liver volume for liver transplantation. Hepatology 1995;21:1317–1321.
9. Sugawara Y, Makuuchi M, Takayama T, Imamura H, Kaneko J, Ohkubo T. Safe donor hepatectomy for living-related liver transplantation. Liver Transpl 2002;8:58–62.
10. Motomura N, Takamoto S, Murakawa T, Yoneda N, Shibusawa S, Maeda K, et al. Short-term result of aortic valve replacement with cryopreserved homograft valve in the University of Tokyo Tissue Bank. Artif Organs 2002;26:449–452.
11. Sugawara Y, Makuuchi M, Imamura H, Kaneko J, Kokudo N. Outflow reconstruction in extended right liver grafts from living donors. Liver Transpl 2003;9:306–309.
12. Sugawara Y, Makuuchi M, Imamura H, Kaneko J, Ohkubo T, Kokudo N. Outflow reconstruction in recipients of right liver graft from living donors. Liver Transpl 2002;8:167–168.
13. Sano K, Makuuchi M, Miki K, Maema A, Sugawara Y, Imamura H, et al. Evaluation of hepatic venous congestion: proposed indication criteria for hepatic vein reconstruction. Ann Surg 2002;236:241–247.
14. Ghobrial RM, Hsieh CB, Lerner S, Winters S, Nissen N, Dawson S, et al. Technical challenges of hepatic venous outflow reconstruction in right lobe adult living donor liver transplantation. Liver Transpl 2001;7:551–555.
15. Marcos A, Orloff M, Mieles L, Olzinski AT, Renz JF, Sitzmann JV. Functional venous anatomy for right-lobe grafting and techniques to optimize outflow. Liver Transpl 2001;7:845–852.
16. Kinkhabwala MM, Guarrera JV, Leno R, Brown RS, Prowda J, Kapur S, et al. Outflow reconstruction in right hepatic live donor liver transplantation. Surgery 2003;133:243–250.
17. Fan ST, Lo CM, Liu CL. Technical refinement in adult-to-adult living donor liver transplantation using right lobe graft. Ann Surg 2000;231:126–131.
18. Lo CM, Fan ST, Liu CL, Wong J. Hepatic venoplasty in living-donor liver transplantation using right lobe graft with middle hepatic vein. Transplantation 2003;75:358–360.
19. Kaneko T, Kaneko K, Sugimoto H, Inoue S, Hatsuno T, Sawada K, et al. Intrahepatic anastomosis formation between the hepatic veins in the graft liver of the living related liver transplantation: observation by Doppler ultrasonography. Transplantation 2000; 70:982–985.
20. Cattral MS, Greig PD, Muradali D, Grant D. Reconstruction of middle hepatic vein of a living-donor right lobe liver graft with recipient left portal vein. Transplantation 2001;71:1864–1866.
21. Kuang AA, Renz JF, Ferrell LD, Ring EJ, Rosenthal P, Lim RC, et al. Failure patterns of cryopreserved vein grafts in liver transplantation. Transplantation 1996;62:742–777.
22. 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.

Advances in Adult Living Donor Liver Transplantation: A Review Based on Reports From the 10th Anniversary of the Adult-to-Adult Living Donor Liver Transplantation Meeting in Tokyo

Yasuhiko Sugawara and Masatoshi Makuuchi

In 1993, the Shinshu Group performed the first successful adult-to-adult living donor liver transplantation (LDLT). During the first 10 years of LDLT, many technical innovations have been reported. The major limitation of LDLT for adult recipients is the size of the graft. To overcome the problem, several graft types were designed, including left liver graft with caudate lobe, right liver, modified right liver, and right lateral sector and dual grafts. The necessity and criteria of reconstruction of middle hepatic vein is still on debate in right liver graft without trunk of middle hepatic vein. Biliary reconstruction remains a significant source of morbidity in LDLT. Donor safety must always be the primary consideration in LDLT and the selection criteria and management of the living donor must continue to be refined. On February 21, 2004, the 10th anniversary of the adult-to-adult LDLT meeting was held in Tokyo to review the accumulated experience and the presented information is summarized. (*Liver Transpl 2004;10:715–720.*)

Living donor liver transplantation (LDLT) was first introduced among the pediatric population in 1989,[1] and the first successful case in the total occurred in 1990.[2] On November 2, 1993, the Shinshu Group performed the first successful adult-to-adult LDLT.[3] The patient, who was a 53-year-old woman with primary biliary cirrhosis, received a left liver graft from her son. The number of LDLT procedures for adult patients has increased rapidly since then. By June 2002, there were 433 adult LDLT cases recorded in the European Liver Transplantation Registry[4] with 3-year graft and patient survival rates of 65% and 68%, respectively.

According to the United Network for Organ Sharing,[5] 731 adult LDLT cases had been performed in the United States by October 2001. The 3-year graft survival was 47% between 1998 and 1999 (n = 156), but it improved significantly to 61% between July 1999 and June 2000 (n = 285). According to the Japanese Liver Transplantation Society,[6] 1063 adult LDLT procedures were performed in Japan by the end of 2002. All of the donors were related to the patients; most of them were within the third degree of consanguinity. During the same period, only 10 adult patients underwent liver transplantation using grafts from deceased donors. Death of one living donor was reported from Japan. The donor was a woman in her 40s with complicated mild hypertension and fatty liver preoperatively. Right liver resection was performed, and estimated remnant liver volume was 29% of the total. Postoperatively the donor progressed to liver failure and received a whole liver from a familial amyloid polyneuropathy patient 5 months after her donation. However, she expired 8 months after the donation. The 5-year survival rates were 83% in children and 69% in adults. The lesser outcome in adults compared to that in children ($P < .0001$) indicates that problems remain in adult LDLT.

During the first 10 years of LDLT, many technical innovations have been reported. Now appears to be a good time to review the accumulated experience. On February 21, 2004, the 10th anniversary of the adult-to-adult LDLT meeting was held in Tokyo. The presented information is summarized below.

Donor Safety

Selection and evaluation of a living liver donor for adult recipients is a complex process that involves optimizing graft size in relation to the safety of donors and recipi-

Abbreviations: LDLT, living donor liver transplantation; MHV, middle hepatic vein; HBV, hepatitis B virus; HCV, hepatitis C virus; RHV, right hepatic vein.

From the Artificial Organ and Transplantation Division, Department of Surgery, Graduate School of Medicine, University of Tokyo-Tokyo, Japan.

Supported by a Grant-in-aid for Scientific Research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan, and Grants-in-aid for Research on HIV/AIDS and Research on Measures for Intractable Diseases from the Ministry of Health, Labor, and Welfare of Japan.

Address reprint requests to Yasuhiko Sugawara, MD, Artificial Organ and Transplantation Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. Telephone: 81-3-3815-5411; FAX: 81-3-5684-3989; E-mail: yasusuga-tky@umin.ac.jp

Published online in Wiley InterScience (www.interscience.wiley.com). DOI 10.1002/lt.20179

ents, technical details of liver procurement, and ethical problems of using nonrelated live donors. As in most countries, including the United States and Japan, no legal restrictions exist in for living donation, local ethics committees confirm whether the candidates are appropriate potential donors. Voluntarism is the primary selection criterion and medical evaluation can only be started after confirmation of the voluntary nature of the donation.

Volumetric study using computed tomography scans is mandatory. For patients with advanced liver disease, a graft volume of greater than 40% of the recipient standard liver volume is necessary,[7] while for the living donor the remnant liver mass must be more than 30% of the whole liver.[8] The term "standard liver volume"[9] has become a key concept in LDLT. Estimated liver volume on computed tomography in healthy volunteers is proportional to body surface area and is calculated using the following formula:

$$\text{liver volume (mL)} = 706.2 \times \text{body surface area } (m^2) + 2.4$$

Donor safety must always be the primary consideration in LDLT. At least 3 cases of donor death have been reported in the United States[10] and 1 in Japan. Therefore, the selection criteria and management of the living donor must continue to be refined. Cherqui et al. reported on laparoscopic left lateral segmentectomy in a living donor for pediatric liver transplantation.[11] This laparoscopic technique was used in 8 donors, and early graft function was satisfactory in all cases. Unfortunately, 2 patients were complicated with hepatic arterial thrombosis, and 1 of them died. The application of laparoscopic donor hepatectomy for adult liver transplantation requires further technical advances but should be possible in the near future.

Small-for-Size Graft Problem

The major limitation of LDLT for adult recipients is the size of the graft that can be procured from a living donor, because a small-for-size graft might not meet the metabolic demands of an adult recipient.

Left Liver Graft

In the initial adult LDLT procedures, only a left liver graft was used. In 1998, the Shinshu group reported satisfactory results using a left liver graft in 13 patients.[12] The donor was selected if, based on computed tomography volume examination, the calculated size of the liver graft was larger than 30% of the recipient's standard liver volume. By January, 2004, the group had performed 95 adult LDLTs using left liver grafts. The 5-year graft and patient survival rates were 81% and 82%, respectively. Graft survival did not appear to be related to the graft volume / patient standard liver volume ratio. One-year graft survival was 83%, 83%, and 100% in patients who received grafts with graft volume / patient standard liver volume ratios ranging from 30% to 39%, 40% to 49%, and more than 50%, respectively. Their data indicate that left liver graft provides satisfactory results for appropriately selected recipients.

Miyagawa et al[13] reported on LDLT using the left liver grafts including the left-side caudate lobe (the Spiegel lobe and the left side of the paracaval portion of the caudate lobe). Takayama et al.[14] designed a similar procedure with direct anastomosis to the vena cava of the hepatic vein from the caudate lobe. The caudate lobe corresponds to only 3% to 4% of the whole liver volume. In conjunction with a left liver graft, however, the caudate lobe increases the graft weight by 8% to 12%.

Fifty-six percent of the patients in the University of Tokyo program received a left liver or left liver with caudate lobe graft with patient and graft 5-year-survival rates of 82% and 84%, respectively.[15] The strategy for selection of left or right liver graft, is influenced by the patient's preoperative condition,[16] as patients with advanced liver disease require a larger liver mass. The model for end-stage liver disease score[17] could become a satisfactory criterion for differentiating between high- and low-risk patients and therefore to determine the type of graft to use.

Extended Right Liver Graft

Use of right liver grafts has had a large impact on the results of adult LDLT. The Hong Kong group was the first to transplant a right liver graft including reconstruction of the middle hepatic vein (MHV) in 1996,[18] terming it an extended right liver graft. The outcome of the initial 8 donors and recipients were not without complications. One recipient died, and the recipients as well as the donors experienced high morbidity. The next 92 patients subsequently received extended right liver grafts with the following innovations: elimination of veno-venous bypass from the routine protocol, preservation of segment IV venous drainage in the donor, venoplasty of MHV and right hepatic vein into a single orifice for better venous return and easy vein reconstruction in recipients,[19] and preservation of blood supply to the right hepatic ducts. Over time, the mortality rate of the recipients decreased from 16% in the initial 50 cases to 0% in 50 more recent patients.

