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Original Article

Early period intensive care follow-up after liver transplantation in children: a single center experience

Edin Botan[1], Emrah Gün[1], Setenay Akyüzlüer Güneş[8], Anar Gurbanov[1], Hasan Özen[1], Zarife Kuloglu[2], Ceyda Kırsaçlıoğlu[2], Elvan Onur Kırımker[4], Özlem Can Selvi[7], Ergin Çiftçi[3], Suat Fitöz[6], Meltem Koloğlu[5], Aydan Kansu[2], Deniz Balcı[4], Tanıl Kendirli[1]

[1]Division of Pediatric Critical Care Medicine, Ankara University Faculty of Medicine, Ankara; [2]Division of Pediatric Gastroenterology, Hepatology, and Nutrition, Ankara University Faculty of Medicine, Ankara; [3]Division of Pediatric Infectious Diseases, Ankara University Faculty of Medicine, Ankara; [4]Department of General Surgery and Liver Transplantation, Ankara University Faculty of Medicine, Ankara; [5]Department of Pediatric Surgery, Ankara University Faculty of Medicine, Ankara; [6]Department of Radiology, Ankara University Faculty of Medicine, Ankara, [7]Department of Anaesthesia and Intensive Care, Ankara University Faculty of Medicine, Ankara; [8]Department of Pediatrics Ankara University Faculty of Medicine, Ankara, Türkiye.

ABSTRACT

Background. Liver transplantation (LT) is a well-established, life-saving treatment for children with irreversible acute and chronic liver failure (LF). We aimed to evaluate the factors associated with morbidity and mortality in the early period of LT in children by reviewing our pediatric intensive care unit (PICU) experience.

Methods. We reviewed children's medical records followed in the PICU after LT between May 2015-August 2021, including demographic parameters, indications for LT, operative variables, respiratory and circulatory support requirements, LT-related complications and survival.

Results. During this period, 40 pediatric patients who underwent LT were evaluated. LT was performed in 35 (87.5%) cases of chronic liver disease and 5 (12.5%) cases of acute liver failure. Twenty-four patients had chronic liver failure due to cholestatic liver disease. The patients' Pediatric Risk of Mortality (PRISM) III score was 18.82±SD (2-58) at PICU admission. 1-year survival was 87.5%, and overall survival was 85%. Younger age, low body weight, preoperative pediatric end-stage liver disease (PELD), and model for end-stage liver disease (MELD) values of 20 and higher were important risk factors for unfavorable outcomes after living donor liver transplantation (LDLT). These risk factors are both associated with technically more challenging vascular and bile duct reconstruction and higher complication rates, and increased mortality during the early period after LT.

Conclusions. The early period of optimum PICU management in pediatric LT recipients is crucial for successful outcomes, which is also related to the patients' characteristics, disease severity scores, and surgical procedures.

Key words: liver transplantation, pediatric intensive care, children.

Liver transplantation (LT) is the standard of treatment with excellent outcomes for many end-stage pediatric liver disorders. It can provide a long and healthy life, especially for pediatric patients following recovery from the early period. The classical indication for LT is liver failure causing a life-threatening situation resulting in a mortality risk higher than 90% at one year. End-stage liver disease (ESLD) from biliary atresia remains the most common cause of liver disease leading to transplantation. Progressive familial intrahepatic cholestasis (PFIC), metabolic diseases, fulminant liver failure, and cryptogenic cirrhosis are the other causes of end-stage liver disease leading to LT.[1,2]

✉ Edin Botan
edinbotan65@hotmail.com

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One of the main limitations of pediatric LT is the scarcity of size-matched pediatric deceased donors. As a result, living donor liver transplantation (LDLT) was performed to reduce mortality in children who could not receive timely LT due to a lack of deceased size-matched donors. Despite all efforts, organ donation is not widespread in our country because of cultural, social, and historical background and religious beliefs; thus, LDLT has become the first option for pediatric patients with ESLD.

