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Original Article

Prognostic Factors for Pediatric Living Donor Liver Transplantation: Impact of Zero-mortality Transplant for Cholestatic Diseases

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Living donor liver transplantation (LDLT) is the final therapeutic arm for pediatric end-stage liver diseases. Toward the goal of achieving further improvement in LDLT survival, we investigated factors affecting recipient survival. We evaluated the prognostic factors of 60 pediatric recipients (< 16 years old) who underwent LDLT between 1997 and 2015. In a univariate analysis, non-cholestatic (NCS) disease, graft/recipient body weight ratio, cold and warm ischemic times, and intraoperative blood loss were significant factors impacting survival. In a multivariate analysis, NCS disease was the only significant factor worsening survival ($p = 0.0021$). One-and 5-year survival rates for the cholestatic disease (CS, n = 43) and NCS (n = 17) groups were 100% vs. 70.6% and 97.4% vs. 58.8% ($p = 0.004$, log-rank). Intergroup comparisons revealed that CS was significantly associated with operation time, cold ischemia, hepatomegaly of the native liver, and portal plasty. These data suggest that a cirrhotic, swollen, artery-dominant liver did not increase graft size-related risks despite the surgical complexity of preceding operations. The NCS group's poorer survival originated from recurrence of the primary disease and liver manifestation of systemic disease untreatable by transplantation. Improving the survival of pediatric recipients requires intensive efforts to prevent primary disease relapse and more rapid diagnoses to exclude contraindications from NCS disease.

Key words: liver transplantation, living donor, pediatrics, prognostic factor, cholestatic disease

The outcomes of living donor liver transplantation (LDLT) for children with acute or chronic hepatic failure are known to be excellent. Studies in pediatric liver transplantation have reported that the average recipient and graft survival rates of pediatric LDLT at 1 and 4 years are 90% and 85%, and 89% and 78%, respectively [1]. LDLT has enabled the optimization of the timing of transplantation and the shortening of the cold ischemic time (CIT), contributing to a decreased mortality rate among pediatric candidates on the pediatric waiting list [2, 3]. Because the main procedure for donor surgery is a lateral segmentectomy or left hepatectomy, relatively better physical safety of the donor is also maintained [4]. LDLT has therefore been accepted as a powerful treatment for end-stage liver failure in children. We conducted the present study to determine the factors that affect the survival of pediatric recipients in our cohort to identify measures and achieve further improvements in the survival of pediatric LDLT recipients.

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Patients and Methods

Patients. This study was approved by the Ethics Committee at Okayama University Graduate School of Medicine, Dentistry and Pharmaceutical Sciences and Okayama University Hospital (approval no. 1701-507) and was conducted in accordance with the Declaration of Helsinki. We performed this retrospective cohort study for consecutive pediatric recipients under 16 years old who underwent an LDLT between August 1997 and December 2015 at Okayama University Hospital. Sixty patients < 16 years old underwent 60 primary LDLTs. Prior to transplantation surgery, written informed consent regarding a future retrospective study was obtained from all of the patients. At study enrollment, all of the enrolled patients had been observed for > 1 year. Patients were observed preoperatively and followed-up after surgery as outpatients of Okayama University Hospital.

The patients were 27 boys and 33 girls (Table 1) ranging in age from 83 days to 16.5 years and with body weights (BWs) ranging from 3.9 kg to 66.4 kg. We divided the patients' primary diseases into two categories (cholestatic vs. non-cholestatic disease) according to final histological diagnoses: cholestatic disease (CS) including biliary atresia (BA; n = 37), Alagille syndrome (n = 4), and primary sclerosing cholangitis (PSC; n = 2); and non-cholestatic (NCS) disease including acute hepatic failure (n = 8), metabolic disease (n = 4), and tumor (n = 3, hepatoblastoma: 2, chronic active EBV infection: 1), and liver cirrhosis (LC; n = 2).