Right Liver Graft

In 1998, the University of Colorado group[20] introduced the right liver graft without reconstruction of the MHV trunk in adult LDLT. From January 1997 until

July 2003, the group performed 80 adult LDLTs. In the first 10 cases, in which the MHV branches of the graft were not preserved, 3 grafts were lost. Based on the group's preliminary experience, the resection line of the graft in the donor was moved to the left to preserve the MHV branches and their connections with the right hepatic vein (RHV).[21] The new transsection line was set between the right border of the MHV and the left margin of the gallbladder bed. In the subsequent 70 cases, no graft loss due to venous congestion was experienced.

Right Lateral Sector Graft

The small graft problem related to the left liver graft has been overcome by the use of a right liver graft. Right hepatectomy, however, imposes an increased surgical risk on the donor, due to the reduced residual liver volume. Fan and associates[8] concluded that safe donation was possible only when the estimated residual liver volume was over 30%. A recent report indicated that in 25% of the potential donors the right liver had an estimated volume of more than 70% of the whole.[22] Thus, based on these volumetric considerations, right hepatectomy is not possible for some potential donors.

The University of Tokyo group was the first to design the right lateral sector graft, consisting of segments VI and VII.[23] The indication for harvesting this type of graft includes a right liver of over 70% of the estimated total donor liver volume, while the estimated volume of the 2 right lateral sectors is greater than that of the left liver. In addition, this graft needs to be larger than 40% of the recipient's standard liver volume. Between January, 2000, and April, 2001, 6 of 32 adult-to-adult LDLTs with a right lateral sector graft[24] were performed at our institution. The postoperative course was uneventful in all donors. All recipients survived the operation. Three patients experienced bile leakage from the dissection plane of the graft. By January, 2004, 16 adult patients had received right lateral sector grafts, and 15 patients were still alive, with normal graft function.

From a technical point of view, careful attention must be paid to transecting the bile duct of the right lateral sector. When the right lateral duct enters the common bile duct separately (caudal right lateral duct), the duct is divided at its origin. Otherwise, after the right portal branch is dissected first and pulled cranially, the right lateral duct is dissected as far as possible from surrounding connective tissues.

Dual Grafts

Lee et al. were the first to devise dual grafts from two living donors.[25] Most commonly, both donors donate the left liver or left lateral segments, although various combinations of graft types can be used.[26] The first left liver graft is orthotopically implanted at the original left position. The second left liver graft is rotated 180 degrees and positioned heterotopically in the right upper quadrant fossa. Modifications in the surgical technique are needed for implantation of the second graft. Because the bile duct is now located behind the portal vein and the hepatic artery, bile duct reconstruction is necessary before reconstruction of the vessels. An interposition vein graft might be necessary for the reconstruction of the hepatic or portal vein, because the second left liver graft is too small to bridge the distance between the hepatic and portal veins. By the end of 2003, this technique was used in 93 patients with satisfactory results. Also, the Kyoto group has implanted dual grafts in 1 adult patient.[27] However, the procedure has limited appeal due to the high requirements of economic and medical resources: 3 operating rooms and 3 surgical teams are required simultaneously. Therefore, liver transplantation using dual grafts is clearly technically demanding and not widely performed around the world.

MHV Reconstruction in Right Liver Graft

A right liver graft without the MHV trunk can cause severe congestion of the right paramedian sector. However, a strategy to prevent such congestion or the necessity to reconstruct the MHV has not been discussed in detail.

Cons

In the meeting, Igal Kam et al. reported that only 2 of 70 patients who received a right liver graft without the MHV trunk required reconstruction of the MHV tributaries. Their research stated that, in general, the MHV can be ligated during the procurement of right liver graft, as connecting the MHV to the vena cava is unnecessary. They emphasized that reconstruction of the MHV is mainly indicated when right hepatic vein of the graft is small. This policy might[50] affect the selection of the potential recipients of the right hemiliver graft. Whole liver grafts from deceased donors can be used for poor-risk patients, while hemiliver grafts from living donors can be used for good-risk patients who can tolerate lesser parenchymal liver mass.

Pros

In contrast, Lee et al. aggressively reconstructed the MHV tributaries in right liver grafts without the MHV trunk and named this type of graft a modified right liver graft.[28] As it is difficult to predict the degree of right paramedian sector congestion, they recommended rou-

tine reconstruction of MHV tributary veins. Ghobrial et al.[29] also recommended reconstruction of the MHV tributary veins when RHV in graft was less than 1.5 cm in diameter. From July, 1997, to February, 1998, 2 of 5 right lobe grafts without MHV drainage reconstruction were complicated with severe congestion of the paramedian sector. Since then, 42 adult recipients, who received right liver grafts with fairly sized MHV tributaries, underwent reconstruction of these veins.[30] All MHV tributaries with a size of >5 mm were preserved during donor hepatectomy and were reconstructed with the autogenous interposition vein grafts of the recipient during bench surgery.

Indications

It remains unclear whether all modified right liver grafts require MHV drainage. Sano et al.[31] proposed clear criteria for MHV reconstruction. During the donor operation, hepatic venous congestion in the right paramedian sector was investigated after transsection of the liver parenchyma. First, liver surface discoloration in the right paramedian sector was observed after 5 minutes of simultaneous clamping of MHV tributaries and the right hepatic artery. Next, intra-operative Doppler ultrasonography was performed after declamping only the hepatic artery. If the portal flow of the paramedian sector was found to be hepatofugal, the area was considered congested. If the congestive area was significant, as determined by the clamping test and ultrasonography, bench reconstruction of MHV tributaries was performed. Using these criteria, we performed MHV reconstruction in 18 of 30 grafts, resulting in an uneventful functional recovery of all grafts.[32] The necessity of short hepatic vein reconstruction can be determined using the same criteria.

Biliary Reconstruction

Biliary reconstruction remains a significant source of morbidity in liver transplantation, with a complication rate of 6% to 47%. Complications include anastomotic leakage and stenosis, problems related with T or stent tubes, and rarely, nonanastomotic strictures or intrahepatic bilomas. These complications can lead to cholangitis, sepsis, and eventually retransplantation and death. Therefore, due to the diminished functional reserve of the hemiliver graft, it might lead to serious complications in adult LDLT.

Initially, the type of biliary anastomosis commonly used in LDLT was the hepaticojejunostomy. Kiuchi and colleagues[33] were the first to report preliminary results of duct-to-duct biliary reconstruction in adult LDLT. Now duct-to-duct biliary reconstruction is enthusiastically performed in a growing number of programs.[34-39] The reports advocate the advantages of duct-to-duct biliary reconstruction over hepaticojejunostomy, such as an aseptic surgical field and shorter duration for reconstruction. The physiologic bilioenteric circulation and bowel continuity can also be preserved, preventing delayed peristalsis. Duct-to-duct reconstruction allows easy endoscopic access to the biliary tree for diagnostic and therapeutic instrumentation and management. For the management of biliary stenosis, the duct-to-duct anastomosis is usually converted to the hepaticojejunostomy. However, the Kyoto group[40] recently reported that 13 of 14 patients were successfully treated with an internal stent. The endoscopic approach appears to be a therapeutic alternative to reoperation. However, the follow-up period in these patients is still short. Long-term postoperative observation is necessary to confirm the safety and feasibility of this procedure.

Viral Hepatitis and Hepatocellular Carcinoma

Hepatitis B Virus

The results of liver transplantation in patients with hepatitis B (HBV) have improved significantly as a result of the rapid evolution in strategies for postoperative prophylaxis. Hepatitis B immunoglobulin, which is costly, was the first effective prophylactic agent. Lamivudine monotherapy prevents emergence of viral mutants. Now, combination therapy with hepatitis B immunoglobulin and lamivudine has become a widely adopted approach. Other nucleotide analogs, such as adefovir, are promising alternative agents.

The HBV prophylactic regimen at Queen Mary Hospital in Hong Kong consists of lamivudine monotherapy,[41,42] while adefovir is reserved for breakthrough reinfection after transplantation. Lo et al. performed 180 liver transplants for HBV-positive patients (120 LDLT and 60 grafts from deceased donors). The 5-year cumulative mutant-free survival was 86%. In contrast, the Tokyo University group[43] presented satisfactory results of LDLT for HBV (n = 20) using hepatitis B immunoglobulin monotherapy. The use of lamivudine was limited to the perioperative period to avoid generating mutants.

One recent report of active production of HBV-antibodies after liver transplantation suggests the possibility of adoptive transfer of immunity against HBV through a liver graft from an immune donor.[44] Active immunization with standard hepatitis B vaccines was recently reported, with conflicting results.[45]

Hepatitis C Virus

Early experience suggested rapid and severe recurrence of hepatitis C (HCV) following adult LDLT.

Ghobrial et al.[46] reported that the time interval to HCV recurrence (n = 11) was significantly shorter in LDLT patients than in patients who received grafts from deceased donors (n = 510). The University of Colorado group[47] reported that serum alanine aminotransferase and total bilirubin levels increased more rapidly after the operation in LDLT patients (n = 24) than in cadaveric graft recipients (n = 41). In addition, LDLT patients had greater serum aspartate aminotransferase levels at 1, 3, and 6 months, compared with a matched group of cadaveric controls.[48]

Gaglio et al.[49] reported that the overall incidence of severe sequelae of hepatitis C recurrence—either cholestatic hepatitis, grade III-IV inflammation, and/or hepatitis C–induced graft failure requiring retransplantation—were not different between cadaveric grafts (n = 45) and those grafts from living liver donors (n = 23). However, the morbidity of cholestatic hepatitis C was more severe in LDLT patients (0% vs. 17%, respectively; $P = .001$). These preliminary reports indicate that more intensive antiviral therapy might be necessary for recipients of living donor grafts. All of these reports, however, have some limitations, which include small numbers of patients, lack of standard virologic evaluation, and short-term follow-up. The results must be confirmed in larger, multicenter studies.

Hepatocellular Carcinoma

LDLT is an established therapeutic option for patients with hepatocellular carcinoma. From 1990 to the end of 2002, LDLT for hepatocellar carcinoma was performed in 225 cases in Japan.

Prof. Furukawa from the Hokkaido University reported in the Tokyo meeting that 160 patients were alive, with a recurrence rate of 5%, while 65 patients were dead, with a recurrence rate of 32%. Multivariate analysis revealed that alpha-fetoprotein levels, tumor size, and invasion of hepatic and portal veins are significant predictors for outcome. When the subjects were categorized into two groups (patients meeting the Milan criteria, and those beyond), difference both in patient and recurrence-free survival reached significance (76% vs. 52%, respectively; $P = .001$; and 76% vs. 50%,respectively; $P = .001$).

