Pediatric Transplantation

WILEY

ORIGINAL ARTICLE

Failure to Rescue Pediatric Recipients of Living Donor Liver Transplantation: A Single-Center Study of Technical Complications in 500 Primary Grafts

Aniss Channaoui[1] | Catherine de Magnée[1] | Roberto Tambucci[1] | Eliano Bonaccorsi-Riani[2] | Thierry Pirotte[3] | Natalia Magasich-Airola[3] | Thierry Detaille[4] | Laurent Houtekie[4] | Renaud Menten[5] | Dana Dumitriu[5] | Marguerite van den Hove[1] | Pamela Baldin[6] | Françoise Smets[7] | Isabelle Scheers[7] | Giulia Jannone[7] | Etienne Sokal[7] | Xavier Stephenne[7] | Raymond Reding[1]

[1]Pediatric Surgery and Transplant Unit, Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium | [2]Abdominal Transplant Unit, Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium | [3]Department of Anesthesiology, Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium | [4]Pediatric Intensive Care Unit, Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium | [5]Pediatric Radiology Unit, Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium | [6]Department of Pathology, Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium | [7]Division of Pediatric Gastroenterology and Hepatology, Cliniques Universitaires Saint-Luc, UCLouvain, Brussels, Belgium

Correspondence: Aniss Channaoui (aniss.channaoui@student.uclouvain.be)

Received: 8 August 2024 | **Revised:** 28 August 2024 | **Accepted:** 8 September 2024

Funding: The authors received no specific funding for this work.

Keywords: failure to rescue | immunological complication | living donor liver transplantation | pediatrics | technical complication

ABSTRACT

Background: The concept of failure to rescue (FTR) has been used to evaluate the quality of care in several surgical specialties but has not been well-studied after living donor liver transplantation (LDLT) in children.

Methods: This study retrospectively reviewed 500 pediatric LDLT performed at a single center between 1993 and 2022. The recipient outcomes were assessed by means of patient and graft survival rates, retransplantation rates, and arterial/portal/biliary complication rates. Graft and patient losses secondary to these complications were calculated regarding FTR for patients (FTRp) and grafts (FTRg).

Results: Overall 1- and 5-year patient survival rates were 94.5% and 92.1%, respectively, the corresponding figures for graft survival being 92.7% and 89.8%. One-year hepatic artery complication rate was 3.6% ($n = 18$ cases), the respective rates for portal vein complications and biliary complications being 5.7% ($n = 57$) and 15.6% ($n = 101$). One-year FTRp rates for hepatic artery thrombosis, portal vein thrombosis, anastomotic biliary stricture, and intrahepatic biliary stricture were 28.6%, 9.4%, 3.6%, and 0%, respectively. The corresponding FTRg rates being 21.4%, 6.3%, 0%, and 36.4%.

Conclusion: Such novel analytical method may offer valuable insights for optimizing quality of care in pediatric LDLT.

Abbreviations: ABS, anastomotic biliary stricture; AR, acute rejection; BA, biliary atresia; CDC, Clavien–Dindo classification; FTR, failure to rescue; FTRg, failure of graft rescue; FTRp, failure of patient rescue; HA, hepatic artery; HAT, hepatic artery thrombosis; IBS, intrahepatic biliary stricture; IS, immunosuppressive; IVC, inferior vena cava; LD, living donor; LT, liver transplantation; MOF, multiple organ failure; POD, postoperative day; PTLD, post-transplant lymphoproliferative disease; PV, portal vein; PVT, portal vein thrombosis.

Presented at the 79th French Congress of Pediatric Surgery (Poitiers, September 20–22, 2023), at the Belgian 2024 Transplantation Society Congress (Brussels, March 15, 2024), and by poster presentation at the 2023 European Society for Organ Transplantation Congress (Athens, September 17–20, 2023).

1 | Introduction

Pediatric liver transplantation (LT) has been established for more than 30 years as a valid therapy for children with acute or chronic liver failure [1, 2]. Our center in Brussels initiated a LT program in children in 1984, and the first living donor (LD) LT took place in 1993 [3, 4]. Since then, more than 500 LDLTs have been performed at Cliniques universitaires Saint-Luc, Brussels, Belgium, this program being one of the longest-running programs worldwide. Nowadays, pediatric LT still constitutes a complex, high-end procedure performed in a limited number of transplant centers [5]. In this specific field, the occurrence of postoperative complications is related to the special characteristics of this pediatric population including undernutrition status of the child, small recipient weight, and need for complex vascular reconstructions. In this context, inadequate management of post-transplant complications may be responsible for wide variations in post-transplantation outcomes across centers around the world [6–8]. The concept of "Failure to Rescue" (FTR) of a given postoperative complication was first described in 1992 by Silber et al. and refers to the death of a patient directly linked to a particular complication [9]. FTR has been proposed as a valid indicator of surgical quality in adult general surgery, but only limited data on its use in pediatric transplantation are available [10, 11]. For children, studies using FTR concept in general, neonatal, heart, or trauma surgery do exist, with one single study in 2016 having specifically addressed this concept in pediatric LT [7, 10, 12–15]. A North American registry study across 21 centers, including 2330, children focused on inter center variability of mortality and liver graft loss and suggested that FTR might be relevant as a quality improvement tool in the field of transplantation [7]. The present work aimed to evaluate the effectiveness of our high-volume, monocentric, pediatric LDLT program using FTR as a novel results/quality assessment tool. By focusing on the relationship between a specific postoperative complication and its impact on the child's outcomes (death or graft loss), we sought to identify areas for improvement in care.

