0.77 ($P<0.001$) and that the AUCs of the APRI for ≥ F3 and F4 fibrosis were 0.92 and 0.91, respectively. By contrast, Lind *et al.*[13] reported that the APRI was not significantly different according to the fibrosis stage in 31 patients at the time of hepatoportoenterostomy. In 23 patients after successful hepatoportoenterostomy (median, 4.2 years; range, 1.6–18.9 years after surgery), Lampela *et al.*[14] described a significant correlation between the APRI and Metavir fibrosis score ($r=0.63$, $P<0.001$) and a good diagnostic accuracy of the APRI for ≥F3 with 93% sensitivity and 67% specificity. Another noninvasive fibrosis marker, transient elastography (Fibroscan), was more recently investigated to assess liver

Table 4 Cutoff values and diagnostic accuracies of the infant biliary atresia liver fibrosis (iBALF) score for predicting histological fibrosis stages

	n (%)	Cutoff	Sensitivity	Specificity	Accuracy
Development cohort (n = 73)					
≥F2	63 (86.3%)	3.00	77.8%	80.0%	78.1%
≥F3	44 (60.3%)	3.99	86.4%	86.2%	86.3%
=F4	24 (32.9%)	5.75	91.7%	93.9%	93.2%
Validation cohort (n = 117)					
≥F2	109 (93.2%)	3.56	83.5%	75.0%	82.9%
≥F3	86 (73.5%)	4.34	80.2%	80.6%	80.3%
=F4	59 (50.4%)	5.12	84.7%	79.3%	82.0%

