virus-specific cell-mediated immunity could not be evaluated [24]. In general, after LT, a majority of patients receive immunosuppressants such as tacrolimus. Other commonly administered immunosuppressants include calcineurin inhibitors, which affect cellular immunity and potentially seroconversion and antibody levels after LAV immunization. A recent data in varicella vaccine in post-LT patients emphasized the importance of cellular immunity against varicella vaccine [25]. Further sequential data is needed for the evaluation of cellular immunity against each organism. Third, investigation of strain-by-strain differences in seropositivity after each vaccination, such as the difference in seropositivity between the two mumps vaccine strains, was not performed. Fourth, there is no well-accepted cutoff level of antibodies. Hence, we cannot be certain that the threshold adopted in this current study reflected the actual protective potency against each pathogen. Finally, the timing of blood sampling varied among patients due to the outpatient-based study design. As such, primary vaccine failure could not be distinguished from secondary vaccine failure. We suggest that future studies should address this issue with a consideration for a booster dose after LT in the event that secondary failure is a significant issue.

In conclusion, LAVs administration prior to LT was relatively effective for rubella, but was suboptimal for others. We found that several factors were associated with the seronegativity of LAVs, including patients <12 months of age at the time of immunization for measles, a lower body weight

for varicella, and underlying diseases other than biliary atresia for mumps. Further evaluation of sequential data, including cell-mediated immunity and nutritional status, is warranted.

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Figure legend

Figure 1. Changes in antibody levels of measles (A), rubella (B), varicella (C), and mumps (D) vaccines in patients who enrolled the study before liver transplantation. The first blood withdraw was performed before liver transplantation (without immunosuppressants) and the second blood withdraw was performed at a median of 6 post-operative months (range: 5-15 post-operative months). The result of '<50' in enzyme-linked immunosorbent assay was expediently replaced to '10' in the (**C**) and (**D**) graphs. X-axis represents post-operative months. Y-axis represents antibody levels of each live attenuated vaccine. The dot-lines indicate cut-off levels of antibody titers of each live attenuated vaccine.

Abbreviations: POM, post operative month; IDU, interdilution unit; EU, enzyme-linked immunosorbent assay unit

Figure 2. Comparison of seropositive rates between patients who received live attenuated vaccines <12 months of age and ≥12months of age.

Open boxes, vaccinated <12 months of age; filled boxes, vaccinated ≥12 months of age. The seropositivity rates of measles and varicella vaccines were significantly lower in those who received the vaccines <12 months of age compared to those who received the vaccines ≥12 months of age (P

= 0.001, P = 0.007, respectively). No differences in seropositivity rates were found in those who received the rubella and mumps vaccines <12 months of age compared to those who received the vaccines ≥12 months of age (P = 0.357, P = 1.000, respectively).

* indicates statistically significant (P<0.05)

Supplementary Figure 1. Numbers of patients enrolled and samples obtained before and after liver transplantation

Numbers of specimens are listed in parentheses. *indicates that one patient was excluded due to invalid results caused by technical error. **indicates number of patients whose blood samples were obtained both before and after liver transplantation. §indicates number of patients whose blood samples were obtained one time point only after liver transplantation. ¶indicates number of patients whose blood samples were obtained two time points after liver transplantation.

Abbreviations: PMH, past medical history; LT, liver transplantation

Table 1. Patients' characteristics and seropositivity after live attenuated vaccines

Patients characteristics		Live attenuated vaccines administered			
		Measles[#]	**Rubella**	**Varicella**	**Mumps**
		(n = 49)	**(n = 48)**	**(n = 40)**	**(n = 41)**
Age (median, months)		45	45	42	45
	(range)	(12-228)			
Gender (male) (%)		17 (35%)	16 (33%)	15 (38%)	13 (32%)
Body weight (median, kg)		17.7	14.8	15.3	15.7
	(range)	(8.5-53.5)			
Simultaneous vaccination (%) YES		14 (29%)	14 (30%)	14 (35%)	14 (34%)
Dose(s) of vaccination	one (%)	44 (90%)	43 (90%)	40 (100%)	41 (100%)
	two (%)	5 (10%)	5 (10%)	0 (0%)	0 (0%)
Underlying diseases or conditions					
	Biliary atresia	27 (55%)	27 (57%)	26 (65%)	24 (59%)
	Metabolic disorders	13 (27%)	14 (29%)	11 (28%)	12 (29%)
	Fulminant hepatic failure	5 (10%)	4 (8%)	2 (5%)	2 (5%)
	others	4 (8%)	3 (6%)	1 (2%)	3 (7%)
Age at transplantation (median, month)		18	18	17	18
	(range)	(6-187)			
Timing of blood collection (post-operative months,		21	19	18	19
median)	(range)	(5-222)			
Immunosuppressants					
(at the time of blood sampling)	TAC	41 (84%)	40 (83%)	30 (75%)	34 (83%)
	TAC + MMF	4 (8%)	4 (8%)	5 (13%)	3 (7%)
	TAC + MMF + PSL	1 (2%)	1 (2%)	1 (2%)	1 (3%)
	TAC + PSL	3 (6%)	3 (7%)	4 (10%)	3 (7%)
WBC (/μL, median)		6,350	6,295	6,485	6,360
	(range)	(1,940-14,010)			
ANC (/μL, median)		2,641	2,573	2,767	2,819
	(range)	(143-7,369)			(495-7,369)
ALC (/μL, median)		2,774	2,781	3,203	2,766
	(range)	(1,164-7,866)			
Seropositivity (%)		23 (46.9%)	42 (89.4%)	27 (67.5%)	20 (48.8%)