Conclusions

During the 10-year period, many technical innovations have been developed for LDLT, contributing to a better patient outcome. LDLT was originally devised and performed in countries where organs from deceased donors are extremely scarce. The contributions made by Asian countries with regard to the design of several graft types, including left liver graft with caudate lobe, right liver, modified right liver, and right lateral sector grafts, are noteworthy. A recent review by Grewal,[50] however, has failed to acknowledge the significant Asian contribution to LDLT.

In LDLT, the physical and psychological sacrifice by the donor is significant and is associated with high expectations regarding a good outcome for themselves and the recipient. We should not be satisfied with the present outcome and need to strive to achieve 0% donor mortality.[15] Firm criteria for graft selection and further technical advances will be helpful in reaching this goal.

References

1. Raia S, Nery JR, Mies S. Liver transplantation from live donors. Lancet 1989;2:497.
2. Strong RW, Lynch SV, Ong TH, Matsunami H, Koido Y, Balderson GA. Successful liver transplantation from a living donor to her son. N Engl J Med 1990;322:1505–1507.
3. Hashikura Y, Makuuchi M, Kawasaki S, Matsunami H, Ikegami T, Nakazawa Y, et al. Successful living-related partial liver transplantation to an adult patient. Lancet 1994;343:1233–1234.
4. Adam R, McMaster P, O'Grady JG, Castaing D, Klempnauer JL, Jamieson N, et al. European Liver Transplant Association. Evolution of liver transplantation in Europe: Report of the European Liver Transplant Registry. Liver Transpl 2003;9:1231–1243.
5. Data from US transplant organization. Available at: http://www.ustransplant.org/index.php. Accessed on March 27, 2004.
6. The Japanese Liver Transplantation Society. Liver Transplantation in Japan. Registry by the Japanese Liver Transplantation Society [Japanese]. Jpn J Transplant 2004;38:401–408.
7. Lo CM, Fan ST, Liu CL, Chan JK, Lam BK, Lau GK, et al. Minimum graft size for successful living donor liver transplantation. Transplantation 1999;68:1112–1116.
8. Fan ST, Lo CM, Liu CL, Yong BH, Chan JK, Ng IO. Safety of donors in live donor liver transplantation using right lobe grafts. Arch Surg 2000;135:336–340.
9. Urata K, Kawasaki S, Matsunami H, Hashikura Y, Ikegami T, Ishizone S, et al. Calculation of child and adult standard liver volume for liver transplantation. Hepatology 1995;21:1317–1321.
10. Surman OS. Transplantation of the right hepatic lobe. N Engl J Med 2002;347:618.
11. Cherqui D, Soubrane O, Husson E, Barshasz E, Vignaux O, Ghimouz M, et al. Laparoscopic living donor hepatectomy for liver transplantation in children. Lancet 2002;359:392–396.
12. Kawasaki S, Makuuchi M, Matsunami H, Hashikura Y, Ikegami T, Nakazawa Y, et al. Living related liver transplantation in adults. Ann Surg 1998;227:269–274.
13. Miyagawa S, Hashikura Y, Miwa S, Ikegami T, Urata K, Terada M, et al. Concomitant caudate lobe resection as an option for donor hepatectomy in adult living related liver transplantation. Transplantation 1998;66:661–663.
14. Takayama T, Makuuchi M, Kubota K, Sano K, Harihara Y, Kawarasaki H. Living-related transplantation of left liver plus caudate lobe. J Am Coll Surg 2000;190:635–658.
15. Sugawara Y, Makuuchi M, Kaneko J, Ohkubo T, Matsui Y,

Imamura H, et al. Living-donor liver transplantation in adults: Tokyo University experience. J Hepatobiliary Pancreat Surg 2003;10:1–4.
16. Sugawara Y, Makuuchi M, Kaneko J, Kokudo N. MELD score for selection of patients to receive a left liver graft. Transplantation 2003;75:573–574.
17. Wiesner RH, McDiarmid SV, Kamath PS, Edwards EB, Malinchoc M, Kremers WK, et al. MELD and PELD: Application of survival models to liver allocation. Liver Transpl 2001;7:567–580.
18. Lo CM, Fan ST, Liu CL, Wei WI, Lo RJ, Lai CL, et al. Adult-to-adult living donor liver transplantation using extended right lobe grafts. Ann Surg 1997;226:261–269.
19. Lo CM, Fan ST, Liu CL, Wong J. Hepatic venoplasty in living-donor liver transplantation using right lobe graft with middle hepatic vein. Transplantation 2003;75:358–360.
20. Wachs ME, Bak TE, Karrer FM, Everson GT, Shrestha R, Trouillot TE, et al. Adult living donor liver transplantation using a right hepatic lobe. Transplantation 1998;66:1313–1316.
21. Bak T, Wachs M, Trotter J, Everson G, Trouillot T, Kugelmas M, et al. Adult-to-adult living donor liver transplantation using right-lobe grafts: Results and lessons learned from a single-center experience. Liver Transpl 2001;7:680–686.
22. Leelaudomlipi S, Sugawara Y, Kaneko J, Matsui Y, Ohkubo T, Makuuchi M. Volumetric analysis of liver segments in 155 living donors. Liver Transpl 2002;8:612–614.
23. Sugawara Y, Makuuchi M, Takayama T, Mizuta K, Kawarasaki H, Imamura H, et al. Liver transplantation using a right lateral sector graft from a living donor to her granddaughter. Hepatogastroenterology 2001;48:261–263.
24. Sugawara Y, Makuuchi M, Takayama T, Imamura H, Kaneko J. Right lateral sector graft in adult living-related liver transplantation. Transplantation 2002;73:111–114.
25. Lee S, Hwang S, Park K, Lee Y, Choi D, Ahn C, et al. An adult-to-adult living donor liver transplant using dual left lobe grafts. Surgery 2001;129:647–650.
26. Lee SG, Hwang S, Park KM, Kim KH, Ahn CS, Lee YJ, et al. Seventeen adult-to-adult living donor liver transplantations using dual grafts. Transplant Proc 2001;33:3461–3463.
27. Kaihara S, Ogura Y, Kasahara M, Oike F, You Y, Tanaka K. A case of adult-to-adult living donor liver transplantation using right and left lateral lobe grafts from 2 donors. Surgery 2002;131:682–684.
28. Lee S, Park K, Hwang S, Lee Y, Choi D, Kim K, et al. Congestion of right liver graft in living donor liver transplantation. Transplantation 2001;71:812–814.
29. Ghobrial RM, Hsieh CB, Lerner S, Winters S, Nissen N, Dawson S, et al. Technical challenges of hepatic venous outflow reconstruction in right lobe adult living donor liver transplantation. Liver Transpl 2001;7:551–555.
30. Gyu Lee S, Min Park K, Hwang S, Hun Kim K, Nak Choi D, Hyung Joo S, et al. Modified right liver graft from a living donor to prevent congestion. Transplantation 2002;74:54–59.
31. Sano K, Makuuchi M, Miki K, Maema A, Sugawara Y, Imamura H, et al. Evaluation of hepatic venous congestion: Proposed indication criteria for hepatic vein reconstruction. Ann Surg 2002;236:241–247.
32. Sugawara Y, Makuuchi M, Sano K, Imamura H, Kaneko J, Ohkubo T, et al. Vein reconstruction in modified right liver graft for living donor liver transplantation. Ann Surg 2003;237:180–185.
33. Kiuchi T, Ishiko T, Nakamura T, Egawa H, Uemoto S, Inomata Y, et al. Duct-to-duct biliary reconstruction in living donor liver transplantation. Transplant Proc 2001;33:1320–1321.
34. Azoulay D, Marin-Hargreaves G, Castaing D, Adam R, Bismuth H. Duct-to-duct biliary anastomosis in living related liver transplantation: The Paul Brousse technique. Arch Surg 2001;136:1197–1200.
35. Sugawara Y, Makuuchi M, Sano K, Ohkubo T, Kaneko J, Takayama T. Duct-to-duct biliary reconstruction in living-related liver transplantation. Transplantation 2002;73:1348–1350.
36. Ishiko T, Egawa H, Kasahara M, Nakamura T, Oike F, Kaihara S, et al. Duct-to-duct biliary reconstruction in living donor liver transplantation utilizing right lobe graft. Ann Surg 2002;236:235–240.
37. Takatsuki M, Yanaga K, Okudaira S, Furui J, Kanematsu T. Duct-to-duct biliary reconstruction in adult-to-adult living donor liver transplantation. Clin Transpl 2002;16:345–349.
38. Soejima Y, Shimada M, Suehiro T, Kishikawa K, Minagawa R, Hiroshige S, et al. Feasibility of duct-to-duct biliary reconstruction in left-lobe adult-living-donor liver transplantation. Transplantation 2003;75:557–559.
39. Sugawara Y, Sano K, Kaneko J, Akamatsu N, Kishi Y, Kokudo N, et al. Duct-to-duct biliary reconstruction for living donor liver transplantation: Experience of 92 cases. Transplant Proc 2003;35:2981–2982.
40. Hisatsune H, Yazumi S, Egawa H, Asada M, Hasegawa K, Kodama Y, et al. Endoscopic management of biliary strictures after duct-to-duct biliary reconstruction in right-lobe living-donor liver transplantation. Transplantation 2003;76:810–815.
41. Lo CM, Cheung ST, Lai CL, Liu CL, Ng IO, Yuen MF, et al. Liver transplantation in Asian patients with chronic hepatitis B using lamivudine prophylaxis. Ann Surg 2001;233:276–281.
42. Lo CM, Fan ST, Liu CL, Lai CL, Wong J. Prophylaxis and treatment of recurrent hepatitis B after liver transplantation. Transplantation 2003;75(3 Suppl):S41–S44.
43. Sugawara Y, Makuuchi M, Kaneko J, Akamatsu N, Imamura H, Kokudo N. Living donor liver transplantation for hepatitis B cirrhosis. Liver Transpl 2003;9:1181–1184.
44. Lo CM, Fung JT, Lau GK, Liu CL, Cheung ST, Lai CL, et al. Development of antibody to hepatitis B surface antigen after liver transplantation for chronic hepatitis B. Hepatology 2003;37:36–43.
45. Bienzle U, Gunther M, Neuhaus R, Vandepapeliere P, Vollmar J, Lun A, et al. Immunization with an adjuvant hepatitis B vaccine after liver transplantation for hepatitis B-related disease. Hepatology 2003;38:811–819.
46. Ghobrial RM, Amersi F, Farmer DG, Chen P, Anselmo DM, Baquerizo A, et al. Rapid and severe early HCV recurrence following adult living donor liver transplantation. Am J Transplant 2002;2(Suppl 3):163.
47. Taniguchi M, Wachs M, Bak T, Trotter J, Kugelmas M, Everson G, et al. Hepatitis C recurrence in living donor liver transplantation. Am J Transplant 2002;2(Suppl 3):138.
48. Trotter JF, Schiano T, Wachs M, Kim-Schluger L, Bak T, Everson G, et al. Preliminary report: Hepatitis C occurs earlier and is more severe in living donor liver transplant recipients [abstract]. Am J Transplant 2001;1:316A.
49. Gaglio PJ, Malireddy S, Levitt BS, Lapointe-Rudow D, Lefkowitch J, Kinkhabwala M, et al. Increased risk of cholestatic hepatitis C in recipients of grafts from living versus cadaveric liver donors. Liver Transpl 2003;9:1028–1035.
50. Grewal HP. Impact of surgical innovation on liver transplantation. Lancet 2002;359:368–370.