The patients received preoperative care as an outpatient (n = 38), on admission (n = 9), or in an intensive

Table 1 Preoperative demographic data of the recipients and donors

Factors			Values	Range or %
Recipient				
Gender (M/F)			27/33	45/55
Mean age (years, range)			3.25 ± 4.1	(89d–16.5y)
Mean body weight (kg), (range)			13.5 ± 11.2	(3.9–66.9)
Primary disease	Cholestatic disease (CS, n = 43)	Biliary atresia	37	61.7%
		Alagille's syndrome	4	6.7%
		Primary sclerosing cholangitis	2	3.3%
	Non-cholestatic disease (NCS, n = 17)	Acute hepatic failure (AHF)	8	13.3%
		Metabolic disease	4	6.7%
		Tumor	3	5.0%
		Liver cirrhosis	2	3.3%
Preoperative condition	Outpatient		38	63.3%
	Admission		9	15.0%
	ICU stay		13	21.7%
ABO blood type combination	identical		40	66.7%
	compatible		12	20.0%
	incompatible		9	15.0%
Mean graft /body weight ratio (GRWR), (range)			2.84 ± 1.12	(1.00–6.16)
Preceding history of abdominal surgery (times)	0		20	33.3%
	1		23	38.3%
	2		17	28.3%
Donor				
Mean age (years, range)			37.8 ± 11.6	(20.0–70.4)
Mean body mass index (kg/m^2, range)			22.4 ± 3.0	(16.0–30.5)
Relation to recipient	Grandfather		4	6.7%
	Grandmother		6	10.0%
	Father		29	48.3%
	Mother		20	33.3%
	Unrelated (father-in-law)		1	1.7%

care unit (ICU; n = 13). The blood type of the donor was identical to that of the recipient in 39 cases, compatible in 12, and incompatible in 9. The graft/recipient body weight ratio (GRWR) of the recipients ranged from 1.06 to 6.16 (median, 2.84 ± 1.12).

Clinical data. For the 60 enrolled pediatric recipients, we evaluated the following demographic and clinical data as recipient preoperative factors: sex, age, weight, primary disease, preoperative condition, ABO-blood type compatibility, GRWR, and preceding history of major abdominal surgery. The donor factors evaluated were: age, body mass index (BMI), and familial relationships. We also analyzed intraoperative factors including CIT, warm ischemic time (WIT), microscopic reconstruction of the hepatic artery, requirement of portal plasty, actual volume of explanted native liver, operation time, and blood loss. We examined the occurrence of acute cellular rejection (ACR), steroid-resistant rejection (SRR), cytomegalovirus (CMV) infection, post-transplant lymphoproliferative disease (PTLD), and postoperative hospital stay as postoperative factors. We then analyzed whether these perioperative factors affected recipient survival.

Transplant surgery. In each case, the donor surgery was started 1 h before the recipient surgery. The details of the surgical procedures have been described [5, 6]. Partial liver grafts were anastomosed to the orifices of the hepatic veins in a piggyback manner. Reconstruction of the hepatic artery was performed microscopically until 2005, at which point the reconstruction procedure was switched to direct anastomosis under a 3.5× magnified surgical loupe due to the rationalization of surgical job loading [7]. Mainly a hepatico-jejunostomy was chosen as the standard procedure for biliary reconstruction, although a small number of duct-to-duct anastomoses were conducted for right lobe grafts.

The graft-type selection depended on the patient's GRWR. To avoid small-for-size graft-related mortality, right lobe grafts were selected in some recipients after 2005. Sixty percent (36 cases) of the grafts were lateral segment grafts. Extended lateral segment and left lobe grafts (excluding or including the Spiegel lobe) comprised 20% and 18% of grafts, respectively. Four pediatric patients of good physique underwent transplantation using a right lobe graft. Segment 2 mono-segment grafts (requiring additional *in situ* reduction procedures) were introduced in 2010, and were used for four small infants with estimated GRWRs > 5%.

When the post-explanted abdominal capacity seemed smaller than the calculated graft volume, complete closure of the abdomen was abandoned and temporary closure was achieved instead using skin flaps separated from the fascial layer. Disrupted muscular layers under the skin flap were reconstructed after growth as the repair of the incisional herniation. Each liver graft was maintained in University of Wisconsin solution until the expired liver of the recipient had been removed.