Pediatric intensive care unit (PICU) management of the patients following LT is crucial for preventing morbidity and mortality.[3] In these patients, effective and sufficient early respiratory and circulatory support, maintenance of fluid and electrolyte balance, neurological assessment monitoring of surgical complications, initiation of immunosuppressive therapy, and prevention of infection are the basic concepts of PICU management.[4] This study aimed to evaluate the factors associated with morbidity and mortality in the early period of LT in children by reviewing our PICU experience.

Material and Methods

Patients and data collection

In this study, all pediatric LT recipients aged one month to 18 years old who had undergone LT between May 2015 and December 2021 and followed in our PICU during the early period of LT were identified. Each patient's demographic and clinical data (preoperative, perioperative, and early postoperative) were recorded from a prospectively designed database. The following data were collected: age, sex, anthropometric data (weight, height, body-mass index), the underlying disease, presence of another disease, type of liver failure, presence and stage of hepatic encephalopathy, preoperative pediatric end-stage liver disease (PELD) (<12 years)[5], and model for end-stage liver disease (MELD) (>12 years)[6] scores. The following intraoperative details were documented: the donor type, graft type (living, reduced or whole); graft weight/recipient weight (GWRW) ratio and graft volume, number of bile ducts reconstructed, type of bile duct reconstruction, blood loss, cold and warm ischemia time, operative time, type of abdominal wall closure. The following early postoperative data were noted: duration of intensive care, need for respiratory, renal, and circulatory support, including mechanical ventilation, non-invasive mechanical ventilation (NIMV), high-flow nasal cannula (HFNC) treatment, continuous renal replacement therapy (CRRT), plasma exchange (PEX), and blood product requirement, complications, re-operation, and mortality. The mortality score [Pediatric Risk of Mortality III (PRISM III)][7] and Pediatric Logistic Organ dysfunction score (PELOD)[5] were calculated within 24 hours of admission to the PICU. The impact of the duration on mechanical ventilation, postoperative bleeding, vascular complications, length of stay in the PICU, and mortality were investigated.

Postoperative management

All children were admitted to the PICU after LT and were closely monitored for 3-5 days. Standard patient management was performed according to a written protocol. Methylprednisolone + tacrolimus ± mycophenolate mofetil-based immune-suppression were initiated. The first dose of methylprednisolone (10 mg/kg/day) is intravenously administered intraoperatively, and then the steroid dose is gradually reduced to 0.3 mg/kg/day on the sixth day. Tacrolimus was started orally 6-12 hours after LT at 0.1 mg/kg/day. Tacrolimus trough levels are adjusted according to the targeted drug level. Mycophenolate mofetil was added to 600 mg/m^2/day within the first five days. Maintenance fluid therapy was given with non-hypotonic fluids, and was aimed at keeping electrolytes and minerals within normal limits. To maintain optimal serum albumin level (>3 g/dL) and intravascular volume, 5% albumin was given to all patients for at least 5 or 7 days post-

operation, according to the amount of fluid in the drainage tubes. Fluid balance was monitored by measuring central venous pressure (CVP). Portal system Doppler ultrasound (USG) was performed twice in the first 3-5 days to check the patency of the vascular anastomosis. Prostaglandin E1 infusion in the first five days, low-molecular-weight heparin (if INR is <2), and aspirin (if the platelet count is >100 000/ mm^3) treatment were used to prevent vascular complications. Blood product transfusion and hemostatic management were performed according to a protocol for LT, which has a restrictive transfusion policy.

Transfusion policy:

The aim is to keep Hct between 25-30% and Hb between 8-10 g/dl. When the Hct falls below 25% and Hb 7 g/dl, if dilution due to fluid load is not considered or in the presence of bleeding, replacement with erythrocyte suspension (10 mL/kg/4 hours) is applied.

Cytomegalovirus (CMV) prophylaxis in patients

If the recipient is CMV (-) and the donor is CMV (+) then intravenous (IV) gancyclovir is given at 10 mg/kg/day (2 doses) for 14 days, then continued with per-oral (PO) valgancyclovir.

If the recipient is CMV (+) and the donor is CMV (+) then IV ganciclovir is given at 10 mg/kg/day (2 doses) and continued with PO valgancyclovir when the patient is eligible for oral intake (+) / Donor (-)

If the recipient is CMV (-) and the donor is CMV (+) then intravenous (IV) gancyclovir is given at 10 mg/kg/day (2 doses) for 14 days, then continued with per-oral (PO) valgancyclovir.