SURGICAL REPAIR FOR LATE-ONSET HEPATIC VENOUS OUTFLOW BLOCK AFTER LIVING-DONOR LIVER TRANSPLANTATION

NOBUHISA AKAMATSU, YASUHIKO SUGAWARA, JUNICHI KANEKO, YOJI KISHI, TAKASHI NIIYA, NORIHIRO KOKUDO, AND MASATOSHI MAKUUCHI

The incidence of hepatic venous complications in partial liver transplantation is more frequent than that in whole liver transplantation. There are no reports of a surgical strategy for hepatic venous outflow block (HVOB) after living-donor liver transplantation. HVOB was diagnosed when the pull-through pressure gradient across the anastomotic site was over 5 mm Hg. Reoperation for venous anastomosis was performed if the angioplasty was unsuccessful. After dissection around the hepatic venous anastomotic site, a patch venoplasty of the anastomosis was performed. When the inferior vena cava was constricted, venoatrial anastomosis was performed. In 6 years, 5 of 223 patients experienced HVOB. Balloon angioplasty was successfully performed in two patients, a patch venoplasty of the anastomosis in two, and venoatrial anastomosis in one. In all patients, the ascites stopped. HVOB must be diagnosed as soon as possible with Doppler ultrasound and venography. Prompt surgical revision can salvage the grafts.

The limited supply of cadaveric donor organs for liver transplantation has fostered the use of segmental liver graft with reduced-size grafts, split-liver transplantation, and living-donor liver transplantation (LDLT). The overall survival rates of recipients using these technical innovations is equivalent to those achieved with whole liver grafts. Nonetheless, the use of a partial liver graft demands more meticulous surgical procedures, resulting in an increase in various vascular complications. The incidence of hepatic venous complication in partial liver transplantation is more frequent (2%–13%) (*1, 2*) than that in whole liver transplantation (1%–2%) (*2, 3*).

The occurrence of hepatic venous outflow block (HVOB) can be divided into two categories on the basis of the timing of onset (*3*): early, in the immediate postoperative period; and late, thereafter. The cause of early-onset HVOB often includes technical problems, and late-onset HVOB might be caused by subsequent fibrosis with inflammatory processes such as bile leakage, abscess formation, and compression or twisting of the anastomosis caused by the graft growth (*4*). Graft salvage is difficult without prompt revision in both types of HVOB. Our surgical techniques for HVOB are presented in this article.

From January 1996 to April 2003, 223 patients underwent LDLT at our hospital (153 adults and 70 children). The mean follow-up period was 603 days. The indications for LDLT in these patients included biliary atresia (n=69), primary biliary cirrhosis (n=43), hepatitis C virus cirrhosis (n=33), hepatitis B virus cirrhosis (n=22), fulminant hepatic failure (n=18), cryptogenic cirrhosis (n=13), metabolic disorder (n=13), primary sclerosing cholangitis (n=6), and autoimmune hepatitis (n=6). The most commonly used type of graft was the left liver with or without the caudate lobe (n=84), followed by right liver (n=73), segments II and III (n=51), and right lateral sector (segments VI and VII, n=15). The transplantation procedure and donor selection criteria are described elsewhere (*5*).

HVOB was suspected with massive pleural effusion and ascites and one of the following Doppler ultrasound (US) findings: (1) a decrease in hepatic vein flow velocity; (2) a flat waveform of the hepatic vein, especially in cases with a previously multiphasic pattern (*6*); (3) mild dilatation of the distal venous tributaries; and (4) a decrease in portal flow. When HVOB was suspected on the basis of US findings, venography was performed. Patients can be diagnosed with HVOB when the pull-through pressure gradient across the anastomotic site is over 5 mm Hg (*7*). Balloon angioplasty was performed first, followed by 1 week of intravenous administration of heparin (200 U/kg/day). Reoperation for venous anastomosis was performed when the angioplasty was unsuccessful.

When dissection around the hepatic venous anastomotic site was possible, a patch venoplasty of the anastomosis was performed. After vascular exclusion, the right wall of the suprahepatic inferior vena cava (IVC) above the anastomosis was incised longitudinally and passed through the anastomosis and extended to the left and middle hepatic veins (Fig. 1). The IVC defect was covered by a triangle-shaped cryopreserved venous patch, allowing the patch to expand outside. Sutures were continuous using 6-0 monofilament. The vein grafts were provided by the University of Tokyo Tissue Bank. They were obtained from cadavers or non–heart-beating donors within 24 hr after cardiac arrest after obtaining informed consent. When inflammatory changes around the IVC were severe and the IVC was constricted, a venoatrial anastomosis was performed. The pericardium was incised. The bottom of the right atrium was then side-clamped and anastomosed with the hepatic veins of the graft (Fig. 2).

Five patients (2%) experienced HVOB. HVOB was not suspected in any other patients in the series. The demo-

This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan; a Grant-in-Aid for Research on Human Genome, Tissue Engineering, Food Biotechnology, Health Sciences Research; and a Grant-in-Aid for Clinical Study on Indication and Effectiveness of Liver Transplantation for Patients with Hepatocellular Carcinoma from the Ministry of Health, Labor and Welfare of Japan.

Artificial Organ and Transplantation Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, Tokyo, Japan.

Address correspondence to: Yasuhiko Sugawara, M.D., Artificial Organ and Transplantation Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. Email: yasusuga-tky@umin.ac.jp.

Received 1 November 2003.

Revision requested 18 November 2003. Accepted 16 December 2003.

DOI: 10.1097/01.TP.0000131162.35391.9D

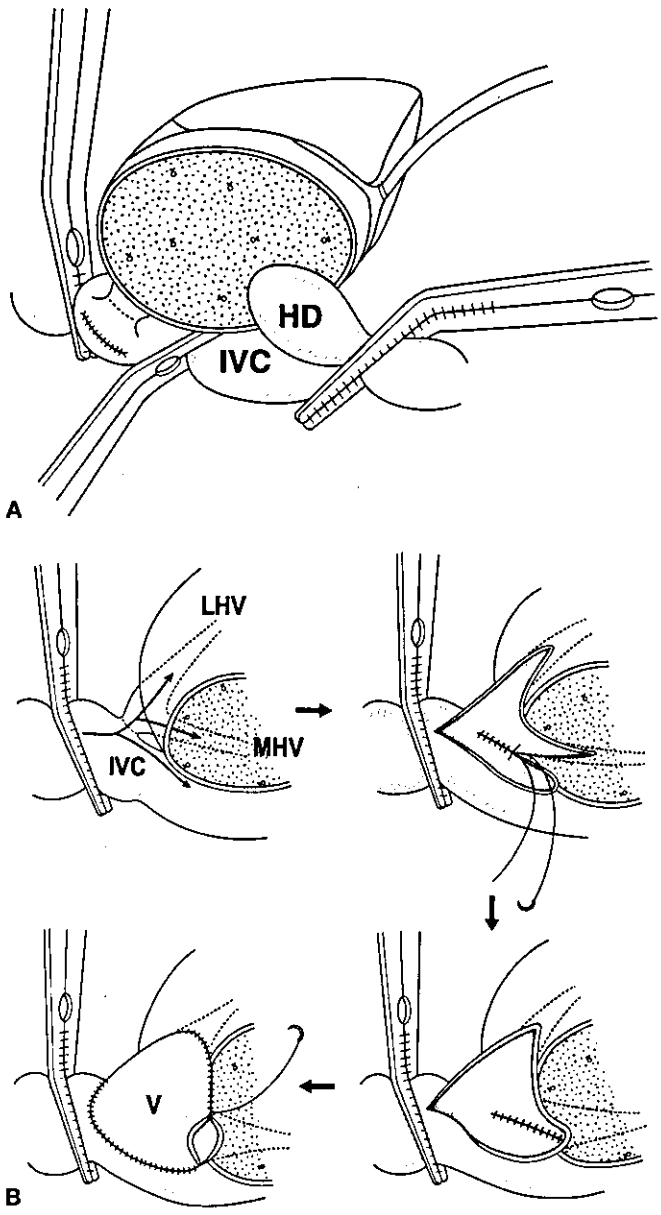

FIGURE 1. **A patch plasty for hepatic venous reconstruction. (A) Total vascular occlusion and cold perfusion of the graft. (B) Venoplasty of the stenotic anastomosis using a venous patch. HD, Hepatic artery, portal vein, and common bile duct; LHV, left hepatic vein; MHV, middle hepatic vein; IVC, inferior vena cava; V, venous patch.**

graphics of the five HVOB patients are shown in Table 1. In two patients, balloon angioplasty was successfully performed. The profile of the other three patients in whom a revision operation was necessitated is described in detail.

In patient 2, during LDLT, a fresh femoral venous graft from a cadaver was used as a conduit from the superior mesenteric vein of the recipient to the graft portal vein because the native portal vein was completely thrombosed. Hepatic venous reconstruction was performed using the technique described previously (*8*). The patient's postoperative course was uneventful, and the patient was symptom-free for 4 years after LDLT. Ascites retention occurred and was first

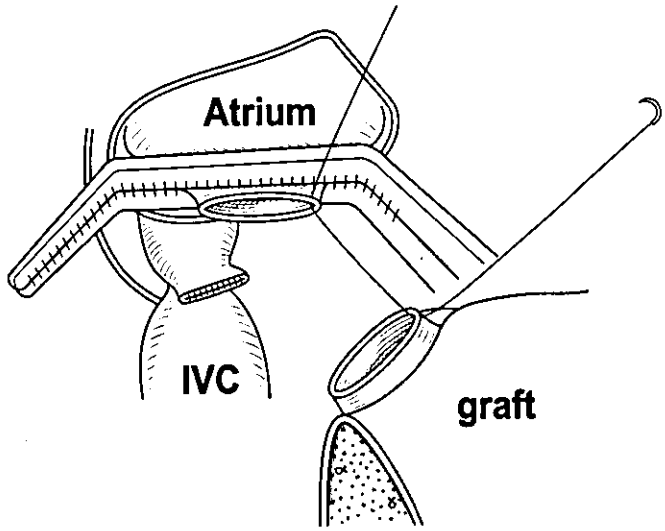

FIGURE 2. **A venoatrial anastomosis. The pericardium was incised. The bottom of the right atrium was then side-clamped and anastomosed with the hepatic veins of the graft. IVC, Inferior vena cava.**

managed with diuretics and periodic abdominocentesis but increased beyond conservative treatment 5 years after LDLT. Doppler US indicated that hepatic venous flow was still biphasic in its waveform and maintained its velocity (30 cm/sec). The portal flow was slow, down to 5 cm/sec. Celiac angiography revealed that the jumping graft was stenotic, probably because of thrombosis. The venogram indicated hepatic venous stenosis with a 7-mm Hg pull-through pressure gradient. The patient underwent surgical venoplasty with the technique shown in Figure 1. After thrombectomy near the anastomotic site of the superior mesenteric vein, portal inflow was reinstated using a cryopreserved femoral vein from a cadaver between the superior mesenteric vein (end-to-side) and umbilical portion of the graft (end-to-side). The ascites completely stopped within 2 weeks after the revision.