1

[#]represents total study subjects. The range of variables in each vaccine is not listed if it they are that same as the ones with measles vaccine. Abbreviations: TAC, tacrolimus; MMF, mycophenolate mofetil; PSL, prednisolone; WBC, white blood cell count; ANC, absolute neutrophil count; ALC, absolute lymphocyte count

Table 2. Univariate analysis for factors associated with serostatus: measles, varicella, and mumps vaccines

Covariates	A) Measles		P-value	B) Varicella		P-value	C) Mumps		P-value
	Seropositive (n = 23)	Seronegative (n = 26)		Seropositive (n = 27)	Seronegative (n = 13)		Seropositive (n = 20)	Seronegative (n = 21)	
Gender, male (%)	9 (39%)	14 (54%)	0.539	10 (37%)	5 (38%)	1.000	5 (25%)	8 (38%)	0.505
Body weight (kg) median (range)	19.4 (9.0-48.0)	13.0 (9.0-28.4)	0.004*	16.7 (9.0-48.0)	11.8 (9.0-18.2)	0.000*	14.2 (9.0-48.0)	15.3 (9.0-28.4)	0.744
Simultaneous vaccination YES (%)	4 (17%)	10 (39%)	0.125	8 (30%)	6 (46%)	0.480	9 (45%)	5 (24%)	0.197
Age at vaccination (≥12month) YES (%)	21 (91%)	12 (46%)	0.001*	19 (70%)	3 (23%)	0.007*	13 (65%)	13 (62%)	1.000
Doses of vaccines One (%)	19 (83%)	25 (96%)	0.173	27 (100%)	13 (100%)	1.000	20 (100%)	21 (100%)	1.000
Two (%)	4 (17%)	1 (4%)		0 (0%)	0 (0%)		0 (0%)	0 (0%)	
Underlying diseases or conditions			0.852			0.511			0.026*
Biliary atresia	14 (61%)	13 (50%)		18 (67%)	8 (62%)		16 (80%)	8 (38%)	
Metabolic diseases	6 (26%)	9 (36%)		7 (26%)	4 (31%)		3 (15%)	9 (42%)	
Fulminant hepatic failure	2 (9%)	2 (7%)		2 (7%)	0 (0%)		0 (0%)	2 (10%)	
others	1 (4%)	2 (7%)		0 (0%)	1 (7%)		1 (5%)	2 (10%)	
Donation Living donor	22 (96%)	25 (96%)	1.000	26 (96%)	12 (92%)	1.000	19 (95%)	21 (100%)	0.488
Deceased donor	1 (4%)	1 (4%)		1 (4%)	1 (8%)		1 (5%)	0 (0%)	
Age at transplantation (months, median)	35	11	0.000*	21	9	0.007*	14	15	0.886
(range)	(6-187)	(5–90)		(6-187)	(5-67)		(5-187)	(6-137)	
Age at blood collection (months, median)	78	35	0.003*	47	27	0.000*	44	44	0.938
(range)	(12–228)	(18–119)		(12-228)	(18-84)		(12-228)	(21-150)	

Timing of blood collection		17	24	0.372	24	16	0.120	17	24	0.522
(post-operative months, median) (range)		(5–222)	(6–53)		(5-222)	(6-33)		(5-222)	(5-68)	
Time from the last vaccination (months,		49	27	0.057	39	19	0.003*	22	29	0.473
median) (range)		(6–137)	(8–103)		(2-119)	(8-34)		(4-188)	(1-112)	
Immunosuppressants (at the time of										
blood sampling)	TAC	21 (92%)	20 (77%)	0.109	24 (89%)	9 (69%)	0.032*	19 (95%)	15 (71%)	0.046*
	TAC + MMF	1 (4%)	6 (23%)		3 (11%)	2 (15%)		0 (0%)	3 (14%)	
	TAC + PSL	0 (0%)	0 (0%)		0 (0%)	1 (8%)		1 (5%)	2 (10%)	
	TAC + MMF + PSL	1 (4%)	0 (0%)		0 (0%)	1 (8%)		0 (0%)	1 (5%)	
TAC trough level (ng/ml)	<1.5	1 (5%)	9 (35%)	0.023*	4 (15%)	7 (55%)	0.001*	4 (20%)	5 (24%)	0.103
	1.5-5.0	19 (82%)	13 (50%)		21 (78%)	2 (15%)		15 (75%)	10 (48%)	
	5.0<	3 (13%)	4 (15%)		2 (7%)	4 (30%)		1 (5%)	6 (28%)	
WBC (/μL, median) (range)		5,420	7,710	0.001*	6,230	8,430	0.168	6,360	6,610	0.602
		(1,940-9,150)	(3,560-14,010)		(1,940-12,290)	(4,200-14,010)		(1,940-12,290)	(3,560-14,010)	
ANC (/μL, median) (range)		2,341	3,037	0.261	2,659	2,767	1.000	2,262	2,961	0.376
		(143-4,616)	(521-7,369)		(143-6,475)	(521-7,369)		(495-6,475)	(521-7,369)	
ALC (/μL, median) (range)		2,069	3,608	0.001*	2,552	3,899	0.018*	2,962	2,766	0.668
		(1,164-6,680)	(1,400-7,866)		(1,164-7,866)	(2,057-5,408)		(1,164-7,866)	(1,400-5,408)	

