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Table 1: Characteristics of APOLT for fulminant hepatic failure

Case	Age (year)	Sex	Blood type	Graft type	GRWR	PVD	Outcome
1	1.8	M	Identical	Left lateral	2.08	−	Died* (POD55, sepsis)
2	1.5	M	Identical	Left lateral	2.00	−	Died† (POD141, sepsis)
3	19.5	M	Identical	Left lobe	0.62	+	Died (POD32, necrotizing enteritis)
4‡	43.3	F	Identical	Left lobe	0.51	+	Died (POD9, graft failure)
5	53.6	M	Compatible	Left lobe	0.61	+	Died (POD25, sepsis)
6	38.6	F	Identical	Right lobe	0.90	+	Died (POD43, sepsis)

GRWR = graft-to-recipient weight ratio (%); PVD = portal vein diversion; POD = post-operative day.
*Portal flow steal phenomenon.
†Retransplantation on day 34 from living donor for recurrent hepatitis.
‡HBV-related fulminant hepatic failure.
Retransplantation on day 29 from living donor for hepatic artery and portal vein thrombosis.

Patient 1, in whom portal blood flow to the native liver was preserved, showed a portal flow steal phenomenon resulting in continuously poor portal blood flow to the graft. Native portal vein diversion at the time of transplantation was indicated in the latter four cases to prevent functional portal flow competition between the graft and remnant native liver (17). Acute cellular rejection that was confirmed by liver biopsy, was observed in 3 patients (patients 2, 4 and 5). Three technical complications occurred in 6 patients, biliary stricture in patient 1 and intra-abdominal bleeding in patients 5 and 6. Retransplantation was indicated in 2 patients: for recurrent hepatitis in patient 2 and for arterial/portal thrombosis in patient 6. All patients died within 5 months of APOLT, due to sepsis in four cases, necrotizing enteritis in one case and graft failure in one case. None of the patients showed sufficient native liver recovery, and none of them were able to withdraw from immunosuppressive therapy.

In the same period, 53 patients had a transplant with standard LDLT for fulminant hepatic failure. Etiology of fulminant hepatic failure was drug-induced in 1, HBV in 15 and of unknown origin in 37. The median age of recipients was 23.3 years (range: 0.1–68.9 years). Recipient and donor characteristics of APOLT or standard LDLT were comparable at the time of transplant. The cumulative 5-year graft and patient survival rates were 58.4% and 60.2% in the standard LDLT group, respectively. The graft survival was significantly lower after APOLT (p < 0.01).

APOLT for non-cirrhotic metabolic liver disease (Table 2)

Six patients had a transplant with APOLT for non-cirrhotic metabolic liver disease. Primary native portal vein diversion was indicated in the last four cases. We reported the case of patient 1 with OTCD who did not receive primary ligation of the native portal branch at the time of APOLT (18). After a severe rejection episode, the graft became smaller and the native liver showed compensatory hypertrophy. As a result of the delayed native portal vein diversion, at 26 months after APOLT the graft volume increased properly and was revealed to have acceptable metabolic function. In our previous study, the resistance of portal venous inflow in the graft liver was higher than in the native liver after APOLT (17), and the dominant portal venous flow to the native liver could be readily observed in the event of severe rejection. After the experience of the first two cases, we changed the standard procedure for APOLT of non-cirrhotic metabolic liver disease to indicate native portal vein diversion in all subsequent cases so that the graft liver received the entire portal venous flow. The native liver was supplied by arterial blood flow. In case 2, native partial hepatectomy was done to compensate the hypertrophy of the native liver after native portal vein diversion (12). No significant difference was found in pericellular or perivenular fibrosis in the native liver between the specimen at APOLT and at native hepatectomy. Despite the native portal vein diversion, steatosis of the native liver improved from 80% to 30% (19).

Table 2: Characteristics of APOLT for non-cirrhotic metabolic liver disease

Case	Age (year)	Sex	Original disease	Blood type	Graft type	GRWR	PVD	Outcome
1	3.0	F	OTCD*	Compatible	Left lateral	2.08	+†	Alive
2	5.8	F	OTCD*	Identical	Left lateral	1.34	+‡	Alive
3	52.7	F	Citrullinemia	Identical	Left lobe	0.84	+	Alive
4	5.5	M	Crigler-Najjar (type I)	Compatible	Left lateral	1.23	+	Alive
5	23.5	M	Citrullinemia	Identical	Left lobe	0.78	+	Alive
6	20.2	M	Citrullinemia	Compatible	Left lobe	1.21	+	Died (POD29, sepsis)

GRWR = graft-to-recipient weight ratio (%); PVD = portal vein diversion; POD = post-operative day; POM = post-operative month.
*Ornithine transcarbamylase deficiency.
†PVD for portal flow steal phenomenon (POM 26).
‡PVD for portal flow steal phenomenon (POM 14), and native hepatectomy for compensate hypertrophy (POM66).

Five patients had an episode of acute cellular rejection (patients 1, 2, 3, 4, 6). Patient 3 had biliary stricture and underwent rehepaticojejunostomy 3 years after transplant. Patient 5 had minor biliary leakage that was successfully managed with percutaneous aspiration drainage under ultrasound guidance. Patient 6 died from sepsis on postoperative day 29. The overall cumulative 5-year graft and patient survival rates were 83.3% and 83.3%, respectively.

Seventeen patients received standard LDLT for non-cirrhotic metabolic liver disease in the same study period. Etiology of liver disease was tyrosinemia in four cases; OTCD in three; citrullinemia in three; glycogen storage disease in three; Crigler-Najjar type I in one; familial amyloidotic polyneuropathy in one; methylmalonic acidemia in one and propionic acidemia in one (20,21). The overall cumulative 1- and 5-year graft and patient survival rates were 70.6% and 62.7% and 70.6% and 62.7%, respectively. There was no significant difference in graft and patient survival between APOLT and standard LDLT for non-cirrhotic metabolic liver disease.

APOLT for small-for-size graft (Table 3)

Thirteen patients underwent transplant with APOLT for a small-for-size graft. Small-for-size grafts can be defined by a recognizable clinical syndrome that results from the transplantation of too small a functional mass of liver for a designated recipient (22,23). The definition of a small-for-size graft in this study is an actual GRWR of less than 0.8% (2,3). The original liver disease was biliary atresia in 2 patients; liver cirrhosis in 2 (of which 1 was HBV-related); primary biliary cirrhosis in 3; primary sclerosing cholangitis in 2; Wilson's disease in 2; autoimmune hepatitis in 1 and Budd-Chiari syndrome in 1. The median GRWR was 0.62% (range: 0.45–0.75%). The decision was made preoperatively in this group of patients to use APOLT.

All patients had histologically proven fibrosis in the native liver, and a pre-operative Doppler study revealed that the blood supply depended on the hepatic artery being dominant rather than the portal vein. Native portal vein diversion was indicated in 10 patients. Six patients had an episode of acute cellular rejection (patients 3, 4, 5, 7, 8, 13) and one patient had chronic rejection (patient 13).

Four patients required relaparotomy for complications: intestinal perforation in patient 3; intra-abdominal bleeding in patients 4 and 9. Patient 7 with primary sclerosing cholangitis underwent native hepatectomy on post-operative day 35 after competent graft regeneration confirmed by CT volumetry and ^{99m}Tc-galactosyl serum albumin scintigraphy, which reflected the general function of the hepatocyte in the graft and native liver (24). The delayed native hepatectomy was intended to eliminate the potential risk of carcinogenecity of the remnant native liver. Interestingly, the explanted native liver showed no histological difference between the specimen at APOLT and at delayed native hepatectomy.

Two patients (patients 4 and 6) had hepatic vein stenosis that was treated by intervention. A metallic stent was inserted in patient 4 after several courses of balloon dilatation, but was thrombosed despite adequate anticoagulation therapy. Biliary complications were observed in 6 patients; biliary leakage in 3 (patients 1, 5 and 10) and stricture in 3 (patients 3, 7 and 8). Hypersplenism was observed in 2 patients (patients 3 and 6) who underwent splenectomy 7 years and 1 year after APOLT, respectively. Patient 6 developed de novo autoimmune hepatitis 2.5 years after APOLT (25).

Retransplantation was indicated in 2 patients due to hepatic vein thrombosis in patient 4 and chronic rejection in

Table 3: Characteristics of APOLT for small-for-size graft

Case	Age (year)	Sex	Original disease	Blood type	Graft type	GRWR	PVD	Outcome
1	23.2	F	Wilson's	Identical	Left lobe	0.72	−	Alive
2	47.1	M	LC (HBV)	Compatible	Left lobe	0.51	−	Died (POD35, sepsis)
3	22.9	F	Biliary atresia	Identical	Left lobe	0.48	+	Alive
4	24.1	M	Wilson's	Identical	Left lobe	0.62	−	Alive*
5	48.7	F	PBC	Compatible	Left lobe	0.62	+	Alive
6	15.9	F	Biliary atresia	Identical	Left lobe	0.54	+	Alive
7	20.6	F	PSC	Identical	Left lobe	0.49	+	Alive†
8	44.1	F	PBC	Identical	Left lobe	0.45	+	Alive
9	50.6	F	LC	Identical	Left lobe	0.67	+	Alive
10	30.0	F	PBC	Identical	Left lobe	0.59	+	Died (POD59, sepsis)
11	39.0	F	Budd-Chiari	Identical	Left lobe	0.69	+	Died (POD22, sepsis)
12	19.2	F	AIH	Identical	Right lobe	0.75	+	Alive
13	30.9	M	PSC	Identical	Right lobe	0.68	+	Died‡ (POD372, sepsis)

GRWR = graft-to-recipient weight ratio (%); PVD = portal vein diversion; POD = post-operative day; POM = post-operative month; LC = liver cirrhosis; PBC = primary biliary cirrhosis; PSC = primary sclerosing cholangitis; AIH = autoimmune hepatitis.
*Retransplantation from living donor for hepatic vein thrombosis (POM 33).
†Native hepatectomy after regeneration of graft (POD 35).
‡Retransplantation from living donor for chronic rejection (POM 6).