In patient 4, who weighed 13 kg, ascites and pleural effusion increased over 700 mL/day, 5% of the patient's body weight, 1 month after the LDLT. On postoperative day (POD) 54, a venogram was obtained using a percutaneous transhepatic approach that revealed hepatic venous obstruction and an 18-mm Hg pull-through pressure gradient. Successive angioplasty using a 12-mm-diameter balloon catheter was performed. The amount of ascites and pleural effusion transiently decreased just after the angioplasty. The hepatic vein, however, thrombosed 1 month after the angioplasty. Retransplantation using the left liver graft from the child's mother was performed 8 months after the first LDLT. The ABO blood-type was incompatible. Because severe fibrosis was observed around the previous venous anastomotic site and suprahepatic IVC, a venoatrial anastomosis was performed. The patient was discharged from the hospital 104 days after the operation; however, the child died because of chronic rejection 28 months after the first LDLT.

In patient 5, on POD 47, open drainage was performed for biloma formation in the right subphrenic space. After the operation, the amount of ascites and right pleural effusion gradually increased. On POD 110, total fluid was over 5,000 mL/day, which was 12% of the body weight. Doppler US

TABLE 1. Profile of the patients with hepatic venous outflow block

Patient	Age (yr)	Gender	Indication	Graft type	Onset (mo after LDLT)	Angioplasty (times)	LDLT to reoperation	Results
1	1	F	BA	SII+III	3	2	—	Alive 74 mo
2	48	F	PBC	Left liver	48	1	Patch plasty	Alive 65 mo
3	12	M	BA	LL+CL	5	3	—	Died 11 mo for biliary infection
4	2	M	BA	SII+III	2	1	Venoatrial anastomosis	Died 28 mo for chronic rejection
5	14	F	FH	LL+CL	2	3	Patch plasty	Alive 9 mo

BA, Biliary atresia; PBC, primary biliary cirrhosis; FH, fulminant failure; LDLT, living-donor liver transplantation; LL+CL, left liver with caudate lobe; SII+III, segments II and III; mo, months after transplantation.

revealed that the hepatic vein waveform was monophasic and the flow speed was 7.6 cm/sec. Venography revealed severe stenosis of the hepatic venous anastomosis, and the patient was diagnosed with HVOB. The pull-through pressure gradient was 19 mm Hg. Balloon angioplasty was performed three times at 14-day intervals with transjugular or transsubclavian catheterization. Even after the angioplasty, the amount of ascites did not decrease. The preoperative splenic volume was 240 mL, which increased to 880 mL in the post-LDLT period. On POD 160, patch venoplasty was performed as shown in Figure 1. Doppler US after the revision revealed a biphasic sharp waveform with the peak flow speed of 120 cm/sec. The amount of ascites dramatically decreased within 10 days after the revision.

Balloon angioplasty might be the first line of treatment for HVOB. Buell and colleagues (*2*) reported a 75% success rate (six of eight). In spite of their successful results, generally balloon angioplasty alone might yield unsatisfactory results as in our cases because of the fibrotic nature of the lesions. Stenosis refractory to angioplasty might be an indication for stent placement. Recent studies on the results of stenting for HVOB (*2*) reported a 72% success rate (18 of 25). In partial liver transplantation, as in whole liver transplantation using piggyback techniques, stenting is not always secure. Double stents might be necessary—one in the IVC and the other across the venous anastomotic site—which can slip off. In our patients, we chose surgical revision instead of stent placement because in patients with partial liver grafts, stent dislocation might occur along with graft regeneration and patient growth in pediatrics.

There are few reports of successful surgical treatment for late-onset HVOB. Lerut and associates (*9*) reported that one patient with a whole liver graft died during the revision operation for HVOB. Eid and colleagues reported successful whole liver graft salvage by retrohepatic cavoatrial shunt using a 16-mm, ring-enforced polytetrafluoroethylene graft (*10*). A French group (*3*) reported a 2% incidence of venous complications (21 of 1,361). Of these, four patients experienced late-onset HVOB. Details of the therapy and the results, however, were not reported. In pediatric LDLT cases, HVOB is treated with angioplasty (*4*) and stenting. There are no reports of a surgical strategy for HVOB, especially in LDLT. The severe liver graft shortage in Japan has made retransplantation extremely difficult, which forces us to choose the most reliable treatment for HVOB.

In an LDLT series of 223 patients, there were 5 cases of late-onset HVOB. It is important to diagnose HVOB as soon as possible with Doppler US and venography before irreversible congestive changes occur in the grafts. Prompt surgical revision could salvage the grafts, although it requires meticulous surgical technique.

REFERENCES

1. Kinkhabwala MM, Guarrera JV, Leno R, et al. Outflow reconstruction in right hepatic live donor liver transplantation. Surgery 2003; 133: 243.
2. Buell JF, Funaki B, Cronin DC, et al. Long-term venous complications after full-size and segmental pediatric liver transplantation. Ann Surg 2002; 236: 658.
3. Navarro F, Moine MC, Fabre JM, et al. Specific vascular complications of orthotopic liver transplantation with preservation of the retrohepatic vena cava: Review of 1361 cases. Transplantation 1999; 68: 646.
4. Egawa H, Tanaka K, Uemoto S, et al. Relief of hepatic vein stenosis by balloon angioplasty after living-related donor liver transplantation. Clin Transplant 1993; 7: 306.
5. Sugawara Y, Makuuchi M, Sano K, et al. Vein reconstruction in modified right liver graft for living donor liver transplantation. Ann Surg 2003; 237: 180.
6. Ko EY, Kim TK, Kim PN, et al. Hepatic vein stenosis after living donor liver transplantation: Evaluation with Doppler US. Radiology 2003; 229: 806.
7. Sze DY, Semba CP, Razavi MK, et al. Endovascular treatment of hepatic venous outflow obstruction after piggyback technique liver transplantation. Transplantation 1999; 68: 446.
8. Takayama T, Makuuchi M, Kawasaki S, et al. Outflow Y-reconstruction for living related partial hepatic transplantation. J Am Coll Surg 1994; 179: 226.
9. Lerut J, Tzakis AG, Bron K, et al. Complications of venous reconstruction in human orthotopic liver transplantation. Ann Surg 1987; 205: 404.
10. Eid A, Rahamimov R, Ilan Y, et al. Cavoatrial shunt: A graft salvage procedure for suprahepatic caval anastomosis obstruction after liver transplantation. Liver Transpl Surg 1998; 4: 239.

Duct-to-Duct Biliary Reconstruction in Adult Living-Donor Liver Transplantation

Ender Dulundu,[1,2] Yasuhiko Sugawara,[2,3] Keiji Sano,[2] Yoji Kishi,[2] Nobuhisa Akamatsu,[2] Junichi Kaneko,[2] Hiroshi Imamura,[2] Norihiro Kokudo,[2] and Masatoshi Makuuchi[2]

Background. Bile duct-to-duct reconstruction is now used in living-donor liver transplantation (LDLT) for adult patients.

Methods. The results of duct-to-duct reconstruction were retrospectively analyzed. The subjects were 81 adult patients who underwent LDLT at the University of Tokyo Hospital with a follow-up period of at least 1 year. The hilar plate of the recipient was dissected to at least the second-order branch of the bile ducts. Duct-to-duct anastomosis was performed with interrupted sutures, and an external stent tube was inserted from the orifice opposite the hilar plate.

Results. During the observation period (median, 664 days), biliary complications were observed in 26 cases (32%). The complications included bile juice leakage at the anastomosis or dissection plane of the graft in 12 patients, anastomotic stenosis in 10 patients, and tube trouble in 6 patients. Two patients had bile juice leakage followed by stenosis. Of the 26 patients, 21 required surgical revision.

Conclusions. The current technique did not reduce morbidity as expected. Further technical advancement and refinement are needed for better results.

Keywords: Bile leakage, Anastomotic stricture, Standard liver volume.

(*Transplantation* 2004;78: 574–579)

Various refinements in surgical techniques, organ preservation, and immunosuppressive management have reduced the incidence of complications after liver transplantation. Biliary tract complications, however, continue to be a significant cause of morbidity after liver transplantation (*1*, *2*).

Living-donor liver transplantation (LDLT) was initially performed for pediatric patients with biliary atresia. Therefore, the type of biliary anastomosis was limited to hepaticojejunostomy. Now, LDLT is widely performed for adults, and duct-to-duct direct biliary reconstruction is enthusiastically presented in some institutions (*3–7*). These reports advocate the advantages of duct-to-duct biliary reconstruction over hepaticojejunostomy (i.e., it could preserve physiologic bilioenteric and bowel continuity, thus preventing delayed bowel movement). Duct-to-duct reconstruction is described as allowing easy endoscopic access to the biliary tree for diagnostic and therapeutic instrumentation and management and to prevent ascending cholangitis (*3*, *7*, *8*).

This work was supported by a Grant-in-aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan and a Grant-in-aid for Research on Human Genome, Tissue Engineering, Food Biotechnology, Health Sciences Research Grants, and Grant-in-aid for Clinical Study on Indication and Effectiveness of Liver Transplantation for Patients with Hepatocellular Carcinoma from the Ministry of Health, Labor and Welfare of Japan.

[1] Foundation for Promotion of Cancer Research, Tokyo, Artificial Organ and Transplantation Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, Tokyo, Japan.

[2] Artificial Organ and Transplantation Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, Tokyo, Japan.

[3] Address correspondence to: Yasuhiko Sugawara, M.D., Artificial Organ and Transplantation Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan. E-mail: yasusuga-tky@umin.ac.jp.

Received 28 December 2003. Revision requested 20 February 2004. Accepted 16 March 2004.

ISSN 0041-1337/04/7804-574
DOI: 10.1097/01.TP.0000128912.09581.46

These advantages are optimistically described but are not clearly established as beneficial. The number of patients who underwent LDLT and received duct-to-duct reconstruction is small, and the length of the follow-up periods is thus far limited. To confirm the feasibility of biliary reconstruction in LDLT, the results of duct-to-duct reconstruction were retrospectively analyzed in our series. The subjects were limited to those with a follow-up of at least 1 year.