*indicates statistically significant (P<0.05)

Abbreviations: TAC, tacrolimus; MMF, Mycophenolate mofetil; PSL, prednisolone; WBC, white blood cell count; ANC, absolute neutrophil count; ALC, absolute lymphocyte cou

Table 3. Multivariate analyses for seroconversion rates for measles (A), varicella (B), and mumps (C) vaccines

A. Measles

Covariates	Regression coefficient ± SE	P-value	Odds ratio (95% CI)
Age at vaccination (≥ 12 months)	2.593 ± 0.834	0.002*	13.364 (2.563-69.685)
Age at blood collection (month)	-0.012 ± 0.033	0.728	0.989 (0.927-1.055)
Body weight (kg)	0.142 ± 0.163	0.384	1.153 (0.837-1.588)
Age at transplantation (months)	0.017 ± 0.019	0.374	1.017 (0.980-1.056)
Tacrolimus trough level (ng/ml)	0.363 ± 0.640	0.571	1.437 (0.410-5.038)
WBC (/μl)	0.000 ± 0.000	0.163	1.000 (0.999-1.000)
ALC (/μl)	0.000 ± 0.000	0.731	1.000 (0.999-1.001)
Constant	-1.946 ± 0.756	0.010	

B. Varicella

Covariates	Regression coefficient ± SE	P-value	Odds ratio (95% CI)
Body weight (kg)	0.382 ± 0.154	0.013*	1.466 (1.084-1.982)
Age at vaccination (≥ 12 months)	2.154 ± 1.475	0.144	8.616 (0.479-155.090)
Age at blood collection (months)	-0.008 ± 0.073	0.914	0.992 (0.860-1.145)
Age at transplantation (months)	-0.047 ± 0.074	0.527	0.954 (0.824-1.104)
Time from the last vaccination (months)	0.079 ± 0.058	0.172	1.082 (0.966-1.213)
Tacrolimus trough level (ng/ml)	0.656 ± 0.716	0.360	1.927 (0.473-7.846)
ALC (/μl)	0.000 ± 0.000	0.305	1.000 (1.000-1.001)
Constant	-4.796 ± 2.069	0.020	

C. Mumps

Covariates	Regression coefficient ± SE	P-value	Odds ratio (95% CI)
Biliary atresia	2.079 ± 0.726	0.004*	8.000 (1.929-33.181)
Immunosuppressants	-2.081 ± 1.225	0.089	0.125 (0.011-1.376)
Constant	-1.253 ± 0.567	0.027	

*indicates statistically significant (P<0.05)

Abbreviations: SE, standard error; CI, confidence interval; WBC, white blood cell count; ALC, absolute lymphocyte count

Supplementary Table 1. Factors associated with seropositivity of the patients who were administered rubella vaccine

1) Univariate analysis

Covariates		Seropositive (n = 42)	Seronegative (n = 5)	P-value
Gender, male (%)		14 (33%)	2 (40%)	1.000
Body weight (kg) median (range)		15.6 (9.0-48.0)	12.8 (9.0-24.4)	0.296
Simultaneous vaccination	YES (%)	13 (31%)	1 (20%)	1.000
Age at vaccination (≥12month)	YES (%)	27 (57%)	2 (40%)	0.357
Doses of vaccines	One (%)	37 (88%)	5 (100%)	
	Two (%)	5 (12%)	0 (0%)	0.449
Underlying diseases or conditions				
	Biliary atresia	27 (64%)	0 (0%)	0.009*
	Metabolic disorders	9 (21%)	4 (80%)	
	Fulminant hepatic failure	4 (10%)	0 (0%)	
	others	2 (5%)	1 (20%)	
Donation	Living donor	40 (95%)	5 (100%)	1.000
	Deceased donor	2 (5%)	0 (0%)	
Age at transplantation (months, median) (range)		17 (6-187)	13 (5-26)	0.095
Age at blood collection (months, median) (range)		44 (12-228)	39 (27-69)	0.228
Timing of blood collection (post-operative months, median) (range)		18 (5-222)	26 (21-43)	0.557
Time from the last vaccination (months, median) (range)		29 (1-131)	28 (24-57)	0.700
Immunosuppressants (at the time of blood sampling)				
	TAC	34 (81%)	5 (100%)	0.512
	TAC + MMF	4 (10%)	0 (0%)	
	TAC + MMF + PSL	1 (2%)	0 (0%)	
	TAC + PSL	3 (7%)	0 (0%)	
TAC trough level (ng/ml)	<1.5	9 (21%)	1 (20%)	1.000
	1.5-5.0	27 (64%)	4 (80%)	
	5.0<	6 (15%)	0 (0%)	
WBC (/μL, median) (range)		6,240 (1,940-14,010)	7,075 (6,080-10,560)	0.256
ANC (/μL, median) (range)		2,573 (143-7,369)	2,864 (1,285-3,844)	0.706
ALC (/μL, median) (range)		2,750 (1,164-7,866)	3,592 (2,262-5,196)	0.142

One specimen could not be evaluated due to technical error.