Table 4: Characteristics of APOLT for ABO-incompatible case

Case	Age (year)	Sex	Original disease	Graft type	GRWR	PVD	Outcome
1	19.6	M	Biliary atresia	Left lobe	0.55	+	Died (POD59, hepatic necrosis)
2	51.4	M	LC (HBV)	Left lobe	0.55	+	Died (POD32, sepsis)
3	13.8	F	Biliary atresia	Left lobe	0.62	+	Alive
4	4.5	F	Biliary atresia	Left lateral	1.37	+	Alive*
5	14.9	M	Biliary atresia	Left lateral	0.63	+	Alive
6	9.8	F	LC	Left lateral	1.16	+	Alive

GRWR = graft-to-recipient weight ratio (%); PVD = portal vein diversion; POD = post-operative day; POM = post-operative month.
*Retransplantation from cadaveric donor (split liver transplantation) for chronic rejection (POM 22).

patient 13. Patient death occurred in 4 of 13 patients, the main cause of death being sepsis. The overall cumulative 1- and 5-year graft survivals were 69.2% and 69.2%, respectively.

Forty patients received standard LDLT for a small-for-size graft during the same period in conjunction with APOLT. The median GRWR in the standard LDLT group was 0.73% (range: 0.60–0.79%). The GRWR was significantly lower for patients receiving APOLT versus those receiving standard LDLT (p < 0.01). The overall cumulative 1- and 5-year graft and patient survivals in the standard LDLT group were 65.0% and 65.0%, respectively. No significant difference was observed between the groups.

APOLT for cases of ABO-incompatibility (Table 4)

Six patients had a transplant with APOLT for ABO-incompatibility. Median recipient age was 14.4 years (range: 4.5–51.4 years). Acute cellular rejection was observed in 4 patients (patients 1, 4, 5 and 6). Patient 4 had chronic rejection.

Relaparotomy was indicated for 2 patients: ligation of the collateral vessel in patient 1 and intra-abdominal bleeding in patient 2. Patient 1 underwent ligation of the collateral vessel on post-operative day 9. After an episode of acute cellular rejection, graft portal venous flow decreased and the steal phenomenon of portal flow to the collateral vessel was confirmed by Doppler ultrasonography even though native portal vein diversion was indicated. The graft function did not recover and the native liver function was not sufficient to support the severe dysfunction of the graft. The patient died from hepatic necrosis on post-operative day 59. Three patients had biliary complications: bile leakage in patients 4 and 5, and biliary stricture in patient 6. Patient 4 underwent retransplantation with a cadaveric split graft in post-operative month 22 for chronic rejection. The overall cumulative 1- and 5-year graft survival rates were 66.7% and 44.4%, and the 1- and 5-year patient survival rates were 66.7% and 66.7%, respectively.

Thirty patients, all over 2 years old, underwent standard LDLT with an ABO-incompatible graft. Median recipient

age was 30.1 years (range: 2.0–59.3 years). Acute cellular rejection was observed in 9 of 30 patients (30%). The overall cumulative 1- and 5-year graft and patient survival rates were 53.3% and 42.7%, respectively. There was no significant difference in graft and patient survival between APOLT and standard LDLT for ABO-incompatibility.

Profiles of APOLT and standard LDLT (Table 5)

Profiles of APOLT and standard LDLT performed in the same study period are shown in Table 5. The GRWR was significantly lower for patients receiving APOLT versus those who received standard LDLT.

The duration of the operation was significantly longer in the APOLT group (831.2 ± 222.0 min) than the standard LDLT group (690.8 ± 198.5 min).

Acute cellular rejection was detected in 18 of 31 (58.1%) cases of APOLT versus 177 of 505 (35.0%) cases of standard LDLT (p = 0.02). Chronic rejection was diagnosed in 2 of 31 (6.5%) cases of APOLT, versus 2 of 505 (0.4%) cases of standard LDLT (p < 0.01). The incidence of rejection was higher in the APOLT group.

There were no significant differences in vascular complications between APOLT and standard LDLT. Biliary leakage was observed in 6 of 31 (19.4%) cases of APOLT, versus 30 of 505 (6.0%) in standard LDLT (p < 0.01). Biliary stricture was observed in 7 of 31 (22.6%) cases of APOLT, versus 28 of 505 (5.5%) in standard LDLT (p < 0.01). Biliary complication was significantly higher in the APOLT group.

The need for retransplantation was significantly greater in the APOLT group (16.1% vs. 4.2% for standard LDLT group, p < 0.01). In-hospital deaths occurred in 13 of 31 patients (41.9%), 10 patient deaths (76.9%) were related to infectious complication. The median delay was 32 days (range: 9–184 days) after APOLT.

The 1- and 5-year cumulative grafts were lower after APOLT versus standard LDLT (57.9 and 50.6% vs. 78.8 and 73.8%, respectively), but the difference did not reach statistical significance (p = 0.45 and 0.18, respectively).

Table 5: Profiles of Auxiliary partial orthotopic liver transplantation and standard living donor liver transplantation

Characteristics	APOLT (n = 31)	Standard LDLT (n = 505)	p-values
Male/female	13/18	213/292	0.87
Age (year)	25.8 ± 16.8 (1.5–53.6)	18.9 ± 20.4 (0.1–69.1)	0.06
Donor age (year)	43.5 ± 10.3 (20–62)	37.9 ± 10.8 (19–66)	<0.01
GRWR* (%)	0.87 ± 0.47 (0.45–2.08)	1.96 ± 1.27 (0.60–9.68)	<0.01
Cold ischemic time (min)	177.4 ± 111.2 (36–460)	116.7 ± 89.5 (14–943)	<0.01
Warm ischemic time (min)	49.4 ± 13.6 (32–77)	46.9 ± 13.8 (16–145)	0.32
Duration of operation (min)	831.2 ± 222.0 (513–1379)	690.8 ± 198.5 (329–1800)	<0.01
Blood loss/recipient boy weight (g/kg)	116.4 ± 140.4 (6.3–607.3)	119.7 ± 146.0 (8.3–1414.1)	0.89
Acute cellular rejection (%)	58.1	35	0.02
Chronic rejection (%)	6.5	0.4	<0.01
Surgical complications (%)			
Intestinal perforation	3.2	4.1	0.83
Intra-abdominal bleeding	16.1	9.4	0.62
Hepatic artery thrombosis	3.2	2.0	0.86
Portal vein thrombosis	3.2	1.4	0.95
Hepatic vein stenosis	6.5	1.4	0.16
Biliary leakage	19.4	6.0	<0.01
Biliary stricture	22.6	5.5	<0.01
Retransplantation (%)	16.1	4.2	<0.01
Graft survival (1-, 5-year survival, (%))			
For fulminant hepatic failure	0, 0	58.4, 58.4 (n = 53)	<0.01
For metabolic liver disease	83.3, 83.3	70.6, 62.7 (n = 17)	1.47
For small-for-size graft	69.2, 69.2	65.0, 65.0 (n = 40)	1.59
For ABO incompatible case	66.7, 44.4	53.3, 42.7 (n = 30)	0.53
Overall	57.9, 50.6	78.8, 73.8	0.45

GRWR = graft-to-recipient weight ratio (%).

Discussion

The most common indication for APOLT in western countries is fulminant hepatic failure (8). The first successful case of APOLT for fulminant hepatic failure, that is, full native liver regeneration and withdrawal of immunosuppressive therapy was reported in 1991 (26). The indication of APOLT for fulminant hepatic failure remains controversial because APOLT does not rule out potential regeneration of the native liver, resulting in unsatisfactory outcomes (6). In our series of APOLT for fulminant hepatic failure, none of the patients achieved long-term survival. The reasons for our poor results might be application of preemptive portal vein diversion and patient selection. The rationale of portal vein diversion is to prevent the portal flow steal phenomenon. We reported that the native liver has less resistant than the graft in fulminant hepatic failure (17), however, sufficient portal blood flow might be essential for native liver recovery and subsequent regeneration. An experimental study reported that the necessity of portal vein diversion in APOLT was dependent on the pathophysiology of the remnant native liver (27). The efficiency of portal vein diversion for fulminant hepatic failure, a paradox between the functional competition and the native liver recovery, remains unclear. Moreover, the optimal APOLT candidate for fulminant hepatic failure has not yet been clearly defined. A previous study suggests that native liver recovery is more likely to occur in those with a short interval between jaundice and encephalopathy (28). The median in-

terval between onset of jaundice and encephalopathy was 42 days in our series. This delay might be one of the reasons for the poor outcome.

Bismuth et al. reported that the main advantage of APOLT for fulminant hepatic failure, that is, the potential for withdrawal of immunosuppressive therapy, was rarely achieved and that the indication of APOLT for fulminant hepatic failure should therefore be reconsidered because of the high degree of technical complications (6,10). We fully agree with this suggestion. While our experience of APOLT for fulminant hepatic failure is limited, based on the poor outcome, we also consider that APOLT should have a limited place in the treatment of fulminant hepatic failure. There might be a possibility, however, that APOLT could be used in toxic injury such as acetaminophen toxicity where recovery of the native liver is more likely than in idiopathic or viral fulminant hepatic failure (29–31).

