Outcomes of Liver Transplantation in Small Infants

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Liver transplantation (LT) for small infants remains challenging because of the demands related to graft selection, surgical technique, and perioperative management. The aim of this study was to evaluate the short-term and longterm outcomes of LT regarding vascular/biliary complications, renal function, growth, and patient/graft survival in infants ≤3 months compared with those of an age between >3 and 6 months at a single transplant center. A total of 64 infants ≤6 months underwent LT and were divided into 2 groups according to age at LT: those of age ≤3 months (range, 6-118 days; XS group, n = 37) and those of age >3 to ≤6 months (range, 124-179 days; S group, n = 27) between 1989 and 2014. Acute liver failure was the main indication for LT in the XS group (n = 31, 84%) versus S (n = 7, 26%). The overall incidence of hepatic artery thrombosis and portal vein thrombosis/stricture were 5.4% and 10.8% in the XS group and 7.4% and 11.1% in the S group, respectively (not significant). The overall incidence of biliary stricture and leakage were 5.4% and 2.7% in the XS group and 3.7% and 3.7% in the S group, respectively (not significant). There was no significant difference between the 2 groups in terms of renal function. No significant difference was found between the 2 groups for each year after LT in terms of height and weight *z* score. The 1-, 5-, and 10-year patient survival rates were 70.3%, 70.3%, and 70.3% in the XS group compared with 92.6%, 88.9%, and 88.9% in the S group, respectively (not significant). In conclusion, LT for smaller infants has acceptable outcomes despite the challenges of surgical technique, including vascular reconstruction and graft preparation, and perioperative management.

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Liver transplantation (LT) is an established treatment for young children with acute liver failure (ALF) and end-stage liver disease. Patient survival has improved with evolving medical management and surgical techniques. Refinements in various surgical techniques, such as liver reduction, living donor liver transplantation (LDLT), and split-liver transplantation, have expanded LT for small infants. However, LT for small infants remains challenging because of technical difficulties related to the size discrepancy between the donor and recipient. Additionally, specific disease states in small infants can have a detrimental impact on their posttransplant course.

In the literature, it has been reported that small infants have acceptable short-term outcomes after LT.[1,2] To date, only a few groups have reported the outcomes following LT for infants <3 months of age. Many of these studies have been limited by small sample size, multicenter data, or short follow-up.[3-8] The aim of this study was to evaluate the short-term and longterm outcomes of LT in small infants ≤6 months at a single transplant center.

Abbreviations: ACR, acute cellular rejection; ALF, acute liver failure; BW, body weight; CLD, chronic liver disease; CR, chronic rejection; DBD, donation after brain death; DCD, donation after circulatory death; D-D, duct-to-duct; DDLT, deceased donor liver transplantation; GRWR, graft-to-recipient weight ratio; HAT, hepatic artery thrombosis; HVS, hepatic venous stenosis; ICU, intensive care unit; IV, intravenous; LDLT, living donor liver transplantation; LL, left lobe; LLS, left lateral section; LMWH, low-molecular-weight heparin; LT, liver transplantation; MOF, multiorgan failure; NA, not available; NCCHD, National Center for Child Health and Development; PTC, percutaneous transhepatic cholangiography; PTLD, posttransplant lymphoproliferative disorder; PV, portal vein; PVS, portal vein stenosis; PVT, portal vein thrombosis; RL, right lobe; R-Y, Roux-en-Y; S, small; TVLT, technical variant liver transplantation; US, ultrasound; XS, extra-small.

Patients and Methods

STUDY COHORT

A prospectively maintained LT database was used to identify pediatric patients (<18 years of age) who underwent LT between October 1989 to December 2014 at a single institution. Out of 1163 pediatric LT

patients, 64 recipients ≤6 months of age were identified and formed the study cohort. Variables related to the recipient, donor, surgery, and outcome (graft/recipient survival) were extracted from the LT database and supplemented by a review of clinical records where needed. The study was performed with institutional ethical approval and within the remit of the ethical guidelines of the Declaration of Helsinki (2008).

