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Liver transplantation in children using organs from young paediatric donors

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Summary

Nowadays, most paediatric liver transplant recipients receive a split or other technical variant graft from adult deceased or live donors, because of a lack of available age- and size matched paediatric donors. Few data are available, especially for liver grafts obtained from very young children (<6 years). We analysed all paediatric liver transplantations between 1989 and 2009. Recipients were divided into five groups (1–5) depending on donor age (<1, ≥1 to <6, ≥6 to <16, ≥16 to <45, ≥45 years). Overall, 413 paediatric liver transplantations from deceased donors were performed; 1- and 5-year graft survival rates were 75%, 80%, 78%, 81%, 74% and 75%, 64%, 70%, 67%, 46%, and 1- and 5-year patient survival rates were 88%, 91%, 90%, 89%, 78% and 88%, 84%, 84%, 83%, 63% for groups 1–5, respectively, without significant difference. Eight children received organs from donors younger than 1 year and 45 children received organs from donors between 1 and 6 years of age. Overall, vascular complications occurred in 13.2% of patients receiving organs from donors younger than 6 years. Analysis of our data revealed that the usage of liver grafts from donors younger than 6 years is a safe procedure. The outcome was comparable with grafts from older donors with excellent graft and patient survival, even for donors younger than 1 year.

Introduction

On the basis of advances in surgical technique, immunosuppressive therapy and general medical care, paediatric liver transplantation (LTX) has shown considerable improvements, with currently excellent results in graft and patient survival [1–4]. Therefore, transplantation is the therapy of choice in children with end stage liver disease and acute liver failure. Initially, only age- and size matched whole organs from paediatric donors could be used for LTX in children [5,6]. At that time, only a small number of suitable organs were available, and therefore the number of children on the waiting list and the mortality on the waiting list increased. The utilization of split-liver grafts from adult deceased [7,8] and living liver donors [9,10] has provided more organs for paediatric recipients, and thereby decreased the number of children on the waiting list. However, recent changes in organ allocation rules and the steady increase in organ shortage along with an increasing proportion of marginal donors have led to a lack of suitable organs for split LTX and a decreased number of organs available for children. On the other hand, with the technical developments of liver splitting, only little attention has been given to the topic of liver allografts obtained from deceased paediatric donors, disregarding a source of potentially high quality organs. The literature shows only few data concerning the usage of paediatric organs for children [11–13] or adults [14–16]. Especially for grafts obtained from young donors (<6 years) and babies, only single cases have been described.

The aim of our study was to analyse the outcome after paediatric LTX using organs from young infants as liver donors.

Patients and methods

Between June 1989 and July 2009, a total of 593 LTX in children were performed at the University Medical Centre Hamburg-Eppendorf. One hundred and eighty of these were living related LTXs and were excluded from the study. The remaining 413 transplantations in 335 infants were accomplished using liver allografts from deceased donors. These paediatric LTXs were divided into five groups depending on the age of the deceased donor.

Group 1: Donor age <1 year; Group 2: Donor age ≥1 to <6 years; Group 3: Donor age ≥6 to <16 years; Group 4: Donor age ≥16 to <45 years and Group 5: Donor age ≥45 years.

Recipient characteristics and diagnoses are given in Tables 1 and 2, donor characteristics are given in Table 3. The five groups were compared regarding recipient/donor characteristics and graft/patient survival. Special attention was given to postoperative complications, including vascular [especially hepatic artery thrombosis (HAT), portal vein stenosis and venous outflow problems] and biliary complications, in group 1 and 2 patients receiving an organ from a paediatric donor <6 years of age.

Transplantation technique

Whole liver transplantation

This procedure was performed analogous to adult orthotopic LTX, either using the classic technique with replacement of the inferior vena cava or using the piggy back technique with preservation of the recipient inferior vena cava. The donor portal vein was anastomosed end-to-end

Table 1. Recipient characteristics.

