Pediatric Liver Transplant: A Single-center Study of 100 Consecutive Patients

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Abstract

Objectives: Here, we present the outcomes of 100 consecutive pediatric liver transplant patients in our center.

Materials and Methods: Five hundred fifteen adult and pediatric liver transplants were performed at Organ Transplantation Center, Sisli Memorial Hospital, Istanbul, Turkey, between August 2006 and November 2012. Of these, the first 100 consecutive pediatric liver transplant patients were retrospectively analyzed.

Results: One hundred three liver transplants were performed in 100 children (mean age, 4.7 y; age range, 4.4 mo to 17.3 y; 53% female, 47% male; mean body weight, 17.2 kg; range, 4.5 to 75 kg). Biliary atresia (27%) and progressive familial intrahepatic cholestasis (18%) were the most common causes of liver disease. Of all the cases, 88.4% were living-donor liver transplants. Arterial reconstruction was performed under an operating microscope in most cases. Duct-to-duct biliary anastomoses were preferred in anatomically favorable cases. Mean hospital stay was 17.5 days. Median follow-up was 19.9 months (range, 6 to 66.1 mo). The main complication after surgery was infection (34%). Postoperative technical complications included hepatic arterial thrombosis (3.9%), portal venous thrombosis (6.8%), and biliary leak (6.8%). One-, 3-, and 5-year patient survivals were 89.8%, 89.8%, and 83.8%. There were no serious postoperative complications in the living donors.

Conclusions: Living-donor liver transplant in pediatric patients is a safe alternative to deceased-donor transplant. It is becoming the most frequent treatment option for end-stage liver disease in pediatric patients in our center, given the paucity of pediatric deceased-donor organs.

Key words: Children, Liver transplant, Outcome

Introduction

Although the first liver transplant was performed by Starzl in 1963, almost 100,000 liver transplants have been performed worldwide since then. During the first 20 years, patient survival was less than 20%. It went up to 90% with better surgical techniques; the discoveries of new immunosuppressive agents and antibiotics; the development of new organ preservation techniques; and better patient care.

Pediatric patients listed as candidates for liver transplant frequently die waiting for transplant. Living-donor liver transplant (LDLT) in pediatric patients is a safe alternative to deceased-donor transplant. It is becoming the most-frequent treatment for end-stage liver disease in pediatric patients. Here, we present the outcomes of the first 100 consecutive pediatric liver transplant patients in our center.

Materials and Methods

Five hundred fifteen adult and pediatric liver transplants were performed at the Organ Transplantation Center, Sisli Memorial Hospital, Istanbul, Turkey, between August 2006 and November 2012. Of these, the first 100 consecutive pediatric liver transplant patients were analyzed retrospectively.

The surgical procedure was performed in a standard piggyback technique. The hepatic veins were
anastomosed to the inferior vena cava using either a triangular or a diagonal opening. Arterial reconstruction was performed with interrupted 7-0 or 8-0 polypropylene sutures under an operating microscope in most cases. Doppler ultrasonographic examination of arterial, portal, and venous flows in the liver were performed by the surgeon before biliary anastomosis and also, before closing the abdomen. All children received aspirin (1 mg/kg/d) on postoperative day 1, if the platelet numbers were above 100,000 per microliter, and the International Normalized Ratio was below 2. Duct-to-duct biliary anastomoses were preferred in anatomically favorable cases, but 60% of the patients had a Roux-en-Y hepaticojejunostomy for biliary reconstruction using interrupted 6-0 absorbable sutures. A short transanastomotic silicon stent (made from the tip of 4.2 or 6.6 French Broviac catheter, Bard Access Systems, Salt Lake City, UT, USA) was used in some Roux-en-Y hepaticojejunostomy cases.

All children received an immunosuppressive protocol consisting of tacrolimus, mycophenolate mofetil, and steroids. The dosage of the steroids was tapered and stopped 1 month after surgery. Antiviral and anti-pneumocystis pneumonia prophylaxis were continued for 6 months after transplant.