CLINICAL PRACTICE

The surgical procedure in recipients and donor organ retrieval has been described previously.[9,10] In brief, the implantation technique was the standard piggyback technique for the inferior vena cava using a triangulation method (continuous for the inferior limbs and interrupted for the superior limbs). Portal vein (PV) anastomosis was performed with the end-to-end technique (continuous for the posterior wall and interrupted for the anterior wall), and hepatic arterial reconstruction was performed with the recipient common hepatic artery in the majority of the patients. Biliary drainage was achieved with Roux-en-Y (R-Y) hepaticojejunostomy, except for duct-to-duct (D-D) anastomosis in 1 patient. Anastomoses (arterial/biliary) were performed using surgical loupes (×4.5), and at other points during surgery, ×2.5 loupes were used. Abdominal closure was either primary closure (skin/muscle) or delayed closure with the use of a temporary silastic mesh (30020R-S; Invotec International, Jacksonville, FL) that was sutured to the muscle sheath, the latter typically used in large-for-size grafts.

Immunosuppression was tacrolimus and prednisolone from 1996 onward and triple therapy with cyclosporine, azathioprine, and prednisolone before then. Episodes of acute cellular rejection (ACR) were treated by pulsing with a 3-day course of intravenous (IV) methylprednisolone therapy (1 mg/kg).[11] The standard longterm immunosuppression strategy was one of immunosuppression minimization and reduction in response to Epstein-Barr virus viremia in addition to the growth of the infant assisting in the reduction of the immunosuppression levels. Prophylactic low-molecular-weight heparin (LMWH) was used postoperatively until the period of needing liver biopsy or surgical re-exploration had passed to facilitate the management of bleeding complications if encountered. LMWH was then converted to aspirin, which was continued for 3 months after LT. Standard antibiotic prophylaxis was Tazocin (90 mg/kg) with antifungals according to clinical risk. Cytomegalovirus prophylaxis was IV ganciclovir (5 mg/kg) started at day 7 after transplant and converted to oral treatment for 4 weeks when the patient was ready for discharge.

STUDY DESIGN

The study cohort (n = 64) was divided into 2 groups based on the age at transplant. The XS group consisted of 37 infants ≤3 months old, and the S group consisted of 27 infants >3 to ≤6 months old. Vascular/biliary complications, ACR, chronic rejection (CR), renal function, posttransplant growth, and survival (graft/recipient) in both groups were analyzed.

DEFINITION OF VASCULAR AND BILIARY COMPLICATIONS

Vascular complications (hepatic artery thrombosis [HAT], portal vein thrombosis [PVT], and hepatic vein stenosis) were initially identified on Doppler ultrasound (US) and further characterized by computed tomography. The present routine clinical practice is to perform US on days 1 and 5 after transplant or in response to a rise in aspartate transaminase or to a clinical concern.

Bile strictures were suspected based on persistent unexplained cholestasis in the graft, leading to initial screening US to detect biliary dilation and confirm

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vascular patency. Subsequent magnetic resonance cholangiopancreatography was used for anatomical definition and to guide in the need for percutaneous transhepatic cholangiography (PTC) and dilation. In this study, any abnormality that needed intervention (radiologically/surgically) was counted as a biliary stricture. Bile leakage was defined as biliary fluid in the abdominal drain or if a significant peritoneal fluid collection was drained (radiologically/surgically) and confirmed to be bile.

STATISTICAL ANALYSIS

The Kruskal-Wallis test was applied respectively for paired and unpaired multiple comparisons. The Mann-Whitney U test was applied respectively for paired and unpaired comparisons between the 2 groups. The correlation of the categorical data and numerical data was evaluated using the chi-square test and Spearman's test, respectively. Cumulative survival rates were calculated by using the Kaplan-Meier method, and differences between curves were evaluated by using the log-rank test. A *P* value <0.05 was recognized as significant. All statistical analyses were performed using the statistical software program SPSS, version 18 (IBM, Armonk, NY).