In the case of non-cirrhotic metabolic liver disease, APOLT had a satisfactory outcome in our series with a 5-year graft survival of 83.3%. After the initial two cases of the portal flow steal phenomenon, we changed the standard procedure for APOLT of non-cirrhotic metabolic liver disease to indicate native portal vein diversion in all subsequent cases whereby the graft liver receives the entire portal venous flow. Concern remains about the dysfunction of the remnant native liver after portal vein diversion, which may

negate the support of a patient's life and the possibility of future gene therapy. However, it has been reported that occluded portal flow induces hepatocyte apoptosis rather than necrosis in the embolized lobe without changing the functional efficiency of the hepatocyte (32,33). Our previous report showed that ligation of the native portal vein had no detrimental effects on the native liver supplied by arterial flow only (17,34). The remnant native liver may sustain the recipient's life if the native portal vein is transected. APOLT with portal vein diversion is an effective technique to induce graft regeneration and to avoid functional portal flow competition in non-cirrhotic metabolic liver disease.

With regard to our experience of APOLT for small-for-size grafts, the patients had high surgical complications and unsatisfactory patient survival. Recent technical improvements in left lobe donation have led to the use of right lobe grafts in adult-to-adult LDLT to overcome problems encountered with small-for-size grafts (35). After a period of APOLT using left lobe grafts, which partially relieved the problems of small-for-size grafts, right lobe LDLT was systematically introduced from February 1998. The cumulative 1-year graft survival rate of right lobe LDLT was 76.8%, which was significantly higher than that of APOLT for small-for-size grafts ($p < 0.01$, $n = 168$). Moreover, in some cases, if the functional volume of the right lobe was not sufficient for recipients, right lobe with middle hepatic vein graft was indicated with special attention to donor safety. The overall cumulative 1-year graft survival rate of right lobe with middle hepatic vein graft was 82.2% ($n = 28$). Our current strategy is to consider the right lobe as the first choice followed by APOLT with a right lobe graft for small-for-size grafts.

The graft survival in children younger than 2 years old receiving an ABO-incompatible graft is similar to those receiving compatible grafts. The survival is gradually affected with age by specific complications associated with blood type mismatching such as focal hepatic necrosis due to microcirculatory disturbance and multiple non-anastomotic biliary strictures attributable to arteriole insufficiency (36). In our LDLT program, an ABO-incompatible graft was unavoidable in 12% of the recipients. Despite the application of pre-operative plasma exchange, splenectomy and enhanced immunosuppression, the 5-year graft survival was less than 50% in an adult population. The application of APOLT to ABO-incompatible cases improved graft survival; however, graft survival was not satisfactory. Recently, an intra-portal infusion protocol was introduced (37), and improved patient survival was observed in ABO-incompatible cases. We modified the protocol from intra-portal to intra-hepatic arterial infusion from December 2001. Although it is still a tentative trial, intra-hepatic arterial infusion protocol dramatically improved survival with 1-year graft survival of 85% (data not shown). After the introduction of a novel immunosuppression protocol, APOLT is not adopted for ABO-incompatible cases. Further study of hepatic artery

infusion therapy is now underway in order to transcend the ABO-barrier.

The higher rejection episodes in APOLT series are a consequence that requires further investigation. Immunological differences in the responses to orthotopic and auxiliary allografts were reported in an experimental study, given the increased expression of class II MHC antigen on hepatocytes in auxiliary liver transplantation, and the increase in the rejection response to the auxiliary grafts (38). Auxiliary liver allografts were also demonstrated to be more susceptible to rejection than non-auxiliary allografts (39). Further histopathological studies into the mechanisms of susceptibility to rejection in APOLT cases are currently underway.

Unlike standard LDLT, the incidence of biliary complications and the need for retransplantation were shown to be higher in APOLT cases. According to our present study, we conclude that APOLT should have a restricted indication in the treatment of fulminant hepatic failure, small-for-size grafts and ABO-incompatibility. Conceptual changes were made in the treatment of small-for-size grafts, through the introduction of LDLT using right lobe with or without middle hepatic vein graft, and in the treatment of ABO-incompatible cases, through the use of a novel intra-hepatic arterial immunosuppression protocol. Non-cirrhotic metabolic liver disease may be a suitable indication for APOLT.

Acknowledgment

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ORIGINAL ARTICLE

Using a radial artery as an interpositional vascular graft in a living-donor liver transplantation for hepatocellular carcinoma

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Summary

With increasing numbers of living-donor liver transplantations (LDLTs) for hepatocellular carcinoma (HCC), cases with some arterial troubles are encountered; because most HCC cases waiting for LDLT have undergone interventional treatments. In these patients, the reconstruction of the graft artery needs to be planned preoperatively. We report a 52-year-old male, with hepatitis C-related liver cirrhosis and advanced HCC, who for 4 years repeatedly underwent continuous intraarterial chemotherapy through an implanted reservoir port. A suitable artery was not available for arterial reconstruction and the patient underwent LDLT using an autologous radial artery conduit based on the infrarenal aorta. Postoperatively, the patient is well with normal liver function and efficient arterial flow. Autologous radial artery can be safely and successfully used as an aortic-based arterial conduit when HCC patients waiting for LDLT have undergone long-term repeated intraarterial chemotherapy.

Introduction

For living-donor liver transplantation (LDLT), successful hepatic artery reconstruction is essential and interpositional vascular grafts are needed in the case of an inadequate or thrombotic hepatic artery. There are several reports regarding vascular grafts in liver transplantation: including of the saphenous vein [1], iliac artery [2], inferior epigastric artery [3] and the cadaveric iliac artery [4]. On the contrary, with increasing numbers of LDLTs for hepatocellular carcinoma (HCC) [5], cases with some arterial troubles are being encountered more often because most HCC cases waiting for LDLT have undergone interventional treatments such as transcatheter arterial embolization (TAE), transcatheter arterial chemoembolization (TACE) and intraarterial chemotherapy through the implanted reservoir. In these patients, the reconstruction

of the graft artery has to be planned preoperatively. We undertook LDLT using the radial artery as an interpositional vascular graft between the graft artery and the infrarenal aorta for an HCC patient who previously had repeated interventional treatments. Although it has routinely been used for coronary artery bypass grafting [6], there are few reports on its utility for the reconstruction of the hepatic artery in LDLT. Here, we report its versatility as an arterial conduit in LDLT.

Case report

A 52-year-old male was found positive for the hepatitis C antibody during a routine health examination in 1991. He was treated with interferon twice and has been followed ever since then because the initial treatment was not effective. In November 1999, three nodular HCC

lesions were diagnosed in liver segment 7 Couinaud's classification, 4 cm in diameter, and segments 2 and 6, both 0.5 cm, by computed tomography (CT) scan; and the patient twice underwent TAE. In May 2000, multiple HCCs were detected in liver segments 2, 3, 4, 5, 7 and 8 with diameters from 1.5 to 0.5 cm. A reservoir port was implanted and he underwent continuous intraarterial chemotherapy through it for 4 weeks. Since then, he has undergone several treatments of intraarterial chemotherapy. In July 2003, because the multiple HCCs could not be controlled by any treatment, and as he complained of liver dysfunction caused by the progression of liver cirrhosis and the HCCs, he was referred to our hospital to undergo LDLT.

Physical examination revealed him to be moderately well built with stable vital signs and with no hepatosplenomegaly or superficial lymph-node enlargement.

Serum total protein level was 6.7 g/dl with an albumin level of 2.9 g/dl. Serum liver function test results showed slightly elevated levels of aspartate transaminase (136 IU/l), alanine aminotransferase (54 IU/l) and gamma GTP (79 IU/l). The value of total bilirubin and direct bilirubim were 4.4 and 3.1 mg/dl respectively. Prothrombin time-international normalized ratio was 1.15. Hepatitis C virus (HCV) antibody, tested by EIA, was positive, and the value of HCV-RNA was 18.5 KI/ml, tested by RT-PCR method. Tumour marker levels of alpha fetoprotein and protein induced by vitamin K antagonist II (PIVKAII) were 39 131 ng/dl and 37 600 U/ml respectively.

A CT scan of the abdomen revealed multiple HCCs in liver segments 2, 3, 4, 5, 7 and 8 with diameters from 5 to 1 cm. Abdominal angiography revealed a complete obstruction of the common hepatic artery and the blood supply to the right hepatic lobe was fed from a collateral artery from the gastroduodenal artery (Fig. 1a). Celiac arterial angiography revealed stenosis of the celiac axis and the splenic, and irregularities of left gastric arteries; the blood supply to the spleen was fed from collateral arteries from the celiac axis (Fig. 1b).

