ってくれば移植を考慮するが、移植適応が新生児型より明確ではなく、より客観的な指標が必要である。近年、堀川らが提唱した「肝移植適応のためのスコアリング（代謝性疾患生体肝移植の手引き）」は、疾患特異性、内科的治療の有効性、QOL、現在の発達・発育、検査結果の項目から点数を加算するもので、10点以上を移植適応とした客観的スコアになっている。

肝移植のためのスコアリング

項目	スコア5	3	1
疾患特異性			
代謝異常が肝臓に限局しているか？	○		
移植治療の実績があるか？		○	
内科的治療の有効性			
頻回の入院を必要とする代謝不全（年間6回以上）	○		
入院を必要とする代謝不全（年間3～5回）		○	
外来治療を必要とする代謝不全（年間6回以上）			○
代謝不全による血液浄化療法・ICU入院（初回発作時を除く、年間2回以上）	○		
服薬・食事療法コンプライアンス・アクセプタンス　著しく不良		○	
服薬・食事療法コンプライアンス・アクセプタンス　不良			○
QOL			
経管栄養・頻回の栄養（改善が見込める場合）		○	
神経学的改善・悪化の防止		○	
現在の状況			
神経学的状況（発達）：日常活動がある程度できる			○
身体的状況（成長）：成長障害（身長<−2.5SD）			○
生化学的所見：異常値の持続＊		○	

＊高アンモニア血症、高乳酸血症、アシドーシス、肝機能異常、高脂血症、低血糖など

スコア　10≦ 適応　7≦ 適応を考慮する

5≦ 適応は慎重に考える　3> 非適応

今回の解析結果に、このスコアを当てはめると、OTCD39例が17.4±8.4、CPSD9例では20.0±9.3であり、本スコアの有用性は高いと思われた。

E. 結論

OTCDやCPSDに対する肝移植治療成績は良好で根治性は高く、新生児発症症例では絶対的な適応と考えられた。遅発型のOTCDでは、内科的に高アンモニア血症のコントロールが不良になってくれば移植を考慮するが、移植適応が新生児型より明確ではなく、より客観的な指標が必要である。新生児発症型、遅発型いずれも、適切なタイミングで肝移植を行うことが重要であり、そのためにも本疾患における治療のガイドラインの作成が必要である。

F. 健康危険情報

G. 研究発表

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H. 知的財産権の出願・登録状況
(予定を含む)

1. 特許取得
なし

2. 実用新案登録
なし

3. その他
なし

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先天代謝異常症に対する移植療法の確立とガイドラインの作成に関する研究
分担研究報告書

糖原病

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研究要旨

糖原病はグリコーゲン代謝に関与する酵素の先天的な欠損により、主に肝臓あるいは筋肉にグリコーゲンが蓄積する疾患であり、蓄積する部位により大きく肝筋型、肝型、筋型に分けられる。移植適応に関しては、欠損酵素を補充する目的で行う場合と肝不全、肝腫瘍の治療目的に行われる場合がある。本研究では、糖原病に対する肝移植のガイドラインを作成することを目的とした。

本邦では 15 例の糖原病患児に対して肝移植が行われており、全例が生体肝移植である。Ⅰ型が 11 例（Ⅰa 型 2 例、Ⅰb 型 9 例）、Ⅳ型が 4 例であり、他の肝型糖原病症例は肝移植が行われていない。ドナーは父親 6 例、母親 8 例、祖父 1 例であり、提供時の年齢は 24 歳ー61 歳、血液型は identical 11 例、compatible 1 例、incompatible 3 例であった。グラフトのタイプは外側区域 11 例、左葉 4 例（APOLT 1 例を含む）であった。Ⅰa 型の 2 例中 1 例が急性拒絶反応により死亡している。Ⅰb 型は 9 例中 2 例が死亡しており、1 例は出血、感染により、1 例は肝不全により死亡している。Ⅰb 型の 5 年生存率は 77.8%であった。また、Ⅰb 型の好中球機能に関しては、肝移植後も G-CSF の投与を必要としている症例もあった。Ⅳ型は 4 例中 3 例死亡しており、1 例は ABO 不適合症例で、急性拒絶反応後の肝不全により再移植後に死亡している。1 例は脾臓摘出術後に門脈血栓起因していた。

肝型糖原病に対してはⅠ型、Ⅳ型に対して肝移植が行われており、Ⅳ型の成績は不良であった。Ⅰ型は内科的にコントロールが不良になってくれば移植を考慮するが、移植適応は明確ではなく、そのためにも本疾患における治療のガイドラインの作成が必要である。