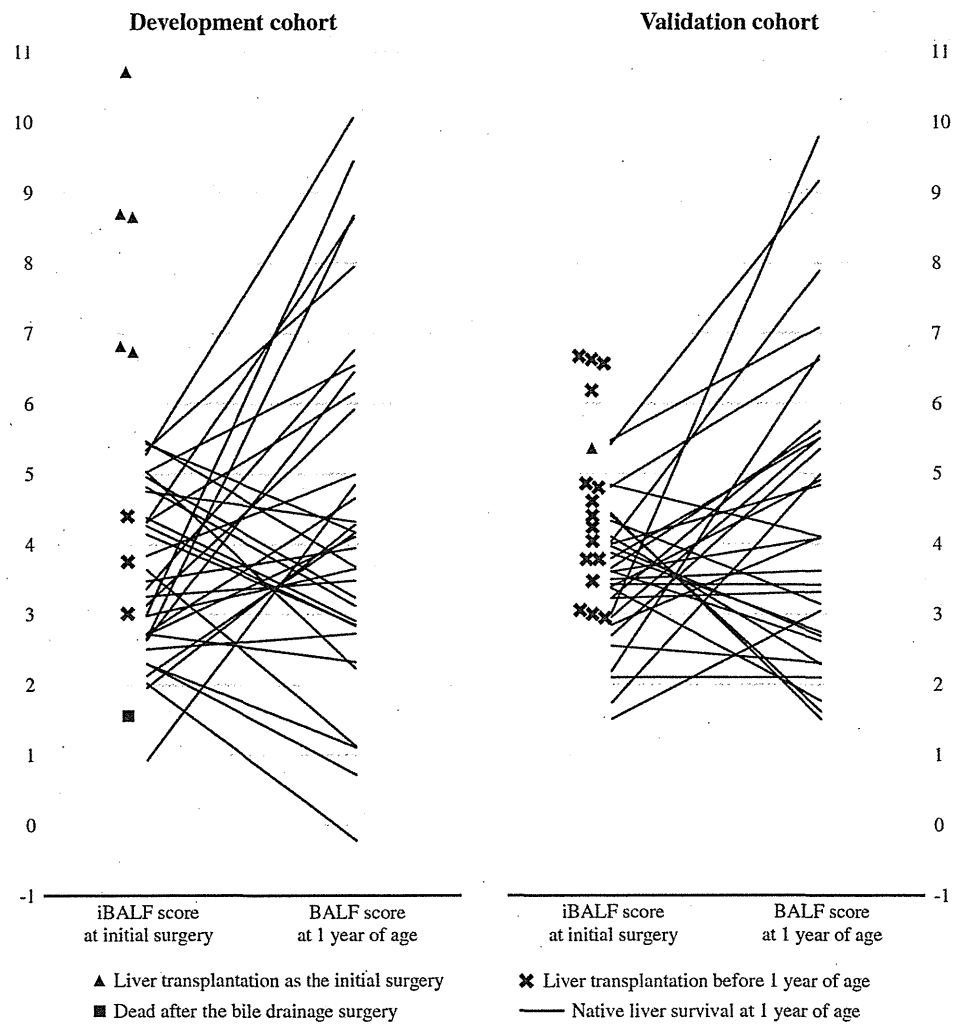

Figure 4 Relationships between the infant biliary atresia liver fibrosis (iBALF) score at the initial surgery and prognosis. Triangles indicate the patients receiving liver transplantation as the initial surgery. Crosses represent the patients requiring liver transplantation after bile drainage surgery before 1 year of age. The square indicates the patient who died after bile drainage surgery. The patients who survived with their native liver at 1 year of age are expressed by lines between the iBALF score at the bile drainage surgery and the biliary atresia liver fibrosis (BALF) score at 1 year of age.

stiffness using the ultrasound technique; Shin *et al.*[15] described that liver stiffness measurements obtained via transient elastography significantly correlated with Metavir fibrosis stages ($r=0.63$, $P<0.001$) and had good diagnostic powers for predicting severe fibrosis (≥F3; AUC = 0.86) and cirrhosis (F4; AUC = 0.96) in 47 BA patients aged <1 year at the time of hepatoportoenterostomy with liver biopsy or liver transplantation. Moreover, the APRI and transient elastography had already been investigated for associations with esophageal varices, an important consequence of liver fibrosis and portal hypertension, in postsurgical BA patients.[14,16–18] The current study suggests the advantages of the iBALF score over the APRI: stronger correlation with the fibrosis stages and more favorable diagnostic power than the APRI. Unlike the elastography methods, the iBALF score has good accessibilities, such as no need for a special device and simple equation components that allow retrospective calculation.

Although the current study indicated that the iBALF was a good noninvasive fibrosis marker even in the validation cohort, it has several limitations. First, patients were selected from three institutions, two of which were assigned to the development cohort and one to the validation cohort, resulting in significant differences in patient characteristics and blood test results between the cohorts. BA patients aged <1 year can be divided into three situations: patients before surgery, patients with a good postsurgical course, and patients requiring liver transplantation after bile drainage surgery. Although we intended that the iBALF-scoring system could apply in all situations, needle biopsy examinations for postsurgical patients with good bile drainage were performed at only one of the three participating institutions, thus the sample size was too small. To reflect the data from patients with a good postsurgical course in the iBALF score composition, we assigned the small number of these patients to the development cohort rather than randomly assigning them to the development cohort or the validation cohort. Thus, the relationships between liver fibrosis stage and the iBALF score of patients with a good postsurgical course could not be validated. In addition, there was a probable difference in the timing of liver transplantation between the institutions. Because of serious deceased donor organ shortages in Japan,[19] the timing of liver transplantation using liver allografts from living donors probably reflected the transplantation policy of each institution, resulting in significantly different ranges of the iBALF score in F4 patients between the cohorts and wide overlap in the ranges of the F3 and F4 groups in the validation cohort. The second limitation was general problems in prior studies of noninvasive fibrosis markers using the biopsy examinations as a reference standard: namely, biopsy sampling errors,[20] and observer variability.[21] Subcapsular wedge biopsy examination, which was used in most subjects in the current study, would tend to overestimate liver fibrosis. Thus, the fibrosis stages evaluated based on liver biopsy examinations might have false-positive and false-negative results.

In this study, we developed the iBALF score as a noninvasive surrogate fibrosis marker for BA patients aged <1 year, in addition to the previously developed BALF-scoring system for BA patients aged ≥1 year. Although some concerns remain, the iBALF score was validated to strongly correlate with liver fibrosis stage and to have good diagnostic powers for predicting liver fibrosis. The iBALF and BALF scores may be useful in future clinical studies as surrogate fibrosis markers.

CONFLICT OF INTEREST

Guarantor of the article: Tatsuo Kuroda, MD, PhD.
Specific author contributions: Hirofumi Tomita designed the study, collected and interpreted the data, performed the statistical analysis, and drafted the manuscript; Yasushi Fuchimoto designed the study, collected the data, and critically reviewed the manuscript. A. Fujino and T. Kuroda designed the study, interpreted the data, and critically reviewed the manuscript. K. Hoshino, M. Sakamoto, M. Kasahara, Y. Kanamori, and M. Nakano designed the study and critically reviewed the manuscript. Y. Masugi, A. Nakazawa, and S. Akatsuka participated in the histological evaluations and critically reviewed the manuscript. Y. Yamada and F. Yoshida collected the data and critically reviewed the manuscript. All authors have seen and approved the final version of the manuscript.
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Potential competing interests: None.