We decided to use the radial artery as an interpositional vascular graft between the graft artery and the aorta. A clinical assessment of the patient's nondominant (left) arm was performed preoperatively using a modified Allen's test. In addition, pulsatile flow in the digital artery of the thumb was confirmed using a Doppler probe, while the radial artery was compressed. With a diagnosis of multiple hepatocellular carcinoma associated with liver cirrhosis, LDLT using his son's right lobe was performed on 19 August 2003. The left radial artery was procured by a cardiothoracic surgeon, highly experienced in this procedure, using previously described techniques [7] (Fig. 2a). The radial artery graft had a diameter of 4 mm and was shortened to a length of 15 cm. Cross clamping
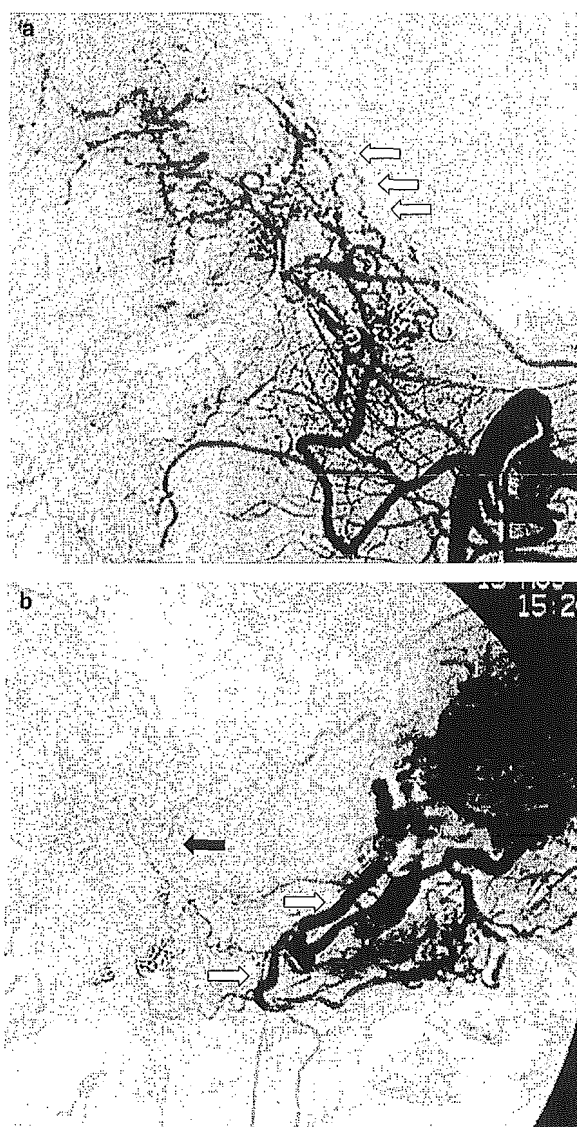
Figure 1 (a) Abdominal angiography demonstrates a complete obstruction of the common hepatic artery and the blood supply of the right hepatic lobe is fed from a collateral artery from the gastroduodenal artery, indicated by white arrows. (b) Celiac arterial angiography reveals stenosis of the celiac axis and the splenic artery, and irregularities of the left gastric arteries. The blood supply to the spleen was fed from collateral arteries from the celiac axis. A white arrow indicates collateral arteries from the celiac axis, black arrows indicate irregularities of the left gastric arteries.

was applied at the infrarenal portion of the aorta and an aortotomy was created with 4-mm aortic punch. Both ends of the radial artery were spatulated and the proximal anastomosis of the graft was carried out with 6-0 polypropylene running suture using parachute technique under 2.5 loupe magnification (Fig. 2a). The radial artery
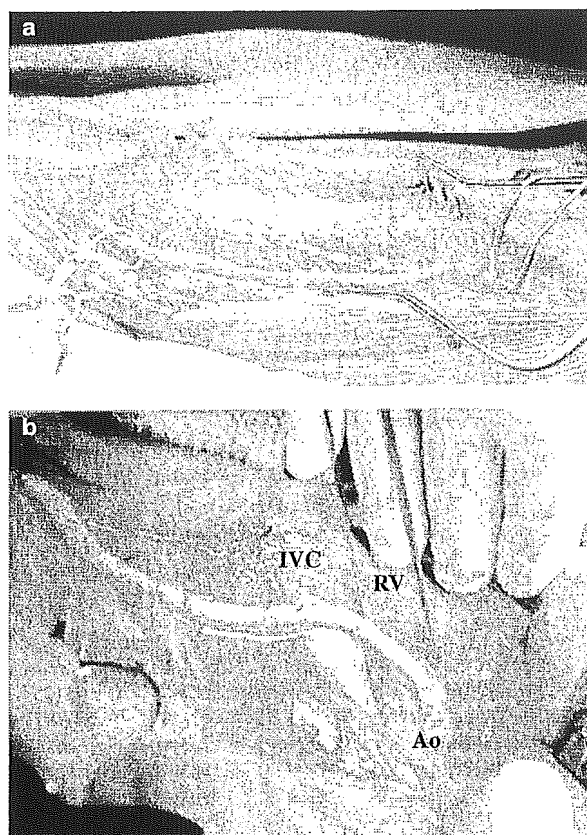
Figure 2 (a) Procurement of the left radial artery. (b) The radial artery graft is anastomosed to the infrarenal aorta. IVC, inferior vena cava; Ao, aorta; RV, renal vein.

graft was then anastomosed to the allograft hepatic artery . using an interrupted 8-0 polypropylene suture under microscopic procedures. Good arterial inflow was then demonstrated by Doppler duplex ultrasound.

The patient had a good postoperative course and the patency of the radial artery graft has been very good. He was discharged on the 23rd postoperative day without any complications. He is currently well and free of disease, 3 months after the operation.

Discussion

In recent years, progress has been achieved in the radical treatment of HCC with several therapeutic modalities, including liver resection, percutaneous ethanol injection (PEI) and radiofrequency cytoablation (RFA) [8]. However, HCC patients with repeated recurrence, tumour progression, and advanced liver dysfunction have been increasing and are unable to undergo such radical treatment; most undergo TACE or intraarterial infusion chemotherapy through implanted reservoirs to prolong

survival [9]. On the contrary, liver transplantation is an excellent treatment for HCC patients because this procedure is able to cure not only the tumour but also the underlying cirrhosis. It is reported that in 56 HCC patients who underwent LDLT most had received treatments for HCC, including TACE in 39 cases, PEI or RFA in 24 cases and liver resection in eight cases [5]. Increasingly, HCC patients are waiting for LDLT; some recipients do not have an adequate artery to reconstruct it to the graft hepatic artery such as a hepatic, gastric or splenic artery because these arteries are often injured by repeated interventional therapies.

In this case, we needed an interpositional artery graft with a length of >15 cm because we had to reconstruct the artery graft to the infrarenal aorta and the graft's hepatic artery. The saphenous vein [1], iliac artery [2], inferior epigastric artery [3] and the cadaveric iliac artery [4] have been described as interpositional arterial grafts. However, these grafts would not have sufficient length or diameter except for the saphenous vein graft. However, there have been several reports of complications of pseudoaneurysms of saphenous vein grafts after coronary bypass [10,11] and it was believed that an autologous arterial conduit would provide better long-term patency.

This is supported in the cardiac surgery literature with reports of <50% patency of vein grafts at 10 years and intraluminal disease in those grafts that were patent. In all angiographic studies, the patency rate for arterial grafts is consistently greater than for vein grafts at any point after coronary surgery [12]. The unsatisfactory patency of saphenous vein grafts compared with that of internal mammary artery grafts in these studies has stimulated a revival in the usage of the radial artery as a coronary artery bypass graft, based on the belief that it should improve long-term results from coronary operations. Carpentier *et al.* [13] first described an arterial conduit in myocardial revascularization in 1971 and the radial artery is now frequently used with excellent long-term patency rates [7,14,15]. A recent report showed an 83% angiographic patency rate of radial artery grafts at 5 years [16]. The excellent long-term patency of radial artery grafts in myocardial revascularization prompted us to use a radial artery graft for the interpositional artery graft in LDLT for this patient. Advances in minimal traumatic arterial-harvesting techniques have limited postoperative morbidity and virtually eliminated ischaemic complications. Because there are some possible complications of the donor arm such as developing of ischaemia or motor dysfunction and there are minor complications of stitch abscesses, skin dehiscence, superficial infection, and small haematomas or seromas, it is important to note that a radial artery graft should be harvested by a surgeon with experience in this technique [17].

Liver transplantation is acknowledged as the treatment of choice for patients with early, unresectable HCC and the Milan criteria have been widely accepted for selection of HCC patients for transplantation [18,19]. On the contrary, Kaihara et al. [5] reported that the 20 HCC patients beyond the Milan criteria showed tumour-free survival of approximately 50% at 2 years after LDLT. These results demonstrated the considerable possibility that even HCC patients, who had been excluded by the Milan criteria, can survive for long periods after transplantation. In our institution, all HCC patients have the extent of tumour involvement evaluated with abdominal, chest and brain CT scans, and by bone scintigraphy within the 2 months before transplantation; but condition, number and size of the tumours are not criteria for exclusion. The present patient underwent LDLT for HCC beyond the Milan criteria. However, as he would get the opportunity for long-term survival, long-term arterial graft patency would be necessary.

In conclusion, we believe that this report is the first documented use of an autologous radial artery for interpositional artery graft in LDLT for HCC patients. Although the radial artery is not a first-line arterial conduit, it can safely and successfully be used when a suitable recipient's artery is unavailable and the use of a saphenous vein or other conduits is believed to be undesirable. Autologous radial artery grafts should be added to the transplant surgeon's armamentarium as needed for interpositional artery graft in LDLT patients who have undergone repeated intraarterial chemotherapy for HCC.

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Impact of Right Lobe with Middle Hepatic Vein Graft in Living-Donor Liver Transplantation

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Technical improvements in adult-to-adult living-donor liver transplantation (LDLT) have led to the use of right-lobe grafts to overcome the problems encountered with 'small-for-size grafts'. The major controversy remains that the venous drainage from anterior segment substantially depends on tributaries of the middle hepatic vein (MHV), and deprivation of such tributaries may critically influence the postoperative graft function. Right-lobe grafts with MHV could resolve the potential problem of congestion in anterior segment. From December 2000 to January 2004, we performed 217 right-lobe LDLTs for adult patients. Of these, 40 patients received a right lobe with MHV graft (18.4%). The overall cumulative 3-year graft survival rate of a right lobe with (n = 40) and without MHV (n = 177) was 86.2% and 74.8% (p = NS). The proximal side of the MHV and the drainage vein of segment IV to the MHV (the left medial superior vein) were preserved in 24 patients. All of them needed venous interposition graft for anastomosis. All patients had a patent right hepatic vein (RHV) and MHV anastomosis during the follow-up period. We adopted the right lobe with MHV graft in 40 LDLT cases. Vein graft is essential for safe MHV anastomosis in cases which preserve proximal side of the MHV.