Results

RECIPIENT AND DONOR CHARACTERISTICS

Recipient characteristics of the 2 groups are summarized in Table 1. In the XS group, most of the infants underwent LT in the first month or less of life (n = 26, 70.3%). The median weight was 3.4 kg in the XS group and 5.8 kg in the S group ($P < 0.01$), and the percentage of recipients with a body weight (BW) <3 kg was 29.7% in the XS group. ALF was the main indication for LT in the XS group (n = 31, 84%) compared with the S group (n = 7, 26%; $P < 0.01$). The leading cause of ALF was hemochromatosis in the XS group and cryptogenic hepatitis in the S group. Of the XS group, 11 (30%) were in the intensive care unit (ICU) at time of transplant compared with 11% in the S group ($P < 0.05$).

In terms of the graft factors, pediatric donors were more often used in the XS group, and ABO-incompatibility was more common (24%; Table 2). Typically, grafts from <3-month-old donors are no longer used because the early experience was associated with a high rate of HAT. However, if in extremis and no other timely graft options are available, then these grafts are still to be considered. Otherwise, there were no significant differences in donor type, graft type, and graft-to-recipient weight ratio (GRWR) between the 2 groups. However, the rate of hyperreduced grafts in the XS group was higher than in the S group (60% versus 26%; $P < 0.05$). With regard to transplant operative factors (Table 3), there were no significant differences in techniques used for vascular reconstruction (hepatic vein, PV, and hepatic artery) and R-Y was the main type of biliary reconstruction in both groups. However, delayed abdominal closure was more commonly used in the XS group ($P < 0.01$).

TABLE 1. Clinical Characteristics of Recipients in the XS (≤3 months) and S (>3 to ≤6 Months) Groups

	XS (n = 37)	S (n = 27)	*P* Value
Age, days	37 (6-118)	164 (125-179)	<0.01
Sex			0.86
Male	17	13	
Female	20	14	
BW, kg	3.4 (1.7-7.0)	5.8 (3.8-9.0)	<0.01
Original disease			<0.01
Hemochromatosis	20 (54)	0 (0)	
Cryptogenic hepatitis	7 (19)	6 (22)	
Biliary atresia	2 (5)	16 (59)	
Others	8 (22)	5 (19)	
ALF	31 (84)	7 (26)	<0.01
CLD	6 (16)	20 (74)	<0.01
Pretransplant status			
ICU	11 (30)	3 (11)	<0.05
Hospital	25 (67)	19 (70)	<0.05
Home	1 (3)	5 (19)	<0.05

NOTE: Data are given as median (range) or n (%). As the percentage is 100, the decimal point was adjusted.

INCIDENCE OF COMPLICATIONS AND RECIPIENT SURVIVAL

Table 4 summarizes the surgical, immunological, and infectious complications that occurred after LT. In terms of complications, there were no significant differences between the XS and S groups. HAT was observed in 2 (5.4%) patients in the XS group and in 2 (7.4%) in the S group. For the 2 patients in the XS group who developed HAT at 2 and 8 days after transplant, 1 was a retransplantation, and the 1 patient with combined HAT and PVT died while waiting for a suitable graft. All transplants were reduced left lobes

TABLE 2. Clinical Characteristics of Donors in the XS (≤3 Months) and S (>3 to ≤6 Months) Groups

	XS (n = 37)	S (n = 27)	*P* Value
Age, years	7 (0.4-26)	20 (1-47)	<0.01
Sex			0.45
Male	20	12	
Female	17	15	
BW, kg	26 (6.0-76.0)	60.0 (5.0-85.0)	<0.01
ABO-incompatibility	9 (24)	1 (4)	<0.05
Donor type			
DBD	35 (94)	21 (78)	0.09
DCD	1 (3)	1 (4)	0.09
LDLT	1 (3)	5 (18)	0.09
Graft type			0.21
LLS	22 (60)	17 (63)	
LL	10 (27)	4 (15)	
RL	0 (0)	4 (15)	
Whole	3 (8)	2 (7)	
Subsegment	2 (5)	0 (0)	
Partition			
Reduced	22 (60)	7 (26)	<0.05
Split	12 (32)	18 (67)	<0.05
None	3 (8)	2 (7)	<0.05
GRWR, %	4.27 (2.4-6.60)	4.35 (2.8-5.7)	0.75

NOTE: Data are given as median (range) or n (%). As the percentage is 100, the decimal point was adjusted.