A.研究目的

糖原病はグリコーゲン代謝に関与する酵素の先天的な欠損により、主に肝臓あるいは筋肉にグリコーゲンが蓄積する疾患であり、蓄積する部位により大きく肝筋型、肝型、筋型に分けられる。肝型糖原病はⅠ型、Ⅲ型、Ⅳ型、ⅥおよびⅨ型であり、空腹時低血糖と肝腫大を特徴とする。

移植適応に関しては、欠損酵素を補充する目的で行う場合と肝不全、肝腫瘍の治療目的に行われる場合がある。本研究では、糖原病に対する本邦での肝移植について、予後検討を含めた実態調査を行い、その結果と既存報告より、糖原病に対する肝移植のガイドラインを作成することを目的とした。

B.研究方法

2012 年 8 月 14 日に一次調査発送、2013 年 2 月 14 日に二次調査発送。対象 194 名、回収率 100%であった。対象の糖原病は 15 例（男 9、女 6）であった。

本邦での肝移植報告は、日本肝移植研究会からの肝移植症例登録報告（移植，第 47 巻, 416, 2012 年）を参照した。

（倫理面への配慮）

本研究は「ヘルシンキ宣言」および「疫学研究に関する倫理指針」に従って実施した。

C.研究結果

糖原病に対する肝移植症例の結果を示す。

症例　15 例（男 9 例、女 6 例）

病型　Ⅰ型 11 例（Ⅰa 型 2 例、Ⅰb 型 9 例

Ⅳ型 4 例

全例生体肝移植

ドナー 父 6例、母 8例、祖父 1例

提供時年齢 24ー61歳

血液型 identical 11例、compatible 1例、incompatible 3例

Graft type 外側区域 11例、左葉 4例（APOLT 1例を含む）

糖原病Ⅰa型肝移植後成績 Ⅰa型 2例

移植時年齢 5歳、6歳

Graft type 外側区域 2例

血液型 identical 2例

死亡 1例（急性拒絶により移植後14日目に死亡）

糖原病Ⅰb型肝移植後成績 Ⅰb型 9例

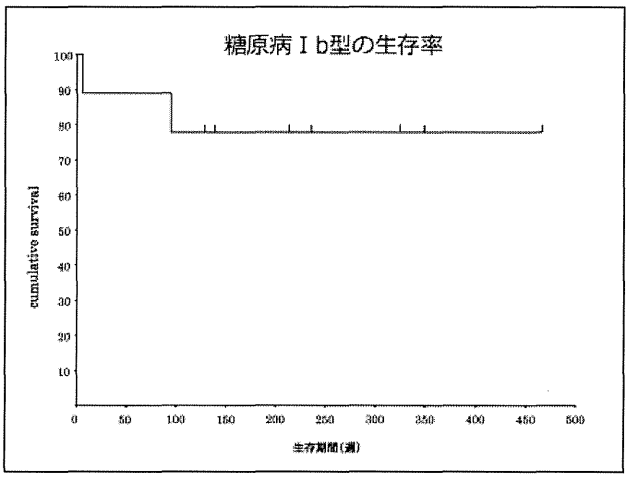
移植時年齢 1~13歳

Graft type 外側区域 5例、左葉4例（APOLT 1例を含む）

血液型 identical 7例, incompatible 2例

死亡 2例（出血、感染 1例、肝不全1例）

Ⅰb型の累積生存率は77.8%であった。



糖原病Ⅳ型肝移植後成績 Ⅳ型 4例

移植時年齢 9ヶ月~4歳

Graft type 外側区域 4例

血液型 identical 2例, compatible 1例, incompatible 2例

死亡 3例

急性拒絶 1例、門脈血栓1例

D.考察

糖原病はグリコーゲン代謝に関与する酵素の先天的な欠損により、主に肝臓あるいは筋肉にグリコーゲンが蓄積する疾患であり、蓄積する部位により大きく肝筋型、肝型、筋型に分けられる。肝型糖原病はⅠ型、Ⅲ型、Ⅳ型、ⅥおよびⅨ型であり、空腹時低血糖と肝腫大を特徴とする。移植適応に関しては以下の適応が考えられる。