PATIENTS AND METHODS

At the University of Tokyo Hospital, duct-to-duct biliary reconstruction was started in May 2000. By the end of 2002, 86 patients received LDLT with the reconstruction. Of these, five patients died within 1 year after LDLT and were excluded from the study. The remaining 81 patients were the subjects of the present study. They were 42 men and 39 women (average age, 50±10 years).

The most common indication for LDLT was viral hepatitis and cirrhosis with or without hepatocellular carcinoma (n=39), followed by cholestatic disease (n=27), including primary biliary cirrhosis, autoimmune hepatitis, primary sclerosing cholangitis, fulminant hepatic failure (n=9), metabolic diseases (n=4), and cryptogenic cirrhosis (n=2). The most commonly used graft type was the right liver in 46 patients, followed by the left liver with or without the caudate lobe in 29 patients, and the right lateral sector in 6. The donors were 56 men and 25 women (average age, 35±11 years). Their relation to the patients was child (n=41), sibling (n=14), spouse (n=12), nephew (n=7), parent (n=4), or other (n=3).

Donor Operation

Standard techniques were previously described (*9*). In brief, after cholecystectomy, a Phycon cholangiocatheter (Fuji Systems Corp., Tokyo, Japan) was inserted through the cystic duct stump for intraoperative cholangiography to ver-

ify the transection point of the hepatic duct. The hepatic duct was sharply severed near the confluence and the remnant stump was carefully sutured closed with 4-0 Vicryl (Ethicon, Inc., Somerville, NJ). After harvesting, completion cholangiography was performed to confirm that there was no bile juice leakage or stricture.

Recipient Operation

The technique was described previously (*4*). In brief, 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.

An end-to-end anastomosis between graft and patient bile duct was performed using an interrupted 4-0 Vicryl suture. When the bile duct of the graft was larger than the recipient's duct, bile duct plasty of the hilar plate was performed (Fig. 1). Then, on the patient's hilar plate, an external stent tube was inserted into the bile duct from the orifice opposite 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. A stent tube was fixed not at the anastomotic site but rather at the orifice site opposite the hilar plate. The anastomosis was begun at the posterior wall. The needle was inserted into the bile duct of the graft from outside to inside, and then to the orifice of the hilar plate from inside to outside. The knots were always outside of the bile duct. The anastomotic site can be turned around for better access. Thereafter, anastomosis of the anterior wall was started. For feeding or injection of the drained bile juice, a 4-French polyethylene tube was inserted from the stump of the cystic duct and introduced into the duodenum. The tubes for bile duct stenting and feeding were removed 3 months after LDLT.

The postoperative care and our immunosuppression regimen have been described previously (*10*). Biliary complications were classified into three categories: bile juice leakage, bile duct stenosis, and tube trouble. Bile juice leakage was diagnosed when the total bilirubin level of the discharge around the dissection plane of the graft was over 5 mg/dL. Bile duct stenosis was suspected on the basis of laboratory data,

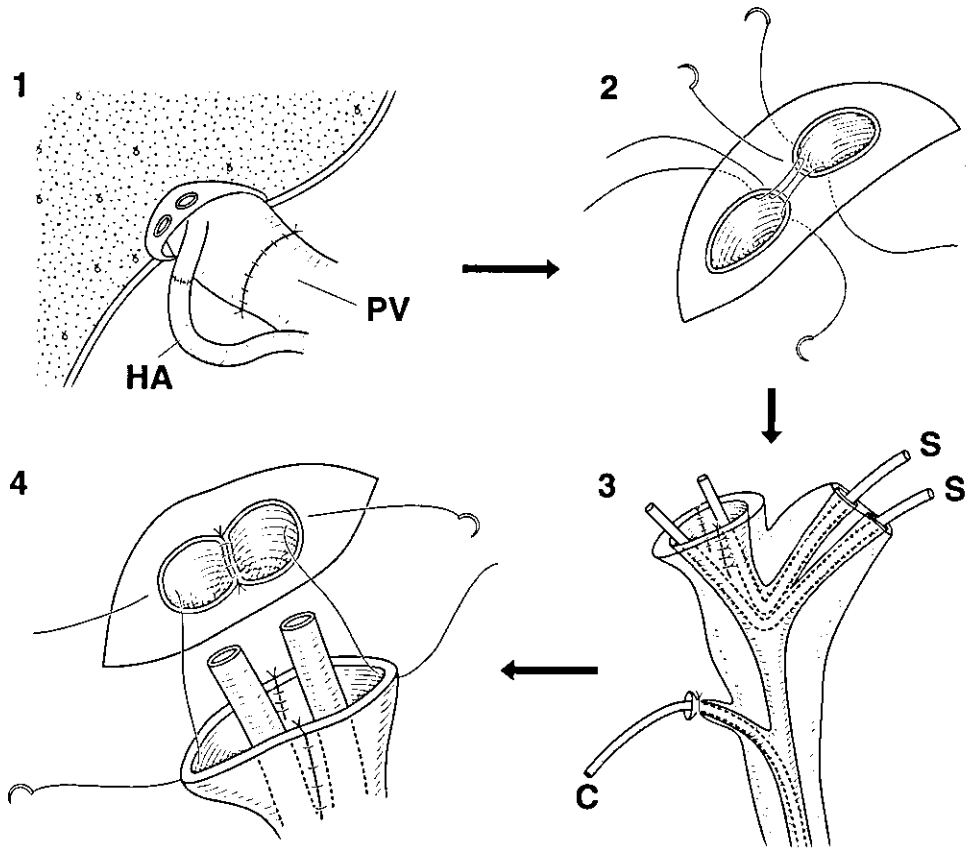

FIGURE 1. When there are two closely located bile duct orifices in the graft, the bile ducts in the hilar plate and graft were sutured into one. A stent tube (*S*) is introduced from the orifice opposite the hilar plate where the tube will be fixed to the plate. For nutrition or bile juice feeding, a 4-French polyethylene tube (*C*) was inserted from the stump of the cystic duct and introduced into the duodenum. The anastomosis was begun at the posterior wall and the needle was inserted into the bile duct in the graft from outside to inside; then, the orifice of the hilar plate was inserted from inside to outside. The knots were always outside of the bile duct. HA, Hepatic artery; PV, portal vein.

including a significant increase of γ-glutamyl transpeptidase and alkaline phosphatase, and was diagnosed radiologically by ultrasound, computed tomography, and cholangiography, showing slight dilatation of the graft bile duct.

A multivariate analysis was performed to find a predictor of bile juice leakage or bile duct stenosis. The independent factors consisted of seven intraoperative and two postoperative factors. Intraoperative factors included graft weight-to-standard liver volume ratio, duration of biliary reconstruction, blood loss per patient body weight, cold ischemic time of liver graft, warm ischemia time, number of bile duct orifices of the graft, and number of sutures used for biliary reconstruction. Two postoperative factors were acute rejection and cytomegalovirus infection. Differences were considered significant at a value of $P<0.05$. Data were shown as mean±SD or median and range.

RESULTS

Donors

The average duration of operation for the donors was 567±93 min. The average blood loss volume was 536±281 mL, which was replaced by 385±351 mL of autologous blood. The most common type of procedure was right liver resection (n=46), followed by left liver resection (n=29) and right lateral sectorectomy (n=6). There were no significant complications in the postoperative period. The mean postoperative hospitalization was 15±2 days. The donors have all returned to their normal daily activity.

Recipients

The average duration of operation for the recipients was 887±184 min. The duration for biliary reconstruction was 66±16 min. The average blood loss volume per body weight was 109±50 mL/kg. The mean graft weight was 577±177 g, which corresponded to 50±11% of the recipient's standard liver volume. Cold and warm ischemic times of the grafts were 99±37 and 71±10 min, respectively. The number of bile duct orifices was one (n=39), two (n=34), or three (n=8), with an average of 1.6±0.7 (Table 1). The number of sutures used for anastomosis was 12±4, ranging from 6 to 23.

During the observation period, biliary complications were observed in 26 patients (32%). The complications included bile juice leakage (n=12), anastomotic stenosis (n=10), and tube trouble (n=6). Two patients experienced complications with leakage followed by stenosis. Of the 26 patients, 21 complications necessitated surgery. For leakage, percutaneous drainage under ultrasound guidance was possible in five patients. The other patients underwent reoperation for drainage. The onset of leakage ranged between 4 and 65 days after LDLT. All of the patients with anastomotic stenosis underwent surgical revision. The procedure included a T-tube insertion from the common bile duct into the intrahepatic bile duct through stenosis (n=5), conversion to hepaticojejunostomy (n=3), dilation of anastomosis using a Kelly clamp under radiographic guidance (n=1), and transhepatic bile duct drainage (n=1). Nine of the 10 events occurred within 1 year after LDLT. The details of the anastomotic stenosis and outcome of the patients after each procedure are shown in Table 2. Briefly, three of the five patients with T-tubes are waiting for T-tube removal, one patient underwent retransplantation for refractory cholangitis, and one was cured. All of the patients with conversion to hepaticojejunostomy were cured and the patient with transhepatic bile duct drainage died as a result of sepsis. Because of the severe adhesion of the hepatic hilum, safe dissection of the bile duct and conversion to hepaticojejunostomy was not possible in one patient. Intraoperative cholangiography of this patient showed an anastomotic stricture and sludge formation on the graft side of the bile duct. A Kelly clamp was inserted into the hepatic hilum from the opposite side of the anastomosis, and all of the sludge was removed. Then, under radiographic guidance, dilatation of the anastomosis was performed and the external tube was changed with a new one. This patient was cured after the procedure.

TABLE 1. Number of bile duct orifices

Graft	1	2	3	Total
Left liver	14	12	3	29
Right liver	20	21	5	46
Right lateral sector	5	1	0	6
Total	39	34	8	81

A common cause of tube trouble was mislocation of the external drainage tube in three patients. The location was corrected in these patients to allow the tube to adequately drain bile juice 1, 3, and 5 days after LDLT. Complications in the other two patients included bile peritonitis after removal of external tubes. One patient was treated conservatively and the other underwent reoperation for irrigation and drainage. In another patient, 13 days after LDLT, there was bile juice leakage around a 4-French polyethylene tube introduced into the duodenum for feeding. Contrast medium injection through the tube revealed leakage from the stump of the cystic duct. The 4-French polyethylene tube was retracted until the tip was in the common bile duct for drainage. The peritonitis subsided thereafter.

Multivariate analyses failed to detect any significant predictors for bile juice leakage or bile duct stenosis (Table 3). The incidence of acute rejection was 27%. Portal vein thrombosis occurred in one patient and was successfully treated with anticoagulants, and none of the patients had hepatic arterial thrombosis. Cytomegalovirus infection occurred in 17% of the patients.