Study Highlights

WHAT IS CURRENT KNOWLEDGE

- ✓ Although liver fibrosis is a prominent feature of biliary atresia (BA) patients, noninvasive liver fibrosis markers in BA patients have been limited.
- ✓ We previously developed a BA liver fibrosis (BALF) score as the first specific liver fibrosis marker for BA patients aged ≥1 year.

WHAT IS NEW HERE

- ✓ We developed a novel noninvasive fibrosis marker for BA patients aged <1 year—the infant BALF (iBALF) score.
- ✓ The iBALF score was validated to be a good noninvasive marker of native liver fibrosis for BA patients during infancy.
- ✓ The iBALF and BALF scores can monitor liver fibrosis in a similar manner before and after 1 year of age, respectively.
- ✓ The BA patients with an iBALF score >6 at presentation had poor outcome on native liver survival at 1 year of age.

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Living donor domino liver transplantation using a maple syrup urine disease donor: A case series of three children – The first report from Japan

Matsunami M, Fukuda A, Sasaki K, Uchida H, Shigeta T, Hirata Y, Kanazawa H, Horikawa R, Nakazawa A, Suzuki T, Mizuta K, Kasahara M. (2016) Living donor domino liver transplantation using a maple syrup urine disease donor: A case series of three children – The first report from Japan. *Pediatr Transplant*, 00: 000–000. DOI:10.1111/petr.12681.

Abstract: As the priority of LD-Domino LT is the safety of the first recipient, limitations and technical difficulties in the second recipient often occur. The most technically challenging part of LD-Domino LT is the reconstruction of the vessels. For the reconstruction of HVs, the native HVs were exteriorized as far as possible using a CUSA because longer extensive HVs are essential for facilitating the reconstruction. At the back table, the HVs of the domino graft were sutured together, and the single cuff of the HVs was anastomosed to the IVC by joining the orifices. The HAs, the presence of insufficient length, and multiple vessels in the whole liver rendered the reconstruction more difficult. We determined the dividing sites of the vessels according to the preoperative 3D-CT findings obtained in two institutions. This is the first case series using grafts in DLT obtained from LDLT for patients with MSUD between two institutions. In conclusion, LD-Domino LT is a safe and feasible therapeutic option to expand the donor pool by technical refinement in the reconstruction of the second recipient. Further studies with a greater accumulation of patients and a longer follow-up will be necessary to establish LD-Domino LT using an MSUD donor.

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Key words: biliary atresia – domino liver transplantation – familial hypercholesterolemia – maple syrup urine disease – protein C deficiency

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LD-Domino LT was developed to expand the donor pool especially in countries where there is limited DDLT for patients such as in Japan. There are only approximately 40–50 DDLT donors each year, with just three donors under six yr of age so far. Therefore, there are few opportunities to receive a whole liver from an age-matched, similarly sized donor. The possibility of amyloidosis as a late complication of DLT using a FAP donor is also a worrisome issue for

Abbreviations: 3D-CT, three-dimensional computerized tomography; BA, biliary atresia; BCAA, branched-chain amino acid; CHA, common hepatic artery; CIT, cold ischemic time; CUSA, cavitron ultrasonic surgical aspirator; DDLT, deceased donor liver transplantation; DLT, domino liver transplantation; FAP, familial amyloidotic polyneuropathy; FFP, fresh frozen plasma; FH, familial hypercholesterolemia; GDA, gastroduodenal artery; GRWR, graft-to-recipient weight ratio; HAs, hepatic arteries; HDL-C, high-density lipoprotein cholesterol; HVs, hepatic veins; IVC, inferior vena cava; LD-Domino LT, living donor domino liver transplantation; LDL-C, low-density lipoprotein cholesterol; LDL-R, low-density lipoprotein receptor; LDLT, living donor liver transplantation; LHA, left hepatic artery; LHV, left hepatic vein; LLS, left lateral segment; LT, liver transplantation; MHV, middle hepatic vein; MSUD, maple syrup urine disease; ND, not detected; PC, protein C; PV, portal vein; RHA, right hepatic artery; RHV, right hepatic vein; SMA, superior mesenteric artery; TC, total cholesterol; TG, triglyceride; WIT, warm ischemic time.

pediatric patients (1, 2). However, for pediatric patients with metabolic liver diseases, such as MSUD, who are undergoing LDLT, DLT is often performed with similarly sized pediatric patients.