A, 欠損酵素を補充する目的で行う場合

B, 肝不全、肝腫瘍の治療目的に行われる場合・肝型糖原病（Ia型, Ib型, Ⅲ型、Ⅳ型、ⅥおよびⅨ型）

糖原病に対する内科的治療は効果的であるため、Ia型についてAを理由として肝移植を行うケースは稀であり、通常は肝移植を行わず特殊ミルクや内科療法による治療を継続することになるが、移植を行えばこれらの治療はほぼ不要となる。Ib型で重度の低血糖を回避するため頻回のミルク摂取（注入など）と好中球減少などに対する感染予防が必要である。肝移植を行った場合には低血糖とそれによる中枢神経障害が回避でき、また、合併する好中球減少・機能低下も改善し、感染症や炎症性腸疾患の罹患のリスクも低下する可能性がある。しかし、好中球機能が改善せず、炎症性超疾患の再発を来した症例の報告もみられる。

肝のadenomaはⅠ型で高頻度に出現し、腫瘍からの出血や悪性化が大きな問題となる。Ⅰ型での肝移植を施行された大部分は多発性のadenomaである。切除できない多発性の肝adenomaや臨床的、病理学的に悪性を示唆

する症例など移植適応に関しては良性・悪性、大きさや数に依存する。

稀なIV型は肝不全を起こす疾患のため肝移植以外での救命は困難であるが、今回調査においては4例中3例死亡しており、移植後の成績は不良である。

E.結論

肝型糖原病に対してはI型、IV型に対して肝移植が行われており、IV型の成績は不良であった。I型は内科的にコントロールが不良になってくれば移植を考慮するが、移植適応は明確ではなく、そのためにも本疾患における治療のガイドラインの作成が必要である。

F. 健康危険情報

G. 研究発表

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H. 知的財産権の出願・登録状況
(予定を含む)

1. 特許取得
   なし
2. 実用新案登録
   なし
3. その他

Ⅲ. 研究成果の刊行に関する一覧表

○研究成果の発表

平成25年度に発表された研究成果は以下のとおりである。

◎は本研究班の課題内容、○は密接に関係する内容である。

[学術雑誌等での公表]

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Ⅳ. 参考資料

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Registry Report

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

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.

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

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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).

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.

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

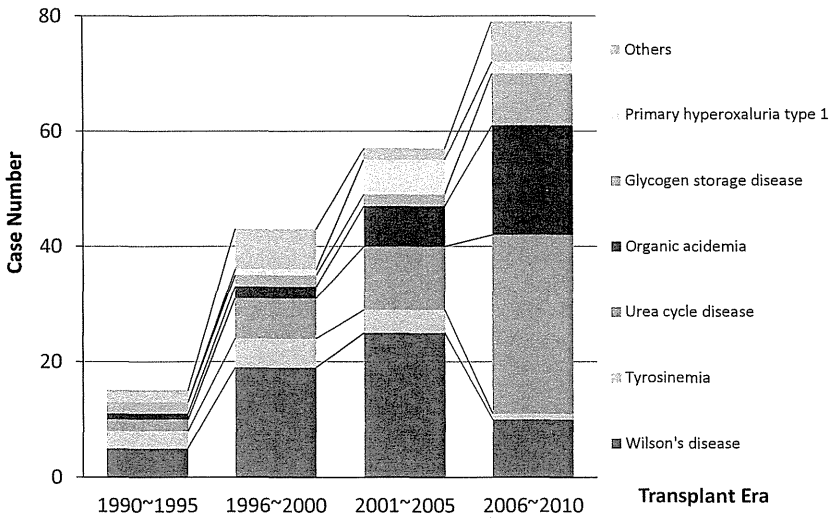

Fig. 1. Number of cases of metabolic disorders according to the transplant era.

score was 16.3 ± 8.2 (3–37) (Table 2). The initial regimen of immunosuppression consisted of tacrolimus and steroids in 91.8% of the cases.

Patient survival

The one-, five-, 10-, and 15-yr patient and graft survival rates of the patients with metabolic disorders undergoing LDLT were 91.2%, 87.9%, 87.0%, and 79.3%, and 91.2%, 87.9%, 86.1%, and 74.4%, respectively. There were no statistical differences in the patient or graft survival rates in the study population ($p = 0.187$; Fig. 2). When the data were analyzed separately, there were distinct differences in outcomes based on the original liver disease. In this study, patients with urea cycle disorder and Wilson's disease exhibited a significantly better patient survival, with 15-yr rates of 96.1 and 77.6% ($p < 0.001$; Fig. 3).

Recipient and donor factors were analyzed with respect to overall recipient survival. The results of the univariate and multivariate analyses are shown in Table 3. According to the univariate analysis, the etiology of liver disease and transplant era were significant predictors of survival. The univariate analysis of the factors predicting patient survival showed no significant associations between survival and donor age, sex, gender combination, relationship of the donor, ABO compatibility, graft type, or recipient age and sex. Factors with $p < 0.1$ were included in the multivariate analysis, and the etiology of liver disease and transplant era were found to be significant predictors of overall survival. Significant improvements in patient survival were obtained within the recent five yr, with one- and five-yr patient survival rates of 94.5 and 89.9%, respectively ($p < 0.001$; Fig. 4).