Rejection therapy

For rejection IV ganciclovir 10 mg/kg/day 2 doses was administered and increased during dosing of immunosuppression.

Antimicrobial, antifungal, CMV, and *Pneumocystis jiroveci* prophylaxis were administered to all LT recipients. In addition, the CMV and Epstein-Barr virus (EBV) PCR of the patients were periodically monitored.

Patients were discharged from the PICU if they had stable vital signs, alert and oriented mental status, and stable laboratory and ultrasound findings.

Because LT is performed at Ankara University Children's Hospital and the surgical team is not comfortable moving the adult donor to the adult hospital in the early postoperative period, the living donors were monitored in our PICU for one night after the transplant surgery. A complication requiring surgical intervention related to the donor was recorded.

Ethical approval for the research was obtained from the Ethics Committee of Ankara University, Medical Faculty (Dated 2021, number: 2021000074, decision number: 74), and the study was conducted in accordance with the Declaration of Helsinki.

Statistical analysis

Numerical data from the findings were expressed as arithmetic mean ± standard deviation (minimum-maximum), while categorical data were expressed as number (n) and percentage (%). Survived and non-survived patients Mann-Whitney U analysis was performed. Kaplan method was used in the analysis. Spearman's rho test was used in the correlation analysis of continuous variables. The statistical significance value (p) was accepted as <0.05.

Results

A total of 43 patients underwent LT in our hospital within six years, and 40 were followed in our unit. Twenty-five (62.5%) of the patients were male, and 15 (37.5) were female. The median age was 61.2±65 (3-197) months, the median body weight was 20.3±16.4 (4.2-61) kg, and the median height was 98.6±36.7 (56-167) cm. The median PELD score in patients under the age of 12 group (n=33) was 24±9.8 (4-54),

and the median MELD score in the age of 12 and up group (n=7) was 29.7±4 (23-35). Hepatic encephalopathy leading to emergent LT was present in 13 (32.5%) patients, and 4 (10%) of these patients required mechanical ventilation before LT.

LT was performed in 35 (87.5%) of the recipients due to chronic liver disease and 5 (12.5%) of the patients due to acute liver failure. Twenty-four (60%) patients had chronic liver failure due to cholestatic liver disease. The demographic data and clinical findings of the patients are also shown in Table I.

Surgical technique

Of the 40 pediatric patients who underwent LT, 39 (97.5%) patients received liver grafts from living donors, and one (2.5%) patient received a liver from a pediatric deceased donor. Left lateral section (LLS) and reduced LLS grafts were used in 20 (53.8%) patients, left lobe grafts in 11 (28.2%) patients, right lobe and right posterior sector grafts in 4 (10.3%), and mono segment grafts in 4 (10.3%) patients. Preoperative portal vein (PV) thrombosis was present in 7 (17.5) patients. PV resection and placement of the PV anastomosis to the level of superior mesenteric artery (SMA) and splenic vein (SV) confluence were done in 4 patients with portal vein thrombosis (PVT). PV reconstructions either by jump graft or patch plasty were done in 3 patients (one for thrombosis and two for narrow and fibrotic PV), inferior vena cava (IVC) reconstruction was done in 3 patients for narrow IVC (n=2), and tumor thrombosis (n=1). The mean graft weight was 318±144gram, mean graft weight/body weight ratio was 2.2±1. Mean cold ischemia time, warm ischemia time, and mean operative time were 48±27, 38±9, and 412±91minutes, respectively. Mean operative blood loss was 275±82 ml. A duct-duct anastomosis was done in 23 (57.5%) patients, and Roux-en-Y-hepaticojejunostomy was done in 17 (42.5%). In 13 (44.8%) patients, initially, the abdomen was closed with either a Bogota bag or Gortex mesh. Complete closure of the abdomen was done in 15-30 days.