MSUD is an autosomal recessive disorder caused by an impaired activity of the branched-chain alpha-keto acid dehydrogenase. MSUD exerts a risk of serious neurologic disability and untimely death, despite recent progress in nutritional and medical management. Ketoacidosis causes cerebral edema that can culminate in brain herniation and cardiorespiratory arrest (3). LT has been performed for satisfactory correction of the enzymatic disorder and the prevention of long-term neurologic consequences (4). Furthermore, a recent report has described the safe use of explanted livers for DLT grafts in 11 cases with an excellent outcome (5). In most cases, however, an excellent outcome is generally obtained only after performing DDLT for MSUD. The most major differences in LD-Domino LT compared with deceased donor lie in the multiple vascular pedicles of insufficient length in the graft for second recipient. The main concern for LD-Domino LT is the safety of the first recipient; native hepatectomy is performed while carefully preserving the retrohepatic IVC, the portal trunk, and the peripheral HAs. The explanted MSUD liver has multiple and insufficient length vascular pedicles, and successful hepatic vascular reconstruction is essential for the second recipient.

In 2014, we presented a case of pediatric PC deficiency that was successfully treated by LD-Domino LT from a pediatric patient with MSUD (5). We applied our experience to three patients who underwent LD-Domino LT using whole liver and evaluated the feasibility and efficacy of the technique. To the best of our knowledge, this is the first case series using grafts in DLT obtained from LDLT for patients with MSUD between two institutions.

Patients and methods

Between November 2005 and May 2015, 330 children underwent LT in our institution, the National Center for Child Health and Development in Tokyo, Japan, with an overall survival rate of 92.2%. Three patients each with PC deficiency, BA, and FH, respectively, were indicated for LD-Domino LT because for two of them (PC deficiency and FH), both parents had heterozygous mutations, while the other (BA) patient was considered to be a low priority on the DDLT waiting list. Analyses of blood amino acids and urine organic acid were performed to exclude the presence of MSUD in the second recipients.

Each patient with MSUD and the first donor of the LLS for the corresponding patient with MSUD underwent 3D-CT for the evaluation of the anatomy of their HAs, PV, and HVs. All three patients with MSUD received an LLS from one of their parents, and all parents of the patients with MSUD agreed to donate their liver.

LD-Domino LT was performed between two institutions. At our department, the immunosuppression regimen consisted of tacrolimus and low-dose steroids. During the follow-up period, the assessments of blood amino acids and urine organic acids were continuously made. The endocrine function was evaluated by determining specific parameters such as serum leucine, isoleucine, valine, and alloisoleucine levels.

This study was approved by the review board of each institution and the Japan Society for Transplantation.

Results

The characteristics of the first donors, together with the first and second recipients, are summarized in Table 1. LD-Domino LT was performed in three cases (cases 1, 2, and 3). Cholesterol-level changes in the FH patient (case 3) are summarized in Table 2. Table 3 shows that BCAA homeostasis was maintained with an unrestricted protein diet in all three cases.

Case 1

A one-yr and 11-month-old girl presented with multiple cerebral bleeding and subcutaneous bleeding on her lower limbs. The patient was found to have a serum PC activity of less than 5%. A genetic mutational analysis confirmed the diagnosis of PC deficiency. The patient had started receiving FFP and activated PC concentrate treatments since one yr and two months of age. She underwent ophthalmectomy due to bilateral vitreous hemorrhages at one month of age. Despite the maximal medical therapy, she had repeated purpura fulminans and was listed for LT. Both her parents had heterozygous mutations in the PC genes and were excluded as living donors; therefore, she was placed on the DDLT waiting list. This patient was selected to receive LD-Domino LT because of physical size matching to the first recipient on our waiting list. We selected the dividing site of the vessels according to the preoperative 3D-CT findings of the first donor and recipient. Because the LHA of the first donor was branched from the right gastric artery, along with having a sufficient length, the GDA was ligated and the CHA was dissected in the first recipient. The RHV, MHV, LHV, and superficial vein were sutured together by venoplasty at the back table, and the single cuff of the HVs was anastomosed to the IVC by joining the orifices. PV anastomosis was performed with the branch patch technique. Roux-en-Y anastomosis was employed for biliary reconstruction. Immunosuppressive treatment was initiated with tacrolimus and low-dose steroids. The patient's

Table 1. Clinical characteristics of the first donors and the first and second recipients

Case no.	1st donor		1st recipient			2nd recipient								
	Donor	Graft	Indication	Age at LDLT	Gender	Indication	Age at DLT	Gender	Body weight (kg)	Operation time	CIT (min)	WIT (min)	GRWR (%)	Follow-up (months)	Complication
1	Father	LLS	MSUD	1 yr	F	PC deficiency	1 yr 11 months	F	9.5	7 h 21 min	237	33	2.57	16	None
2	Mother	LLS	MSUD	3 yr 7 months	M	BA	2 yr 4 months	M	11.3	12 hr 30 min	350	26	3.52	9	None
3	Mother	LLS	MSUD	1 yr 3 months	M	FH	2 yr 10 months	F	13	5 hr 3 min	252	23	1.64	8	None

postoperative course was uneventful except for acute cellular rejection. She was discharged on postoperative day 68 without any surgical complications. One yr and four months after the LD-Domino LT, the patient's PC activity was maintained at more than 80% and she has since remained symptom free.