2 | Patients and Methods

2.1 | Study Population

The electronic medical files of 792 consecutive recipients (less than 17 years old) who received a primary LT at Cliniques Universitaires Saint-Luc, Brussels, Belgium, between July 1993 (launch of our LDLT program in children) and June 2022 were retrospectively reviewed to analyze clinical, surgical, and histological data. Among these transplants, the 500 primary pediatric LDLTs were specifically considered for this study (238 boys and 262 girls; median age at LT: 1.9 years old; range: 0.1–16.5). During the same period, nine retransplantation cases using a LD graft performed at our center were excluded from the present analysis. Median post-LT follow-up of survivors was 7.9 years (range: 1.0–25.3). Data collected retrospectively included demographic data, surgical type of graft, preoperative diagnoses, ABO compatibility status, surgical techniques, occurrence of immunological complications (acute rejection: AR; chronic rejection), and technical complications (hepatic artery: HA, portal vein: PV, biliary tract). For HA, thrombosis and kinking were considered separately. Similarly for PV, both thrombosis and stenosis were recorded pathologic. Diagnoses were established using ultrasonographic (US) Doppler for both HA and PV complications. Definitive diagnosis of biliary complications (stricture or leakage) required cholangiographic assessment. Pretransplant diagnoses were biliary atresia (BA, $n = 321$: 64.2%), other cholestatic diseases ($n = 62$: 12.4%), metabolic disorders ($n = 41$: 8.2%), liver malignancies ($n = 44$: 8.8%), fulminant hepatitis ($n = 9$: 1.8%), and miscellaneous diagnoses in the remaining cases ($n = 23$: 4.6%). Detailed diagnoses are listed in Table 1. More than half of the recipients ($n = 327$: 65.4%) were under 2 years at the time of transplantation, as shown in Figure 1.

2.2 | Types of Donors

Between July 1993 and June 2022, a postmortem liver graft was primarily used in 292 children (36.9%) and a LD graft primarily in 500 children (63.1%). The proportion of LD grafts increased along the successive eras (1993–1997, 1998–2002, 2003–2007, 2008–2012, 2013–2017, and 2018–2022) as shown in Figure 2. Based on the Goldsmith and Woodburne classification, we defined "left lateral lobectomy" ($n = 439/500$; 87.8%) as the removal of Couinaud's segments II and III, and "left lobectomy" ($n = 61/500$; 12.2%) as the removal of segments II, III, and IV including the middle hepatic vein [16, 17]. According to the recipient's age below 1 year ($n = 197$), between 1 and 5 years ($n = 218$), and older than 5 years ($n = 85$), the respective proportions of left lateral lobe grafts were 98.5% ($n = 194/197$), 96.8% ($n = 211/218$), and 40.0% ($n = 34/85$).

2.3 | Type of Familial Donor

Among LD ($n = 500$; median age: 1.9 years; range: 0.1–16.5), donors were mothers in 225 cases, fathers in 209 cases, uncles/aunts in 45 cases, grandparents in 7 cases, cousins in 6 cases, sisters in 2 cases, and unrelated donors in 6 cases, one of them being a good Samaritan donor as previously described by our team [1]. Regarding ABO compatibility, donor to recipient pairs were ABO identical ($n = 369$, 73.8%), compatible ($n = 96$, 19.2%), or incompatible ($n = 35$, 7.0%) [18].

2.4 | Surgical Technique

The medical management and surgical techniques, as progressively optimized in LDLT at our center since 1993, were thoroughly described in previous publications from our team [1, 3, 19–21]. Most recently in 2021, Tambucci et al. described in detail our procurement and graft implantation procedure [22]. In brief: retro-hepatic inferior vena cava (IVC) was preserved during hepatectomy, except in 7.4% of children ($n = 37$), including 36 liver malignancies and one Budd–Chiari syndrome [23]. In the latter cases, en bloc hepatectomy was carried out that included the removal of retro-hepatic IVC and its replacement by the living donor's internal jugular vein (91.9%, $n = 34$), or an iliac vein graft from a cadaveric donor (8.1%, $n = 3$). Hepaticocaval anastomosis was performed using triangulated technique. Regarding portal revascularization, end-to-end anastomosis ($n = 309$, 61.8%) was performed between graft's left portal branch and recipient's portal trunk (or left PV, according to

TABLE 1 | Indications of transplantation in 500 primary pediatric living donor liver transplants performed at Cliniques universitaires Saint-Luc, Brussels, Belgium, between July 1993 and June 2022.