Post-transplant follow-up

The patients' PRISM III score was 18.82 (2-58) at PICU admission. All of the patients were admitted to the PICU while being intubated, and the average time spent on mechanical ventilation was 86.17±139.5 (10-720) hours, the mean duration of stay at the PICU was 172±143.3 (72-809) hours [7.6±5.07 (3-34) days]. The average usage time of epinephrine in 40 patients was 19.78±32 (0-124) hours; the average usage time of norepinephrine in 40 patients was 16.1±25.4 (0-98) hours, and the average usage time of dopamine in 14 patients was 20.01±30.4 (0-120) hours. The duration of stay in the PICU and mechanical ventilator according to age and body weight are given in Figures 1 and 2.

A significant negative correlation was found between age groups and the duration of mechanical ventilation, and the duration of stay

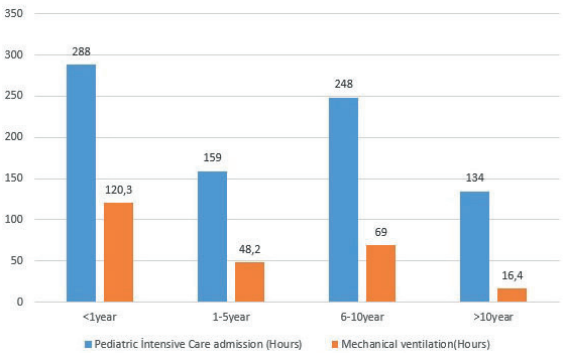

Fig. 1. Patients' length stay of in the pediatric intensive care unit and mechanical ventilation time distributions according to age.

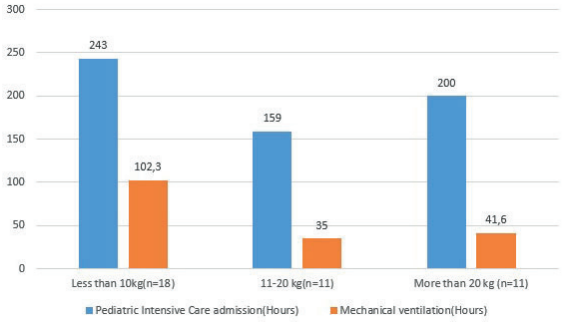

Fig. 2. Patients's length of stay in the pediatric intensive care unit and mechanical ventilation time distributions according to body weight.

Table I. Demographic and clinical findings of patients.

Parameters	n (%)
Gender	
Female	15 (37.5)
Male	25 (62.5)
Age groups	
<1 year	12 (30)
1-5 years	9 (22.5)
6-10 years	10 (25)
11-15 years	5 (12.5)
16-18 years	4 (10)
Anthropometric measurements, median (range)	
Body weight (kg)	20.3 (4.2-61)
Height (cm)	98.6 (56-182)
BMI	16.3 (11.7-20.8)
Scores, median (range)	
PELD	24 (4-54)
MELD	29.7 (23-35)
PRISM III, median (range)	18.82 (2-58)
Concomitant chronic disease	
No	35 (87.5)
Yes	5 (12.5)
Citrullinemia type 1	1
CVID (GMAP5 deficiency), HCC +EBV related lenfoma, hepatopulmonary syndrome	1
Hyperinsulinemic hypoglycaemia (KCNJ 11 mutation)+choledochal cyst	1
Inflammatory myofibroblastic tumor	1
DOCK8 deficiency+ cholestatic cirrhosis	1
Etiology	
❖ Acute liver failure	5 (12.5)
➢ Toxic hepatitis	2 (5)
➢ Idiopathic	3 (7.5)
❖ Chronic liver failure	35 (87.5)
➢ Cholestatic	24(60)
▪ Biliary atresia	10 (25)
▪ Genetic cholestatic disorders	12(30)
• PFIC	6 (15)
• Bile acid synthesis defects	2 (5)
• Mitochondrial depletion syndromes	2(5)
• Alfa-1 antitrypsin deficiency	1 (2.5)
• DOCK8 deficiency+ cholestatic cirrhosis	1 (2.5)
▪ Secondary biliary cirrhosis	2(5)
• Inflammatory myofibroblastic tumor+ Secondary biliary cirrhosis	1(2.5)
• Choledochal cyst +secondary biliary cirrhosis	1 (2.5)
➢ Inherited metabolic disorders	5(12.5)
▪ Wilson's disease	3(7.5)
▪ Tyrosinemia	1 (2.5)
▪ Citrullinemia type 1	1 (2.5)
➢ Chronic viral hepatitis	1 (2.5)
▪ HCV related cirrhosis	1 (2.5)
➢ Cryptogenic	4(10)
▪ Cryptogenic +HCC	1(2.5)
▪ Unknown	3(7.5)
➢ CVID (GMAP5 deficiency), HCC +EBV related lenfoma, hepatopulmonary syndrome	1(2.5)
Clinical and laboratory findings before transplantation	
Hepatic encephalopathy	13 (35.1)
Mechanical ventilation	4 (10.8)