Key words: Hepatic vein reconstruction, liver transplantation, living donor, right-lobe graft

Introduction

The accumulating results of living-donor liver transplantation (LDLT) are comparable to those of cadaveric transplantation (1). Experience of and technical improvements in left-lobe donation have led to the use of right-lobe grafts in adult-to-adult LDLT to overcome the problems encountered with 'small-for-size grafts'. We have reported that the use of 'small-for-size grafts' (<1.0% of recipient body weight) leads to lower graft survival, probably through enhanced parenchymal cell injury and reduced metabolic and synthetic capacity (2).

The major controversy about right-lobe LDLT remains that the venous drainage from the anterior segment depends substantially on tributaries of the middle hepatic vein (MHV), and deprivation of such tributaries may influence the postoperative graft regeneration (3). We have reported that the regeneration of the posterior segment was significantly greater than that of the anterior segment. Despite deprivation of MHV tributaries, a graft will regenerate to meet the metabolic demand (4). However, some patients substantially suffered from complications related to 'small-for-size graft'. In some right-lobe grafts, regional volume of the MHV might be dominated over the right hepatic vein (RHV), and the functional liver volume could be reduced in such type of the grafts. To maximize the benefit of right-lobe graft, several technical modifications have been reported, such as additional venous reconstruction of segment V and VIII (5–8).

The application of right lobe with MHV graft could resolve the potential problem of congestion in the anterior segment (6). However, sufficient drainage veins of the remnant donor liver might not be certified due to the presence of tributaries from segment IV to the MHV (left medial superior vein) (9). Preservation of the drainage veins of segment IV to the MHV in the donor might be important for surgical innovation in right lobe with MHV LDLT.

Recent developments in imaging studies have made it possible to visualize the distribution of the hepatic vessels without hepatic dissection (10). Preoperative three-dimensional (3D) computed tomography (CT) volumetry and computer-assisted volumetric analysis according to the hepatic venous anatomy (MeVis, Germany) were adopted as a noninvasive and objective evaluation for application of a right lobe with MHV graft (11). The computer-assisted preoperative donor risk analysis is helpful for providing volumetric calculations, relating the volume of the compromised areas to total graft or remnant liver. We describe the surgical techniques and outcome in 40 cases of

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hepatic vein reconstruction in LDLT using right lobe with MHV grafts, while preserving the significant drainage veins of segment IV to the MHV remaining in the donor.

Patients and Methods

During the period from June 1990 to January 2004, 966 LDLTs were performed in 922 patients at Kyoto University Hospital. Right-lobe LDLT was first carried out in February 1998, and we have since carried out 345 right-lobe LDLTs. Since the initiation of the right lobe with MHV graft procedure for adult patients (>18 years old) in December 2000, we have performed a total of 217 cases of right-lobe LDLTs for adult patients in the same period. Of these, 40 patients received a right lobe with MHV graft (18.4%). Nineteen cases of right-lobe LDLT with additional vein reconstruction of the anterior segment were excluded from the study.

The patients were 29 males and 11 females, with a median age of 49.7 years (range: 18.8–65.7), and a median weight of 64.3 kg (range: 37.1–99.0). Median model for end-stage liver disease (MELD) score was 19.0 (range: 4.0–37.0). The indication for transplantation was hepatocellular carcinoma with hepatitis C virus (HCV) cirrhosis in 17 patients; hepatocellular carcinoma with hepatitis B virus (HBV) cirrhosis in 4; liver cirrhosis in 9 (HCV in 6, HBV in 1 and alcoholic in 2); biliary atresia in 3; fulminant hepatic failure in 2; primary biliary cirrhosis in 2; glycogen storage disease in 1; retransplantation in 1 and a metastatic neuroendocrine tumor (pancreatic polypeptide-secreting tumor) in 1. Six patients received blood-type incompatible grafts (Table 1).

Immunosuppression consisted of tacrolimus and low-dose steroids (12). Patients who received blood-type incompatible transplants had preoperative plasma exchange or double-filtration plasmapheresis in order to reduce the anti-ABH antibody titer. Prostaglandin E1, cyclophosphamide and additional steroids were administered from the portal vein or hepatic artery postoperatively (13).

Donor evaluation
Potential donors were evaluated through the use of liver function tests, determination of blood type, HLA typing and determination of anatomical variation and graft size using 3D CT volumetry. The potential indication for right lobe with MHV grafting was a graft-to-recipient weight ratio (GRWR) of less than 1.0% with right-lobe graft, as determined by preoperative 3D CT volumetry. If the regional volume of the MHV dominated over the RHV and the remnant liver volume in the donor was shown to be over 35% of the whole liver volume, then the entire MHV could be included with the graft. If not, the proximal side of the MHV, which is the concourse of the segment IV drainage vein (left medial superior vein), should be left in the donor to reduce the risk of venous congestion in segment IV. The MHV dominance in right lobe was defined as follows:

regional volume of vein 5 + vein 8/right-lobe volume × 100 > 40%.

Donor operation
Before parenchymal transection, the right lobe was mobilized and the sizeable right inferior hepatic vein (RIHV; >5 mm) was preserved with a caval cuff for reconstruction. After careful definition of biliary anatomy in the hepatic hilum using intraoperative cholangiography, the right hepatic duct was transected. The right portal vein and the right hepatic artery were temporally clamped to clarify the parenchymal transection line.

The surface markings of the donor liver consisted of a line from a point to the middle of the gallbladder fossa anteriorly and inferiorly/dorsally to the left side of the RHV entry to the vena cava. An 8-mm Penrose drain was passed between the RHV superiorly and the portal bifurcation inferiorly to maintain the cutting plane during parenchymal dissection (hanging maneuver technique) (14).

The initial parenchymal transection line should be same as the standard right-lobe donation. When encountering the MHV or V5 peripherally, the cutting line was modified to the left side of the MHV. Parenchymal transection was continued until the junction of the MHV and left hepatic vein without inflow occlusion. The MHV was transected distal to the common trunk with the left hepatic vein. When the hepatic vein from segment IV (left medial superior vein) had a significant drainage region in the remnant liver as determined by 3D CT volumetry, the proximal side of the MHV and the drainage vein of segment IV to the MHV were preserved in the donor (right lobe with partial MHV graft). Perfusion of the graft was done through

Table 1: Characteristics of 217 Right-Lobe Living-Donor Liver Transplantation With or Without Middle Hepatic Vein

	With MHV (n = 40)	Without MHV (n = 177)	p-value
Donor demographics			
Age (years)	41.3 ± 11.8 (range: 21–61)	40.1 ± 11.4 (range: 19–64)	NS
Weight (kg)	58.5 ± 10.5 (range: 40–80)	63.6 ± 10.9 (range: 42–107)	NS
Operation time (min)	432 ± 74.8 (range: 308–528)	402 ± 82.1 (range: 198–660)	NS
Blood loss (g)	243 ± 217 (range: 25–1030)	239 ± 241 (range: 5–2300)	NS
Blood-type combination	29:5:6	109:34:34	NS
(identical: compatible: incompatible)			
Recipient demographics			
Sex	Male, 29; female, 11	Male, 83; female, 94	
Age (years)	50.1 ± 12.8 (range: 18–66)	42.9 ± 15.2 (range: 16–69)	NS
Weight (kg)	64.3 ± 13.8 (range: 37.1–99.0)	60.0 ± 11.4 (range: 28.3–96.0)	NS
MELD score*	18.8 ± 7.1 (range: 6–37)	20.5 ± 9.2 (range: 6–54)	NS
Operation profiles			
Cold ischemic time (min)	128 ± 83 (range: 30–372)	99 ± 85 (range: 30–372)	NS
Warm ischemic time (min)	59 ± 16 (range: 27–100)	45 ± 16 (range: 22–114)	<0.001
Operation time (min)	781 ± 200 (range: 400–1415)	730 ± 178 (range: 337–1291)	NS
Blood loss (g)	5977 ± 6776 (range: 320–33 000)	7088 ± 9768 (range: 350–60 000)	NS
Graft weight (g)	678.9 ± 165.2 (range: 445–1270)	699.3 ± 120.9 (range: 425–1080)	NS
GRWR** (%)	1.10 ± 0.26 (range: 0.70–1.70)	1.20 ± 0.28 (range: 0.60–2.40)	NS

*Model for end-stage liver disease.
**Graft-to-recipient weight ratio.
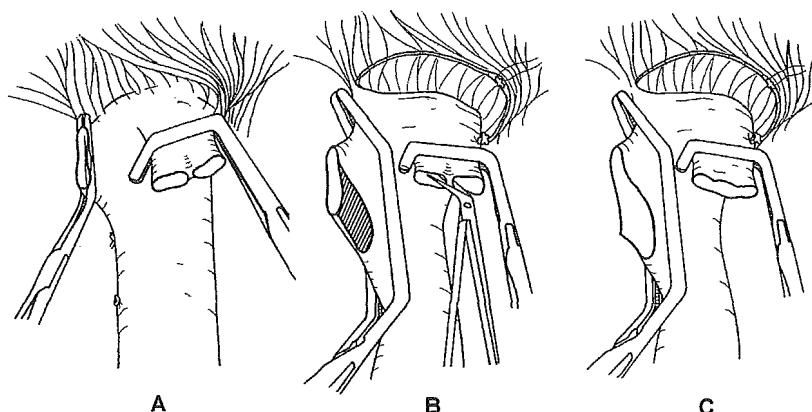
Figure 1: Skeltonization of the inferior vena cava and the hepatic veins to allow adequate spacing for the hepatic vein anastomosis (A,B). The orifice of the RHV was enlarged with a downward incision and an anterior wall excision making an oval orifice to obtain sufficient outflow (B,C).

the right portal vein with a histidine-triptophan-ketoglutarate solution (Dr. Franz Köhler Chemie, Alsbach-Hähnlein, Germany).