(LLs) in the XS group, and in no patient was an aortic conduit used. In the S group, HAT developed at 3 and 13 days after transplant: 1 patient was managed by thrombectomy, and the other was managed conservatively. All were reduced LLs except for 1 whole graft that was used in the S group.

PVT occurred in 4 (10.8%) of the XS group and 3 (11.1%) of the S group. In the XS group, 2 patients had PVT in the first month after transplant and the remaining 2 presented later at 2 and 12 years. Although in the S group, the 3 patients who developed PVT presented at 2 days, 4 months, and 8 years after transplant. These 3 patients (2 in the XS group and 1 in the S group) with late PVT at >1 year after transplant were managed with a shunt surgery (Rex shunt in 2 patients and mesocaval shunt in 1 patient). Similarly, there was no difference in the incidence of biliary complications between the 2 groups. Immunologically, there was also no difference in the occurrence of ACR or CR between groups. Up to this point in time, 1 patient in the S group has developed posttransplant lymphoproliferative disorder (PTLD), and developmental delay was documented in 1 patient from the XS group.

TABLE 3. Surgery-Related Variables in the XS (≤3 Months) and S (>3 to ≤6 Months) Groups

	XS (n = 37)	S (n = 27)	*P* Value
Hepatic vein			0.37
Piggyback	37 (100)	27 (100)	
PV			0.37
End-to-end	37 (100)	27 (100)	
Conduit			
Yes	0 (0)	0 (0)	
No	37 (100)	27 (100)	
Hepatic artery			0.37
End-to-end	37 (100)	27 (100)	
Conduit			
Yes	13 (35)	6 (22)	
No	24 (65)	21 (78)	
Bile duct			0.58
R-Y	36 (97)	27 (100)	
D-D	1 (3)	0 (0)	
Abdominal closure			<0.01
Primary	2 (5)	21 (78)	
Delayed	35 (95)	6 (22)	

NOTE: Data are given as n (%).

TABLE 4. Clinical Outcomes in the XS (≤3 Months) and S (>3 to ≤6 Months) Groups

	XS (n = 37)	S (n = 27)	*P* Value
Surgical complications			
HAT	2 (5.4)	2 (7.4)	0.57
PVT	4 (10.8)	3 (11.1)	0.50
HVS	0 (0.0)	0 (0.0)	—
Biliary stricture	2 (5.4)	1 (3.7)	0.62
Biliary leak	1 (2.7)	1 (3.7)	0.62
Immunological complications			
ACR	3 (8.1)	7 (25.9)	0.06
CR	0 (0.0)	1 (3.7)	0.42
Infectious complications			
PTLD	0 (0.0)	1 (3.7)	0.42

NOTE: Data are given as n (%).

The cumulative patient survival rates are shown in Fig. 1. The 1-, 5-, and 10-year patient survival rates were 70.3%, 70.3%, and 70.3% in the XS group and 92.6%, 88.9%, and 88.9% in the S group, respectively (log-rank $P = 0.074$). The causes of death were sepsis (n = 3), multiorgan failure (MOF; n = 3), combined PVT/HAT (n = 1), pulmonary hemorrhage (n = 1), and others (n = 3) in the XS group and MOF (n = 2) and acute respiratory distress syndrome (n = 1) in the S group.

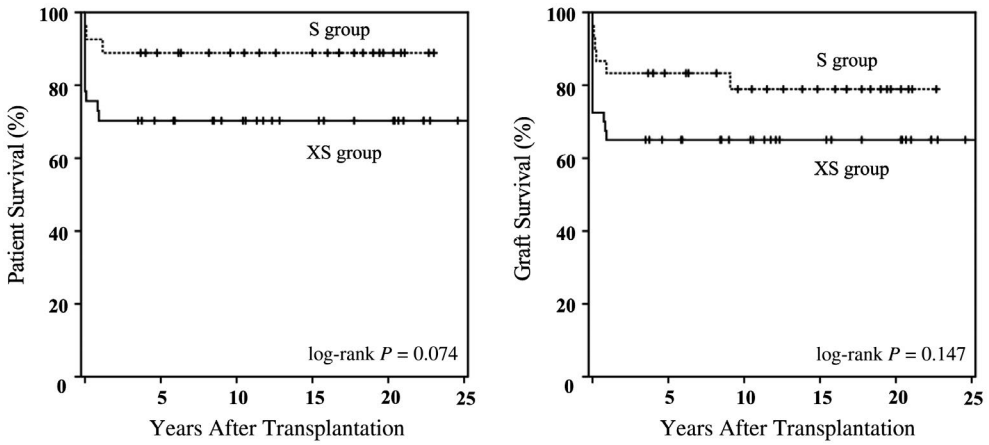

FIG. 1. Cumulative patient and graft survival rates following LT.