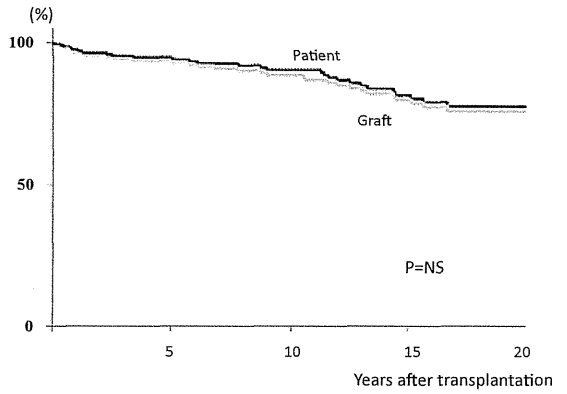

Fig. 2. Patient and graft survival after LDLT.

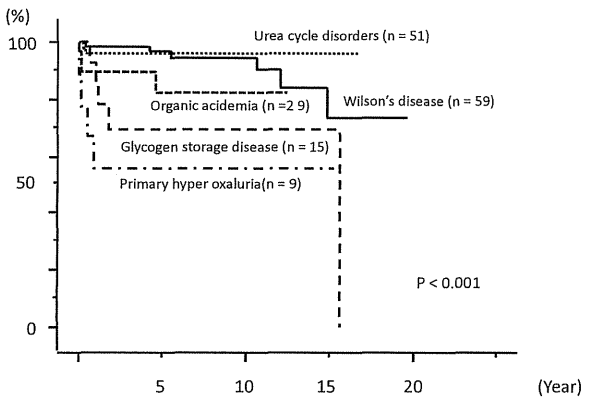

Fig. 3. Patient survival according to the original liver disease.

Original liver disease

When the data were analyzed according to the original liver disease, differences were found in each metabolic disease (Table 4). Wilson's disease was diagnosed at a median age of 11.0 ± 4.4 (range: 6–17) yr. The diagnosis was made based on laboratory data and clinical findings (the serum ceruloplasmin, urinary copper excretion and hepatic copper concentrations, and presence of Kayser–Fleischer rings) in all cases, as ATP7B genetic examinations were performed in the most recent nine cases. Four patients had an affected

Table 3. Factors associated with long-term survival after LDLT for metabolic disorders

	Hazard Ratio	95% confidence interval		p-Value
Univariate analysis				
Donor age groups	1.880	0.853	4.145	0.117
Donor sex	0.809	0.548	1.194	0.285
Gender combination	0.889	0.623	1.269	0.519
Donor relationship to recipient	1.129	0.749	1.702	0.562
Donor ABO status	1.047	0.722	1.519	0.809
ABO compatibility	1.201	0.737	1.955	0.462
Graft type	0.967	0.522	1.794	0.916
Recipient age group	1.186	0.857	1.640	0.303
Recipient age: ≥1 yr vs. <1 yr	1.186	0.446	3.153	0.732
Recipient sex: male vs. female	1.090	0.738	1.608	0.666
Original disease	1.151	1.067	1.243	0.000
UCD vs. others	0.230	0.054	0.976	0.046
Wilson's disease vs. others	0.133	0.018	0.980	0.048
Wilsonian fulminant vs. others	1.847	0.631	5.400	0.263
Primary hyperoxaluria vs. others	4.561	1.566	13.282	0.005
Transplant era	0.599	0.403	0.889	0.011
Multivariate analysis (stepwise forward selection method)				
Original disease	1.179	1.089	1.276	<0.001
UCD vs. others	–	–	–	0.664
Wilson's disease vs. others	–	–	–	0.108
Primary hyperoxaluria vs. others	–	–	–	0.142
Transplant era	0.594	0.409	0.863	0.006

UCD, urea cycle deficiency.