Immunosuppression. In the majority of the cases, immunosuppression was achieved using tacrolimus and corticosteroids. Tacrolimus was administered orally from day 1 every 12 h or by a continuous intravenous infusion. Oral target trough levels were maintained at > 10 ng/mL for the first 2 weeks, 7-10 ng/mL for the next 2 months, and 5.5 ng/mL thereafter. The whole-blood concentration for the intravenous tacrolimus administration was 1.4-fold the oral target trough level to provide an almost equal area under the concentration-time curve. When the recipient had a history of neurological symptoms or manifestation of posterior reversible encephalopathy syndrome, cyclosporine was chosen as the main calcineurin inhibitor.

Methylprednisolone was administered at 10 mg/kg after graft reperfusion, followed by twice-daily dosing at 1 mg/kg for the first 4 days, and programmed pulse therapy at 0.5 mg/kg intravenously per day for the next 3 days (days 5-7). From day 8, prednisolone was given orally, starting with a dosage of 0.3 mg/kg/day and tapered over the first 12 months after LDLT. The aim of including programmed pulse therapy was the early diagnostic treatment of steroid-resistant rejection and compensation for unsettled tacrolimus trough levels in the early post-transplant phase for pediatric recipients, who show a relatively high prevalence of ACR. An episode biopsy sample was obtained whenever liver enzymes and/or the total bilirubin level were found to be elevated.

When the recipient suffered from SRR, full-dose pulse therapy (20 mg/kg for 3 days) with recycle tapering and/or T-cell deletion therapy using muromonab (until 2010) or thymoglobulin (from 2011) was performed. Thereafter, mycophenolate mofetil was also administered at 10 mg/kg for 3-6 months. We did not actively attempt withdrawal from immunosuppression, expecting operational tolerance.

In cases of ABO-incompatible LDLT for children > 2 years old additional immunosuppressants were given to inhibit humoral rejection. The preoperative induction of replacement transfusion or plasma exchange, and the preoperative administration of rituximab were performed. Oral cyclophosphamide was provided at 2 mg/kg/day from 7 days before surgery, switching to azathioprine at 1 mg/kg/day or mycophenolate mofetil at 10 mg/kg from 1 month after surgery.

Statistical analysis. JMP ver. 8 software (SAS Institute, Cary, NC, USA) was used for all statistical analyses. Data are presented as mean, median, and standard deviation for continuous variables. Categorical data are presented as proportions. Differences between groups were assessed using the Mann-Whitney *U*-test for continuous variables and Fisher's exact test or the χ^2 test for categorical variables. To investigate the impact of prognostic factors, patient survival was calculated using the Kaplan-Meier method, the log-rank test was used for the univariate analysis of perioperative risk factors. Stepwise forward Cox regression modeling was used for the multivariate analysis of perioperative risk factors. Hazard ratios (HRs) and 95% confidence intervals were calculated. Values of $p < 0.05$ were considered significant.

Results

Among the preoperative factors including sex, age at the time of transplant, preoperative condition, ABO blood type compatibility, and history of major abdominal surgery, the univariate analysis revealed that the disease category of CS showed significantly better outcomes than NCS ($p = 0.0002$). As intraoperative factors, GRWR, CIT, WIT, and blood loss were significantly associated with recipient survival ($p = 0.0035$, 0.0047, 0.0122, and 0.0055, respectively). The cut-off values for GRWR, CIT, WIT, and blood loss calculated from a receiver operating characteristic analysis were 2.84, 58 min, 50 min, and 100.6 ml/kg, respectively. The graft type, the ratio of explanted liver for recipient body weight, the explanted/transplanted liver weight ratio, the performance of portal vein plasty, microscopic arterial reconstruction, and operation time were not significant prognostic factors affecting recipient survival.