The 1-, 5-, and 10-year graft survival rates were 65.0%, 65.0%, and 65.0% in the XS group and 83.3%, 83.3%, and 78.9% in the S group, respectively (log-rank $P = 0.147$). The indications for retransplantation (n = 3) in the XS group were early HAT, CR (9 months after transplant), and cholangiopathy (12 months after transplant). In the S group, 3 patients were retransplanted for primary nonfunction (4 days after transplant), CR (3 months after transplant), and PVT (12 months after transplant).

RENAL FUNCTION

Figure 2 displays the median change in the serum creatinine levels in the 2 groups. Median serum creatinine levels in the XS and S groups before transplantation were 44 μmol/L (range, 16-182 μmol/L) and 46 μmol/L (range, 6-85 μmol/L), respectively. Median serum creatinine in the XS and S groups 10 years after transplant were 50 μmol/L (range, 42-70 μmol/L) and 52 μmol/L (range, 41-79 μmol/L), respectively. There were no significant differences in terms of renal function between the 2 groups. No child needed renal replacement therapy at the time of transplantation.

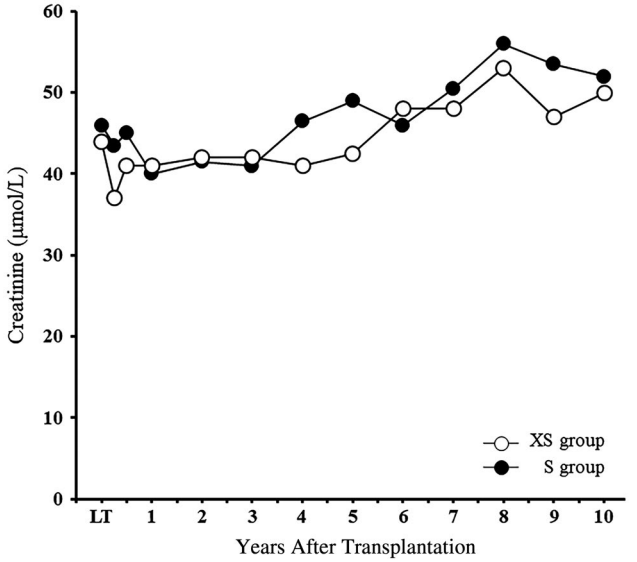

FIG. 2. Changes of serum creatinine after LT. Open circles represent levels for the XS group (≤3 months), and filled circles represent levels for the S group (>3 to ≤6 months).

CATCH-UP GROWTH

Figure 3A shows the growth curve in BW *z* score after transplantation between the 2 groups. Children in both groups had growth impairment at the time of LT: median BW *z* score in the XS group was –1.92 (–4.41 to 4.20) and–1.91 (–3.78 to 1.41) in the S group. Overall, 51% of the XS group and 41% of the S group had a BW *z* score of <–2.00. Median BW *z* scores 10 years after transplant in the XS and S groups were 0.176 (–1.36 to 1.84) and –0.203 (–1.14 to 2.40), respectively. There were no significant differences in BW *z* score between the 2 groups during the follow-up period. Figure 3B shows the growth curve in height *z* score after transplantation. Median height *z* scores at the time of transplantation in the XS and S groups were –1.16 (range, –4.59 to