BMI: body Mass Index, CVID: common variable immunodeficiency, EBV: Epstein-Barr virus, HCC: hepatocellular carcinoma, GMAP5: "GTPase of immunity-associated proteins" protein 5, HCV: Hepatitis C virus, KCNJ 11: potassium inwardly rectifying channel, subfamily J, member 11, PELD: Pediatric end-stage liver disease, MELD: Model for end-stage liver disease, PFIC: progressive familial intrahepatic cholestasis, PRISM: Pediatric Risk of Mortality

in the PICU (p=0.011, p=0.047). While there was a significant negative correlation between body weight and duration of mechanical ventilation, there was no significant correlation between body weight and length of PICU stay (p=0.006, p=0.130). In the first days of transplantation, 37 of 40 patients received erythrocyte suspension, 30 patients received fresh frozen plasma (FFP), and six patients received one unit of platelet suspension. The mean duration of alprostadil infusion was 5.2±2.2 (1-11) days.

Methylprednisolone, tacrolimus, and mycophenolate mofetil were given in appropriate doses to all patients according to the standard treatment protocol. Blood plasma tacrolimus trough level >20 was detected between 2 and 3 days in 5 patients. Hyperglycemia was observed in 2 of these patients, and seizures and sedative status were observed in 2. The average age of these patients was 25.6±32.3 (3-85) months. Severe diarrhea was observed in one patient after the use of mycophenolate mofetil. Apart from routine postoperative antibiotics, 13 patients were treated with meropenem.

We were able to start enteral nutrition in 24 of 40 patients during the PICU course, and their enteral feeding start time was 2.5 (1-8) days. Total parenteral nutrition (TPN) was started in 6 patients. TPN start time was 6 (4-5-9) days. The blood parameters of the patients on the day of transplantation and the first day after transplantation are shown in Table II. The complications that develop during the PICU follow-up and the distribution of these complications among the patients who survived

Table II. Laboratory findings at admission to PICU, and one day after LT.

Parameters	Transplantation Day (Mean ± SD)	First Day After Transplantation (Mean ± SD)	Normal Range
WBC (x10^3/mm^3)	10.70 (14 ± 3.4)	12.79 (18 ± 4.2)	4.5-12.5
Hb (g/dL)	8.6 (12 ± 5.4)	7.2 (11 ± 5.1)	12.5 - 16.2
Platelets (x10^3/mm^3)	115 (158 ± 62)	83 (110 ± 55)	150 – 450
AST (U/L)	1625 (2870 ± 840,4)	1040 (1642 ± 442)	0-50
ALT (U/L)	925 (1720 ± 640)	768 (1400 ± 452)	0-50
GGT (U/L)	68 ((214 ± 34)	38 (89 ± 14)	0-55
ALP (U/L)	205 (284 ± 87)	125 (198 ± 94)	109-449
LDH (U/L)	1345 (2650 ± 1840)	1125 (1804 ± 895)	0-248
Total bilirubin (mg/dL)	7.47 (14 ± 3.4)	6.32 (12 ± 3.1)	0.3- 1.2
Direct bilirubin (mg/dL)	4.06 (10 ± 2.4)	2.67 (8 ± 1.8)	0- 0.2
APTT (sec)	51.9 (87 ± 27)	59.72 (97 ± 34.4)	25.1-36.5
PT (sec)	34.8 (42,8 ± 17.2)	38.2 (68.1 ± 23.4)	9.4-12.5
INR	3.4 (5.1 ± 1.9)	3.11 (4.9 ± 1.4)	0.82-1.09
Albumin (g/dL)	3.1 (3.5 ± 2.2)	4.4 (5.4 ± 2.4)	3.5- 5.2
Glucose (mg/dL)	161 (244 ± 142,4)	143 (213 ± 134)	74-100
BUN (mg/dL)	10.5 (14 ± 3.4)	18.7 (24.1 ± 5.2)	5-18
Creatinine (mg/dL)	0.24 (1,4 ± 0,15)	0.14 (1.2 ± 0.1)	0.57-0.87
Sodium (mmol/L)	137 (155 ± 124)	140 (165 ± 133)	136-146
Potassium (mmol/L)	3.9 (5.9 ± 2.4)	3.8 (5.2 ± 2.5)	3.5-5.1
Magnesium (mg/dL)	2.13 (3.8 ± 1.4)	2.02 (3.4 ± 1.2)	1.7-2.2
Phosphorus (mg/dL)	4.85 (8.31 ± 3.4)	4.3 (7.65 ± 2.4)	3.4-6.2