All but two patients are alive with normal liver function at a median follow-up period of 664 days. The patient with autoimmune hepatitis died 13 months after LDLT because of thrombocytopenic purpura. Bile duct stenosis occurred in the other patient, who underwent transhepatic bile duct drainage. The cholangitis was resistant to conservative therapy, however, and the patient died as a result of sepsis 13 months after LDLT.

DISCUSSION

The morbidity rate was 32% during the 1-year observation period, and the results are comparable among other series of right liver transplantation (Table 4). The rate might be higher, however, than that after whole liver transplanta-

TABLE 2. Detail of bile duct stenosis

Patient	Age/Gender	Onset (day)	Treatment	Result
1	57/F	89	Hepaticojejunostomy	Cured
2	20/M	214	Hepaticojejunostomy	Cured
3	54/F	810	T-tube drainage	Waiting for T-tube removal
4	52/F	334	Hepaticojejunostomy	Cured
5	50/M	73	T-tube drainage	Retransplantation for refractory cholangitis
6	34/F	44	Dilation of anastomosis by Kelly clamp and reinsertion of the external tube under radiographic guidance	Cured
7	67/M	18	T-tube drainage	Cured
8	59/M	310	T-tube drainage	Waiting for T-tube removal
9	43/M	69	Transhepatic bile duct drainage	Died as a result of sepsis
10	53/M	300	T-tube drainage	Waiting for T-tube removal

TABLE 3. Multivariate analysis for detecting predictors of biliary complications

	Leakage		Stenosis	
	Regression index	*P* value	Regression index	*P* value
GW/SLV	–0.366	0.31	0.007	0.10
Duration	–0.001	0.39	0.0005	0.97
Blood loss/BW	–0.001	0.19	–0.0005	0.49
CIT	–0.0004	0.64	–0.0002	0.77
WIT	–0.001	0.40	0.002	0.11
No. of ducts	–0.077	0.30	0.06	0.40
No. of threads	0.01	0.52	–0.01	0.36
Acute rejection	—	—	0.073	0.41
CMV infection	—	—	–0.0005	0.97

GW, Graft weight; SLV, standard liver volume; BW, body weight of the patients; CIT, cold ischemic time of liver graft; WIT, warm ischemic time of liver graft; CMV, cytomegalovirus.

TABLE 4. Comparison with the previous references

	No.	DDR (%)	Median FUT	Morbidity (%)
Icoz et al., 2003[15]	50	72	15	30
Settmacher 2003[26]	50	76	ND	40
Nakamura 2002[27]	120	34	13	24
Testa, 2000[1]	30	ND	ND	27
Marcos, 1999[28]	25	0	5	24
Present study	81	100	22	32

DDR, Rate of duct-to-duct biliary reconstruction to the whole series; FUT, follow-up term (mo).

tion (2%–24%) (*11–14*). This difference might be because of anatomic variations in bile ducts rather than surgical experience. In cadaveric transplantation, the anastomosis is performed on the intact hepatic duct of the donor and the recipient common bile duct so that only one anastomosis with well-vascularized tissue can be performed (*15*). This is not the case for LDLT, which often necessitates multiple and thin bile duct anastomoses.

In our series, 52% of all the grafts and 57% of the right liver grafts had multiple bile duct orifices. The incidence was comparable to the others (*1*). The poorer outcome might be related to the complicated procedure. Some surgeons performed duct-to-duct anastomosis in selected grafts that would secure a single bile duct anastomosis (*8, 16*). The results of the present multivariate analysis, however, contradicted this presumption. Takatsuki and colleagues (*6*) re-

ported that multiple hepatic ducts were not a significant risk factor for biliary reconstruction. In our technique, the hilar plate was dissected distal to the second-order branch of the bile ducts. The extensive dissection enabled us to overcome the technical difficulty of multiple and widely separated graft bile ducts because the corresponding orifices in the recipient hilar plate could be freely selected.

Wide dissection of the hilar plate might be advantageous for tension-free anastomosis but disadvantageous because of decreased arterial supply to the duct (*17*). The common bile duct, if properly dissected, has its own axial blood supply that is provided mainly by branches of the superior posterior pancreaticoduodenal artery or the right hepatic artery (*18–20*). As in the recipient operation, the bile duct was inevitably dissected from the right hepatic artery, and the arterial supply was provided through connective tissues around the bile duct and the bile duct itself. Meticulous attention must be paid to dissection of the hepatoduodenal ligament, and preservation of axial periductal microcirculation is mandatory for successful biliary reconstruction (*15*). Similarly, the ability to preserve the blood supply to the donor's bile duct requires sharp dissection around the duct (*21*). The use of electrocautery should be avoided. The viability of the bile ducts for donor and recipient should be confirmed by the presence of pulsatile arterial bleeding from the cut ends. The venous drainage system of the duct might be more important. Venous blood enters into the portal venous branch, and the direction of the blood flow is from the caudal to the cranial direction in the upper part of the bile duct. It is unclear whether venous drainage can be maintained after anastomosis.

Transanastomotic external drainage or a T-tube is another concern of LDLT (*15*). Marcos and associates (*22*) reported that the biliary complication rate after routine use of an external drainage tube decreased from 24.% to 13%. A transanastomotic external tube could theoretically help to decrease the intrahepatic biliary pressure caused by edema and consequent partial obstruction of the anastomosis (*1*). The tube can also facilitate a postoperative imaging study; however, its advantage over no stenting and relation with the anastomotic biliary complication has not been clearly shown. In our series, six patients had tube complications, including mislocation and leakage, and one of them underwent reoperation. The complications caused by tubes should not be neglected. In the series of Testa and associates (*1*), stenting of the anastomosis was not routinely performed. Some institutions used a T-tube for decompression (*3, 7*). The randomized, controlled trial of biliary reconstruction in whole liver transplantation (*12*) revealed an increase in the biliary complication rate in the T-tube group. In LDLT, a T-tube will help decompress the bile duct but it will not help prevent stenosis at the anastomotic site. Because in LDLT there are often multiple duct orifices in the graft and a size difference between common bile duct and duct orifice in the graft, it is difficult to put the tip of a T-tube across the anastomotic site.

For surgical repair of stenosis, some authors converted duct-to-duct anastomosis directly to the hepaticojejunostomy for biliary complications (*1, 5, 8, 23*). Another strategy was T-tube insertion in the common bile duct with one arm in the stenotic portion. The surgical revision is technically demanding. The hilar plate of the patient often severely adheres to the hepatic artery or portal vein, and it is difficult to isolate the bile duct safely. In repairs using a T-tube, careful attention must be paid to the appropriate localization of the T-tube under intraoperative cholangiography, allowing for appropriate bile juice drainage. The Kyoto group (*24*) recently reported that 13 of 14 patients were successfully treated with an inside stent. The endoscopic approach is a therapeutic alternative to reoperation (*25*).

CONCLUSION

The results of duct-to-duct anastomosis in 81 patients with at least a 1-year follow-up were reviewed. Long dissection of the recipient hilar plate makes our technique unique and enables a tension-free biliary anastomosis and the ability to overcome the size and number discrepancy between graft and recipient bile ducts. In spite of these advantages, the morbidity rate was 32%, which was not as satisfactory as expected. The present results reveal the necessity for technical modifications to reduce the morbidity rates.

REFERENCES

1. Testa G, Malago M, Valentin-Gamazo C, et al. Biliary anastomosis in living related liver transplantation using the right liver lobe: Techniques and complications. *Liver Transpl* 2000; 6: 710.
2. Fan ST, Lo CM, Liu CL, et al. Biliary reconstruction and complications of right lobe live donor liver transplantation. Ann Surg 2002; 236: 676.
3. Azoulay D, Marin-Hargreaves G, Castaing D, et al. Duct-to-duct biliary anastomosis in living related liver transplantation: The Paul Brousse technique. *Arch Surg* 2001; 136: 1197.
4. Sugawara Y, Makuuchi M, Sano K, et al. Duct-to-duct biliary reconstruction in living-related liver transplantation. *Transplantation* 2002; 73: 1348.
5. Ishiko T, Egawa H, Kasahara M, et al. Duct-to-duct biliary reconstruction in living donor liver transplantation utilizing right lobe graft. *Ann Surg* 2002; 236: 235.
6. Takatsuki M, Yanaga K, Okudaira S, et al. Duct-to-duct biliary reconstruction in adult-to-adult living donor liver transplantation. *Clin Transpl* 2002; 16: 345.
7. Soejima Y, Shimada M, Suehiro T, et al. Feasibility of duct-to-duct biliary reconstruction in left-lobe adult-living-donor liver transplantation. *Transplantation* 2003; 75: 557.
8. Kawachi S, Shimazu M, Wakabayashi G, et al. Biliary complications in adult living donor liver transplantation with duct-to-duct hepaticocholedochostomy or Roux-en-Y hepaticojejunostomy biliary reconstruction. *Surgery* 2002; 132: 48.
9. Sugawara Y, Makuuchi M, Takayama T, et al. Safe donor hepatectomy for living related liver transplantation. *Liver Transpl* 2002; 8: 58.
10. Sugawara Y, Makuuchi M, Kaneko J, et al. Correlation between optimal tacrolimus doses and the graft weight in living donor liver transplantation. *Clin Transplant* 2002; 16: 102.
11. Neuhaus P, Blumhardt G, Bechstein WO, et al. Technique and results of biliary reconstruction using side-to-side choledochocholedochostomy in 300 orthotopic liver transplants. *Ann Surg* 1994; 219: 426.
12. Scatton O, Meunier B, Cherqui D, et al. Randomized trial of choledochocholedochostomy with or without a T tube in orthotopic liver transplantation. *Ann Surg* 2001; 233: 432.
13. Randall HB, Wachs ME, Somberg KA, et al. The use of the T tube after orthotopic liver transplantation. *Transplantation* 1996; 61: 258.
14. Greif F, Bronsther OL, Van Thiel DH, et al. The incidence, timing, and management of biliary tract complications after orthotopic liver transplantation. *Ann Surg* 1994; 219: 40.
15. Icoz G, Kilic M, Zeytunlu M, et al. Biliary reconstructions and complications encountered in 50 consecutive right-lobe living donor liver transplantations. *Liver Transpl* 2003; 9: 575.
16. Malago M, Testa G, Hertl M, et al. Biliary reconstruction following