Preoperative diagnosis	Number of cases
Biliary atresia	*n* = 321; 64.2%
Other cholestatic diseases	*n* = 62; *12.4%*
• Alagille syndrome	*n* = 25
• Progressive familial intrahepatic cholestasis type 1	*n* = 12
• Progressive familial intrahepatic cholestasis type 2	*n* = 10
• Progressive familial intrahepatic cholestasis type 3	*n* = 6
• Primary sclerosing cholangitis	*n* = 5
• Caroli disease	*n* = 2
• Cirrhogen cholestasis of unknown origin	*n* = 2
Metabolic disorders	*n* = 41; 8.2%
• Crigler–Najjar syndrome	*n* = 7
• Tyrosinemia type 1	*n* = 7
• Glycogenosis type 1	*n* = 6
• Alpha-1 antitrypsin deficiency	*n* = 3
• Cystic fibrosis	*n* = 3
• Propionic acidemia	*n* = 3
• Homozygous familial hypercholesterolemia	*n* = 2
• Mitochondrial disease	*n* = 2
• Refsum disease	*n* = 2
• Zellweger syndrome	*n* = 2
• Hemochromatosis	*n* = 1
• Ornithine transcarbamylase deficiency	*n* = 1
• Oxaluria	*n* = 1
• Wilson disease	*n* = 1
Liver malignancies	*n* = 44; 8.8%
• Hepatoblastoma	*n* = 38
• Hepatocarcinoma	*n* = 3
• Epitheloid hemangioendothelioma	*n* = 1
• Hemangiosarcoma	*n* = 1
• Rhabdomyosarcoma	*n* = 1
Fulminant hepatitis	*n* = 9; 1.8%
• Unknown origin	*n* = 6
• Hepatitis A	*n* = 1
• Valproate hepatotoxicity	*n* = 1
• Recurrent infantile hepatitis	*n* = 1
Miscellaneous diagnoses	*n* = 23; 4.6%
• Cryptogenic cirrhosis	*n* = 9
• Budd–Chiari syndrome	*n* = 4
• Congenital hepatic fibrosis	*n* = 4
• Autoimmune	*n* = 2
• Graft-versus-host disease	*n* = 1
• Portal vein thrombosis and hepatocellular adenoma	*n* = 1
• Histiocytosis with hepatopulmonary syndrome	*n* = 1
• Short bowel syndrome with cirrhosis secondary to parenteral nutrition	*n* = 1

caliber congruency and length), except in cases of portal hypoplasia (defined as a PV diameter of 4 mm or less) [1, 22]. In this specific situation (*n* = 153, 30.6%), longitudinal portoplasty was constructed using a patch of donor's inferior mesenteric vein, as described by de Magnée et al. in 2011 [24]. Arterial anastomosis was performed as a single end-to-end anastomosis between graft's left HA and recipient's HA, using 3.0–6.0x magnifying spectacles and interrupted non-absorbable 8/0 sutures according to a semi-microsurgical "no touch" technique in all cases, except for one historical case performed under surgical microscope [1]. Eighty-nine LD grafts had two HA, whereas three HA were present in the remaining three cases. It was not necessary to suture all HA if satisfactory arterial backflow was observed after the reconstruction of the main artery [22, 25]. Among the former subgroup, only 15 children (16.9%; *n* = 15/89) had two anastomoses performed to revascularize the graft, whereas in the latter only one anastomosis of the main artery was performed in each case (*n* = 3). Biliary drainage was constructed using existing or de novo Roux-en-Y jejunal loop of 30–50 cm (*n* = 496) [26]. Biliary duct-to-duct anastomosis was done in three cases, and a duct-to-duodenum in the remaining specific situation of short bowel in one case. Immediate abdominal closure was performed in 450 children, whereas delayed closure using a mesh (or skin closure only) was used in 50 children [27].

2.5 | Immunosuppressive Protocols and Rejection Diagnosis

The immunosuppressive (IS) therapy varied along the years, as documented in details in our previous works [19, 28–30]. In brief, three main immunosuppressive eras were considered. Group 1 (*n* = 23) received triple drug therapy from 1993 until 1997, including cyclosporine (Neoral-Sandimmun; Novartis Pharma), steroids, and azathioprine (Imuran; Aspen); Group 2 (*n* = 96):