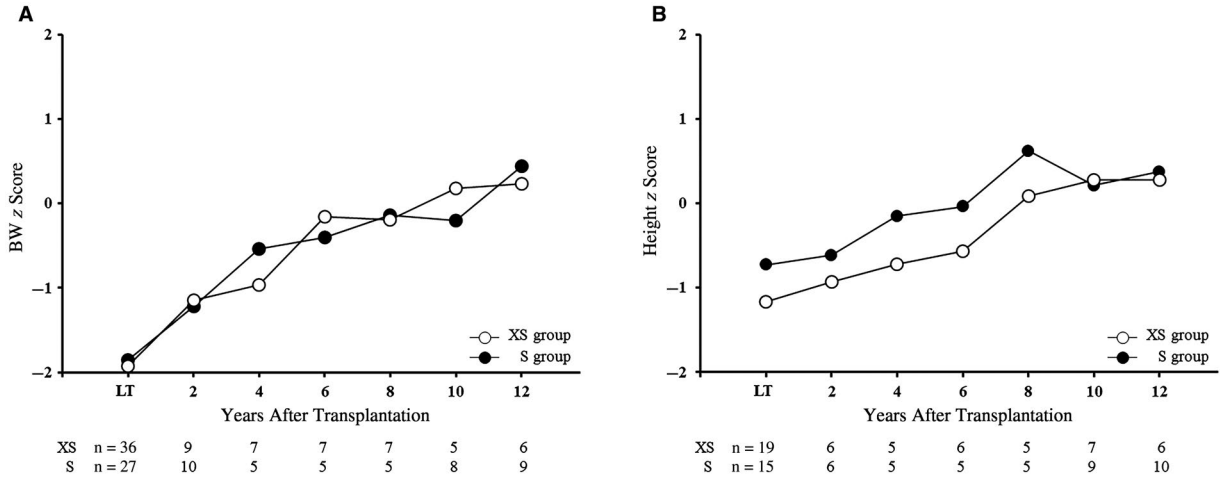

FIG. 3. Changes of BW *z* score and height *z* score after LT: (A) BW *z* score and (B) height *z* score. Open circles represent levels for the XS group (≤3 months), and filled circles represent levels for the S group (>3 to ≤6 months).

3.71) and –0.73 (range, –2.47 to 2.35), respectively. Median height *z* scores 10 years after transplant in the XS and S groups were 0.28 (–1.00 to 1.87) and 0.21 (–2.00 to 1.52), respectively, with no significant difference between the 2 groups again being demonstrated during follow-up period.

Discussion

This study describes the short-term and longterm outcomes of LT in infants 3 months old or younger in a single institution. Other centers have reported variable survival rates between 60% and 90.9% in small infants ≤3 months.[3-5] Many of these earlier studies showed that patient survival in the recipients <3 months of age was poorer and, thereby, contributed to the etiology of liver disease being different to that of older infants.[7,8] However, other studies and present work have refuted this observation.[4,5] Table 5 summarizes the published literature and present series on LT in small infants ≤3 months old.

In the present study, the longterm outcomes of small infants ≤3 months of age at the time of LT was similar to those of infants >3 to ≤6 months of age, and on surviving the first year after transplant reaching adulthood. In our series, the main causes of early death in small infants were sepsis and MOF. Immaturity of the immune system in small infants is a recognized problem and makes the child vulnerable to systemic infection.[12] Also, desferrioxamine given in the management of neonatal hemochromatosis can have an immunosuppressive effect. Therefore, perioperative management, especially control of infection, is a crucial element in the success of LT in this age group.

The main indication for LT in small infants (≤3 months) is ALF secondary to neonatal hemochromatosis.[3,5-8] In the present series, this indication accounted for half of the patients in the XS group. ALF in smaller infants is difficult to recognize and diagnose, and encephalopathy is a late and often devastating complication. The mortality of ALF in small infants without LT has been reported to range from 24% to 47.5%,[13,14] and the rate is significantly higher than the 10.5% seen in older children with ALF managed without LT.[13] However, as the present data shows, if neonatal hemochromatosis is referred promptly, there can be a good outcome.