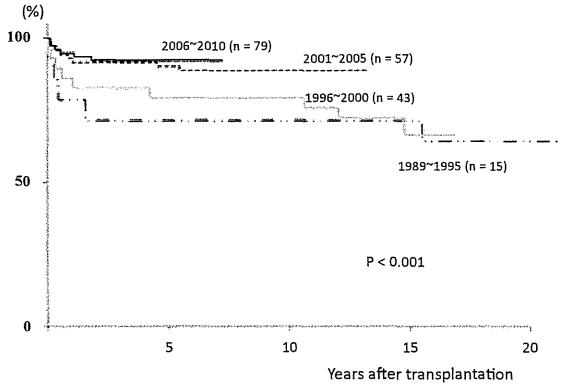

Fig. 4. Patient survival according to the transplant era.

family history. The indication for LT was chronic liver failure in 42 patients (71.1%), including the fulminant form in 17 patients. Fifty patients received medical treatment (D-penicillamine, trientine, zinc sulfate, ammonium tetrathiomolybdate) prior to LDLT. The mean transplantation score was 17.7 ± 3.2. Retransplantation was indicated in a total of four patients due to chronic rejection in three cases and graft failure secondary to portal vein thrombosis in one case. Four patients showed tacrolimus-related seizure, which were successfully treated with cyclosporine conversion therapy. The one-, five-, 10-, and 15-yr patient and graft survival rates were 98.4%, 96.6%, 94.7% 77.5%, and 96.6%, 94.7%, 90.1%, 62.9%, respectively. There were six patient mortalities: *Pneumocystis* Pneumonia in one case, recurrent hepatitis C (a paternal graft with HCV-RNA +ve) in one case, de novo autoimmune hepatitis in one case, hypoxic ischemic encephalopathy in one case, and sepsis in two cases.

Fifty-one patients underwent LDLT for urea cycle deficiency (OTCD in 40 patients, CPS1D in nine patients, and ASS in two patients). The median age at LDLT was 3.8 ± 4.6 (0.2–16) yr. There were significant differences in age and body weight at LDLT between the patients with OTCD and patients with CPS1D (4.7 ± 7.8 and 0.8 ± 0.7 yr, 8.1 ± 2.9 vs. 4.7 ± 4.8 kg; $p < 0.001$), given that the patients with CPS1D exhibited a trend toward undergoing earlier LDLT than the patients with OTCD. The diagnosis was made according to a genetic analysis in 35 patients (68.6%). Seventeen patients (33.3%) demonstrated a relevant family history, including six patients with early death of a newborn(s) and 11 patients with a genetically proven heterozygote mother. Despite the administration of conventional medications with severe protein restriction, frequent hyperammonemia was observed in all patients. Four patients showed postoperative tacrolimus-related seizure. The mean transplantation score was 18.6 ± 3.0. The one-, five-, 10-, and 15-yr patient and graft survival rates were 96.1%, 96.1%, 96.1%, and 96.1%, respectively. Two patients died from hemophagocytic syndrome at three months and a traffic accident at four months after LDLT.

Twenty-nine patients received LDLT for organic acidemia (MMA in 20 patients and PA in nine patients) at a median age of 2.2 ± 2.8 (0.4–12) yr. Despite the administration of protein restriction (mean: 1.46 ± 0.81 g/kg/day) with medications (cobalamin, carnitine supplementation, and antibiotics to eradicate gut flora), recurrent metabolic decompensation was observed in all patients. The mean transplantation score was 18.6 ± 3.0. Two patients with PA had a family history of early death of a newborn. Four patients developed septic complications that resulted in mortality after LDLT. Post-transplant medications for the original liver disease were continued in all patients, with mild relief of protein restriction (mean; 1.72 ± 0.72 kcal/kg/day). Among the patients with MMA, four patients (20%) exhibited progressive renal insufficiency, and three patients (15%) demonstrated new onset of seizures following successful LDLT. None of the patients with PA developed cardiac insufficiency after LDLT. The one-, five-, and 10-yr patient and graft survival rates were 89.7%, 85.2%, and 85.2%, respectively.

LDLT for GSD was indicated in 15 patients, with a median age of 4.9 ± 4.3 (0.8–13) yr. The classification of GSD was type 1a in two patients, 1b in nine patients, and IV in four patients. The diagnosis was made based on a liver biopsy in five patients and a genetic analysis in 10 patients. The indication for LDLT was life-threatening hypoglycemia in 11 patients, chronic liver failure in three patients, and acute liver failure in two patients. There were six patient mortalities, five of which were due to septic complications after LDLT. Three of the five mortalities included patients with GSD type IV. The one-, five-, and 10-yr patient and graft survival rates were 80.0%, 66.7%, and 66.7%, respectively.

Nine patients received LDLT for PH1, with a mean age of 7.7 ± 6.2 (1–17) yr. Deficiency of alanine-glyoxylate aminotransferase of the liver was confirmed in all cases, and a genetic diagnosis was made in three cases. Three patients had a relevant family history. Five patients were on dialysis treatment at the time of LDLT, and four patients received sequential liver–kidney transplantation from a living donor(s). Three patients