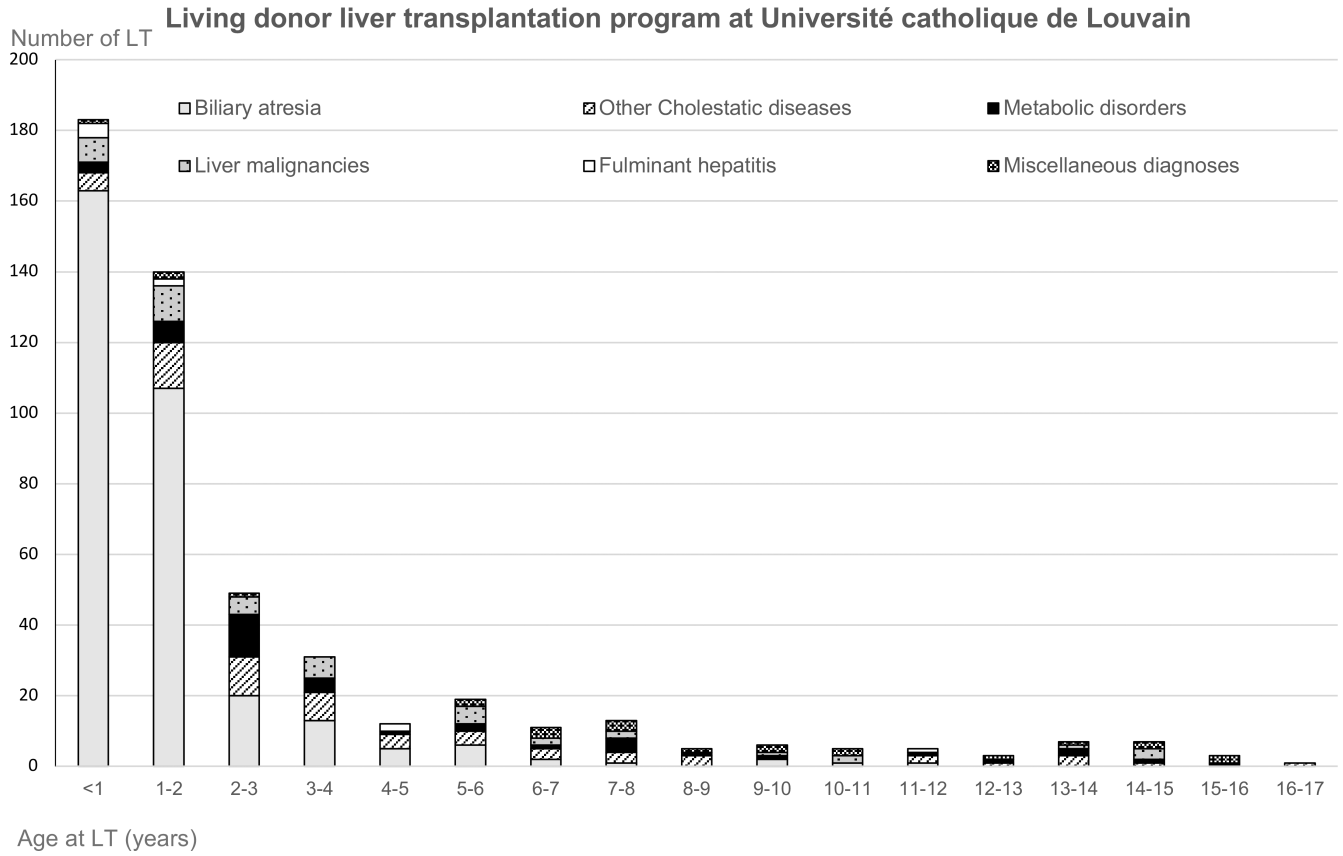

FIGURE 1 | Histogram describing the number of liver transplantations (LT) and respective preoperative diagnoses according to age at transplant in the series of 500 primary pediatric living donor LT at Cliniques universitaires Saint-Luc, Brussels, Belgium, between July 1993 and June 2022.

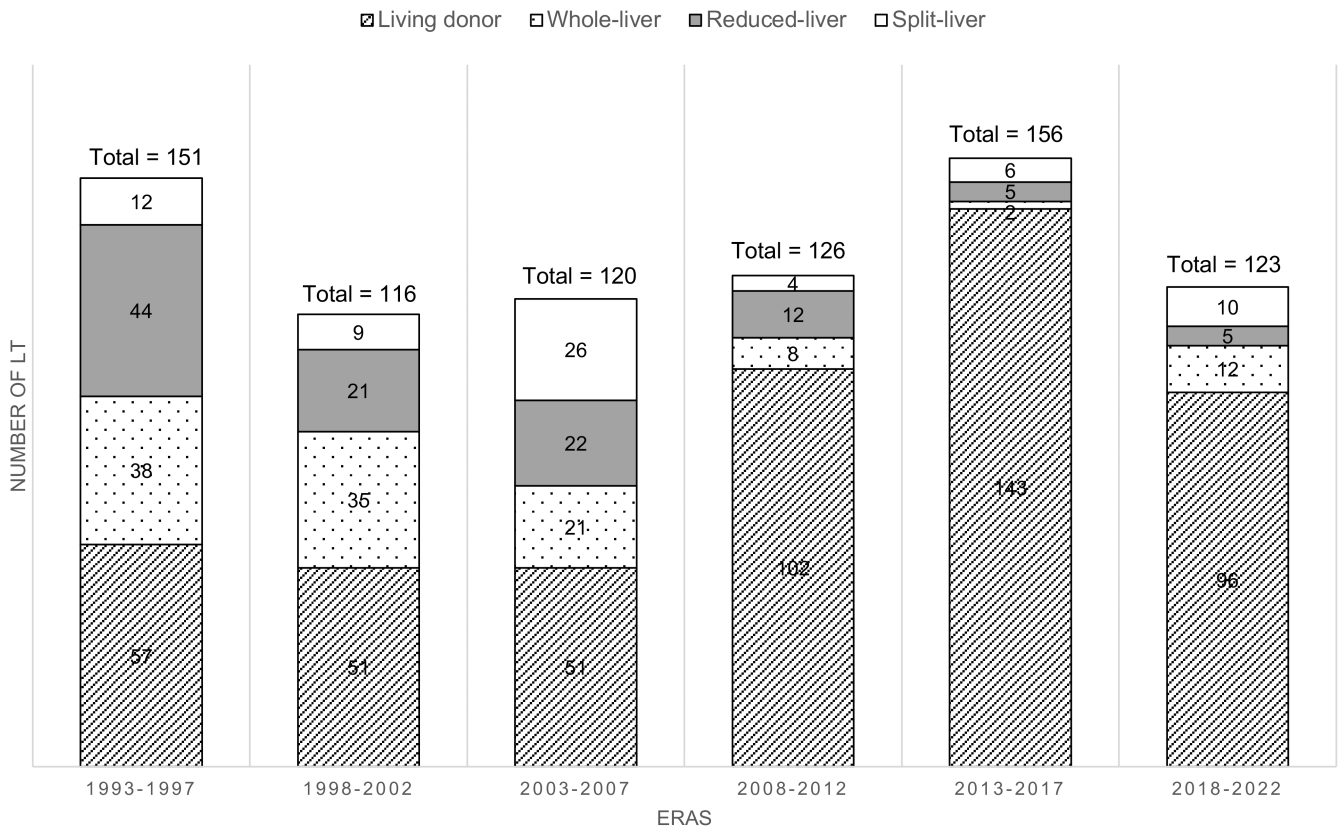

FIGURE 2 | Distribution of 792 pediatric liver transplantation (LT) performed at Cliniques universitaires Saint-Luc between July 1993 and June 2022, according to eras and liver graft technical alternatives.