Back-table operation

In the case of a right lobe with partial MHV graft, the stump of the MHV was too short to be anastomosed directly to the recipient MHV, and the MHV orifice was not always close enough to the RHV to make a common cuff plasty. The vein graft, i.e. the recipient's portal branch, left portal vein or inferior mesenteric vein or donor's ovarian vein, was prepared according to the size of MHV and was anastomosed as an interposition graft to the MHV stump on the back table (6-0 polypropylene, Prolene, Ethicon, Japan).

Recipient operation

After a total hepatectomy, the top vena cava was freed from its diaphragmatic attachments, by dividing the phrenic veins, and was skeltonized to allow adequate spacing for the hepatic vein anastomosis (Figure 1). During the anhepatic period, a portosystemic shunt was made between the right portal branch and the inferior vena cava (IVC) to prevent portal hypertension in the patients without collaterality. The orifice of the RHV was enlarged with a downward incision and an anterior wall excision making an oval orifice to obtain sufficient outflow. Anastomosis of the RHV was accomplished in an end-to-end fashion with a continuous suture (5-0 Prolene). Significant RIHV was anastomosed to the sidewall of the IVC, the recipient RIHV or the stump of the portosystemic shunt. The interposition vein graft was anastomosed to the recipient's MHV with an interrupted suture in the anterior wall. The patch graft technique was used with an interrupted suture if tension was seen in the anterior wall of the MHV anastomosis. Portal and arterial reconstructions were carried out according to our previous report (15). Biliary reconstruction was carried out with duct-to-duct anastomosis in 36 cases, and with Roux-en-Y hepaticojejunostomy in four cases with 6-0 polydioxanone suture.

Statistical analysis was performed using the generalized Wilcoxon test. Actuarial survival rate was calculated with the nonparametric Kaplan-Meier method and was compared with the Wilcoxon test throughout the study. p-values < 0.02 were considered significant.

The study was approved by the international review board and informed consent was obtained in all the cases.

Results

Donor outcome

A comparison was made between right lobe with MHV grafts from living donors (n = 40) and graft cases without MHV (n = 177).

The median right lobe with MHV graft donor operation time was 420 min (range: 308–528), and median blood loss was 195 g (range: 25–1030). No blood transfusion was given during the donor operation. Four (10%) out of 40 donors experienced complications that required treatment, including two cases of biliary leakage, one of biliary stricture and one of liver failure. Biliary leakage was successfully resolved with percutaneous aspiration. Biliary stricture was treated by reexploration surgery. The liver failure was caused by unsuspected nonalcoholic steatohepatitis and small remnant liver volume. The donor underwent domino liver transplantation, but died from sepsis 9 months after the initial operation (16).

Of 177 donors of a right lobe without MHV graft in our center, duration of the donor operation was 402 ± 82.1 min and blood loss was 239 ± 241 g. There was no significant difference in duration of surgery or blood loss in the donors between right lobe with or without MHV graft operation. Nineteen (10.7%) out of 177 donors experienced complications that required treatment: 14 cases of biliary leakage; 1 of pulmonary embolization; 3 of wound infection and 1 of wound hernia. Nine donors with biliary leakage required endoscopic nasobiliary tube drainage (17).

To evaluate the impact of right-lobe donation, postoperative liver function tests in the donors were analyzed in relation to the type of graft carried out. However, asparate aminotransferase (AST) and serum bilirubin levels showed no significant difference between right-lobe donation either with or without MHV graft (Figure 2).

Recipient outcome

The median recipient operation time for right lobe with MHV graft was 753 min (range: 400–1415), and the median blood loss was 4100 g (range: 320–33 000). The median cold and warm ischemic time was 103 (range: 30–372) and 57 min (range: 27–100). The median graft weight was 675 g (range: 445–1270), and the median GRWR was 1.10% (range: 0.70–1.70%).
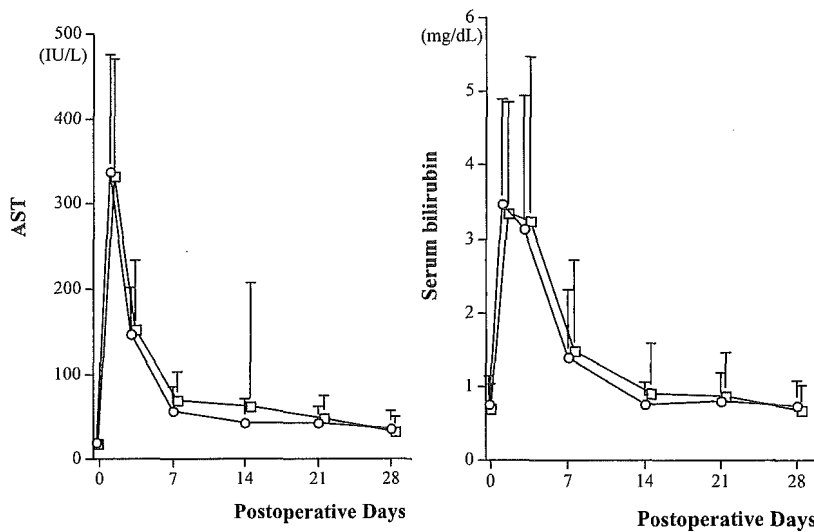
Figure 2: Postoperative liver function tests in the donors. O: Right lobe with middle hepatic vein graft; □: Right lobe without middle hepatic vein graft.

Among 177 recipients of a right lobe without MHV graft, duration of the recipient operation was 730 ± 178 min and blood loss was 7088 ± 9768 g. The graft weight and GRWR range was 699.3 ± 120.9 g and 1.20 ± 0.28%. The cold and warm ischemic time was 99 ± 85 and 45 ± 16 min, respectively. There was no significant difference in duration of surgery, blood loss and GRWR in the recipients between right lobe either with or without MHV graft. However, the warm ischemic time was significantly longer in the right lobe with MHV graft group (p < 0.001).

With regard to liver function tests, there was no significant difference in AST or prothrombin levels between the two groups. Although preoperative serum bilirubin level was significantly lower in the right lobe with MHV graft group (p < 0.02), serum bilirubin clearance was much delayed and persistent hyperbilirubinemia was observed in the right lobe without MHV graft group (Figure 3).

Venous reconstruction

With regard to the patients who had right lobe with MHV graft, a direct MHV anastomosis was possible in 12 patients in an end-to-end fashion (30.0%). Of these cases, the common cuff technique of the MHV and RHV in the graft after venoplasty, as reported by Lo et al. (18), was indicated in four. The proximal side of the MHV and the drainage vein of segment IV to the MHV (left medial superior vein) were preserved in 24 donors and a venous interposition graft was necessary in these cases: native portal vein in 19 cases; native inferior mesenteric vein in 2; donor's ovarian vein in 2 and native portal vein patch graft in 1. A Y-shaped portal vein graft was adopted in 13 cases, an I-shaped vein graft in 10 and a patch graft in 1, according to the distance between graft and recipient MHV (Figure 4).

Fourteen RIHV were reconstructed in 13 patients (46.4%). All patients had a patent RHV and MHV anastomo-

sis confirmed by routine Doppler ultrasonography and/or CT/magnetic resonance imaging (MRI) at least 1 month after transplantation. There were no complications related to the hepatic vein anastomosis during the follow-up.

One patient had portal vein thrombosis 19 days after LDLT, and this was successfully treated by reexploration surgery. Two patients developed biliary leakage, which was resolved by percutaneous aspiration. Four cases developed biliary stricture, and this was treated with endosopic retrograde biliary drainage (19). Causes of death were sepsis in one patient, intraabdominal bleeding in one, multiple organ failure secondary to small intestinal perforation in one and severe pneumonia in one. The overall cumulative 3-year graft survival rate of right lobe with MHV graft was 86.2%, with a median follow-up of 18 months (range: 6–36). The cumulative 3-year graft survival rate of 143 right lobe without MHV graft for the same period was 74.8% (Figure 5; p = 0.38, NS).

Discussion

Right-lobe LDLT can provide an adequate graft size to compensate for the metabolic demands in most adult recipients, and the clinical outcome has improved in our series (5). One of the controversies in right-lobe LDLT is the potential congestion in the graft anterior segment due to the deprivation of the MHV tributaries. Techniques of venous reconstruction and the graft selection remain an open question.