Case 2

A two-yr and four-month-old boy presented with jaundice and white feces. At five months of age, he was diagnosed with BA and the Kasai procedure was performed. However, his clinical condition did not improve and he exhibited growth failure, repeated cholangitis, and progressive esophagus varix with a pediatric end-stage liver disease score of 17; therefore, the patient was listed for LT. Because his father had disk herniation and was under the treatment for a gastric ulcer and his mother had repeated episodes of pyelonephritis, he was on the DDLT waiting list. However, because he was considered to be a low priority on the waiting list, LD-Domino LT was taken into account as an option. The operative finding at LD-Domino LT revealed severe adhesion. The operation employed the removal of multiple intestinal adhesions, which was achieved with synechiotomy. The HVs were exteriorized as far as possible in the native liver parenchyma using a CUSA (Fig. 1a). The RHV, MHV, LHV, and superficial vein were sutured together by venoplasty at the back table, and the single cuff of the HVs was anastomosed to the IVC by joining the orifices (Fig. 1b). PV anastomosis was performed with the branch patch technique. A sufficient hepatopetal flow was obtained following the devascularization of the collateral vessels. Because the RHA of the first recipient was branched from the SMA, two arterial anastomoses were required in the second recipient. The first recipient's LHA and RHA were directly anastomosed to the second recipient's LHA and posterior RHA, respectively, because of a suitable orifice diameter. A new Roux-en-Y anastomosis was employed for biliary reconstruction. Immunosuppressive treatment was initiated with tacrolimus and low-dose steroids. The patient was discharged on postoperative day 31 without any surgical complications and was found to be doing well nine months after the LD-Domino LT.

Case 3

A two-yr and 10-month-old girl presented with cutaneous xanthomas on the wrists, elbows, and ankles (Fig. 2a). She suffered from high TC

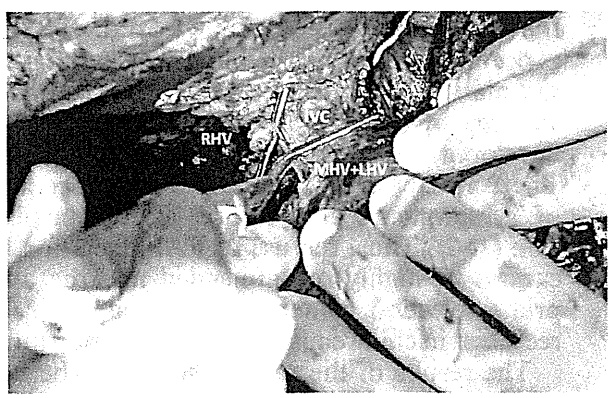
Table 2. Lipid profile in case 3 showing levels at baseline prior to any treatment; on maximal lipid-lowering drug and dietary therapy; and after liver transplantation without lipid-lowering drug therapy

			Postoperative day					
mg/dL	No treatment	On medication	Liver transplantation	1	7	30	90	180
TC (125–240)	1092	735	239	246	115	164	201	201
HDL-C	49	21	–	7	31	47	57	50
LDL-C (70–139)	975	732	–	230	68	100	129	135
TG (32–237)	129	60	–	19	87	223	70	52

Table 3. Amino acid levels before and after DLT

		Case 1						Case 2					Case 3			
Amino acids	Normal range (nmol/mL)	Before DLT	After 1M	After 3M	After 6M	After 9M	After 12M	Before DLT	After 1M	After 3M	After 6M	After 9M	Before DLT	After 1M	After 3M	After 6M
Leucine	80.9–154.3	96.8	113.8	107.3	87.3	86.9	81.1	139.0	102.2	76.3	71.7	90.7	120.5	132.7	154.7	143.8
Isoleucine	41.3–84.9	50.3	68.6	59.9	50.8	51.7	43.4	79.4	55.8	47.4	37.5	55.2	71.7	85.9	100.4	89.3
Valine	158.4–287.7	197.6	156.8	166.8	174.8	175.5	185.6	267.8	219.4	165.7	179.5	217.7	240.9	265.5	344.4	291.2
Alloisoleucine	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND	ND

