

Long-term follow-up results of pediatric liver transplants at our center

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The only curative treatment for irreversible liver damage and chronic liver disease is liver transplantation (LT).

OBJECTIVES: to determine long-term follow-up results, liver graft functions, and survival rates of pediatric LT recipients at our center.

MATERIALS AND METHODS. All pediatric LT recipients performed between March 15, 1990 and August 11, 2022 were included in our study. Demographic characteristics, preoperative clinical features, LT indications, early and late postoperative complications, survival rates, and long-term outcomes of pediatric LT recipients were evaluated.

RESULTS. Between March 15, 1990, and August 11, 2022, we performed 341 pediatric LTs (307 from living related donors and 34 from deceased donors). The most common indication for LT was biliary atresia. There were 3 hepatic vein, 5 portal vein, and 54 hepatic artery complications. Biliary stenosis was observed in 62 patients, and biliary leakage was observed in 54 patients. The overall five-year survival rate was 84.1%, and the 10-year survival rate was 77.7%.

CONCLUSIONS. According to the long-term outcomes of pediatric liver transplants performed in our center, liver transplantation is a successful treatment option for pediatric patients with end-stage liver disease and irreversible liver damage. The patients' survival rates are also satisfactory.

KEYWORDS

pediatrics, liver transplantation, end stage liver disease.

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Liver transplantation (LT) is the only curative treatment for end-stage liver disease and acute liver failure. The incidence of chronic liver disease in newborn children is 1 in 2700 [1]. Especially in the last 20 years, there has been an improvement in graft and patient survival as a result of the developments in immunosuppressive therapy, advances in technology, and surgical technique [2, 3]. Unfortunately, the insufficiency of the deceased donor pool, especially pediatric, makes living-related liver transplantation a mandatory option in the world [4].

Technological, immunological, and strategic advances, as well as the use of a living related donor as

an alternative to a deceased donor, have increased graft and recipient survival in pediatric LT to > 20 years [5, 6]. This research aims to present one of the largest single-center studies in the literature by examining the long-term outcomes of pediatric LT recipients at our center.

Materials and methods

From November 8, 1988, to August 11, 2022, we performed 709 LT procedures, and 341 of these were pediatric LT. In March 1990, a pediatric left lobe living related donor LT treatment was first

carried out in Turkey, the Middle East, and Europe. In April 1990, our center performed the first adult left lobe living related donor LT procedure in the world [7]. In May 1992, a combined liver and kidney transplantation procedure from a living related donor was the first transplantation of its kind ever carried out anywhere in the world [8].

During the pandemic period, most of the transplant centers in the world stopped their solid organ transplantation activities [9]. Since it is unacceptable for our center to stop the organ transplant procedure and delay the treatment of patients, we quickly developed our own strategy and decided to continue with organ transplantation [10]. We did not limit our organ transplant activities within our country. We have performed kidney and liver transplants on many patients with end-stage kidney disease and end-stage liver disease in many countries of the world. Some of these countries were: Jordan, Kazakhstan, Bulgaria, Somalia, Kenya, Russia, Uzbekistan, Azerbaijan, Kosovo, Saudi Arabia, the Turkish Republic of Northern Cyprus, and Ukraine.

We analyzed all 341 pediatric LT recipients retrospectively. Liver transplant recipients were followed up at regular intervals before and after transplantation. Demographic features including body weight, Child-Pugh score, etiology of liver disease, blood type, perioperative patient condition, immunosuppression protocol, postoperative complications, cause of death, and outcome at last follow-up (survival or death) of LT recipients were analyzed.

The biliary and vascular anastomoses of LT recipients were performed by the same surgical team. Ultrasonographic evaluation was done twice daily during the first week after LT. Further ultrasonographic evaluation was done in the first month after surgery. Then it was repeated every 3 months. All recipients received triple immunosuppression therapy (tacrolimus, methylprednisolone, and mycophenolate mofetil).

Results and discussion

Between November 8, 1988, and August 11, 2022, 709 LT procedures were performed by our team, and 341 of these were pediatric LT. Of these pediatric LTs, 307 (90%) were from living related donors and 34 (10%) were from deceased donors. All living related liver transplant recipients were relatives to their donors. The mean body weight of recipients was 24.7 kg (a range of 4.5–81.0 kg). 98 (28.7%) of the recipients weighed less than 10 kilograms, and 92 (26.9%) were under 1 year old. When we grouped the recipients according to their gender, 208 (60.9%) were male and 133 (39.1%) were female.

The most common indication for LT was biliary atresia. The other common indications were Wilson disease, fulminant hepatitis, progressive familial intrahepatic cholestasis, hepatocellular carcinoma, and cryptogenic cirrhosis (Table).

When we evaluated the vascular complications, we found that hepatic vein complications occurred in 3 patients. In all three patients, stenosis was detected in the portal vein anastomosis region and was successfully treated with interventional radiological methods by placing a stent in the anastomosis region. Portal vein complications occurred in 5 patients. In one of these patients, hemostasis was performed by surgical method due to bleeding from the portal vein anastomosis. In three patients, the anastomosis was surgically revised due to thrombus formation in the portal vein. In one patient, due to a stenosis of more than 50% in the portal vein anastomosis, a stent was placed in the anastomosis region after balloon dilation using interventional radiological methods, and blood flow was successfully maintained. Hepatic artery complications occurred in 54 patients. Hepatic artery thrombosis occurred in 31 patients, hepatic artery stenosis in 13 patients, bleeding from hepatic artery anastomosis in 7 patients, hepatic artery dissection in 2 patients, and pseudoaneurysm in the hepatic artery in 1 patient. Of these patients, 43 were successfully treated with interventional radiological methods, 11 of them surgically. When the recipients were evaluated in terms of biliary complications, we found that biliary leakage occurred in 54 (15.8%) patients and biliary stenosis in 62 (18.1%) patients.