We evaluated the data regarding the patient’s characteristics, source of the transplanted organ, surgical details, postoperative complications, and 1-, 3-, and 5-year patient survival rates. Statistical analyses were performed with SPSS software (SPSS: An IBM Company, version 13.0, IBM Corporation, Armonk, NY, USA). Survival rates were estimated by the Kaplan-Meier method. The log-rank test was used to compare different factors such as age, PELD/MELD (pediatric end-stage liver disease/model for end-stage liver disease) score, body weight, graft weight-body weight ratio (GWBWR), and indication for transplant were analyzed in terms of patient survival. P value less than .05 was accepted as statistically significant.

Results

One hundred three liver transplants were performed in 100 children (53% female, 47% male; mean age, 4.7 years; age range, 4.4 mo to 17.3 y; Figure 1) between August 2006 and June 2012. The mean body weight of the children was 17.2 kg (range, 4.5 to 75 kg) (Figure 2). Of these 100 children, 28% were younger than 1 year old and 34% weighed less than 10 kg. Biliary atresia (27%) and progressive familial intrahepatic cholestasis (18%) were the most common causes of liver disease (Figure 3). In all, 7% of the patients had a liver transplant for fulminant hepatic failure (FHF). The cause of FHF was mushroom poisoning in 1 patient, there was no specific cause for other FHF patients. In all of the patients, 88.4% were LDLT. Forty-three percent of the patients received grafts from their mothers. In all, 71.8% received a left lateral segment graft, 8.7% received a right lobe graft, 9.7% received a left lobe graft, and 9.7% had a full-sized graft from a deceased donor. Only 2 cases were performed from a split-graft of deceased donor. The mean GWBWR was 2.6% (range, 0.86% to 5.38%).

The mean hospital stay was 17.5 days. The median follow-up was 19.9 months (range, 6 to 66.1 mo). The main complication after surgery was infection (34%). Postoperative technical complications included hepatic...
arterial thrombosis (3.9%), portal venous thrombosis (6.8%), and biliary leak (6.8%). Liver retransplant was performed either from a living donor or a deceased donor in 3 cases with hepatic artery thrombosis (HAT). Iliac artery graft reconstruction between the aorta and the hepatic artery was performed in 1 patient with HAT. Early reoperation, thrombectomy, and reconstruction of the portal vein was performed in all cases with portal vein thrombosis (PVT). There was no correlation between PVT and primary disease. All cases with biliary leak were reoperated on, and treated with either Roux-en-Y conversion or a biliary reanastomoses with drainage. Late biliary strictures were treated with interventional radiology in most cases. Roux-en-Y conversion was needed in 1 patient resistant to conservative treatment for 2 years after the liver transplant. One-, 3-, and 5-year patient survivals were 89.8%, 89.8%, and 83.8% (Figures 4 and 5). The factors affecting survival rates were PELD, body weight, and GWBWR. Patients with less than 25 PELD points, having GWBWR less than 3%, and weighing more than 7 kg had significantly better survival rates. There were minor postoperative complications such as wound infection, pulmonary infection, and biliary leakage controlled conservatively in the living donors.

Discussion

Advances in surgical techniques, postoperative care, and immunosuppressive treatment have allowed liver transplant to be an effective treatment modality for patients with liver failure. Biliary atresia is the most common indication for liver transplant in the pediatric population.\(^2\) In our series, 27% of the liver transplants were performed for patients with congenital biliary atresia.

Hepatic artery thrombosis remains a significant cause of graft loss after a liver transplant in children, with an incidence ranging from 5.7% to 8.4%.\(^3\) In our series, HAT occurred in 3.9% of the children. To overcome this, microvascular surgery using a surgical microscope has been introduced by the Kyoto group in living-related donors.\(^4\) Contrary to this, Emre and associates have reported 0% HAT in 48 consecutive liver transplants anastomoses performed by a single surgeon using 3.5 to 4.5 magnification loupes.\(^5\) Microsurgical techniques with an operational microscope were used in our series for hepatic arterial anastomosis reconstruction. We think delicate surgical technique and no-touch anastomosis with microsurgical techniques are more important than magnification tools. To minimize the risk of vascular thrombosis, flow measurements by color Doppler ultrasound were performed routinely after reperfusion, before closing the abdomen, and twice a day for the first 7 postoperative days.