*indicates statistically significant (P<0.05)

Abbreviations: TAC, tacrolimus; MMF, mycophenolate mofetil; PSL, prednisolone; WBC, white blood cell count; ANC, absolute neutrophil count; ALC, absolute lymphocyte count.

Supplementary Table 2. Summary of the factors associated with seropositivity after administration of live attenuated vaccines administered before liver transplantation by univariate and multivariate analyses

Variables	Univariated analysis				Multivariated analysis			
	Measles	Rubella	Varicella	Mumps	Measles	Rubella	Varicella	Mumps
Age at vaccination (≥ 12 months)	○		○		○			
Age at blood collection (month)	○		○					
Body weight (kg)	○		○				○	
Age at liver transplantation (months)	○		○					
Number of Immunosuppressants			○	○				
TAC trough level (ng/mL)	○		○					
WBC (/μL)	○							
ALC (/μL)	○		○					
Underlying diseases								
Biliary atresia		○		○				○

○ indicates that the factor significantly impacted on the seropositivity of vacccine ($P<0.05$).

Abbreviations: LAVs, live attenuated vaccine; TAC, tacrolimus; WBC, white blood cell count; ALC, absolute lymphocyte count, N/A, not available

Figure 1

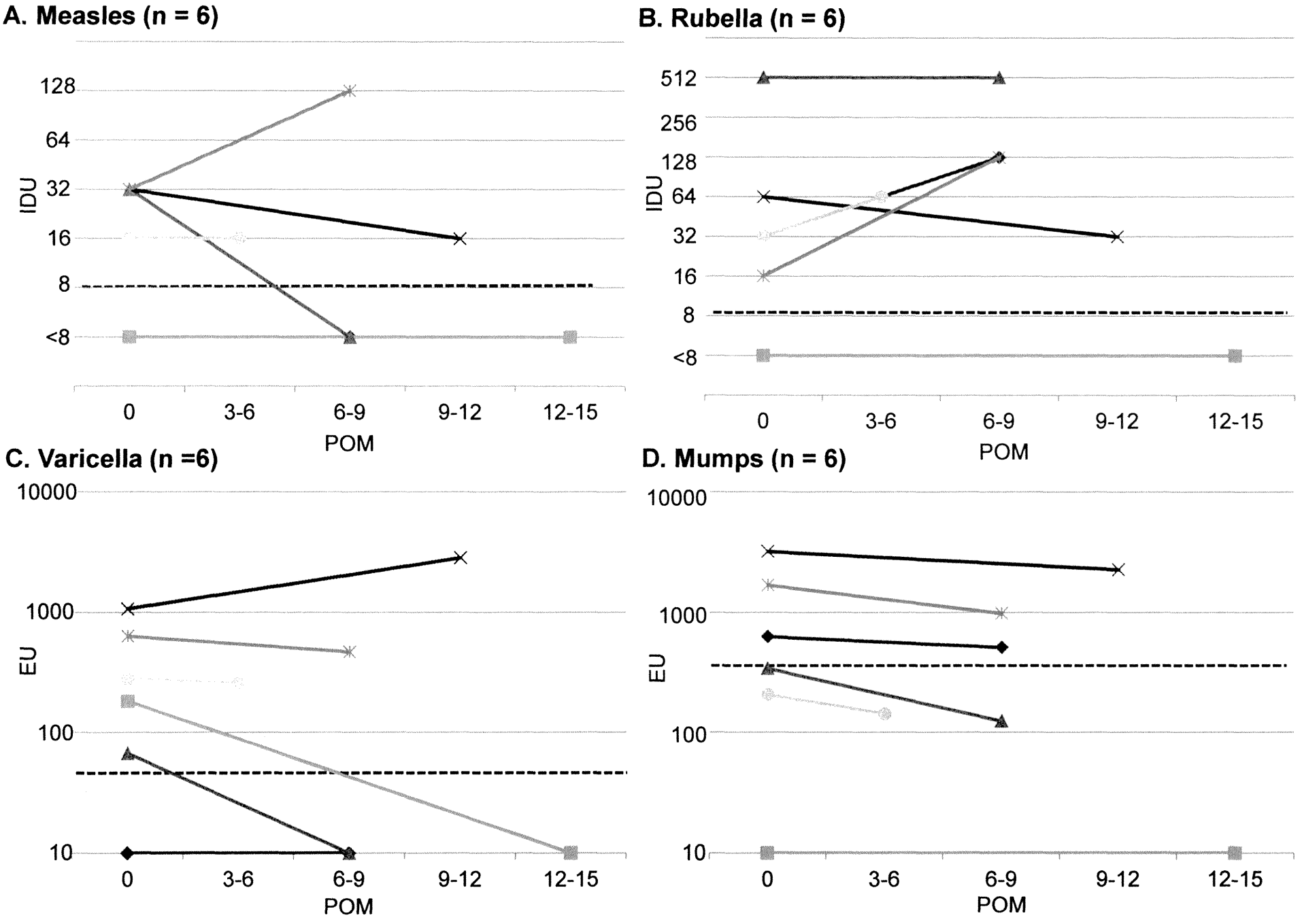
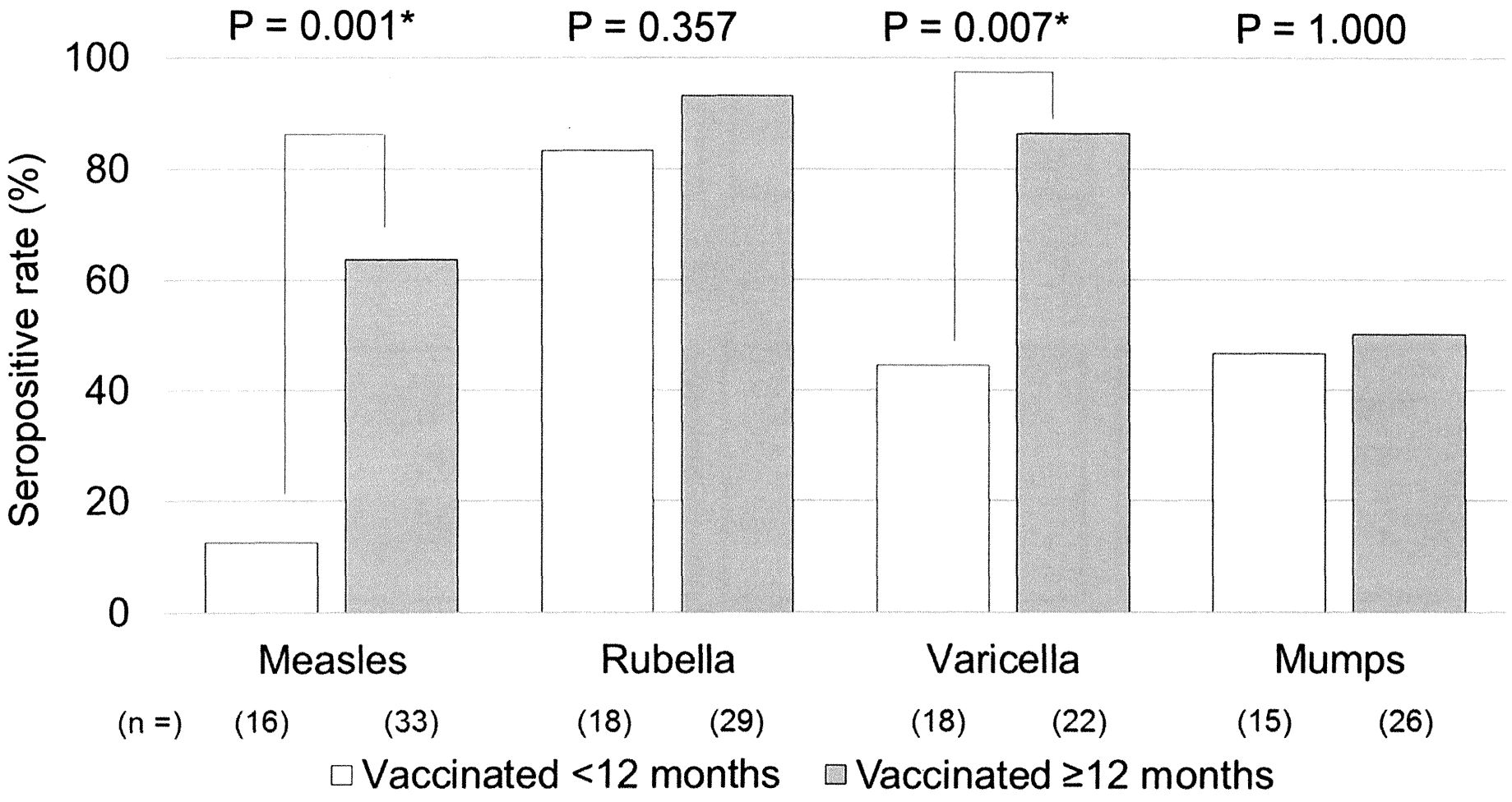
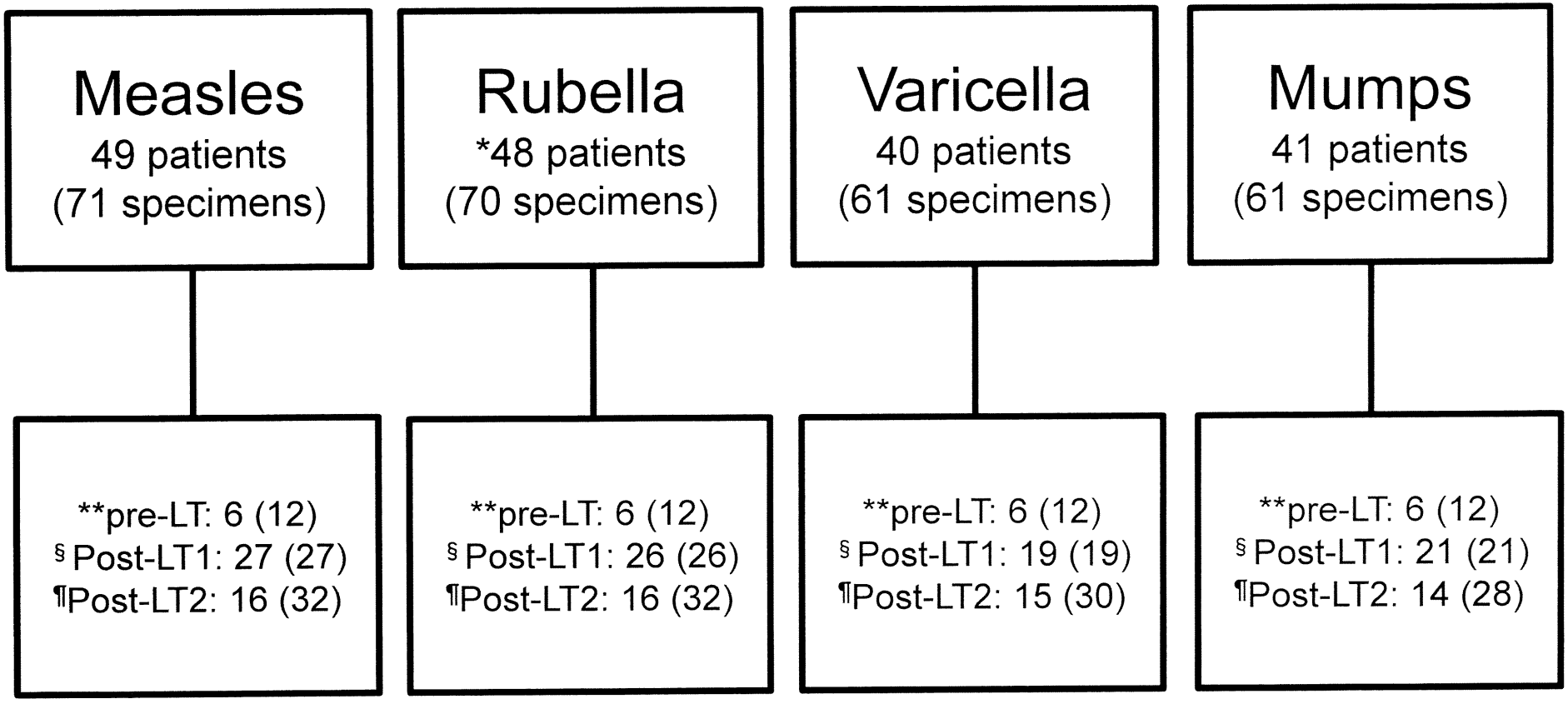