tacrolimus (Prograft; Astellas) and steroids, between 1998 and 2001; Group 3 ($n=380$): steroid-free tacrolimus-based immunosuppression from 2001, including induction with anti-CD25 monoclonal antibody basiliximab (Simulect; Novartis Pharma). A last patient in our series of 500 LDLTs did not require any immunosuppressive therapy after LT because the child previously received a bone marrow transplant from the same LD prior LT [31]. AR was confirmed by hepatic biopsy according to Banff classification in case of elevated liver enzymes and/or cholestasis, and treated by intravenous methylprednisolone boluses [1, 32]. Chronic rejection was confirmed histologically, considering ductopenia and cholestasis at liver pathology [33]. AR-free survival was studied for each group, as well as the overall incidence of chronic rejection.

2.6 | Complication Rate and Failure to Rescue

Technical complications were analyzed by types (arterial, portal, biliary) and ranked according to Clavien–Dindo classification (CDC) [34]. Surgical complication rate was described using the following ratio:

$$\text{Complication rate} = \frac{\text{Number of patients with a given postoperative complication}}{\text{Number of patients undergoing a specific surgery}}$$

Based on the current literature and our experience, FTR rate was defined as the inability to prevent postoperative death (or graft lost) after at least one, specific, possibly curable, postoperative complication [8]. FTR were calculated at 6 months and 1 year post-complication using the following ratio, graft losses due to patient death being censored from FTRg [7, 9].

$$\text{FTRp} = \frac{\text{Number of deaths at 6 months (or 1 year) after one specific postoperative complication in transplant patients}}{\text{Total number of transplant patients who developed this postoperative complication}}$$

$$\text{FTRg} = \frac{\text{Number of lost grafts at 6 months (or 1 year) after one specific postoperative complication in transplant patients}}{\text{Total number of transplant patients who developed this postoperative complication}}$$

Specific FTRp and FTRg rates were calculated with respect to the most frequent postoperative arterial, portal, and biliary complications: hepatic artery thrombosis (HAT), portal vein thrombosis (PVT), and biliary stricture including anastomotic (ABS) or intrahepatic (IBS) stricture. In the setting of sequential postoperative complications, the FTR is calculated for the index complication (the first one).

2.7 | Statistical Methods

Categorical variables were expressed as absolute number and percentage, numeric variables as median and range. Survival analysis (patients, grafts, AR-free survival) were estimated using the Kaplan–Meier method and compared by the log-rank test, as appropriate. Technical complication rate and FTR rate were also expressed as percentage. A value of $p<0.05$ was considered as statistically significant. The analyses were performed using the software GraphPad Prism (version 10.0 for macOS, GraphPad Software, Boston, MA, USA).

2.8 | Ethics Committee

The pediatric LDLT protocol was approved by the ethics committee of Louvain Medical School, Brussels, Belgium, in 1992 and lastly amended in 2005. This observational retrospective, single-center study was conducted after approval of the Committee on Human Experimentation of Cliniques universitaires Saint-Luc, UCLouvain, Brussels, Belgium (Approval number: 2023/02NOV/441).

3 | Results

3.1 | Overall Results

Overall patient survival rates at 1 month (patients at risk: $n=494$), 3 months ($n=487$), 6 months ($n=476$), 1 year ($n=447$), 5 years ($n=316$), and 10 years ($n=188$) were 98.6%, 97.2%, 96.4%, 94.5%, 92.1%, and 91.4%, respectively. Forty patients died during the follow-up (median post-LT interval: 128 days, range: 2–8528). Corresponding graft survival rates at 1 month ($n=490$), 3 months ($n=483$), 6 months ($n=469$), 1 year ($n=438$), 5 years ($n=310$), and 10 years ($n=183$) were 97.8%, 96.4%, 94.9%, 92.7%, 89.8%, and 89.6%, respectively. The retransplantation rates at 1 month, 3 months, 6 months, 1 year, 5 years, and 10 years were 0.8%, 1%, 1.6%, 2.1%, 2.8%, and 2.8%, respectively. In total, 13 patients needed a retransplantation (median post-LT interval: 119 days, range 3–1484), using postmortem split liver grafts in five cases, whole-liver grafts in three cases, reduced-liver grafts in three cases, and LD grafts in two cases. Causes of death ($n=40$) and indications for retransplantation ($n=13$) are listed in Table 2.

3.2 | Technical Complications

One-year HA complication rate was 3.6% ($n=18$, all ≥ CDC III) in the series of 500 LDLT, with 14 thromboses, and four kinking/extrinsic compressions. One-year PV complication rate was 5.7% ($n=57$, with 50 ≥ CDC III), with 32 thromboses, and 25 stenoses. The most frequent technical complications after LT involved the biliary tract, with 1-year rate of 15.6% ($n=101$, with 97 ≥ CDC III), including 55 anastomotic strictures, 35 biliary leakages (anastomotic: $n=22$; cut surface: $n=6$; Roux-en-Y loop: $n=7$), and 11 intrahepatic stenoses with anastomotic strictures in five cases. The complication rates for each technical complication

TABLE 2 | Causes of death ($n=40$) and indications for retransplantation ($n=13$) in 500 primary pediatric living donor liver transplantations performed at Cliniques universitaires Saint-Luc, Brussels, Belgium, between July 1993 and June 2022. The technical complications that led/contributed to the final cause of death or retransplantation are presented *in italic*.