Patients (*n*) Donor age [years]	Group 1 *n* = 8 <1	Group 2 *n* = 45 ≥1 to <6	Group 3 *n* = 90 ≥6 to <16	Group 4 *n* = 223 ≥16 to <45	Group 5 *n* = 47 ≥45	Statistics
Age; median (range) [years]	1.6 (0.0–3.6)	1.3 (0.0–15.9)	5.3 (0.0–16.0)	3 (0.1–16.0)	2.2 (0.0–16.0)	Mann–Whitney *U*-test Group 1,4 *P* = 0.12 Group 2,4 *P* = 0.001
Weight; median (range) [kg]	8 (3–14)	7 (2–40)	16 (3–67)	12 (3–75) 1*	11 (3–75) 1*	Mann–Whitney *U*-test Group 1,4 *P* = 0.116 Group 2,4 *P* = 0.000
Height; median (range) [cm]	73 (50–83) 1*	65 (43–162) 12*	98 (44–173) 24*	84 (43–177) 30*	86 (51–175) 9*	Mann–Whitney *U*-test Group 1,4 *P* = 0.073 Group 2,4 *P* = 0.001
Graft weight; median (range) [g]	300 (157–327) 3*	450 (210–800) 26*	479 (150–1100) 34*	330 (190–1900) 38*	325 (190–960) 11*	Mann–Whitney *U*-test Group 1,4 *P* = 0.078 Group 2,4 *P* = 0.06
Graft-to-recipient weight ratio median (range) [%]	3.8 (1.9–6) 3*	5.5 (1.1–7.5) 26*	3.5 (1.3–9.3) 34*	3 (0.9–12) 38*	3.3 (1.1–9.2) 11*	Kruskal–Wallis test *P* = 0.239
Gender (male/female)	5/3	24/21	48/42	120/103	29/18	χ^2-test *P* = 0.862
Whole/reduced/split liver transplantation	8/0/0	30/15/0	38/19/33	16/28/179	6/5/36	χ^2-test Group 1,4 *P* = 0.000 Group 2,4 *P* = 0.000
High urgent liver transplantation; *n* (%)	2 (25)	8 (18)	15 (17)	71 (32)	23 (49)	χ^2-test Group 1,4 *P* = 0.683 Group 2,4 *P* = 0.059
Primary LTX (%)	7 (88)	37 (82)	72 (80)	163 (73)	34 (72)	χ^2-test *P* = 0.453
Re-LTX; *n* (%)						
First		6 (13)	15 (17)	47 (21)	9 (19)	
Second	1 (13)	2 (4)	2 (2)	12 (5)	4 (9)	
Third			1 (1)	1 (0)		
Combined liver-kidney transplantation; *n* (%)		3 (7)	2 (2)	7 (3)	2 (4)	χ^2-test *P* = 0.686

LTX, liver transplantation.
*Lost data.

Table 2. Recipient diagnoses.

Patients (*n*)	Group 1 *n* = 8	Group 2 *n* = 45	Group 3 *n* = 90	Group 4 *n* = 223	Group 5 *n* = 47
Donor age [years]	<1	≥1 to <6	≥6 to <16	≥16 to <45	≥45
Cholestatic liver disease (%)	5 (63)	26 (58)	47 (52)	107 (48)	19 (40)
Metabolic disease (%)	1 (13)	4 (9)	9 (10)	32 (14)	6 (13)
Alagille syndrome (%)		2 (4)	6 (7)	17 (8)	2 (4)
Fulminant hepatic failure (%)	2 (25)	6 (13)	7 (8)	22 (10)	10 (2)
Liver tumour (%)			2 (2)	2 (1)	
Other (%)		7 (16)	19 (21)	43 (19)	10 (21)

No significant difference in the distribution of diagnoses among the five groups (χ^2-test 0.632).

Table 3. Donor characteristics.