a



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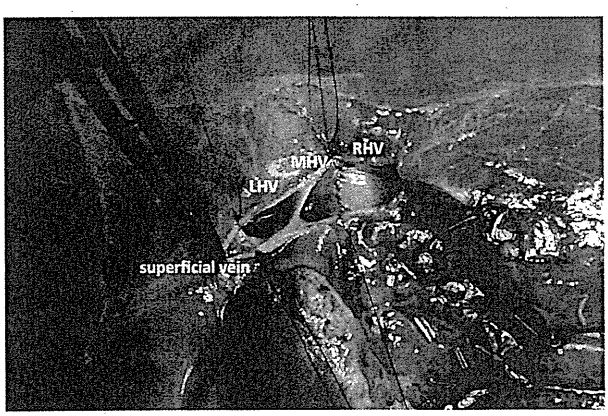
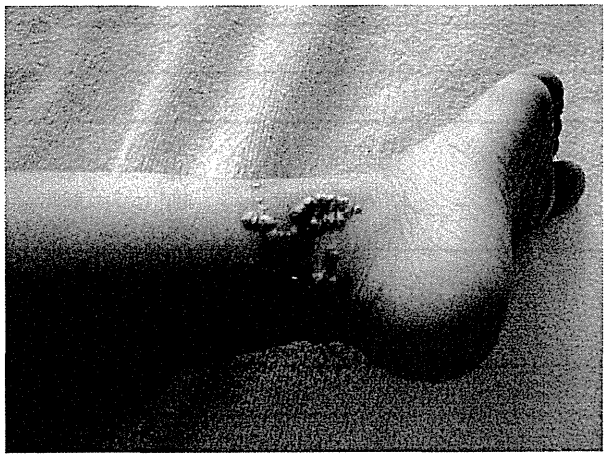


Fig. 1. (a) The HVs were exteriorized as far as possible using a CUSA. (b) The RHV, MHV, LHV, and superficial vein were sutured together to create a single cuff by venoplasty on the back table.

levels (>900 mg/dL) and was treated for hypercholesterolemia at one yr and four months of age. Sequencing of the LDL-R gene identified two mutations (c.418G>A and p.E119K/c.IVS12 + 2T>C). The LDL-R activity of the patient was 0%. Due to the patient's clinical history, she was diagnosed with compound heterozygous FH and was treated with a low-fat diet and medication. She had persistent severe hypercholesterolemia and her skin lesions enlarged. However, she showed no findings of coronary artery disease according to echocardiography and coronary vessel angiography. In addition to a cholesterol-restricted diet, medications including statins, cholesterol absorption inhibitors, and cholesterol dissimilation accelerators were administered. Despite the medications, her general condition was unresponsive and the TC level could not be controlled. Her parents had been evaluated as possible donors for LT, but were eventually excluded because they were heterozygous for FH and had low LDL-R activities (51% and 43%, respectively). For this reason, she was on the DDLT waiting list. The patient was selected to receive LD-Domino LT because of physical size matching to the first recipient on our waiting list. LD-Domino LT was performed at two yr and 10 months of age. The HVs were exteriorized as far as possible in the native liver parenchyma using a CUSA in order to create a longer vascular pedicle in the second recipient. The RHV, MHV, and LHV were sutured together by venoplasty at the back

a



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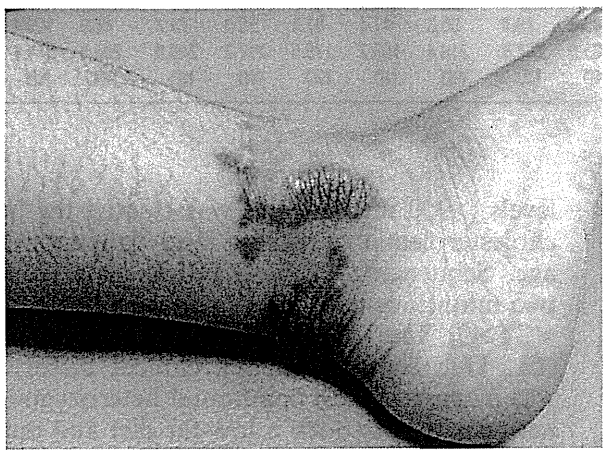

Fig. 2. Cutaneous xanthomas. Appearance at diagnosis time (a) and after six months from liver transplantation (b).