ALP: alkaline phosphatase, ALT: alanine aminotransferase, APTT: activated partial thromboplastin time, AST: aspartate aminotransferase, BUN: blood urea nitrogen, Hb: hemoglobin, GGT: gamma-glutamyl transferase, INR: international normalized ratio, LDH: lactate dehydrogenase, LT: liver transplantation, PICU: pediatric intensive care unit, PT: prothrombin time, SD: standard deviation, WBC: white blood cells

and who did not survive are given in Table III. Four patients received both CRRT and PEX therapy. In addition, one patient received only CRRT.

Graft loss leading to mortality occurred in the initial four patients due to insufficient portal flow (n:3) and insufficient graft outflow (n:1). These patients were less than 6 kg and had hypoplastic and fibrotic PV with less than 3mm diameter and insufficient portal flow. These four patients were listed for retransplantation, but they could not receive a timely liver graft from a deceased donor. After experiencing portal inflow issues in these patients, the surgical team changed their approach to removing hypoplastic and fibrotic portal veins in small pediatric recipients and placed the PV anastomosis at the level of SMVa and SV confluence.

Acute antibody-related rejection was observed in only one LT recipient with PFIC2 one week after LT. Even though aggressive immune suppressive and supportive therapies were applied, she died due to hemodynamic instability developed during PEX therapy. No graft or patient loss occurred in the latest 24 consecutive pediatric LDLT recipients. One patient with a mitochondrial disease died of pulmonary hypertension related to his primary disease 13 months after LDLT.

Table III. Complications after liver transplantation and comparison between survived and non-survived patients.

	Complications	n (%)	Survived (n)	Non-survived (n)	p
Operative	Portal flow issues	3 (7.5)	0	3	0.001
	Hepatic outflow issues	1 (2.5)	0	1	
	Postoperative bleeding	4 (10)	4	0	
	Bile leak (from parenchymal dissection site and Roux limb stump)	2 (5)	2	0	
Respiratory system	Atelectasis	12 (30)	11	0	0.023
	Pleural effusion	4 (10)	3	1	0.560
	Pneumothorax	4 (10)	3	1	0.790
Gastrointestinal tract	Hematemesis	2 (5)	0	2	0.008
	Melena	2 (5)	0	2	0.007
	Intestinal perforation (terminal ileum)	1(2.5)	0	1	0,067
Circulatory system	Hypertension	9 (22.5)	7	2	0.836
	Inotropic need after 24 hours	14 (35)	10	4	0.148
	Cardiac arrest	5 (12.5)	0	5	0.001
Infection	Blood infection	7 (17.5)	6	1	0.790
	VAP	2 (5)	1	1	0.319
Renal system	UTI	1 (2.5)	1	0	0.499
	Hematuria	4 (10)	3	1	0.024
	CRRT	5 (12.5)	3	2	0.142
Central nervous system	Intracranial bleeding	1 (2.7)	0	1	0.065
	Brain death	1 (2.7)	0	1	0.499
	Seizures	2 (5)	1	1	0.324
Central nervous system	Hyperglycemia	8 (20)	6	2	0.679
Acute humoral rejection		1 (2.5)	0	1	0.459
Re-operation		10(25)	6	4	0.012

CRRT: continuous renal replacement therapy, UTI: urinary tract infection, VAP: ventilator associated pneumonia

At discharge from the PICU, neurological examinations of the patients were normal, and there was no patient who required respiratory support.