Patients (*n*)	Group 1 *n* = 8	Group 2 *n* = 45	Group 3 *n* = 90	Group 4 *n* = 223	Group 5 *n* = 47	
Donor age [years]	<1	≥1 to <6	≥6 to <16	≥16 to <45	≥45	Statistics
Age; median (range) [years]	0.7 (0–0.9)	2.9 (1–5.7)	9.8 (6–15.9)	27.8 (16–44.9)	50 (45.2–67.8)	
Weight; median (range) [kg]	9 (5–10)	14 (8–30)	30 (11–80)	75 (40–110)	70 (47–90)	Mann–Whitney *U*-test Group 1,4 *P* = 0.000 Group 2,4 *P* = 0.000
Height; median (range) [cm]	77 (62–90)	96 (70–127) 1*	140 (106–190) 1*	175 (145–195)	170 (158–198)	Mann–Whitney *U*-test Group 1,4 *P* = 0.000 Group 2,4 *P* = 0.000
Gender (male/female)	5/3	24/21	65/25	139/84	25/22	χ^2-test *P* = 0.137
Cause of death (%)						
Trauma	2 (25)	19 (42)	44 (49)	103 (46)	9 (19)	χ^2-test
Cerebral bleeding	1 (13)	2 (4)	16 (18)	76 (34)	29 (62)	*P* = 0.000
Other	5 (63)	24 (53)	30 (33)	44 (20)	9 (19)	
Cold ischaemic time; mean ± standard deviation [min]	528 ± 109	599 ± 160 4*	610 ± 141 3*	588 ± 163 3*	534 ± 159 1*	One-way ANOVA-test *P* = 0.072
Creatinine; median (range) [mg/dl]	0.4 (0.1–0.9) 2*	0.4 (0.2–1.1) 20*	0.7 (0.3–2.4) 27*	0.8 (0.1–5.3) 24*	0.8 (0.4–1.9) 6*	Mann–Whitney *U*-test Group 1,4 *P* = 0.004 Group 2,4 *P* = 0.000
Bilirubin total; median (range) [mg/dl]	0.7 (0.2–0.9) 4*	0.4 (0–2.4) 21*	0.6 (0–3) 29*	0.7 (0–4.1) 30*	0.6 (0–2) 6*	Mann–Whitney *U*-test Group 1,4 *P* = 0.572 Group 2,4 *P* = 0.002
Alanine aminotransferase (ASAT); median (range) [U/l]	118 (5–215) 2*	37 (6–414) 23*	49 (9–471) 27*	35 (4–493) 27*	17 (5–231) 12*	Mann–Whitney *U*-test Group 1,4 *P* = 0.017 Group 2,4 *P* = 0.393
Aspartate aminotransferase (ALAT); median (range) [U/l]	54 (10–584 2*	48 (6–242) 24*	25 (2–368) 25*	25 (3–546) 30*	14 (3–175) 10*	Mann–Whitney *U*-test Group 1,4 *P* = 0.068 Group 2,4 *P* = 0.009

*Lost data.

to the recipient portal vein with a running suture, followed by porto-venous reperfusion. Reconstruction of the hepatic artery depended on size and anatomy. Anastomoses were performed in an end-to-end fashion by interrupted sutures using magnifying loops, without the use of interposition grafts. The bile duct was anastomosed end-to-end, or in case of underlying biliary disease or small size donor bile duct as hepatojejunostomy with a Roux-en-Y jejunal limb using interrupted sutures in both instances. Absorbable Polydioxanone suture material was utilized for all anastomoses.

Reduced-size liver transplantation

Reduction of the whole liver was performed on the back table depending on graft and recipient size. The central vascular and biliary structures remained untouched.

Implantation of the reduced graft was performed similar to whole organ transplantation.

Split liver transplantation

Selection criteria for donors suitable for liver splitting were analogous to the criteria defined by Broering *et al.* [17]. Only haemodynamically stable deceased donors under the age of 55 years and an intensive care stay under 5 days and good liver quality (fatty degeneration of the liver <30%, aspartate aminotransferase <60 U/l, gamma-glutamyl transpeptidase <50 U/l, sodium <160 mM) were used. Splitting of liver allografts was performed *in-situ* or *ex-situ*, following whole liver procurement. The transsection line, mostly dividing the whole organ into a left lateral graft (segments II and III) for a child and a right extended graft (segments I and IV to VIII) for an adult, was identical for both *in-situ* and *ex-situ* splitting. In selected cases, full left (segments I to IV) and full right (segments V to VIII) grafts were used.