table, and the single cuff of the HVs was anastomosed to the IVC by joining the orifices. PV anastomosis was performed with the branch patch technique. Because the RHA of the first donor was branched from the SMA, along with a sufficient length, the GDA was ligated and the CHA was dissected in the first recipient. The first recipient's CHA was anastomosed to the second recipient's CHA. A new Roux-en-Y anastomosis was employed for biliary reconstruction. Within one day of LT, the plasma LDL-C level significantly decreased to 239 mg/dL and the lipid profile promptly normalized (Table 2). Her immunosuppressive protocol was the same as that of cases 1 and 2. A histological examination of the explanted liver showed low lipid content with oil red O staining. The patient's postoperative course was uneventful, and on postoperative day 19, she was discharged. Over time, the patient improved and the cutaneous xanthomas gradually decreased within six months with average LDL-C levels of 120 mg/dL (Fig. 2b). Subsequent liver ultrasounds were normal with no visible steatosis.

Discussion

This case series highlighted two important clinical issues: (i) LD-Domino LT is technically complicated compared with deceased donor Domino LT; however, LD-Domino LT is a safe and feasible therapeutic option for expanding the donor pool through the use of technical refinement in the reconstruction of the second recipient and 3D-CT to determine the dividing site of the vessels of both recipients preoperatively between two institutions. Using a living donor offers advantages for making a satisfactory image assessment and preparing for operation. (ii) DLT using the whole liver from a pediatric patient with MSUD can be effective in a pediatric patient with proper physical size matching.

DLT was first performed in 1995 in Portugal as a strategy for addressing the disproportionate supply of deceased organ donors and the rising waiting list for DDLT (2). The latest update of the DLT registry displayed a total of 1085 DLT procedures performed with patients with FAP as the main donors (2). However, the main disadvantage of using a FAP donor is the risk of developing amyloidosis in the DLT recipient. There have been several reports of the occurrence of symptomatic amyloidosis after transplantation (1, 2). Thus, the use of FAP livers for DLT cannot be highly recommended and the appropriate selection of suitable livers as the second recipient in children is particularly important.

The results of the present study on the use of whole liver graft obtained from pediatric patients with MSUD who had undergone LDLT rendered the procedure technically complex, but excellent postoperative functional recovery was achieved in the second recipient. This benefit may be related to the larger size of the graft and by not performing resection or reduction. Our findings demonstrated that whole liver graft could be safely used.

Potential candidates for LD-Domino LT are patients on DDLT waiting lists with good physical size matching to a donor. In this case series, all second recipients were unable to undergo LDLT for various reasons. In case 2, the parents had medical problems which made them ineligible as donors for LDLT, and in cases 1 and 3, the parents were excluded due to heterozygous disease mutations.

LD-Domino LT recipients generally have a longer CIT, ranging from 237 to 350 min

(Table 1), compared with our usual LDLT series; the reason for this is most likely because LD-Domino LT was performed between two institutions. The surgical procedure of LD-Domino LT was technically demanding due to the second recipient's original disease, and the case with a previous surgical history had a longer operation time than the other two metabolic disorder cases. However, the continued success of LD-Domino LT may help to determine which disease is suitable for the second recipient.

FH is an autosomal dominant disorder characterized by markedly increased plasma LDL-C and can progress rapidly to premature cardiovascular risk (6). Homozygous and compound heterozygous FH patients exhibit the rapid development of atherosclerosis with death due to coronary artery disease even in childhood. Because LDL apheresis delays, but does not prevent the development of atherosclerosis, heart and heart–LT have been applied in these patients (6). According to previous evidence, 75% of the LDL-R concentration is located in the liver, and LT becomes the treatment of choice for FH. LT provides a source of normal LDL-R, which may clear cholesterol from the plasma so effectively that the disease would be completely cured without additional medication (7). Therefore, LT before the onset of coronary artery disease offers the best chance for a potential cure for patients with compound heterozygous FH.

To date, 18 previous cases of successful LT for FH have been reported (7); however, there have been no such reports of LD-Domino LT for FH. A few studies have reported the use of a heterozygous donor graft, but the patients required additional medications to control their cholesterol levels after LT (8). Therefore, LDLT from a heterozygous donor for FH is not recommended.