Cause of death	# Patients	Postoperative day (POD)
Sepsis/Bacterial infection	$n=7$	2–18–33-80-219-425-500
PTLD	$n=7$	128–140–224-273-595-919-1299
Cancer recurrence	$n=6$	155–278–521-794-1025-1165
Multiple organ failure secondary to: • *HAT in three cases* • *PVT in two cases* • *Peritonitis in one case*	$n=6$	2–17–24-71-83-133
Viral hepatitis	$n=3$	28-35-1897
Death after retransplantation	$n=3$	32–1540-2817
Hepatic failure secondary to *PVT*	$n=1$	31
Cerebral bleeding	$n=1$	14
Inhalation pneumonia	$n=1$	261
Macrophagic hyperactivation syndrome	$n=1$	303
Hypersplenism febrile erythema	$n=1$	320
Sudden death	$n=1$	240
Unknown	$n=2$	359–8530

Indication for retransplantation	# Patients	Postoperative day (POD)
Chronic rejection	$n=4$	210–538–672-1484
Biliary complications secondary to: • *IBS in all cases*	$n=4$	94–119–131-196
Portal vein thrombosis	$n=2$	3–22
Hepatic artery thrombosis	$n=2$	9–34
Primary non-function	$n=1$	3

Abbreviations: HAT, hepatic artery thrombosis; IBS, intrahepatic biliary stricture; PTLD, post-transplant lymphoproliferative disease; PVT, portal vein thrombosis.

after LT at 7 days, 1 month, 3 months, 6 months, 1 year, and beyond 1 year are illustrated in Table 3.

3.3 | Failure to Rescue Technical Complications

Hepatic artery thromboses. Six-month FTRp and FTRg secondary to HAT were 21.4% ($n=3/14$) and 14.3% ($n=2/14$), respectively. The causes of patient death following HAT were as follows: (1) 0.5-year-old girl (body weight: 6.0 kg) at LT for BA, 200 g left lateral lobe LD graft, ABO compatible, HAT on postoperative day (POD) 2 with failure of surgical revascularization, death due to multiple organ failure (MOF) on POD 2; (2) 1.5-year-old boy (11.3 kg) at LT for cholestatic disorder, 284 g left lateral lobe LD graft, ABO identical, HAT on POD 5 with failure of surgical revascularization, anastomotic biliary leakage and leakage on Roux-en-Y loop on POD 11, death due to MOF on POD 17; (3) 1.6-year-old girl (8.2 kg) at LT for BA, 270 g left lateral lobe LD graft, ABO compatible, HAT on POD 4 with partial success of surgical revascularization, iatrogenic PVT during arterial rescue procedure (POD 4), and biliary leakage on Roux-en-Y loop on POD 10, death due to MOF on POD 24. Indications for retransplantation following HAT were as follows: (1) 0.5-year-old girl (5.9 kg) at LT for BA, 280 g left lateral lobe LD graft, ABO identical, HAT on POD 6 with failure of arterial bypass, retransplanted with a whole-liver graft from a cadaveric donor on POD 9; (2) 0.6-year-old girl (8.9 kg) at LT for BA, 230 g left lateral lobe LD graft, ABO compatible, HAT on POD 7 with partial success of surgical revascularization and second look after 3 days for extrinsic compression, retransplanted with a split liver graft from a cadaveric donor on POD 35 for hepatic failure secondary to HAT recurrence. One-year FTRp was 28.6% ($n=4/14$). The additional cause of death beyond 6 months post-LT was inhalation pneumonia with cardiac arrest on POD 261. One-year FTRg was 21.4% ($n=3/14$). The additional case of retransplantation beyond 6 months post-LT was a 0.9-year-old girl (7.2 kg) at LT for cryptogenic cirrhosis, 235 g left lateral lobe LD graft, ABO identical, HAT on POD 7 with surgical exploration on the same

TABLE 3 | Post living donor liver transplantation complication rates, in 500 primary pediatric grafts performed at Cliniques universitaires Saint-Luc, Brussels, Belgium, between July 1993 and June 2022.

	7 days (%)	1 month (%)	3 months (%)	6 months (%)	1 year	Overall (%)
Hepatic artery complications ($n=18$)	2.8	3.4	3.4	3.4	3.6	3.6
Thromboses ($n=14$)	2.4	2.6	2.6	2.6	2.8	2.8
Kinking/extrinsic compressions ($n=4$)	0.4	0.8	0.8	0.8	0.8	0.8
Portal vein complications ($n=57$)	1.4	2.0	3.3	4.3	5.7	11.4
Thromboses ($n=32$)	0.6	1.2	2.3	2.3	3.0	6.4
Stenoses ($n=25$)	0.8	0.8	1.2	2.0	2.7	5.0
Biliary complications ($n=101$)	1.6	5.9	8.0	11.7	15.6	20.2
Anastomotic strictures ($n=55$)	0	0.2	1.7	4.2	7.2	11.0
Intrahepatic strictures ($n=11$)	0	0	0.2	1.1	1.6	2.2
Leakages ($n=35$)	1.6	5.7	6.1	6.4	6.8	7.0

day (kinking), and second look on POD 8 in the context of no arterial flow at preoperative US Doppler control with success of surgical revascularization, ultimately retransplanted with a LD graft on POD 199 for intrahepatic biliary stenoses and recurrent cholangitis.