Disposition of the main arterial trunk (common hepatic artery and coeliac axis) was variable and principally remained with the part of the split liver assigned to the primary recipient. The left lateral graft was implanted by performing an end-to-side anastomosis between the donor left hepatic vein and the preserved recipient inferior vena cava. In detail, the opening of the recipient right hepatic vein was closed during hepatectomy, the common trunk of the middle and left hepatic vein was connected and the orifice was enlarged by cutting the anterior face of the vena cava. Portal vein anastomosis was performed between the left portal vein of the left lateral graft and the recipient portal vein bifurcation. Arterial reconstruction depended on the remaining structures of the split graft and was performed analogous to techniques described above. Biliary reconstruction was performed as an end-to-side hepato-jejunostomy in all transplantations using left lateral grafts. In case of large-for-size liver grafts or elevated intra-abdominal pressure, a widening synthetic patch was used for abdominal closure. Definitive abdominal closure was achieved by stepwise reduction of the widening patch in one or more operative revisions.

Monitoring of the paediatric ICU directly after transplantation included clinical examination and blood tests, at least twice daily. To optimize liver allograft blood flow, haemoglobin levels were adjusted between 7 and 10 g/dl and unfractionated heparin was administered with a partial thromboplastin time target of 40–50 s. Patency of vascular anastomoses was verified intraoperatively, as well as postoperative days, 1 to 7, using duplex-sonography performed by a single radiologist.

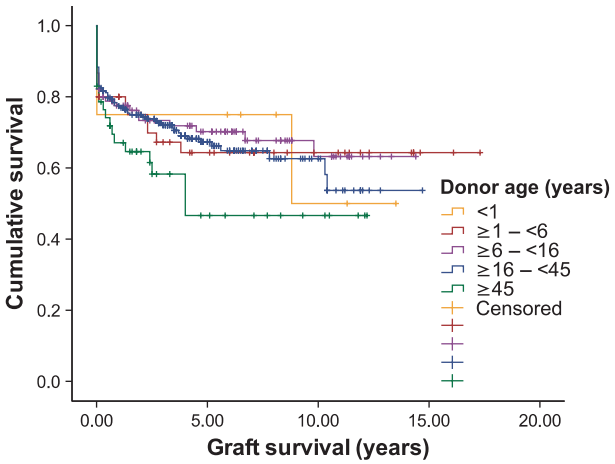
Statistics: The distribution of continuous data was analysed by Kolmogorov–Smirnov-test. In case of normal distribution, data were expressed as mean/standard deviation and differences between continuous data were analysed using one way ANOVA (>2 groups) and *t*-test (2 groups), respectively. Otherwise, data were expressed as median/range and analysed using Kruskal–Wallis test (>2 groups) or Mann–Whitney *U*-test (2 groups). Categorical variables were illustrated as number/percentage. Differences between categorical variables were evaluated using chi-square test. All data were analysed regarding differences among the five groups. In case of a significant difference among these groups, group 1 and group 2 were tested against group 4 patients (standard donors) separately. Graft and patient survival were assessed using Kaplan–Meier survival curves and Log Rank test. All statistics were performed using the SPSS 18.0 software (IBM, München, Germany). Significance levels were set at a *P*-value of ≤0.05.

Results

Recipient characteristics

All recipients were divided into groups according to donor age; group 1 (donor age <1 year) $n = 8$, group 2 (donor age ≥1 to <6 years) $n = 45$, group 3 (donor age ≥6 to <16 years) $n = 90$, group 4 (donor age ≥16 to <45 years) $n = 223$, group 5 (donor age ≥45 years) $n = 47$. Overall, 53 children received organs from donors younger than 6 years of age. Distribution and development of donor age over time is illustrated in Fig. 1. The median follow-up of all patients was 57 months (range: 2–202 months). As a result of the classification of the patients based on donor age, there were significantly lower values for recipient age, weight and height in group 2 and a trend towards lower values in group 1, compared with group 4 (defined as standard donors). Irrespective of these differences, the graft-to-recipient weight ratio was comparable among the five groups. In consequence of the small organs in group 1 and 2, the ratio of whole organ transplantation versus reduced and split LTX was significantly higher in these groups compared with standard group 4.