Our standard technique of harvesting the right-lobe graft requires the transection of the MHV tributaries from the anterior segment to leave the entire MHV in the donor (20,21). To prevent congestion in the anterior segment, several technical modifications were reported. Fang et al. have adopted an extended right-lobe graft with the MHV
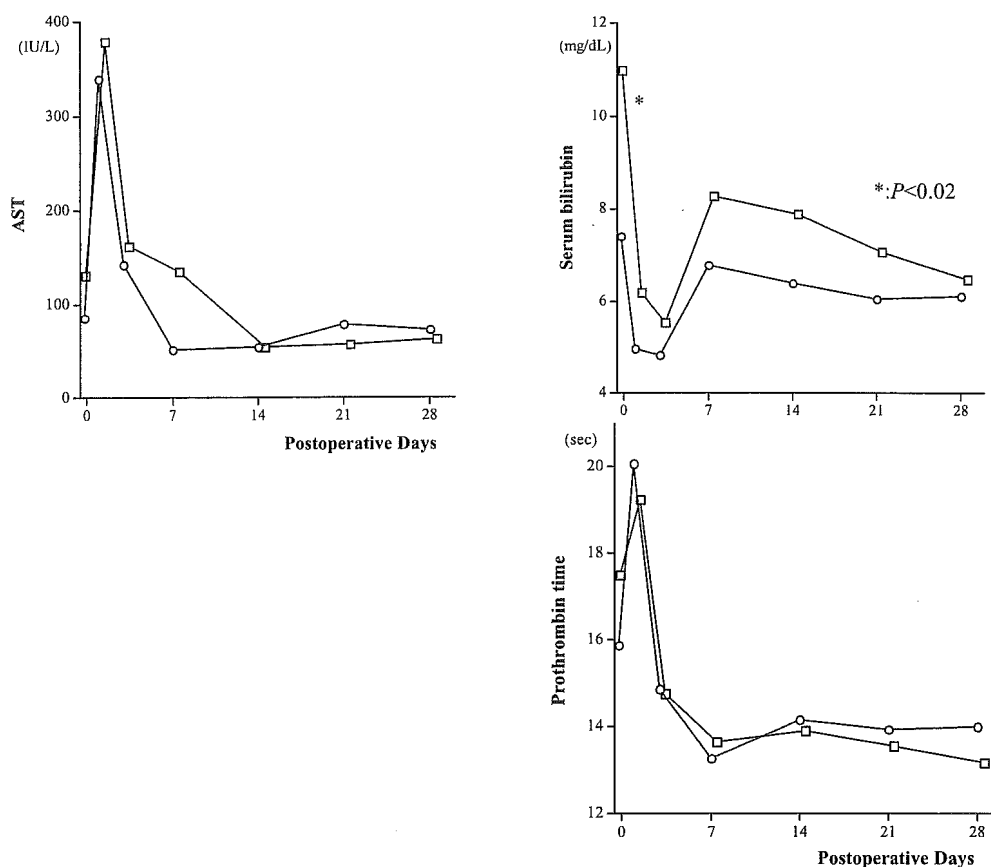
Figure 3: **Postoperative liver function tests in the recipients.** O: Right lobe with middle hepatic vein graft; □: Right lobe without middle hepatic vein graft.
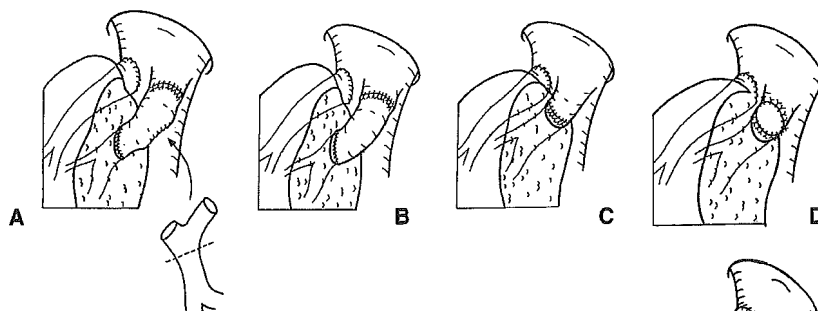

Figure 4: The type of middle hepatic vein anastomosis with/without the use of interposition vein graft. (A) Y-shaped portal vein graft (n = 13), (B) I-shaped vein graft (n = 10), (C) direct anastomosis (n = 12), (D) patch graft (n = 1); and (E) venoplasty (n = 4).

- A. Y-shaped portal vein graft   (n=13)
- B. I-shaped vein graft   (n=10)
- C. Direct anastomosis   (n=12)
- D. Patch graft   (n=1)
- E. Venoplasty   (n=4)

(6,22), and reconstruction of the MHV with an interposition vein graft has also been adopted by the Toronto group (23). Reconstruction of the segment V/VIII branches using jump grafts has been reported both with and without the intraoperative MHV clamp test to confirm graft congestion in some centers (8,24). However, additional venous reconstruction of the anterior segment did not significantly reduce graft congestion defined on MRI despite the patency of reconstructed drainage veins in our previous series (25).
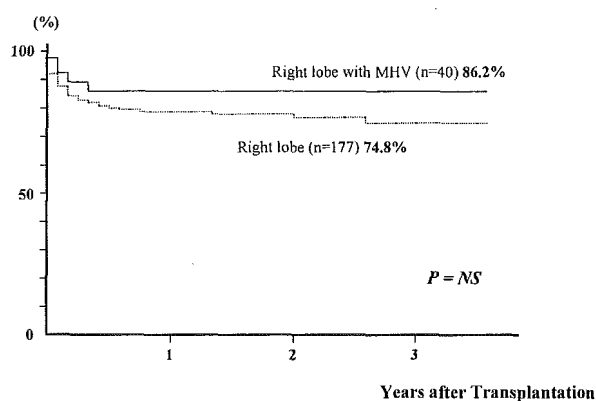
Figure 5: The overall cumulative graft survival rate in right lobe with/without middle hepatic vein.

Based on our previous study, graft congestion in the anterior segment could be well tolerated and improved through intrahepatic anastomosis when the portal and arterial inflow and the RHV outflow were preserved (5,25). Although the regeneration of the posterior segment was shown to be superior to that of the anterior segment, the lack of anterior segment regeneration was resolved by a compensatory regeneration of posterior segment and the graft congestion in the anterior segment did not affect the overall graft regeneration (4). After the initiation of right lobe with MHV graft, however, we experienced some patients who suffered from complications related to 'small-for-size graft'.

Our recent study revealed that right lobe with MHV graft showed no congestion on MRI imaging (26). However, it remains open to question whether or not right lobe with MHV graft should be indicated in all adult recipients. Nakamura et al. suggested that 26.5% of the MHV had proper branches that internally drained from the anterior segment (27). Kinkhabwala et al. reported that 26% of the accessory venous reconstruction from the anterior segment was necessary in right-lobe LDLT (28). We agree with these results that the reconstruction of MHV tributaries was not always necessary and should be indicated according to the preoperative imaging study.

A graft without MHV reconstruction would be given a 'functional liver volume' that corresponded to area drained by the RHV (and RIHV if reconstructed), while a graft with MHV reconstruction would have the anterior segments included in the right-lobe calculation with 3D volumetry. In our preliminary study of 3D CT volumetry in right-lobe LDLT series, the regional volume of V5 and V8 in right lobe was $29.4 \pm 11.1\%$ (range: 12.4–56.7%) and 18.0% of the grafts showed MHV dominant (n = 52; data not shown). The importance of drainage vein in the anterior segment could be emphasized in the MHV dominant graft. Moreover, the tolerability of congestion in anterior segment and the compensate regeneration of posterior segment might not be

guaranteed in the MHV dominant right-lobe graft. We recommend right lobe with MHV graft or additional vein reconstruction of the anterior segment in the MHV dominant right-lobe graft.

Recently, the Kaohsiung group provided an adequate algorithm for determining the extent of donor hepatectomy in right-lobe LDLT either with or without MHV. The decision to take MHV with the graft was made based on the donor-to-recipient body weight ratio and the size of the MHV tributaries from the anterior segment (29). The initial indication for right lobe with MHV graft in our institution was the GRWR < 1.0% using right-lobe graft. Figure 6 shows our current algorithm for the graft selection after the initial experience of 40 right lobes with MHV LDLTs. The graft selection should be made according to the RHV/MHV dominance, GRWR and remnant liver volume. It is important for avoiding the possibility of anterior segment congestion having information of the MHV dominant before an operation with 3D volumetry. If the graft selection is inconclusive, further discussion should be necessary to secure the recipient benefit as well as donor safety considering the graft quality and metabolic load of the recipient.

The inflow modulation of in 'small-for-size graft' might be an another important issue. Our study showed that elevated portal vein pressure (>20 mmHg) is strongly associated with poor patient survival attributable to 'small-for-size syndrome'. Further elucidation of the pathogenesis behind this phenomenon and efforts to modify portal vein pressure will be a key to improving results (30). Moreover, our recent study suggested that partial diversion of portal flow to systemic circulation and splenic artery ligation might be effective for avoiding injuries that occur in 'small-for-size graft' (31). The same technical modification was adopted in some centers in order to avoid graft congestion and failure by portal overperfusion (32,33). The decrease of portal vein pressure may be able to be used as an effective method to attenuate the 'small-for-size syndrome'. Further discussion about portocaval shunt and splenic artery ligation should be necessary to make a conclusion for the graft selection in right-lobe LDLT.

In determining whether a donor can provide adequate liver volume at acceptable risks, it is important to know not just the remnant liver volume but also the anatomical factors that may affect the functional capacity of the donor remnant liver. It was reported that 9.5% of patients had a left medial superior vein originating from the MHV and draining predominantly the left medial superior segment (27). The impairment of regeneration and functional recovery of segment IV after right lobectomy with MHV has been reported, while the overall regeneration of the remnant liver was not affected by the MVH harvesting in right-lobe LDLT (34).