Portal vein thromboses. Six-month FTRp secondary to PV thromboses was 9.4% ($n=3/32$), and FTRg was 6.3% ($n=2/32$). Causes of patient death following PVT were as follows: (1) 13-year-old boy (30 kg) at LT for cystic fibrosis, 320 g left lobe LD graft, ABO compatible, PVT on POD 28, death due to hepatic failure on POD 32 post-LT; (2) 6.2-year-old girl (20.1 kg) at LT for BA, left lobe LD graft, ABO compatible, PVT on POD 69 in a context of small bowel volvulus with extensive bowel resection, suture dehiscence, and ileostomy, death due to MOF on POD 83; (3) 1.3-year-old boy (9.0 kg) at LT for BA, 195 g left lateral lobe graft, ABO identical, PVT on POD 10 with successful meso-Rex shunt performed on POD 18, death due to MOF on POD 71. Indications for retransplantation following PVT were as follows: (1) 1.1-year-old girl (7.4 kg) at LT for BA, 265 g left lateral lobe LD graft, ABO identical, PVT on POD 1, retransplanted for PVT with a reduced-liver graft from a cadaveric donor on POD 3; (2) 14.1-year-old boy (35.0 kg) at LT for hepatopulmonary syndrome with cryptogenic cirrhosis, 402 g left lobe LD graft, ABO identical, PVT on POD 12 with unsuccessful meso-Rex shunt performed on POD 13, with upper gastro-intestinal bleeding secondary to portal hypertension, retransplanted on POD 22 with a whole-liver graft from a cadaveric donor, death due to severe cellular rejection and upper gastro intestinal bleeding on POD 33. One-year FTRp was 9.4% ($n=3/32$), and 1-year FTRg was 6.3% ($n=2/32$).

Anastomotic biliary strictures. Six-month FTRp and FTRg secondary to ABS were 0% ($n=0/55$) and 0% ($n=0/55$), respectively. One-year FTRp was 3.6% ($n=2/55$). The additional causes of these late deaths ($n=2$) were post-transplant lymphoproliferative disease (PTLD) on POD 224 for the first child, and mycotic aneurysm rupture at POD 240 for the second child. Finally, the 1-year FTRg for ABS was 0% ($n=0/55$) in the series.

Intrahepatic biliary strictures. Six-month FTRp and FTRg secondary to IBS were 0% ($n=0/11$) and 27.3% ($n=3/11$), respectively. Indications for retransplantation following IBS were as follows: (1) 1.9-year-old boy (12.8 kg) at LT for Crigler–Najjar syndrome, 260 g left lateral lobe LD graft, ABO incompatible, IBS diagnosed on POD 72, retransplanted on POD 119 for recurrent cholangitis and severe humoral rejection, with a LD liver graft; (2) 2.3-year-old girl (10.7 kg) at LT for BA, 250 g left lateral lobe LD graft, ABO incompatible, progressive development of IBS retransplanted on POD 94 with a cadaveric split liver graft; (3) 13-year-old boy at LT for BA, left lateral lobe LD graft, ABO incompatible, surgical exploration on POD 5 for Roux-en-Y perforation, retransplanted on POD 131 for acute rejection leading to IBS, biliary necrosis, and multiple hepatic abscesses, with a cadaveric split liver graft. One-year FTRp and FTRg were 0% ($n=0/11$) and 36.4% ($n=4/11$), respectively. The additional case of retransplantation beyond 6 months post-LT was a 0.9-year-old girl (7.2 kg) at LT for BA, 253 g left lateral lobe graft, ABO incompatible, retransplanted for IBS and recurrent cholangitis on POD 196.

The analysis of FTR rates at 6 months and 1 year post-complication is summarized in Table 4.

3.4 | Immunological Complications

The overall 1-year AR-free survival rate in the present LDLT series was 54.4% among 273 recipients at risk. As shown in Figure 3, AR-free survivals were studied in the three IS groups: cyclosporine + steroids + azathioprine (Group 1, $n=23$); tacrolimus + steroids (Group 2, $n=96$); and steroids-free tacrolimus + basiliximab (Group 3, $n=380$). The 1-year AR-free survival in the three groups were as follows: 34.2% (patients at risk:

TABLE 4 | Failure of patient or graft rescue rates for the most frequent postoperative technical complications at 6 months and 1 year post-complication, in a series of 500 primary pediatric living donor liver grafts performed at Cliniques universitaires Saint-Luc, Brussels, Belgium, between July 1993 and June 2022.

	Failure of patient rescue (FTRp)		Failure of graft rescue (FTRg)	
Technical complication	**6 months**	**1 year**	**6 months**	**1 year**
Hepatic artery thrombosis (HAT, $n=14$)	21.4% ($n=3/14$)	28.6%[a] ($n=4/14$)	14.3% ($n=2/14$)	21.4%[b] ($n=3/14$)
Portal vein thrombosis (PVT, $n=32$)	9.4% ($n=3/32$)	9.4% ($n=3/32$)	6.3% ($n=2/32$)	6.3% ($n=2/32$)
Anastomotic biliary stricture (ABS, $n=55$)	0% ($n=0/55$)	3.6%[c] ($n=2/55$)	0% ($n=0/55$)	0% ($n=0/55$)
Intrahepatic biliary stricture (IBS, $n=11$)	0% ($n=0/11$)	0% ($n=0/11$)	27.3% ($n=3/11$)	36.4%[d] ($n=4/11$)

Note: Graft loses secondary to death were excluded from FTRg figures.
[a]The additional death was due to an event not directly related to HAT (inhalation pneumonia with cardiac arrest).
[b]The additional graft loss was due to intrahepatic biliary stenoses and recurrent cholangitis.
[c]Both deaths were due to events not directly related to ABS (post-transplant lymphoproliferative disease or mycotic aneurysm rupture).
[d]The additional graft loss was due to recurrent cholangitis.