In group 1 (donor age <1 year), all organs were transplanted as whole liver grafts into recipients with a median age of 1.6 years (range: 0–3.6 years). The donor age in group 2 was defined from ≥1 to <6 years with a median of 2.9 years; by contrast, the median recipient age was lower, with a median of 1.3 years and a range of 0–15.9 years. That is, in this group most organs were transplanted into younger children, with two-thirds (30/45) of the children in group 2 being younger than 2 years of age. However, three whole organs from young paediatric donors (1, 2.3 and 5.7 years, respectively) were transplanted in older children (10.1, 11.4 and 15.9 years,



	Time point (years)																				
Patients at risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Group 1	8	6	6	6	6	6	5	4	4	2	2	2	1	1	0	0	0	0	0	0	0
Group 2	45	34	30	25	22	20	18	16	14	12	11	10	7	6	6	2	2	1	0	0	0
Group 3	90	62	52	49	48	41	34	26	23	15	14	9	5	2	1	0	0	0	0	0	0
Group 4	223	163	142	114	90	63	48	35	27	21	16	9	4	1	1	0	0	0	0	0	0
Group 5	47	28	22	16	15	11	9	9	7	6	5	3	2	0	0	0	0	0	0	0	0

Figure 1 Graft survival depending on donor age. The figure shows the Kaplan–Meier graft survival curves for the five groups. Statistical analysis by Log Rank test showed no significant difference in the graft survival between the groups.

respectively) with excellent results. All three children were alive with well-functioning graft at last follow-up (0.6, 38.5 and 32.3 months, respectively). Whole organ (30/45 = 67%) versus reduced organ (15/45 = 33%) LTX dominated in group 2.

The main diagnoses for LTX were cholestatic liver disease in all groups followed by metabolic disease. No significant difference in the distribution of diagnoses was detectable between the groups. In addition, we analysed total bilirubin concentration and international normalized ratio (INR) as marker of liver function and the status of the patient, preoperative. The mean bilirubin concentration was 8.4 mg/dl, 14.9 mg/dl, 11.9 mg/dl, 10.6 mg/dl and 13.3 mg/dl for groups 1–5, respectively, without a significant difference ($P = 0.761$). Likewise, we found no statistically significant difference ($P = 0.794$) in the INR between the five groups (mean INR 1.4, 1.4, 1.2, 1.4, 1.3, for groups 1–5, respectively). With regard to other characteristics possibly affecting recipient outcome, like gender, ratio elective to high urgent LTX, ratio primary to re-LTX and ratio single LTX to combined liver and kidney transplantation, groups 1 and 2 were comparable with standard donors (group 4).

Recipient characteristics are given in Tables 1 and 2.

Donor characteristics

As a result of the classification of the donors by age, there were also significant lower values of donor weight and height in groups 1 and 2, compared with group 4 containing standard donors. Donor characteristics and causes of donor death are shown in Table 3. Trauma was the leading cause of death in donors aged between 6 years and 45 years (groups 3 and 4), whereas in older donors (age >45 years, group 5) intracerebral bleeding represented the main cause of death. Special regard was given to donors younger than 6 years. Although trauma represented the most common single cause of death ($n = 21$) in these donors, the majority of causes of death were classified as ''other'' ($n = 29$) which is in contrast to the conditions encountered in donors older than 6 years. Thus, a variety of diagnoses in donors younger than 6 years was observed, including hypoxia ($n = 12$, thereof four patients because of drowning), infection (meningitis $n = 3$, myocarditis $n = 1$) and intracerebral bleeding ($n = 3$). The remaining 13 patients died because of aspiration ($n = 1$), hydrocephalus ($n = 1$), sudden infant death ($n = 1$) or other multifactorial disorders or unknown reasons ($n = 10$). Analysis of donor laboratory serum chemistry results revealed significantly lower creatinine levels in paediatric donors (groups 1 and 2) and also significantly lower total bilirubin levels (group 2), compared with standard donors (group 4). By contrast, alanine aminotransferase and aspartate aminotransferase showed higher values in groups 1 and 2 compared with group 4. Unfortunately, laboratory values of the donors were not available for all children; the exact number of missing data per parameter and group is included in Table 1. Therefore, the significance of the statistical analysis for these parameters is reduced.

No significant difference (One-way ANOVA $P = 0.072$) between the five groups was observed for the mean cold ischaemic time (528, 599, 610, 588, 534 min for groups 1–5, respectively).