On a technical level, the major concern for LT in small infants is a shortage of size-matched donors, which contributes to the increased wait-list mortality reported in this age group.[15] This has led to the development of the technical graft variants of reduced,[16,17] split,[10,16,18] living donor,[16,19] partial graft, and hyper-reduced[20] to expand the potential pool of donors. The introduction of technical variant liver transplantation (TVLT) has reduced both the time on the waiting list and wait-list mortality.[21] However, the survival advantages of TVLT over whole-liver transplantation have not been consistently demonstrated in the literature.[22]

TABLE 5. Published and Present Series Experience of LT in Small Infants ≤3 Months Old

Program	Number of Centers	Year	Number of Patients	BW (kg) (Number <3 kg)	Donor Type		Vascular Complications (%)	Biliary Complications (%)	Survival Rates (%)	
					DDLT	LDLT			Patient	Graft
University of Chicago*	3	1998	23	Mean, 3.8 (NA)	19	4	14.0	NA	60	60
University of Colorado†	39	2008	38	Mean, 3.9 (NA)	34	4	HAT 5.3/PVT 10.5	21.1	87.8	76.1
NCCHD, Tokyo‡	1	2017	12	Median, 4.0 (2)	0	12	0	Stricture 16.7/leak 0	90.9	90.9
King's College Hospital§	1	2019	37	Median, 3.4 (11)	36	1	HAT 5.4/PVT 10.8	Stricture 5.4/leak 2.7	70.3	65

*Woodle et al.[3] (1998).
†Sundaram et al.[4] (2008).
‡Kasahara et al.[5] (2017).
§Present study.

In contrast, superior graft survival of living donor partial grafts compared with deceased donor partial and whole grafts has been more consistently demonstrated in the literature.[23] In the present study, most small infants in the XS group received a partial liver graft that included reduced-sized (60%), split (32%), living donor (3%) graft, and whole graft (8%). Although the left lateral section (LLS) is used in TVLT for the pediatric population, this graft may be too large for small infants. Large-for-size grafts can be problematic with microcirculatory hypoperfusion due to a combination of low portal blood flow and external compression by the small size of the abdominal cavity.[24] One option to overcome large-for-size grafts is further reduction of the LLS. When deciding whether reduction of the graft is necessary or not, the relationship between the shape (thickness and length), volume, conformation of the graft, and the size of the abdominal cavity has to be taken into consideration. With some centers, using a GRWR >4.0% combined with a ratio of graft thickness and abdominal depth can be a guide to when reduction should be undertaken.[25,26] In such infants, monosegment LT appears to be a satisfactory option with both deceased[2] and living donor grafts.[26] Previous reports on monosegments have described the use of a nonanatomically reduced LLS graft that consists of mainly segment 3 or an anatomically reduced LLS graft of segment 2.[26,27] Another option to prevent large-for-size grafts is delayed abdominal closure using a silastic mesh or skin closure.[26,28] In our series, 95% of the XS group had delayed abdominal closure to avoid the risk of abdominal compartment syndrome and graft compression with no adverse effect on graft/patient survival.[28]

The use of ABO-incompatible grafts is another way to increase graft options for small infants. In the present study, ABO-incompatible graft usage in the XS group was higher than in the S group and was more often used in the context of ALF for infants in both the XS and S groups with good outcomes, and no desensitization manipulations were used. Both pediatric and adult ABO-incompatible LT survival has improved markedly and has become comparable to ABO-compatible LT on the introduction of rituximab prophylaxis before LT.[29,30] However, infants are able to accept ABO-incompatible grafts without desensitization therapy because the immune system is still developing,[30] which can be verified by confirming low levels of anti-A and anti-B antibody titers (<1/8).

The multidisciplinary approach in the management of small infants with ALF continues to contribute to

the improvement in outcomes, with medical care in intensive care aiming to prevent or treat major complications of ALF (ie, encephalopathy, brain edema, bleeding, infections, and MOF). The availability of continuous venovenous hemodiafiltration for small infants is reported by some centers as the standard procedure for brain protection and liver support in ALF,[31] thereby providing a window for the native liver to recover or as a bridge to LT.