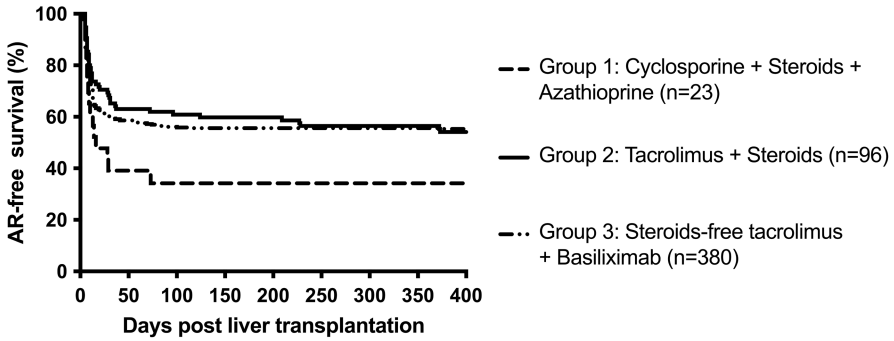

FIGURE 3 | Kaplan–Meier acute rejection (AR)-free survival curves of 499 primary pediatric living donor (LD) liver transplantation (LT) recipients, among a total of 500 LDLT performed at Cliniques universitaires Saint-Luc, Brussels, Belgium, between July 1993 and June 2022. One patient did not require immunosuppressive therapy. The difference between Groups 1 and 2 ($p=0.0027$, log-rank test), and Groups 1 and 3 ($p=0.0031$) were significant, whereas no differences were observed between Groups 2 and 3 ($p=0.9012$).

$n=8$), 56.5% ($n=50$), 55.6% ($n=180$), respectively (log-rank test: *S*—$p=0.0082$; Group 1 vs. 2: *S*—$p=0.0027$; Group 1 vs. 3: *S*—$p=0.0031$; Group 2 vs. 3: *NS*—$p=0.9012$). One patient in the series did not need IS therapy after LDLT. Among the 500 pediatric LDLT, the overall incidence of chronic rejection was 2.2% ($n=11/500$).

4 | Discussion

In the present series of 500 primary pediatric LDLT, 1-year and 5-year patient survival rates reached 94.5% and 92.1%, respectively. The corresponding graft survival rates were 92.7% and 89.8% with retransplantation rates at 2.1% and 2.8%. This series compares favorably with the series of Shanghai ($n=430$ primary cases), Sao Paulo ($n=615$), Tokyo ($n=414$), and Kyoto ($n=568$) [35–38]. The present 3-month HAT rate of 2.6% appeared to be lower than the 7.4% observed in the SPLIT multicentric registry of 3801 patients [39]. Regarding overall PVT rate, the 6.4% observed in this work was comparable to 9% figure of the monocentric Regensburg series of 115 patients [40]. The corresponding biliary complication rate of 20.2% was also comparable to the 18.6% figure observed in the monocentric Tochigi series of 290 recipients [41]. Beyond these figures describing overall survivals and post-transplant technical complications, the main objective of this study was to investigate the relationships between the occurrence of a particular technical complication and the final outcome of the patient affected. The concept of FTR might constitute a relevant tool to explore such relationship.

After careful analysis of the clinical events sequence between the complication occurrence and their outcomes, we arbitrarily choose to only interpret FTR figures at 6 months post-complication, with the hypothesis that the cause of death may become more multifactorial at 1 year. In Table 4, the 6-month FTRp rates reached 21.4% for HAT, versus 9.4% for PVT. The corresponding FTRg rates were 14.3% versus 6.3%. Obviously, the occurrence of HAT was associated with the worst FTRp and FTRg when compared to PVT and anastomotic biliary stricture. Regarding HAT, prevention and management strategies to improve patient outcome should include risk anticipation, early detection, and rescue measure. These preventive and therapeutic strategies have been discussed in detail in a previous paper from our group [21]. Similarly, PVT could be better prevented by anticipation of native portal vein hypoplasia using preoperative US Doppler, and use of surgical alternative as portoplasty

or mesenterico-portal jump graft [24, 42]. Diffuse intrahepatic biliary strictures induced 27.3% FTRg at 6 months post-complication, in the context of ABO incompatibility in all cases. Possible future development of novel immunosuppressive strategies for ABO incompatible LT might lead to revise this limitation [18]. In the present series, anastomotic biliary stricture constituted the most frequent postoperative technical complication, requiring percutaneous dilatation or surgical redo. In our center, the therapeutic strategy is to reoperate anastomotic strictures, reserving interventional radiology for recurrences [43].

Overall, FTR seemed to constitute a valid instrument for establishing the final outcome of a given postoperative surgical complication and to identify among these, the ones where management improvement is required. Multidisciplinary management of identified complications could then be discussed among various teams from transplant centers with significantly different FTR rates for the same complication, to share practices enhancement. Accordingly, we hypothesized that such FTR data may contribute to quality improvement in the complex practice of pediatric LDLT through multicentric collaborations. Further analyses will be needed to determine the outcome benefits expected from such approach.

Acknowledgments

All the authors wish to thank the residents and nursing staffs of the operating theater, intensive care department, hospitalization, and outpatient clinic for their daily devoted involvement in the care of our transplanted children and their families.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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