A. Measles (n = 6)
128
64
32
16
8
<8
IDU
0
3-6
6-9
9-12
12-15
POM
B. Rubella (n = 6)
512
256
128
64
32
16
8
<8
IDU
0
3-6
6-9
9-12
12-15
POM
C. Varicella (n =6)
10000
1000
100
10
EU
0
3-6
6-9
9-12
12-15
POM
D. Mumps (n = 6)
10000
1000
100
10
EU
0
3-6
6-9
9-12
12-15
POM

Figure 2


P = 0.001*
P = 0.357
P = 0.007*
P = 1.000
100
80
60
40
20
0
Seropositive rate (%)
Measles
Rubella
Varicella
Mumps
(n =)
(16)
(33)
(18)
(29)
(18)
(22)
(15)
(26)
Vaccinated <12 months
Vaccinated ≥12 months

Supplementary Figure 1



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Registry Report

Living donor liver transplantation for pediatric patients with metabolic disorders: The Japanese multicenter registry

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Key words: living donor liver transplantation – liver transplantation – long-term results – pediatric liver transplantation – metabolic disease

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Kasahara M, Sakamoto S, Horikawa R, Koji U, Mizuta K, Shinkai M, Takahito Y, Taguchi T, Inomata Y, Uemoto S, Tatsuo K, Kato S. Living donor liver transplantation for pediatric patients with metabolic disorders: The Japanese multicenter registry.

Abstract: LDLT is indicated for a variety of metabolic disorders, primarily in Asian countries due to the absolute scarcity of deceased donor LT. We analyzed data for all pediatric LDLTs performed between November 1989 and December 2010, during which 2224 pediatric patients underwent LDLT in Japan. Of these patients, 194 (8.7%) underwent LDLT for metabolic disorders. Wilson's disease (n = 59; 30.4%) was the most common indication in the patients with metabolic disorders, followed by OTCD (n = 40; 20.6%), MMA (n = 20; 10.3%), and GSD (n = 15; 7.7%). The one-, five-, 10-, and 15-yr patient and graft survival rates were 91.2%, 87.9%, 87.0%, and 79.3%, and 91.2%, 87.9%, 86.1%, and 74.4%, respectively. Wilson's disease and urea cycle deficiency were associated with better patient survival. The use of heterozygous donors demonstrated no negative impact on either the donors or recipients. With regard to X-linked OTCD, symptomatic heterozygote maternal donors should not be considered potential donor candidates. Improving the understanding of the long-term suitability of this treatment modality will require the registration and ongoing evaluation of all patients with inherited metabolic disease considered for LT.