Vascular complications are a major concern in LT for small infants and can lead to graft loss, with the small size of vessels driving technical challenges.[22,32,33] The incidence of early HAT is significantly higher in pediatrics (8.3%; range, 1.0%-20.2%) compared with adults (2.9%; range, 0.0%-6.8%)[34] with the reported incidence of HAT ranging from 0.0% to 9.5% in small infants.[3-6] Similarly, in the present study, the incidence of HAT was 5.4% with no difference between the XS group and S group. Traditionally, retransplantation has been the first choice of therapy for early HAT in pediatrics (61.9%) compared with adults (50%).[34] However, revascularization is being increasingly used in pediatrics with reported success rates ranging from 10.5% to 25%[33,35] with retransplantation in reserve, if unsuccessful.[35] In the present series, revascularization was used successfully for graft salvage in 1 patient from the S group.

The incidence of early and late portal vein stenosis (PVS)/PVT reported after pediatric LT in the literature range from 2.7%-23.3% to 4.5%-7.4%, respectively,[27,33,36-39] with the incidence of PVT in small infants ranging from 0.0% to 10.5%.[3-5] Data from the present study are similar with an incidence of PVT at 10.8% overall (5.4% in early PVT and 5.4% in late PVT). In previous reports, risk factors associated with PV complications include young age, BW <6 kg, high hematocrit level, PV hypoplasia, and technical problems.[36,39,40] Technical problems with PV reconstruction in small infants are related to the increased tension on the anastomosis due to the short length between the recipient and donor PV, size discrepancy, small caliber vessels, and the use of an interposition vein graft.[36,38,40] Interventional radiology (balloon angioplasty, stent replacement) is used to treat, and recanalization with stent placement is limited to cases that need repeat balloon dilatation for PVS recurrence.[36,38,40] Access for PV angioplasty and stent placement is typically via a percutaneous transhepatic approach,[40] but a percutaneous transsplenic[41] or transileocolic approach by minilaparotomy[42] has been described.

Additionally, the feasibility of the intraoperative segment 4 PV stump stenting approach has been reported.[43] The reported success rate of interventional radiology for PV complications range from 60.7% to 100%.[37,38,42] However, when stent placement for PVS/PVT in small infants is needed, a potential problem that arises as the child grows is that a stented PV may not be able to adjust to size, and more longterm follow-up data is needed to confirm safety. An alternative way to re-establish PV flow after LT is by a meso-Rex shunt, with the use of the left internal jugular vein as a graft being reported to have 100% patency in the long term.[44] In the present series, a meso-Rex shunt with a deceased iliac vein was performed in 2 late PVTs in the XS group and both remain patent on follow-up.

The incidence of biliary stricture after pediatric LT ranges from 4.5% to 14.9%[4-6,45,46] and from 8.9% to 16.7% in smaller infants,[5,6,46] which is comparable to the incidence of 5.4% reported in the present series. Similarly, reported biliary leak ranges from 0% to 21.4% in pediatric LT,[5,45,46] and in our study, the incidence of biliary leak in smaller infants was 2.7%. Some studies have suggested that the incidence of biliary complications in smaller infants is similar to that of older children.[4,5] However, other groups have reported a higher incidence of biliary strictures in infants <3 months old.[5] In our series, however, there was no significant difference between the XS and S groups.

When the renal function of smaller infants was evaluated in our study, we could not observe a major difference between the XS and S groups throughout the posttransplant course, with stabilization of renal function observed in the longterm follow-up, which is consistent with other reports.[47,48] Many studies have demonstrated that growth is improved after LT[49,50] with early catch-up height and weight being observed during the first 2 years after transplant.[50] In our study, patients in both the XS and S groups had good catch-up growth following LT. However, catch-up growth in the XS group when the indications for LT was ALF was slower. Supporting this observation, other groups have reported that children with biliary atresia had less growth impairment compared with those with metabolic disease or ALF.[49]

Two limitations associated with our study deserve further comment: the retrospective nature of the study and the small sample size. As a result, the power of the study is reduced, and there is a lack of statistical significance in patient and graft survival. Although

this work does describe one of the largest cohorts with the longest follow-up from a single center, further prospective and multicenter studies would help clarify the longterm outcome of LT in smaller infants.

In conclusion, LT for smaller infants has acceptable and improving outcomes despite the challenges of a surgical technique that encompasses both vascular reconstruction and graft preparation as well as perioperative management. Additionally, the judicious use of graft variants to deal with size mismatch between the recipient and graft has been a key to improving outcomes in LT for small infants.

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