The median warm ischaemic time was comparable (Kruskal–Wallis test $P = 0.271$) among the five groups; group 1: 32 min (24–55 min), group 2: 40 min (20–65 min), group 3: 40 min (17–95 min), group 4: 38 min (14–76 min), group 5: 44 min (20–72 min).

Graft and patient survival

For groups 1–5, the 1-year graft survival rates were 75%, 80%, 78%, 81%, 74%, the 5-year graft survival rates were 75%, 64%, 70%, 67%, 46% and the 10-year graft survival rates were 50%, 64%, 63%, 62%, 46%, respectively. Statistical analysis by Log Rank test revealed no significant difference between the graft survival rates in the different groups.

Patient survival rates were 88%, 91%, 90%, 89%, 78% after 1 year, 88%, 84%, 84%, 83%, 63% after 5 years and 88%, 80%, 84%, 81%, 63% after 10 years for groups 1–5, respectively. Moreover, statistical analysis by Log Rank test revealed no significant difference between the patient survival in the different groups, but there was a trend to a reduced patient survival in group 5 for children receiving organs from donors older than 45 years.

Kaplan–Meier survival plots are given in Figs 1 and 2.

Patient outcome using organs from donors younger than 6 years

Special regard was given to the postoperative course and complications in patients receiving organs from donors younger than 6 years (groups 1 and 2).

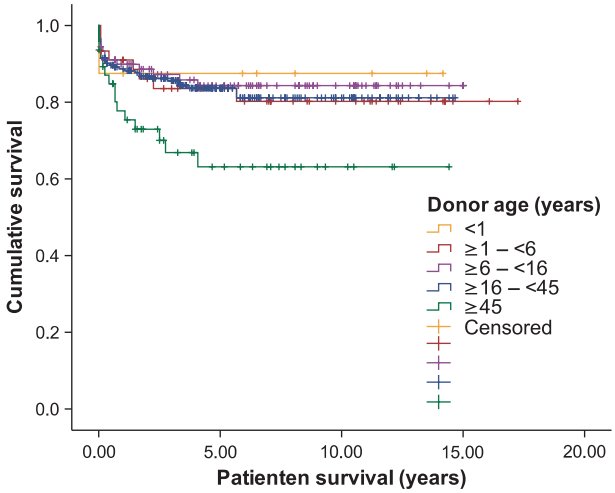
Intraoperative course

The mean warm ischaemic time was 37 ± 13 min in group 1 and 40 ± 13 min in group 2, respectively. A 3-year-old girl in group 1, who was undergoing fourth LTX, died during reperfusion because of cardiac failure. All other children in groups 1 and 2 overcame surgery without severe complications.

Vascular complications

One patient in group 1 (12.5%) suffered from a hepatic artery thrombosis (HAT) diagnosed at the first postoperative day on routine ultrasound examination. The patient underwent immediate operative revision of the hepatic artery, which was unsuccessful. Re-LTX was performed at the fourth postoperative day. Three patients in group 2 (6.7%) developed HAT on the 2nd, 6th and 8th postoperative day. In two patients, immediate operative revision of the hepatic artery was successful; one patient needed re-transplantation 2 days after ineffective operative revision.

Two patients in group 1 (25%) developed portal vein thrombosis after transplantation. One patient was treated



	Time point (years)																					
Patients at risk	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Group 1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	0	0
Group 2	45	39	35	32	30	27	24	22	19	16	15	13	9	7	6	2	2	1	0	0	0
Group 3	90	74	67	61	58	49	42	33	32	23	21	14	9	4	3	2	0	0	0	0	0
Group 4	223	185	170	150	115	85	62	48	41	35	28	18	12	7	3	0	0	0	0	0	0
Group 5	47	33	26	21	18	16	14	12	9	7	5	3	3	1	1	0	0	0	0	0	0

Figure 2 Patient survival depending on donor age. The figure shows the Kaplan–Meier patient survival curves for the five groups. Statistical analysis by Log Rank test showed no significant difference in the patient survival between the groups.

with interventional angioplasty and one patient underwent operative revision, both with a successful outcome.

One patient in group 2 (2.2%) showed hepatic vein stenosis accompanied by reduced outflow, 6 weeks after LTX. Radiological intervention was performed twice with eventual successful outcome.