Postoperatively, the aforementioned programmed pulse therapy was constantly induced after the 7th pediatric recipient. Hepatic artery thrombosis (HAT) and hepatic artery stenosis (HAS), which are life-threatening complications, were not significantly associated with survival in this series because none of the four recipients who experienced HAT or HAS was lost. One recipient who experienced simultaneous arterial and portal thromboses underwent an urgent re-transplant using a maternal liver graft 7 days after the initial LDLT of a paternal liver graft. Two recipients experienced juxta-operational HAT within 24 h after the primary LDLT, and both of them were saved by surgical re-anastomosis. The fourth recipient (with HAS) suffered from severe vascular rejection that caused the HAS, which was detected by a tardy waveform on ultrasonography on postoperative day 5. Although balloon dilation was attempted to correct the patient's HAS using an angiographic technique, an unexpected rupture of the dilatation balloon caused a disruption of the anastomosis and the completion of HAT. However, the arterial supply was maintained via a rapid and vigorous development of collateral arteries.

Portal vein stenosis occurred in five cases but was not identified as a significant factor in survival. Among these 5 cases, 4 were successfully revised by percutaneous trans-hepatic portal dilation. The fifth recipient died of progressing hepatic failure due to the failure of surgical repair of the portal vein stenosis.

The prevalence of ACR as proven by episode biopsy was 60%, and eight patients (13.3%) developed SRR. No early graft failure resulted from uncontrolled ACR or SRR. CMV infection was found in 50% of the recipients, but was not a significant prognostic factor worsening the recipients' survival because all of the recipients who were identified as pp-65 antigen-positive were administered ganciclovir or valganciclovir to prevent life-threating CMV disease.

Six recipients (10%) manifested PTLD. One infant who received an LDLT at 6 months earlier from an ABO-incompatible donor manifested high fever and dyspnea caused by PTLD of Waldeyer's ring. Since a sharp decrease in immunosuppressant doses led to fatal ABO-humoral rejection during chemotherapy, that patient died of hepatic failure. The other five recipients with PTLD were successfully treated by dose reduction, switching immunosuppressants, and chemotherapy. PTLD was therefore also not a postoperative factor that significantly affected recipient survival (Table 2).

We conducted a multivariate analysis to analyze the

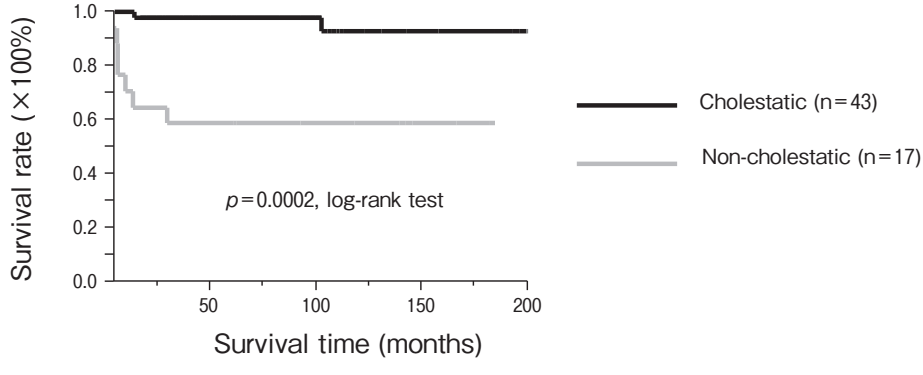
Table 2 Univariate analysis of perioperative factors affecting the recipients' survival