As the concept of LD-Domino LT is generally well established with the priority being the safety of the first recipient, limitations and technical difficulties often occur in the second recipient (9). The biggest challenge of LD-Domino LT using a whole MSUD liver without a sufficient length of HVs pedicle and multiple HAs is the reconstruction of the vessels. For the reconstruction of the HVs, native HVs that are hidden under the liver parenchyma were exteriorized as far as possible in the native liver parenchyma using a CUSA because longer, extensive HVs were essential to facilitate the reconstruction in the second recipient. By venoplasty at the back table, the RHV, MHV, and LHV were sutured together to create a single cuff. Few reports have discussed the optimal techniques of outflow reconstruction (10–15). In this case series, we employed the

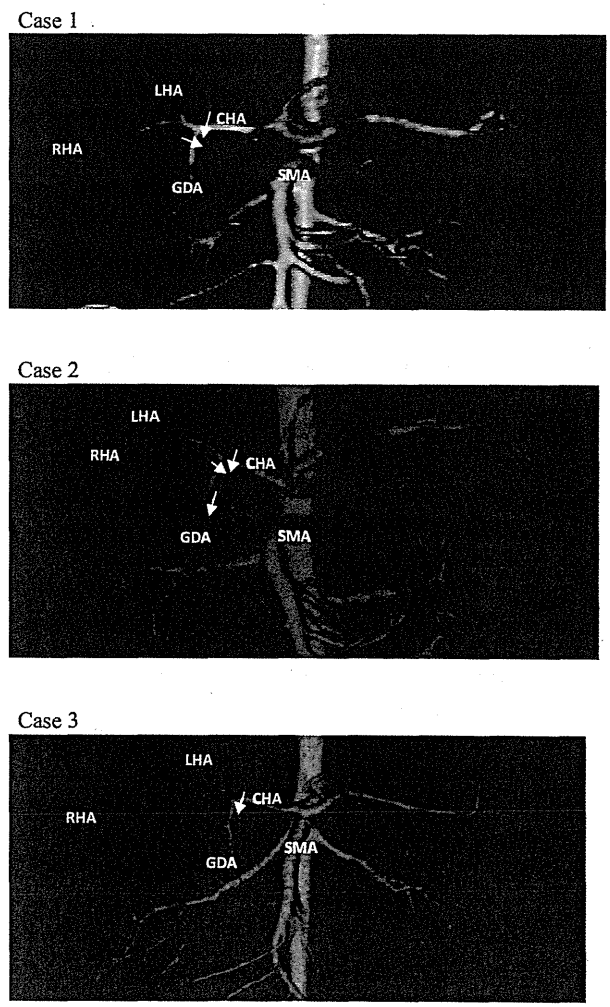

Fig. 3. Three cases of HAs according to the 3D-CT findings in the first recipient. Arrows denote the sites of dissecting.

technique described by Chan et al. (12), which was venoplasty of the RHV, MHV, and LHV stumps and the single cuff of the HVs anastomosed to the IVC without an interpositional graft or patch. The successful outcomes reassure us of the usefulness of this technique.

The vessels of the living donor graft from the first donor were not sufficiently long to allow anastomosis. Therefore, it was necessary to leave the HAs as long as possible when removing the liver from the patient with MSUD to ensure safety for vascular construction. This led to the presence of multiple vessels with insufficient length in the whole MSUD liver graft, which added to the difficulty of the HAs reconstruction. Notably, the success of LD-Domino LT largely depends on the reconstruction of the HAs. To that end, we determined the dividing sites of the vessels according to the preoperative 3D-CT findings (Fig. 3) between two institutions. During implantation of the graft in the second

recipient, we ligated the GDA to gain mobility and to obtain sufficient length for the anastomosis. The anastomosis was end-to-end and performed using 9-0 nylon under the operating microscope maintaining careful alignment. Patency and satisfactory pulsatility of the hepatic arterial flow was confirmed by intraoperative Doppler ultrasonography.

For the reconstruction of the PV, PV anastomosis was performed with the branch patch technique in all the cases. There were no surgical complications, and all recipients had good postoperative functional recovery. In addition, all second recipients maintained normal plasma BCAA levels on an unrestricted protein diet after LD-Domino LT (Table 3). These findings are supported by our previous report (5).

In conclusion, according to the early results from this case series, LD-Domino LT was effective and safe for patients who are on the DDLT waiting list and are likely to die without an LT. In Japan, the number of deceased donors remains extremely low, and the use of LD-Domino LT may relieve some of the challenges of organ shortage. In general, most patients with MSUD requiring LT are pediatric patients, and thus, LD-Domino LT may offer a valuable and potential opportunity for physical size matching in such patients. Further studies with a greater accumulation of patients and a longer follow-up will be necessary to establish LD-Domino LT using an MSUD donor.

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Conflict of interest

The authors of this manuscript have no conflict of interest.

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