Biliary complications

In both groups, no early bile duct complications occurred. Only one patient in group 1 (12.5%) developed bile duct stenosis 8 months after LTX and was treated successfully by two operative bile duct revisions with re-procedure of the biliodigestive anastomosis.

Early postoperative course (first 3 months after LTX)

In group 1, one patient died during reperfusion and another child underwent re-LTX for HAT; hence, 3-month patient survival was 87.5% (7/8) and graft survival 75% (6/8) for children receiving organs from donors younger than 1 year of age. In group 2, the 3-month patient survival was 93% (42/45). Among the three children who died, two suffered from multi-organ failure of unknown origin and one child died from pulmonary embolism. The 3-month graft survival rate in group 2 was 80% (36/45); causes for graft loss were primary non-function ($n = 4$), HAT ($n = 1$), acute rejection ($n = 1$) and other unclear reasons ($n = 3$).

Discussion

In our study, recipients of organs from young paediatric donors showed favourable results with a low rate of vascular complications and an excellent graft and patient survival. This positive outcome was not necessarily to be expected in view of the few studies published about the outcome of paediatric LTX depending on donor age. In two studies, young donor age was found to be a risk factor for HAT [11,18]. In another study, a diameter of the hepatic artery of <3 mm was shown to be a risk factor for HAT [19]. Tanaka *et al.* [20] described 69 LTX in children using paediatric liver grafts (age ≤15 years, median age 8 years). In this study, 1-year graft survival rates were 68–84% (depending on the type of graft) with an 11.5% incidence of HAT, which is within the range described in the literature for paediatric LTX using grafts from adult donors. One publication described 16 paediatric LTX recipients receiving liver grafts from neonatal donors with an age of 28 days or less. As a result of the small number of cases, no significant conclusion was possible when compared with recipients who received grafts from older donors. However, there was a trend towards a lower graft and patient survival, a higher rate of HAT and re-transplantation, and a prolonged time to functional recovery after transplantation of these grafts from extremely young donors [13].

As a result of the aggravation of organ shortage in adults, today paediatric liver grafts are also directed to adult recipients. Studies analysing the outcome of paediatric liver grafts in adults showed a reduced graft survival and an elevated risk for hepatic artery complications [12,14,16]. On the other hand, because of the expected size mismatch and the likelihood of a small-for-size situation when paediatric liver grafts are used for adult recipients, these results might not be generally applicable to paediatric recipients. McDiarmid postulated that the use of liver grafts from paediatric donors will be beneficial for paediatric recipients, but unfavourable for adult recipients. Therefore, she concluded that, based on the United Network for Organ Sharing (UNOS) data, paediatric liver grafts should be allocated to paediatric recipients [12].

This analysis, for the first time, assessed the outcome of paediatric LTX with special regard to donor age analysed in a large group of over 400 children.

Recipients of organs from donors younger than 6 years were significantly (group 2) or by trend (group 1) younger, lighter and smaller, compared with recipients in the standard donor group 4. Although in group 1 recipient and donor age were almost comparable (median 1.6 vs. 0.7 years), in group 2 the age of the recipients showed a trend to lower values (median 1.3 years) compared with the donors (median 2.9 years). As a result of the unbalanced distribution of age in children with end stage liver disease with a maximum in the first year and another maximum during adolescence, there are few recipients in the same age like the donors in group 2. Hence, in the majority of cases the organs from the donors between 2 and 6 years were transplanted into younger children, possibly based on expected risks of immature organs and the size mismatch for adolescent children. Nevertheless, three whole liver grafts from young paediatric donors (1, 2.3 and 5.7 years, respectively) were transplanted into considerably older children (10.1, 11.4 and 15.9 years, respectively) with excellent results. Although graft-to-recipient weight ratio showed no significant difference between group 1/2 and group 4, the range of graft-to-recipient weight ratio within the groups was high (group 1: 2–6%, group 2: 1–8%) implying a high variability in tolerated liver volume. Likewise, analysis of the liver volume in our paediatric donors younger than 6 years of age revealed a high variance in the real liver size relative to body weight (2.1–5.0%). In our study population, the minimum transplanted liver volume was 1% of body weight; however, maximum liver volume (regarding all groups) was more than 10-fold higher, with 12%. This means except for minimal liver volume, avoiding small-for-size syndrome, no stringent graft to recipient ratio has to be applied. In

case of oversized liver grafts for small children, we used temporarily mesh grafts for initial abdominal wall closure, to avoid elevated intra-abdominal pressure and vascular compromise. In all these cases, the mesh graft size could be reduced step-by-step until definitive abdominal closure was achieved.