Factors		Values, mean value ± SD	Range or %	Number of lost patients	Cut-off value for continuous parameters	Odds ratio (95%CI)	*P* values
Preoperative factors							
Sex	Male	27	45.0%	4			0.971
	Female	33	55.0%	5			
Recipient age at transplant (years)		3.25 ± 4.1	(89d–16.5y)		–	–	0.1304
Disease category	Cholestatic disease	43	71.7%	2			0.0002*
	Non-cholestatic disease	17	28.3%	7			
Preoperative condition	Outpatient	38	63.3%	2			0.7377
	Admission	22	36.7%	7			
ABO blood type combination	Identical or compatible	51	85.0%	7			0.4375
	Incompatible	9	15.0%	2			
Surgical history of abdominal surgery	0 or 1	43	71.7%	7			0.6338
	2	17	28.3%	2			
	Intraoperative factors						
Type of graft	Mono-segment (S2)	4	6.7%				
	Lateral segment	35	58.3%				
	Left lobe	12	20.0%				
	Extended left lobe	6	10.0%				
	Right lobe	3	5.0%				
Explanted liver/recipient body weight ratio		4.20 ± 1.8	(1.00–8.71)		–	–	0.1343
GRWR		2.84 ± 1.12	(1.00–6.16)		2.34	−2.91	0.0035*
Explanted/transplanted liver weight ratio		1.56 ± 0.57	(0.36–3.07)		–	–	
Cold ischemic time (CIT, min)		79.7 ± 67.3	(7–373)		58	−0.0326	0.0047*
Warm ischemic time (WIT, min)		43.9 ± 15.4	(20–102)		50	−0.1122	0.0122*
Portal vein plasty	yes	21	35.0%	2			0.9511
	no	39	65.0%	7			
Microscopic reconstruction of hepatic artery	yes	19	31.7%	4			0.9326
	no	41	68.3%	5			
Blood loss (ml/kg)		100.6 ± 122.4	(2.7–597.0)		22.5	0.0055	0.0055*
Operation time (min)		529 ± 169.0	(353–1154)		–	–	0.32
	Postoperative factors						
Programmed pulse therapy	yes	54	90.0%	9			0.265
	no	6	10.0%	0			
Hepatic artery thrombosis or stenosis	yes	4	6.7%	0			0.2453
	no	56	93.3%	9			
Portal vein stenosis	yes	5	8.3%	1			0.4139
	no	55	91.7%	8			
Acute cellular rejection (ACR)	yes	36	60.0%	7			0.8618
	no	24	40.0%	2			
Steroid-resistant rejection (SRR)	yes	8	13.3%	1			0.633
	no	52	86.7%	8			
CMV infection	yes	30	50.0%	5			0.0996
	no	30	50.0%	4			
Post-transplant lympho-proliferative disease (PTLD)	yes	6	10.0%	8			0.3141
	no	54	90.0%	1			

5 perioperative factors identified as significant by the univariate analysis. The disease category of CS remained as the only independent predictor of better prognosis ($p=0.0021$, Table 3). The overall survival among the 60 recipients was 91.4% at 1 year, and 85.9% at both 3 and 5 years. Since the only re-transplant case showed HAT-related early graft loss and since that re-transplanted recipient was doing well, we evaluated the outcomes of our series based solely on patient survival. The 1-, 3-, and 5-year survival rates by group were 100%, 97.7%, and 97.7% in the CS group, and 70.6%, 70.6%, and 58.8% in the NCS group, respectively (Fig. 1). Two recipients were lost in the CS group; one to viral infection, and the other to chronic hepatic failure due to poor medication originating from parental neglect. In the NCS group, 6 of the 9 lost patients experienced acute or chronic hepatic failure. Of note, in the NCS group, hepatocellular liver failure requiring urgent LDLT included some cases of incurable systemic disease and malignant tumor. In the NCS group, the early loss of three recipients resulted from the recurrence of malignant tumors (chronic active Epstein-Barr

Table 3 Multivariate analysis of prognostic factors

Factors	Exp.	Standard error	Confidential interval	*P*-value
Cholestatic/non-cholestatic	1.255	0.4577	0.4372837 < CI < 2.3037148	0.0021*
GRWR	0.556	0.4045	−0.228276 < CI < 1.3883422	0.1644
CIT (min)	−0.01	0.0131	−0.040273 < CI < 0.0109811	0.407
TIT (min)	−0.071	0.0434	−0.167739 < CI < 0.0046094	0.0679
Blood loss (ml/kg)	0.00157	0.00287	−0.004872 < CI < 0.0070256	0.5927