The mean length of hospital stay of the recipients was 13 days (6–121) and the mean length of intensive care unit was 3 days (1–12). Revision transplants were performed 14 times in 12 children. The mortality rate in the first 3 months after LT was 9.1% (n=31). The mortality rate was 10.5% (n=36) 3 months after LT. The most common causes of early and late mortality were sepsis (58%

Table. **Indications for pediatric liver transplantation**

Etiology	Number
Biliary atresia	72 (21.0%)
Wilson's disease	64 (18.7%)
Fulminant hepatitis	44 (12.9%)
Progressive familial intrahepatic cholestasis	38 (11.1%)
Hepatocellular carcinoma	34 (9.9%)
Cryptogenic	27 (7.9%)
Other	62 (18.1%)

and 47 %, respectively). Fortunately, the overall five-year survival rate was 84.1 % (n = 287) and the 10-year survival rate was 77.7 % (n = 265).

When we evaluated the long-term results of pediatric liver transplants performed at our transplantation center, we found excellent five-year (84.1 %) and 10-year (77.7 %) survival rates. Compared to previously published studies, we found that our results were more successful [11, 12]. In our opinion, the reason for this difference is the surgical techniques we have developed and the experience of our team. In addition, we have achieved excellent long-term results in pediatric LTs thanks to our disciplined treatment and follow-up algorithms from patient preparation for LT to post-discharge controls [13].

Studies in the literature have shown that vascular complications are observed to occur more frequently in LTs performed with large-size grafts [14]. On the other hand, biliary complications are more common in LTs from living-related donors with reduced-size grafts [15]. The incidence of hepatic artery thrombosis in the early period in pediatric LTs is between 9 % and 14.9 %. This rate rises to 30 % in patients under 1 year of age [16]. Although 26.9 % of our patients are under the age of 1, the incidence of hepatic artery thrombosis is only 9 %. Portal vein thrombosis should be suspected in patients with clinical signs of portal hypertension and hypersplenism in the early post-LT period. The incidence of portal vein thrombosis after pediatric LT is 2–10 % [17]. In our series, the rate of portal vein thrombosis was only 0.88 %. The reason for our success is that the smaller-sized portal vein is spatulated (anterior and posterior walls) to make a wide anastomosis when there is a difference in diameter between the graft and the recipient portal vein. Previous studies have shown that there is no significant difference in long-term outcomes between duct-to-duct and Roux-N-Y hepaticojejunostomy in biliary tract anastomoses in pediatric liver LTs [18]. In our center, we generally prefer the duct to duct anastomosis technique since it can be intervened with endoscopic retrograde cholangio pancreatography after LT except for patients with biliary atresia [19].

Conclusions

Since the beginning of pediatric liver transplantation, survival rates of pediatric liver disease patients have increased, especially in the last 30 years as a result of the technical, surgical, immunological, and pharmacological developments that have taken place in recent years. In spite of high success rates in vascular complications, biliary complications following liver transplantation are still common and continue

to be a challenging aspect in the management of such patients. Therefore, we should continue to work on finding solutions to eliminate post liver transplantation biliary complications. On the other hand, we should try to encourage pediatric hepatologists to convince patients with liver disease to undergo early transplantation given that these patients live completely normal lives after transplantation with only a few immunosuppressive medications.

In conclusion, LT performed in experienced centers has become the optimal and standard treatment method for pediatric patients with end-stage liver disease and irreversible liver damage.

DECLARATION OF INTERESTS

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Віддалені результати трансплантації печінки у дітей у нашому центрі

Трансплантація печінки — єдиний метод лікування незворотних уражень та хронічних захворювань печінки.

Мета — визначити віддалені результати спостереження, функції трансплантата печінки та виживаність дітей-реципієнтів у нашому центрі.

Матеріали та методи. У дослідження було залучено дітей-реципієнтів, прооперованих у період із 15 березня 1990 р. до 11 серпня 2022 р. Оцінювали демографічні характеристики, доопераційну клінічну картину, показання до трансплантації печінки, ранні та пізні післяопераційні ускладнення, виживаність і віддалені результати.

Результати. У період із 15 березня 1990 р. до 11 серпня 2022 р. виконано 341 трансплантацію печінки у дітей (307 — від живих родичів, 34 — від померлого донора). Найчастішим показанням до трансплантації печінки була атрезія жовчовивідних шляхів. Виявлено 3 ускладнення з боку печінкових вен, 5 — з боку ворітної вени, 54 — з боку печінкової артерії. Стеноз жовчних шляхів спостерігали у 62 пацієнтів, витік жовчі — у 54. Загальна 5-річна виживаність становила 84,1 %, 10-річна виживаність — 77,7 %.

Висновки. Віддалені результати проведених у нашому центрі трансплантацій печінки у дітей свідчать, що трансплантація печінки є успішним методом лікування дітей із термінальною стадією захворювання печінки та незворотним ураженням печінки, а виживаність пацієнтів є задовільною.

Ключові слова: педіатрія, трансплантація печінки, термінальна стадія захворювання печінки.

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