Portal vein thrombosis was another complication seen in our patients (6.8%). Portal vein thrombosis reportedly affects approximately 5% to 10% of pediatric recipients.\(^6\) The diameter of the portal vein tends to decrease because of a reduced flow in children with portal hypertension. Additionally, in patients with biliary atresia, the inflammation can extend to the hepatoduodenal ligament, increasing the possibility of inflammation of the portal vein.\(^7\) Also the length and diameter of portal vein is more important in left lateral segment liver transplant because of a long gap and size discrepancy in infants. Portal vein thrombosis could be prevented by taking care of the GWBWR, technical perfection, and avoiding redundancy, kinking, or stretching. The
mean airway pressure, peak inspiratory pressure, and intra-abdominal pressure should be measured just before closing the abdomen for patients with a GWBWR > 3%. In patients with high intra-abdominal pressure, we close only the skin, and let the patient heal while he or she waits for a secondary hernia repair after the age of 2 years.

The Studies in Pediatric Liver Transplantation (SPLIT) group reported the overall incidence of early biliary complications were more frequent in segmental liver transplants (21.8%) than in whole liver transplants (5.8%). Early biliary problems were seen in 6.8% of our cases. However, duct-to-duct biliary anastomoses were preferred in anatomically favorable cases, but most of our patients had a Roux-en-Y hepaticojejunostomy for biliary reconstruction. Our experience shows that a Roux-en-Y hepaticojejunostomy should be the first choice for left lateral segment liver transplant. The decision on the type of biliary reconstruction should be done according to the vascularity of bile duct, the availability of an expert interventional radiologist and gastroenterologist to perform endoscopic retrograde cholangiopancreatography.

Infection was the most frequent cause of morbidity and mortality in our cases. Rejection was problematic in managing infection, whereas balancing infection and rejection remains an important consideration for clinicians. The main complication in our series was infection after surgery (34%). Our acute rejection rate was 29%.

The SPLIT study showed patients who received LDLT had statistically fewer rejection episodes than those who received a whole organ. They also indicated that by 1 year, 46.6% of those who received a whole organ, and 40.5% who received LDLT, had experienced > 1 rejection episode.

Other important complications of immunosuppressive therapy are developing opportunistic infections, Epstein-Barr virus-related posttransplant lymphoproliferative disease, and cytomegalovirus infection. The morbidity from posttransplant lymphoproliferative disease was reduced by early detection of Epstein-Barr virus infection, decreasing the dosage of immunosuppressive medication, and continuing intravenous ganciclovir. We have been using intravenous or oral ganciclovir as a prophylactic medication against cytomegalovirus and Epstein-Barr virus infection, and 2% of our patients developed posttransplant lymphoproliferative disease.

Recent outcomes of pediatric liver transplant are good. According to recent United States Organ Procurement and Transplantation Network and SPLIT, patient survival rates at 1 and 5 years after a pediatric liver transplant are now 91% to 91.4% and 84% to 86.5%. One-, 3-, and 5-year patient survivals in our center are 89.8%, 89.8% and 83.8% (Table 1). It must be borne in mind that lower patient survival rates should be expected because of high complication rates in LDLT. The only factors affecting survival rates were PELD, body weight, and GWBWR in our series. Patients in our series having less than 25 PELD points, having GWBWR less than 3%, and weighing more than 7 kg had significantly better survival rates. It has been reported that small babies with the GWBWR equal to or higher than 4% have been successfully liver transplanted closing the abdominal incision primarily. Infections and primary nonfunction of liver were the most frequent causes of mortality in our series.

### Table 1. Survival According to the Age Compared With the US Data

<table>
<thead>
<tr>
<th>Age (y)</th>
<th>Istanbul Sisli Memorial (88.4% LDLT)</th>
<th>US OPTN* (3.6%** LDLT)</th>
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<tbody>
<tr>
<td></td>
<td>1 year</td>
<td>3 years</td>
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<td>11-17</td>
<td>84.6</td>
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Abbreviations: LDLT, living donor liver transplant; OPTN, Organ Procurement and Transplantation Network
*Based on OPTN data as of January 11, 2013.
**The rate for both adults and children.

### Conclusions

Transplant, especially liver transplant, is a teamwork procedure. The team players must work well together to achieve a successful program. Living-donor liver transplant in pediatric patients is becoming the most frequent treatment option of end-stage liver disease in pediatric patients. The surgical skills, experience, and close follow-up are the most important keys for success in any solid-organ transplant.

### References