Group / % survival	1 year	3 years	5 years
Total (n=60)	91.4	85.9	85.9
Cholestatic (n=43)	**100**	97.4	97.4
Non-cholestatic (n=17)	70.6	58.8	58.8

Fig. 1 Survival curves for the 60 pediatric recipients. The overall survival at 1-, 3-, and 5 years were 91.4%, 85.9%, and 85.9%, respectively. The survival rates for the cholestatic (CS) group vs. non-cholestatic (NCS) groups at 1, 3, and 5 years were 100% vs. 70.6%, 97.4% vs. 58.8%, and 97.4 vs. 58.8%, respectively. Significant differences in survival rates were seen between the CS and NCS groups ($p=0.0002$, log-rank test).

virus infection-associated diffuse T and natural killer cell lymphoma, and hepatoblastoma) and multi-organ failure from mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes (MELAS) [8,9]. Interestingly, 85.7% of the lost recipients in the NCS group experienced ACR (Table 4).

To clarify the characteristics of CS associated with better prognosis, we analyzed the influences of disease category on perioperative factors. A history of multiple major surgeries ($p=0.0042$), a larger ratio of explanted liver for recipient body weight ($p=0.0449$), a high frequency of portal plasty ($p=0.0193$), longer total operation time ($p=0.0335$), and elongated CIT (0. 0421) were significant in the CS group (Table 5).

Discussion

Pediatric LDLT, currently the only alternative to

Table 4 Details of the 9 mortality cases

Disease category	Case	Age	Sex	ABO compatibility	Initial diagnosis	Final diagnosis	ACR	Survival (months)	Cause of death
Cholestatic (CS)	1	2y2m	M	Compatible	BA	BA	+	102.7	Hypoxic encephalopathy → poor adherence
	2	1y4m	F	Identical	BA	BA	−	13.7	Influenza encephalo-pneumonitis
Non - cholestatic (NCS)	3	6m	M	Incompatible	AHF	AHF (unknown)	+	6.1	PTLD → dose down of CNI → humoral rejection (ABO)
	4	1y6m	F	Identical	Cryptogenic LC	Tyrosinemia	+	12.7	Other cause of death
	5	1y2m	M	Identical	AHF	AHF (unknown)	+	5	Portal stenosis → revision → portal obstruction
	6	10m	F	Compatible	Cryptogenic LC	Cryptogenic LC	+	29	Cardiac failure
	7	4y7m	F	Compatible	Cryptogenic LC	Chronic invasive EB lymphoma*	+	2.5	MOF by tumor progression
	8	8m	F	Incompatible	AHF	S/O MELAS*	−	6.1	MOF by MELAS (defined by muscle biopsy)
	9	2y	M	Identical	Hepatoblastoma	Hepatoblastoma	+	9.4	Lung metastasis

AHF, acute hepatic failure; LC, liver cirrhosis; EB, Epstein-Barr; MOF, multi-organ failure; MELAS, mitochondrial myopathy, encephalopathy, lactic acidosis, and stroke-like episodes.
*Out of indication for LT at postoperative final diagnosis.

Table 5 Significant factors affected by disease category (except for recipient survival)

Disease category/Significant factors		Cholestatic group (n = 43)	Non-cholestatic group (n = 17)	*P*-value
Surgical history of abdominal surgery	0 or 1	27	16	0.0042*
	over 2	16	1	
Native liver/RBW ratio		4.494 ± 1.641	3.449 ± 2.101	0.0449*
Operation time (min)		535.4 ± 214	458.5 ± 62.6	0.0335*
Cold ischemic time (min)		88.0 ± 77.8	59.6 ± 25.7	0.0421*
Portal plasty		19/24	2/15	0.0193*

*Statistically significant.

deceased donor LT, has become accepted practice around the world because of its advantages including a lower pediatric waiting-list death ratio, shorter waiting periods, reduced ischemia times, and more precise donor screening, all of which contribute to better recipient survival [10, 11]. Despite the clear increase in surgical complexity due to the preceding hepatoportoenterostomy (*e.g.*, the extended surgical time and CIT), the reasons for the good transplantation results for cholestatic cirrhosis warrant examination.