Abbreviations: ASS, argininosuccinic aciduria; CPS1D, carbamoyl phosphate synthetase 1 deficiency; GSD, glycogen storage disease; JLTS, Japanese Liver Transplantation Society; LDLT, living donor liver transplantation; LLS, left lateral segment; LT, liver transplantation; MMA, methylmalonic acidemia; OTCD, ornithine transcarbamylase deficiency; PA, propionic acidemia; PH1, primary hyperoxaluria type 1.

Although optimal treatment with medical and nutritional management has been adopted, many inborn errors of metabolism that affect the liver have a poor prognosis. Metabolic decompensation can result in severe neurological sequelae and even mortality in some patients with inborn errors of metabolism (1). LT has become an important therapeutic modality and may offer a complete/partial cure for many metabolic disorders (2).

Metabolic disorders have become the second largest indication for LT (3). LDLT is indicated for a variety of metabolic disorders, primarily in Asian countries due to the absolute scarcity of deceased donor LT, such as in cases of Wilson's disease (4–6), urea cycle disorders (7, 8), tyrosinemia (4), organic acidemia (9, 10), glycogen storage disorders (11), PH1 (12), and mitochondrial respiratory chain disorders (13), without mortality or morbidity related to the use of heterozygous donors at the time of publication. However, the indications and long-term outcomes in this pediatric population and the use of potentially heterozygote donors have not been fully documented.

The JLTS, a cooperative research consortium, was established in 1989 to characterize and follow trends in patients and graft survival and post-transplant complications in all liver transplant centers in Japan. The aim of this study was to evaluate pediatric patients who have undergone LDLT for metabolic disorders among the largest LDLT cohort in the world. A nationwide survey was supported in part by grants from the Scientific Research Fund of the Ministry of Education and a Research Grant for Immunology, Allergy and Organ Transplant, Rare and Intractable Disease from the Ministry of Health, Labor and Welfare, Japan (H24-08, H24-014, H25-06). This study was conducted with the approval of the ethics committee of the National Center for Child Health and Development, Tokyo (NCCHD #595), and the use of the annual LDLT registry data was approved by the committee of the JLTS.

Patients and methods

Study design

We analyzed data for all living donors and recipients receiving primary LDLT enrolled in the JLTS between the registry's inception in November 1989 and December 2010. The study patients were followed before LDLT then yearly after transplantation. During the study period, 6097 LDLTs were performed in Japan. Of these cases, 2224 patients were children less than 18 yr of age (36.5%), with an overall cumulative patient survival of 88.3% at one yr, 85.4% at five yr, 82.8% at 10 yr, and 79.6% at 20 yr (14). Biliary atresia was the leading indication for LDLT in Japan (n = 1471; 66.1%), followed by metabolic disorders (n = 194; 8.7%), acute liver failure (n = 190; 8.5%), Alagille syndrome (n = 70; 3.1%), and hepatoblastoma (n = 52; 2.3%). Of these 2224 children, 194 (8.7%) underwent LDLT for metabolic disorders and were enrolled in this study (Table 1). The median follow-up period was 7.4 yr (range: 2.0–19.7 yr).

Indication scores for LT for inherited metabolic disorders (Transplantation score)

The indications for LDLT were retrospectively evaluated according to a grading score system based on the guidelines recommended by the Japanese Ministry of Health, Labour and Welfare (Table 2) (15). The metabolic disorders were divided into groups based on the following: Whether the disorder predominantly involved the liver (liver-oriented disease; Wilson's disease, urea cycle disorder, citrullinemia,

Table 1. Pediatric LDLT for metabolic disorders in Japan

Original liver disease	n	%
Wilson's disease	59	30.4
Ornithine transcarbamylase deficiency	40	20.6
Carbamoyl phosphate synthetase 1 deficiency	9	4.6
Argininosuccinic aciduria	2	1.0
Methylmalonic academia	20	10.3
Propionic academia	9	4.6
Citrullinemia	6	3.1
Tyrosinemia	13	6.7
Glycogen storage disease	15	7.7
Primary hyperoxaluria type 1	9	4.6
Bile acid synthetic defect	4	2.1
Crigler–Najjar syndrome type 1	3	1.5
Mitochondrial respiratory chain disorders	2	1.0
Familial hypercholesterolemia	2	1.0
Erythropoietic protoporphyria	1	0.5
Total	194	100

Table 2. Scoring system for indication of LT for metabolic disorders (Transplantation score)

	Score 5	Score 3	Score 1
Original disease			
Liver-oriented disease	○		
Previous case report		○	
Effectiveness of medical treatment			
Metabolic decompensation which necessitated hospitalization			
≥6 times/yr	○		
3–5 times/yr		○	
Metabolic decompensation which necessitated admission			
≥6 times/yr			○
Metabolic decompensation which necessitated ICU care with apheresis			
≥2 times/yr	○		
Extremely poor response/adherence for medical treatment		○	
Poor response/adherence for medical treatment			○
Quality of life			
Nasogastric tube feeding/frequent meal		○	
Progressive neurological impairment		○	
Present status			
Good social interaction, full ambulation, partially impaired gross and fine motor skills, use of language, mildly delayed development, only modest learning deficits			○
Growth retardation (height<2.5 s.d.)			○
Continuous abnormal laboratory test (NH3, lactate, base excess, liver function, cholesterol, glucose)		○	