The mean regional volume of the left medial superior vein in 3D CT evaluation was 159.3 ± 28.8 mL and the
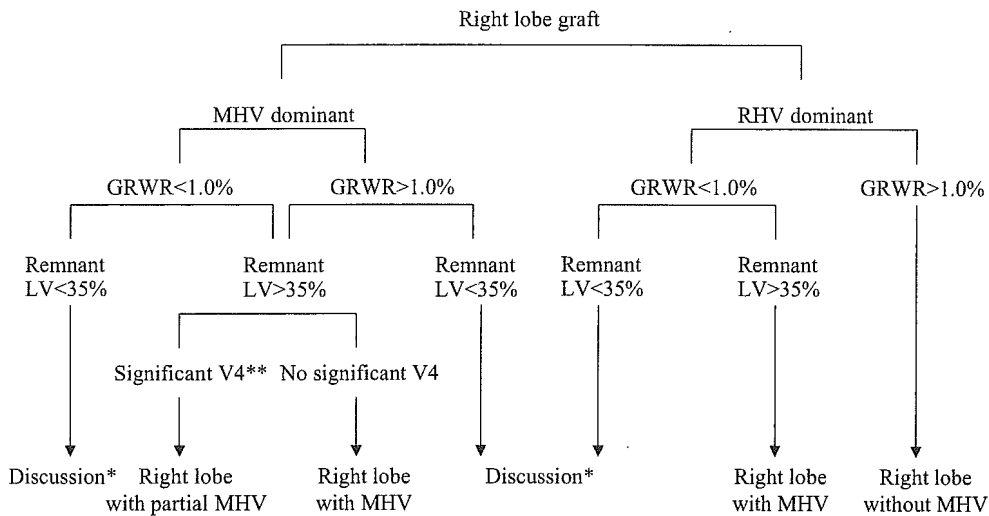
Figure 6: Algorithm for the graft selection. RHV: right hepatic vein; MHV: middle hepatic vein; GRWR: graft-to-recipient weight ratio; LV: liver volume. RHV dominant: regional volume of vein 5 + vein 8/right-lobe volume × 100 < 40% MHV dominant: regional volume of vein 5 + vein 8/right-lobe volume × 100 > 40% *Discussion for; additional vein reconstruction of V5/8, dual graft, auxiliary liver transplantation, ligation of splenic artery and/or partial portocaval shunt, exclude from potential donor candidate **V4: drainage vein of segment IV to the MHV (left medial superior vein).

percentage of the regional volume of left medial superior vein in remnant liver was 40.5 ± 8.0% (range: 27.9–49.9%) in our series (n = 52, data not shown). To obtain more evidence of the segment IV drainage vein and RIHV, a further study of '3D volumetric analysis' is now underway in order to clarify the exact role of these drainage veins. Evaluation of the regional volume of the left medial superior vein is important for the donor safety.

If the regional volume of the left medial superior vein was significant, then the proximal side of the MHV and the left medial superior vein were preserved in the donor, given that the MHV was divided at the side proximal to the left medial superior vein. If the remnant liver volume was revealed to be less than 35% of the whole liver volume, the potential donor was excluded and another donor candidate or option was considered, such as auxiliary liver transplantation, dual liver transplantation and additional vein of the anterior segment reconstruction (35–37).

Manner of the MHV reconstruction is controversial. It was reported that 7.6% of MHV anastomoses were found to be occluded intraoperatively even in an experienced center (22). Direct end-to-end MHV reconstruction was possible in 40.0% of the patients with entire MHV graft. Skeltonization of the IVC and the hepatic veins are important to allow adequate spacing for the hepatic vein anastomosis. In the case of a MHV divided proximal to the left medial superior vein, vein graft should be used to prevent torsion and tension in the anastomosis, as the MHV is considered too short for safe anastomosis. Recently, the common cuff of the MHV and RHV in the graft after venoplasty has been reported (18). While it is an excellent technique, reconstruction of

the outflow of the RHV and distal part of the MHV into a single opening may not be possible if their orifices are far apart, and both may need to be implanted separately into the recipient IVC.

In conclusion, we adopted right lobe with MHV graft in 40 LDLT cases. Although no significant differences were revealed in the donor and recipient liver function tests nor in patient survival between right-lobe LDLT with or without MHV, right lobe with MHV graft should be indicated in very selected patients according to algorithm for the graft selection paying special attention to donor safety. It is hoped that as experience increases and refinements are made to the technique, improved outcomes in right-lobe LDLT will be seen.

Acknowledgment

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Living-donor liver transplantation for situs inversus: 2 case reports

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Index words:
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Abstract Two cases of living-donor liver transplantation performed in patients with situs inversus arereported. The authors discuss the operative management for a situs inversus recipient to undergo liver transplantation.
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Liver transplantation has been accepted as the treatment of choice for patients with end-stage liver disease. Biliary atresia is one of the most common indications in children for liver transplantation. The disorder is associated with other congenital abnormalities in 10% to 27% of patients, which includes situs inversus [1].

Situs inversus is characterized by a mirror image orientation of the abdominal and thoracic viscera relative to the midline. The etiology of this disease is unclear, and the incidence is very low, as it occurs in less than 0.005% of the general population [2]. Situs inversus may occur in up to 28% of children with biliary atresia [3,4].

Situs inversus was once considered a contraindication to liver transplantation because of technical difficulties inherent in the procedure. Patients with a combination of vascular anomalies, including an interrupted inferior vena cava (IVC), a preduodenal portal vein, and an anomalous hepatic arterial anatomy, have been highly questionable candidates for liver transplantation [5], but it is very controversial.

We present 2 cases of living-donor liver transplantation performed in patients with situs inversus. In this report, we discuss the operative management for a situs inversus recipient to undergo liver transplantation.

1. Case report

1.1. Case 1

A 5-year-old boy presented with end-stage liver disease for living-related liver transplantation. He had a history of biliary atresia and had undergone a Kasai portoenterostomy at the age of 13 months. At that time, he was noted to have situs inversus, polysplenia, intestinal malrotation, and preduodenal portal vein.

After the Kasai operation, ascending cholangitis frequently occurred, and he developed liver failure. The father, who was selected as an organ donor, had normal abdominal anatomy by computed tomography scan. A left lateral segment was harvested as a graft. The procedure was performed as reported previously [6].

In the recipient operation, complete situs inversus, including nonrotation of the gut, polysplenia, and a preduodenal portal vein, was verified. The retrohepatic IVC was absent, and the hepatic veins drained directly into

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the right atrium. The right and left hepatic arteries independently originated directly from the supraceliac aorta. The graft was placed in the midline position to align the vascular anastomoses.

The donor left hepatic vein was anastomosed directly to the shared hepatic vein ostium in an end-to-end fashion. Because of sclerosis and narrowing of the wall, the portal vein of the recipient was resected at the confluence of the splenic vein and the superior mesenteric vein superior to the pancreas. The inferior mesenteric vein of the donor, which was the interposition vein graft, was anastomosed to the recipient portal vein in an end-to-end fashion. On the opposite side, transversing over the duodenum, it was anastomosed to the donor left portal branch in an end-to-end fashion. In spite of transversing over the duodenum, the anastomotic site was not under tension. The recipient hepatic artery was anastomosed to the donor left hepatic artery using microvascular techniques [7]. The bile duct was anastomosed to the previously created Roux-en-Y limb. A 4F polyvinylalcohol tube was inserted as an external stent to prevent anastomotic stenosis or obstruction.

Postoperatively, the graft function was excellent. During the 9-year follow-up, the patient did well without any surgical complications.

1.2. Case 2

A 2-year 4-month-old girl presented at Kyoto University Hospital with progressive hepatic failure secondary to biliary atresia after a Kasai portoenterostomy. She had undergone the procedure at the age of 2 months, at which time she was noted to have situs inversus with dextrocardia, polysplenia, intestinal malrotation, and a preduodenal portal vein. After the Kasai operation, the patient had frequent episodes of ascending cholangitis and had developed liver failure 2 years after the initial Kasai operation.

Her parents were evaluated as potential organ donors for liver transplantation, and both of them had normal anatomic findings on computed tomography scan. The mother was selected as the organ donor because the father had a fatty liver. A left lateral segment from her mother was harvested as a graft.

In the recipient operation, complete situs inversus, including nonrotation of the gut, polysplenia, a left-positioned vena cava, and a preduodenal portal vein, was verified. The proper hepatic artery arose directly from the supraceliac aorta and bifurcated into a left and right hepatic artery.

The graft was placed in the left side of the abdominal cavity. The graft had separate segments 2 and 3 veins, and both veins were independently anastomosed to the recipient hepatic vein orifice, because they were too far apart to make a single anastomosis. An orifice was created to connect the left and middle hepatic veins by incising the IVC, and this structure was then anastomosed end-to-end to the graft segment 2 vein. The right hepatic vein of the recipient was sutured from the left corner to adjust the size and anasto-

Table 1   Profiles of cases

	Case 1	Case 2
Age (y)	5	2
Weight (kg)	15	10.5
Native liver abnormalities	Absence of retrohepatic IVC preduodenal PV right and left HA direct from aorta independently	Left-sided IVC preduodenal PV proper HA direct from aorta
Donor relation	Father	Mother
Blood type combination	Identical	Identical
GRWR	1.56	2.28

GRWR indicates graft-to-recipient weight ratio; PV, portal vein; HA, hepatic artery.

mosed end-to-end to the graft segment 3 vein. Because of sclerosis and narrowing of the wall, the portal vein of the recipient was resected superior to the pancreas. Then, the donor ovarian vein, which was the interposition vein graft, was anastomosed to the recipient portal vein in an end-to-end fashion. On the opposite side, transversing the duodenum, the vein graft was anastomosed to the donor left portal branch in an end-to-end fashion without tension. The recipient right hepatic artery was anastomosed to the donor left hepatic artery using microvascular techniques. The bile duct anastomosis was created with the Roux-en-Y limb in the usual fashion, and a 4 French polyvinylalcohol tube was inserted. Postoperatively, the graft function was excellent. Currently, 2 years and 9 months after liver transplantation, the patient is doing well.

2. Discussion

The prevalence of situs inversus in the general population is difficult to establish. The estimated incidence is between 0.002% and 0.1% [8]. Nearly 80% of these patients are affected with other congenital malformations, including visceral and vascular anomalies and biliary atresia, which is one of the most common indications for liver transplantation [3,9]. Biliary atresia in association with other congenital structural anomalies has a poor prognosis, and these patients continue to have poor bile secretion after Kasai portoenterostomy [10]. Complex vascular anomalies associated with situs inversus increased the technical difficulty of the operation and resulted in a high mortality rate in these patients, especially in the context of an interrupted IVC, a preduodenal portal vein, and an anomalous hepatic artery origin. The technical aspects of performing liver transplantation in these patients are more challenging than simply overcoming the mirror-image liver anatomy.

Mattei et al [11] described the results of 26 patients with situs inversus who had undergone liver transplantation. In that report, they stated that the anatomic variations