As a consequence of the small donor organs in group 1 and 2, all liver grafts in group 1 and 67% of liver grafts in group 2 were transplanted as whole organs, whereas in group 4, 80% of the transplantations were split LTX. However, as shown in Table 1, there was a relevant rate of missing data for recipient height, graft weight and graft-to-recipient weight ratio varying from 10% to 40%. Therefore, a reduced statistical significance of the above statement has to be postulated.

Other factors possibly influencing the outcome, like recipient gender, high urgency versus elective recipient status, preoperative total bilirubin concentration, preoperative INR, primary LTX versus re-LTX, combined liver-kidney transplantation versus LTX alone were comparable between group 1/2 and group 4. Likewise, distribution of recipient diagnoses showed no significant difference among the five groups.

In adult donors, the dominating causes of donor death were cerebral bleeding and trauma. By contrast, in paediatric donors, besides trauma the main causes of death consisted of a variety of miscellaneous diagnoses like hypoxia, infection and infrequent other reasons. Median creatinine levels in paediatric donors (groups 1 and 2) were significantly lower than those in standard adult donors (group 4). Most likely, this finding is attributed to lower standard values of serum creatinine in children than in adults without any clinically relevant differences in renal function between the groups. Transaminases showed higher levels in donors in groups 1 and 2, compared with group 4. It might be postulated that the willingness to accept elevated liver values is greater in case of young donors with presumed high quality organs in contrast to organs from adult donors. In summary, we could not identify any difference in donor characteristics that would predict a different outcome in the recipients. As mentioned earlier, donor laboratory values showed a high rate of missing data, for which reason the evidence is reduced.

The incidence of HAT in paediatric LTX varies from 8% to 26% [11,18,19,21]. In our series, HAT were seen in 12.5% in children receiving organs from donors younger than 1 year and 6.7% in children receiving organs from donors between 1 year and younger than 6 years. Therefore, we did not find an apparent increase in HAT when using very young paediatric donors for LTX in children. Portal vein thrombosis has been described in 4–9% of paediatric LTX recipients [22–25], a range that might increase up to 20% in living related liver donation [26,27]. Two cases of portal vein stenosis were observed in group 1 (donors <1 year), resulting in an incidence of 25% (2/8 patients). In group 2 (donors ≥1 to <6 years), no child developed portal vein complications. Altogether, the risk of portal vein thrombosis in our study was 3.8% (2/53 patients) for paediatric recipients receiving organs from donors younger than 6 years. We therefore conclude that the use of organs even from very young donors will not imply an increased risk of portal vein stenosis.

Hepatic vein stenosis occurred in one patient (2.2%) in group 2, whereas no outflow complications were seen in group 1. Overall, vascular complications of any kind using liver grafts from donors under 6 years were present in only 13.2% (7/53 patients) of our paediatric recipients. Compared with the literature results reporting up to 31% vascular complications after paediatric LTX [28–31], the rate of vascular complications in our recipients transplanted with organs from very young donors was low.

The majority of children receive technical variant (split or reduced size) liver grafts to match graft and recipient size. Publication of single centre series report a comparable complication rate for the transplantation of technical variant and whole organ grafts in children and adults [8,32] with similar short-term [6] and long-term [33] outcomes. Registry data, however, suggest slightly inferior results including an increased risk for graft loss and postoperative complications, e.g. biliary complications and portal vein thrombosis for reduced and split LTX compared with whole organ transplantation in children [34,35]. The potentially higher complication rate and inferior outcome using technical variant grafts support the use of paediatric donors allowing whole organ LTX in paediatric recipients with compatible graft and recipient size.

Authorship

UH: collected and analysed the data, wrote the paper. RG: analysed the data. AB-R and KH: collected the data. BN: study design. LF: study design, wrote the paper.

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