Score	Liver transplantation
≧10	Absolute indication
10> score ≧5	Relative indication
5> score ≧3	Prudence indication
3>	Contraindication

tyrosinemia type 1, bile acid synthetic defects, and Crigler–Najjar syndrome type 1) or partly involved the liver; the effectiveness of conventional medical treatment; the quality of life; and the mental/physical status. Each parameter was classified into three scores. A score of ≧10 points was defined as an absolute indication for LT, a score of 10 > points ≧5 was defined as a relative indication; a score of 5 > points ≧3 was defined as a prudent indication; and a score of 3> points was defined as a contraindication.

Evaluated variables

The following variables were obtained from the nationwide survey: disease etiology, laboratory data at presentation, medications and protein restriction therapies, the regimen of immunosuppression, post-transplant complications, and cause of death. The dates for the following events were also obtained: disease onset, jaundice, grade II or higher severe encephalopathy, and LT outcome.

Statistical analysis

Continuous variables are reported as medians and interquartile ranges, and categorical variables are reported as proportions. Cumulative survival is shown using Kaplan–Meier curves, and differences in survival between groups were analyzed using the log-rank test. Medians were compared using the Wilcoxon test, and proportions were compared using the chi-square test. Factors associated with long-term patient survival were analyzed with Cox regression analyses. The backward stepwise procedure was used for variable selection with retention criteria at a p Value of <0.1 level of significance. Variables with $p < 0.1$ according to the univariate analysis were included in the multivariate analysis. All recipients were followed until death and/or graft loss or until December 2010. All statistical tests were two-sided, and $p < 0.05$ was considered to be significant. The statistical analyses were performed using the SPSS, version 19.0 software program (SPSS, IBM, Chicago, IL, USA).

Results

The potential donors were evaluated using liver function tests, and the blood type, anatomical variations, and graft size were evaluated using computed tomography volumetry. All patients received grafts from family members. There were 95 men (48.5%) and 99 women donors, with a median age of 37.0 yr (range: 20–68 yr) and a median body weight of 58.5 kg (range: 39–89 kg). The donors were parents in 95.4% cases, including fathers and mothers in 46.9 and 48.5% of cases, respectively, followed by grandparents in 2.6% of cases. The blood-type combination was identical in 118 (60.8%) cases and compatible in 46 (23.7%) cases, while 30 (15.3%) recipients received ABO-incompatible grafts. The graft types included reduced LLSs (n = 7; 3.6%), LLSs (n = 108; 55.7%), left-lobe grafts (n = 63; 32.5%), and right-lobe grafts (n = 16; 8.2%). Three patients (OTCD in two patients and Crigler–Najjar disease in one patient) received auxiliary orthotopic LDLT with LLS. There were no donor mortalities related to surgery in this study population.

There were 89 male (45.9%) and 104 female recipients, with a median age of 5.9 yr (range: one month–17.9 yr) and a median body weight of 23.5 kg (range: 3.0–74.0 kg). Wilson's disease (n = 59; 30.4%) was the most common indication in the patients with metabolic disorders, followed by OTCD (n = 40; 20.6%), MMA (n = 20; 10.3%), and GSD (n = 15; 7.7%). The two decades comprising the study period can be categorized into four eras. The number of cases of LDLT for metabolic disorders increased over the past two decades (Fig. 1). Although there were no significant differences, the number of cases of recipients with urea cycle deficiency, organic acidemia, and GSD increased, while the number of transplanted recipients with Wilson's disease decreased according to the transplant era, respectively. The median transplantation

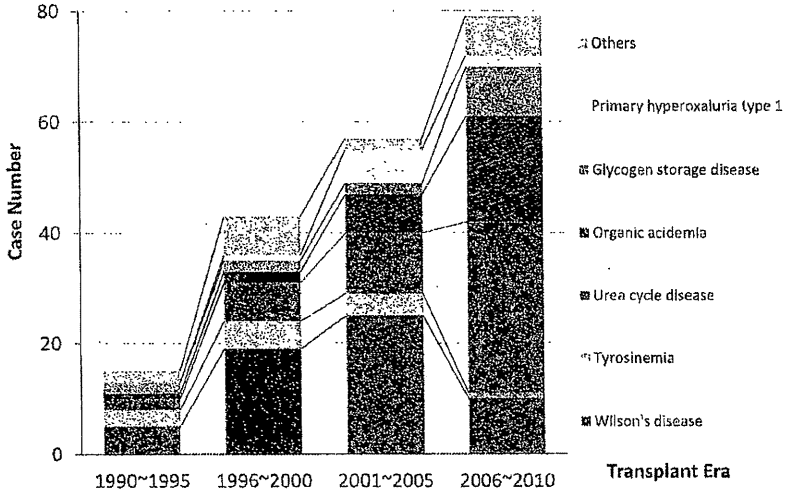

Fig. 1. Number of cases of metabolic disorders according to the transplant era.