First, the recipients in our CS group had mainly non-recurrent diseases, with the exception of a small number of PSC recipients. Three cases of death due to recurrence or progression of the primary disease after transplantation occurred in the NCS group. These included a case of recurrent hepatoblastoma, the development of MELAS, and liver invasion of EBV-derived malignant lymphoma. Since the latter 2 recipients manifesting acute and subacute forms of hepatic failure were transferred to receive an urgent LT under an initial diagnosis of meeting LT indications, their LDLTs were subsequently performed. A histological diagnosis of both cases was obtained after the LT. If these patients' histological diagnoses had been obtained before the LT, both of them would have been excluded as LT candidates. Strong expectations from the patients' families and referral doctors for LT, the sudden onset of liver failure, imminent symptoms, and the temporal urgency for transplants led us to select immediate LDLT.

Fulminant hepatic failure is known to be a primary disease with poor prognosis among pediatric LT cases. The reported overall prognosis for children with acute liver failure remains poor, with a mortality rate of 44-67% [12-15]. We have lost 2 of 8 recipients with acute hepatic failure (AHF) among these 60 pediatric LDLT cases. One recipient experienced respiratory failure that developed from Wardiel's lymphoma 6 months after an ABO-incompatible LDLT. However, that patient died of hepatic necrosis due to the development of ABO-incompatible humoral rejection. In the current rituximab era, this case may be savable [16, 17]. Another patient showed strong stricture of the hepato-duodenal ligament at the duct-to-duct anastomotic level after strong ACR and was lost due to portal vein occlusion after revision surgery on the bile duct.

Another factor contributing to better outcomes of LT in our CS group is the larger intraperitoneal space in the CS group. Kasahara *et al.* reported that the recipients under 1 year old who received grafts with a GRWR >4.0% showed significantly worse survival [18]. However, as our data show, patients with CS can accept a graft with a 1% greater GRWR compared to patients with NCS because of hepatomegaly due to cholestatic cirrhosis, thus avoiding the risk of a large-for-size graft. Moreover, the significant increase in the requirement for portal plasty shows that portal veins are narrower in the CS group compared to the non-CS group. The relatively high risk of portal vein complications among BA recipients reported by Takahashi *et al.* may support a scarce portal feed and dominant arterial supply for the cirrhotic native liver before transplantation in a CS patient [19]. In other words, the arteries in the present CS group were relatively thick and arterial complications may thus have been less likely to occur. Whether arterial anastomosis was performed under fixed microscopy or a surgical loupe was not a prognostic factor for the recipients in our series.

Pediatric recipients are more likely to experience early acute rejection, at approx. twice the frequency of adults [20-22]. However, this history of early acute rejection has some advantages, inducing donor-specific hyporesponsiveness and improvement of both recipient and graft survival [23-25]. In terms of the pattern of postoperative hemodynamics early after LDLT, a portal vein-dominant blood supply increases the port/arterial flow volume ratio to 8.3 in a deceased donor LT and to 14.6 in an LDLT [26]. This portal hyperperfusion results in a relative decrease in arterial supply, and is considered one contributor to the unique complications in LDLT, termed "small-for-size syndrome" [27, 28].

In early acute rejection, portal hyperperfusion decreases as sinusoidal resistance rises, and the arterial supply is secondarily enhanced by the hepatic artery buffer response [29-32]. This reciprocal increase in arterial blood flow may be favorable in maintaining patency of the anastomotic site in the early phase after a pediatric LT, and may contribute to physically stable graft blood flow thereafter.

In conclusion, pediatric CS disease required a more complicated surgical technique and significantly prolonged operation time, but is very suitable for LDLT therapy and offers an excellent prognosis. The further improvement of the survival of pediatric recipients requires the intensive prevention of the relapse of the patients' primary disease and more rapid diagnoses in order to exclude contraindicated diseases which mani-

fest hepatic failure as initial symptoms from NCS diseases.

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