One year and overall Kaplan Meier survival curves of pediatric LDLT recipients are shown in Fig. 3. 1- year survival was 87.5%, and overall survival was 85%.

Discussion

This study reports the early postoperative experience after LT in children admitted to our PICU. The main indication for LT was cholestatic liver disease, including biliary atresia (60%), which was in accordance with previous reports in children.[8] The majority (97.3%) of the LTs were LDLT in our series due to the lack of available deceased donors in our country. LDLT is technically more challenging than deceased donor LT and requires the highest level of technical expertise in pediatric patients, especially those of younger age and lower body weight. Meticulous surgery and tailoring the graft to each recipient by providing sufficient and balanced inflow and outflow dynamics are mandatory for a successful LDLT in children.

Young age, low body weight, PELD, and MELD values of 20 and higher are important risk factors for unfavorable outcomes after LDLT.[5,6] These risk factors are both associated with technically more challenging vascular and bile duct reconstruction and higher complication rates, and increased mortality during the early period after LT. LDLT is even more challenging in pediatric patients with low body weight given that often there is a big graft for the patient's size, which needs to be reduced to provide sufficient portal flow, and there are short and smaller vascular structures, and bile ducts, which is more difficult to reconstruct.

Our recipients' mean PELD (24) /MELD (29.7) scores were higher than the literature. Haseli et al.[9] reported 392 patients with a mean age of 102±68.4 months and a mean PELD/MELD score of 20.3±8.9. They reported an increased risk of post-transplant complications and death when the PELD/MELD score was more than 20. In accordance with this report, the mean PELD/MELD score of patients who died was 25.3±7.5, suggesting that a high PELD score is associated with higher mortality. Similarly, Kukreti et al.[1] reported the mean PRISM III score of the patients as 7 (4-12) in a study of 145 children who underwent LT between 1988 and 2011. In another study, 17 LT patients in the pediatric intensive care unit were shown to have a PRISM III score of 5.7 (0-14).[10] In our study, the PRISM III score was 18.82 (2-58) higher than the literature, which correlated with our mortality.

The short mechanical ventilation time after LT in children positively affects the prognosis.[11] In the literature, the mean duration of mechanical ventilation in pediatric patients varies between 1-10 days.[12] In the study conducted by Qian et al.[13], the mean duration of mechanical ventilation for 81 LT patients with a median age of 8.2 months and a mean body weight of 8.4±4.6 kg was 120 hours. Alaçakır et al.[14] published that

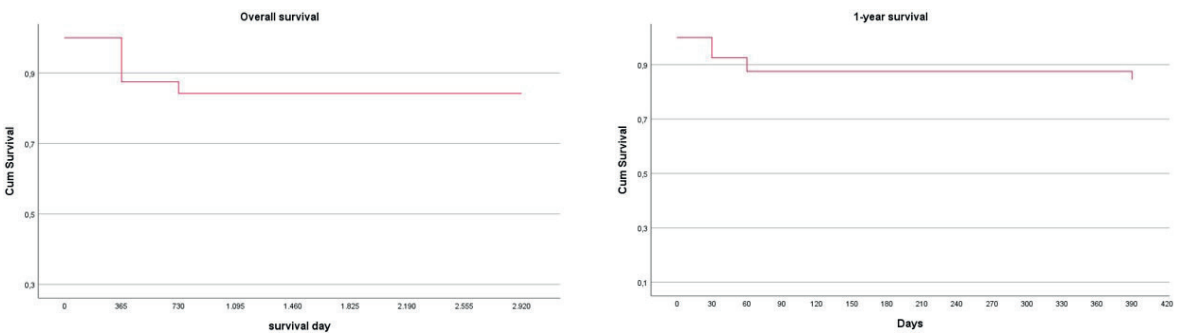

Fig. 3. One year and overall Kaplan Meier survival curves of pediatric LDLT recipients.

the mean mechanical ventilation time of 31 LT recipients with a mean body weight of 14 ± 3.01 kg was 18.4 hours. In agreement with previous reports, in our series, the time on mechanical ventilation was longer when the recipient was younger and smaller.