right adult living donor liver transplantation end-to-end or end-to-side duct-to-duct anastomosis. *Langenbecks Arch Surg* 2002; 387: 37.
17. Northover JM, Terblanche J. A new look at the arterial supply of the bile duct in man and its surgical implications. Br J Surg 1979; 66: 379.
18. Northover J, Terblanche J. Bile duct blood supply. *Transplantation* 1978; 26: 67.
19. Stapleton GN, Hickman R, Terblanche J. Blood supply of the right and left hepatic ducts. *Br J Surg* 1998; 85: 202.
20. Rath AM, Zhang J, Bourdelat D, et al. Arterial vascularization of the extrahepatic tract. *Surg Radiol Anat* 1993; 15: 105.
21. Grewal HP, Shokouh-Amiri MH, Vera S, et al. Surgical technique for right lobe adult living donor liver transplantation without venovenous bypass or portocaval shunting and with duct-to-duct biliary reconstruction. *Ann Surg* 2001; 233: 502.
22. Marcos A. Right lobe living donor liver transplantation: A review. *Liver Transpl* 2000; 6: 3.
23. Marcos A, Ham JM, Robert AF, et al. Surgical management of anatomical variations of the right lobe in living donor liver transplantation. *Ann Surg* 2000; 231: 824.
24. Hisatsune H, Yazumi S, Egawa H, et al. Endoscopic management of biliary strictures after duct-to-duct biliary reconstruction in right-lobe living-donor liver transplantation. *Transplantation* 2003; 76: 810.
25. Park JS, Kim HM, Lee SK, et al. Efficacy of endoscopic and percutaneous treatment for biliary complications after cadaveric and living donor liver transplantation. *Gastrointest Endosc* 2003; 57: 78.
26. Settmacher U, Steinmuller TH, Schmidt SC, et al. Technique of bile duct reconstruction and management of biliary complications in right lobe living donor liver transplantation. *Clin Transplant* 2003; 17: 37.
27. Nakamura T, Tanaka K, Kiuchi T, et al. Anatomical variations and surgical strategies in right lobe living donor liver transplantation: lessons from 120 cases. *Transplantation* 2002; 73: 1896.
28. Marcos A, Fisher RA, Ham JM, et al. Right lobe living donor liver transplantion. *Transplantation* 1999; 68: 798.

Abdominal Imaging

Received: 30 October 2003 / Accepted: 17 December 2003 / Published online: 27 May 2004

Abdom Imaging (2004) 29:603–605
DOI: 10.1007/s00261-003-0156-1

Prediction of hepatic artery thrombosis by protocol Doppler ultrasonography in pediatric living donor liver transplantation

J. Kaneko,[1,2] Y. Sugawara,[1,2] N. Akamatsu,[1,2] Y. Kishi,[1,2] T. Niiya,[1,2] N. Kokudo,[1,2] M. Makuuchi,[1,2] K. Mizuta[1,2]

[1]Artificial Organ and Transplantation Division, Department of Surgery, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo 113-8655, Japan
[2]Department of Transplantation Surgery, Jichi Medical School, 3311-1 Yakushiji, Minamikawachi-machi, Kawac-gun Tochigi, Japan

Abstract

Hepatic arterial thrombosis (HAT) after liver transplantation is a life-threatening event. Previous reports have suggested that the resistive index (RI) of the hepatic artery predicts HAT. Doppler ultrasonography (US) to measure RI, however, is not routinely performed. The subjects were 70 pediatric patients who underwent living donor liver transplantation (LDLT). Protocol Doppler US was performed once or twice a day for 2 weeks postoperatively and 692 records were examined. Changes in RI values were examined separately in patients with and without HAT complications. The incidence of HAT was 10% (seven of 70). HAT was diagnosed an average of 6.2 days after LDLT. In patients without HAT complications (n = 63), average RI levels at 14 days after LDLT were 0.71 ± 0.1 (records, n = 625). In patients with HAT complications, RI decreased gradually within 2 days before the onset of HAT. RI values of less than 0.6 predicted HAT within 2 days before onset, with 83% sensitivity and 85% specificity. RI during the first 2 weeks after LDLT is a sensitive predictor for HAT. Thrombectomy and reanastomosis should be considered when RI values are less than 0.6 in Doppler US.

Key words: Hepatic artery thrombosis—Living donor—Liver transplantation—Doppler ultrasonography—Resistive index

Hepatic arterial thrombosis (HAT) after liver transplantation is a life-threatening event associated with a high rate of graft loss or death [1]. The incidence of HAT during the first 30 days has been reduced to approximately 5% by recent technical advances [2]. HAT is more common, however, in split or living donor liver transplantation (LDLT) [3].

Although arteriography remains a standard of reference for the diagnosis of HAT, Doppler ultrasonography (US) is a useful diagnostic tool for detecting HAT and the need for urgent revascularization. Rescue of liver graft from HAT depends on its early detection [4]. Protocol postoperative Doppler US appears to be mandatory for early detection [5]. Some studies [6–8] have proposed that decreases in the resistive index (RI) of the hepatic artery might predict HAT. Doppler US is not routinely performed, however, and the indication for Doppler US remains unclear from previous reports. The purpose of our study was to evaluate the significance of RI as a predictor of HAT in protocol Doppler US after pediatric LDLT.

Materials and methods

Seventy-two patients younger than 18 years underwent LDLT procedures at the University of Tokyo from January 1996 to December 2002. Of these, two patients were excluded from the analysis because they died due to simultaneous HAT and portal vein thrombosis. The remaining 70 patients (33 male, 37 female; mean age, 4.6 years) comprised the subjects of this study. The most common indication for LDLT was biliary atresia (n = 61), followed by Wilson disease (n = 2), fulminant hepatic failure (n = 2), cryptogenic cirrhosis (n = 2), and metabolic diseases (n = 1). The remaining two patients had indications for retransplantation. The most commonly used graft was the left lateral sector (n = 50), followed by the left liver (n = 15), right liver (n = 3), and right lateral sector (n = 2).

The operative procedure and postoperative management have been described elsewhere [3]. In brief, the donor and patient hepatic arteries were anastomosed end to end with an

Correspondence to: Y. Sugawara; *email:* yasusuga-tky@umin.ac.jp

interrupted suture using 9-0 monofilament under a microscope. Anticoagulant therapy with prostaglandin E1 (0.01 μg/kg per hour) and a protease inhibitor (mesylate gabexate; 1 mg/kg per hour) was administered intravenously just after the operation for 14 days. Antithrombin III concentrates and low-molecular-weight heparin were also used.

Protocol Doppler US was performed once or twice a day for 2 weeks postoperatively with an SSD 2000 or SSD 6500 (Aloka Co. Ltd., Tokyo, Japan). The patencies of the hepatic artery, portal vein, and hepatic vein were assessed. Hepatic artery flow was determined near the porta hepatis. If intrahepatic artery flow was absent, then emergent laparotomy was performed without a confirmatory angiogram. RI ([systolic velocity − diastolic velocity]/systolic velocity) was calculated during each examination.

A total of 692 Doppler US records was collected. Changes in RI values were examined for 2 weeks after LDLT in patients without HAT complications. In patients with HAT complications, changes in RI values were analyzed for 1 week before the onset of HAT. The RI values in patients without HAT, those in patients with HAT within 2 days before the onset, and those in patients with HAT 7 to 2 days before the onset were compared with an unpaired t test. $P < 0.05$ was considered statistically significant. Values were recorded as average ± standard deviation.

Results

Clinical results

The incidence of HAT was 10% (seven in 70). HAT was diagnosed an average of 6.2 days after LDLT. Laparotomy was performed immediately after the diagnosis in each patient. In one patient, thrombus was not apparent but reanastomosis was performed because of anastomotic kinking. In the remaining six patients, a thrombus was detected at the anastomotic site and extended a few millimeters proximally into the reconstructed hepatic artery and was successfully removed. All patients survived the reoperation without retransplantation. One patient died 47 days after LDLT despite successful thrombectomy.

RI levels

In patients without HAT complications ($n = 63$), RI levels for 14 days after LDLT were 0.71 ± 0.1 (record $n = 625$; Fig. 1). In patients with HAT complications ($n = 7$), RI decreased gradually within 2 days before the onset of HAT. RI levels within 2 days before the onset (record $n = 28$) and those 7 to 2 days before the onset (record $n = 39$) were 0.52 ± 0.08 and 0.66 ± 0.09, respectively (Fig. 2). There was a significant difference between the two values ($p < 0.001$; Fig. 3).

Ten records in four patients without HAT showed an RI of less than 0.5, recorded on the fourth, fifth, sixth, and ninth days after LDLT. In each patient, the RI level spontaneously recovered within 12 h. When the threshold was set at 0.6, the sensitivity and specificity of RI for HAT detection were 83% and 85%, respectively (Table 1).

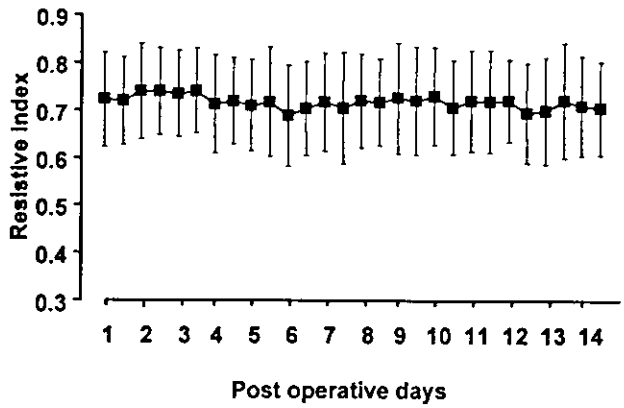

Fig. 1. Changes in RI values in patients without HAT ($n = 63$). RI was constant around 0.7 during the observation period.

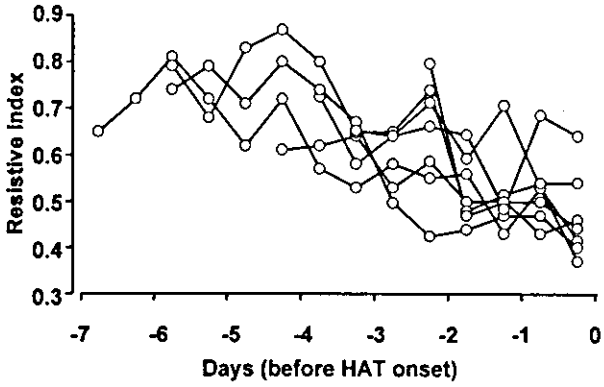

Fig. 2. Changes of RI values in patients with HAT complications ($n = 7$). RI decreased gradually 2 days before the onset of HAT.

Discussion

RI is a popular parameter that reflects vascular resistance and compliance [9] and is used to characterize the arterial waveform of Doppler US. Dodd and associates [7] emphasized that RI provides excellent screening for the detection of liver graft arterial stenosis or thrombosis. Of the 72 transplant recipients, 42 had normal arteries, 27 had substantial stenoses, and six had thromboses at angiography. Arterial flow was detected using Doppler US in 26 of 27 patients with stenosis, three of six patients with thrombosis, and in all patients with normal angiograms. In patients with HAT and flow detected by Doppler US, only RI was statistically significantly different from that in patients with normal angiograms. Another report [10] concluded that duplex Doppler US is useful for the diagnosis of HAT. In these reports [7,