During PICU admission, the most common complications in our patients were respiratory system complications in 51.3% (n=19), followed by circulatory system complications in 43.2% (n=16). Atelectasis was observed to be frequent in patients with long mechanical ventilation days. Patients with pneumothorax and pleural effusion did not have long durations of mechanical ventilation.

We believe that early mobilization has positive effects on both the respiratory and musculoskeletal systems and is very important in reducing complications. Our average mobilization time in older children was 2-3 days postoperatively. McDiarmid et al.[15] reported that complications such as vascular thrombosis, intestinal perforation, septicemia, and retransplantation were the primary risks for mortality in pediatric LT recipients. A higher incidence of pulmonary complications has been reported among pediatric LT recipients.[16] Similarly, the frequency of pulmonary complications (atelectasis n=14, pneumothorax n=4, pleural effusion n=3) was high in the early period of our series. The higher incidence of respiratory system complications in pediatric patients can be attributed to a diaphragmatic malfunction related to dissection of the bare area of the recipient's native liver from the diaphragm, phrenic nerve injuries during recipient hepatectomy and ligation of the diaphragmatic veins during IVC cross-clamping and graft implantation. Moreover, in LDLT for small infants, liver grafts can be too big for small infants depending on the small space of the recipients' abdomen or graft thickness. In most infants undergoing LDLT, staged abdominal closure is preferred to avoid large for size syndrome and graft inflow and outflow problems. When full-thickness abdominal closure cannot be achieved, respiratory issues are induced in small infants due to the lack of abdominal wall support.

Five early graft losses and recipient mortality occurred in this series. Thus, the early mortality rate within the first 28 days was 12.5%, higher than other data provided in the literature.[1] Four of these patients were small infants with hypoplastic portal veins (portal vein diameter <3mm) and high PELD and PRISM III scores. Retransplantation is not a rare condition in pediatric liver transplants, it is reported in the literature at a rate of approximately 10% to 20%.[17] In another study, this rate was 9% in 167 LT patients.[18] Unfortunately, we could not retransplant these patients with vascular issues due to the lack of deceased donors. Even though these patients were listed in the first place for more than a week, they could not get a suitable graft from a deceased donor. If these patients had had a chance of retransplantation, our mortality rate might have been lower.

Also, donor-specific antibodies (DSA) cause antibody-mediated rejection (AMR); however, their pathogenic role after LT has not yet been adequately investigated. Kovandova et al.[19] reported that preformed complement-binding DSA to HLA Class I antigens is associated with an increased risk of acute antibody-mediated rejection, while chronic AMR is more common in patients with de novo-produced antibodies to HLA Class II antigens after liver transplantation. In our study, acute antibody-associated rejection was observed in only one patient, followed one week later. HLA Class I antigens were detected in the liver biopsy.

In conclusion, careful pediatric intensive care monitoring according to established protocols and timely dealing with complications are essential to decreasing morbidity and mortality after LT in children. Small children and patients with high disease severity scores such as PRISM III, PELD, and MELD have a higher risk of morbidity and mortality.

Ethical approval

This study was approved by the local Institutional Ethics Committee of Ankara University, Medical Faculty (Dated 2021, number: 2021000074, decision number: 74).

Author contribution

The authors confirm contribution to the paper as follows: study conception and design: TK,EB; data collection: AG, EB, SAG; analysis and interpretation of results: HÖ, ZK, EB, TK, EG, EÇ; draft manuscript preparation: CK, EOK, ÖCS, SF, MK, AK, DB, TK. All authors reviewed the results and approved the final version of the manuscript.

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Conflict of interest

The authors declare that there is no conflict of interest.

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