Liver Transplantation in Children

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KEYWORDS

• Pediatric liver transplant • Immunosuppression • Split liver • Living donor
• Liver failure

KEY POINTS

- Liver transplantation (LT) is a lifesaving procedure in children with acute or chronic liver disease, hepatic tumors, and some genetic metabolic diseases.
- A multidisciplinary team is required to address the clinical needs of patients and assure optimal outcome.
- Because of scarcity of donors and better size matching between graft and recipients, most of the pediatric LTs in recent practice consist of variant techniques instead of whole LTs. The outcomes are similar to those following whole LTs.
- Advances in surgical techniques, postoperative management, and immunosuppressive treatment have allowed LT to be an effective treatment modality for patients with liver failure. LT for children has excellent short- and long-term patient and graft survival.

INTRODUCTION

Since the first successful pediatric liver transplant (LT) by Dr Starzl in 1967 in a patient with biliary atresia (BA), LT is now preformed in approximately 600 children a year in the United States and there are more than 15,000 pediatric recipients (Scientific Registry of Transplant Recipients [SRTR] data). Pediatric transplants account for about 7% to 8% of total number of LTs performed in the United States. Improvement in pretransplant management, patient selection, surgical techniques, organ preservation, immunosuppression, and posttransplant follow-up has led to outstanding results in patient and graft survival and quality of life (QOL). LT has become the standard of care for children with end-stage liver disease, acute or chronic, selected liver tumors; and metabolic disorders. The indications for LT in children are different than in adults, with BA remaining the most common cause. Many children are transplanted at a

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young age, necessitating the use of technical variants with improving success. The scarcity of cadaveric donors has led to using living donor grafts that are currently approximately 15% of transplants.[1] In 2002, the Pediatric End-Stage Liver Disease (PELD) for patients younger than 12 years and Model of End-Stage Liver Disease (MELD) for patients older than 12 years were implemented to allocate organs according to clinical need.

There are LT recipients who survive beyond 20 years after transplant. Tailoring the immunosuppressant to the individual patient is pertinent, on one hand, for prevention of acute cellular, chronic, and antibody-mediated rejection and, on the other hand, for avoiding significant morbidities such as infection, posttransplant lymphoproliferative disease (PTLD), and medication side effects.[2] Patients need close monitoring of liver enzymes, function, immunosuppressant levels, and viral polymerase chain reactions. Adherence with lifelong medication is challenging, in particular with adolescents. Nonadherence is associated with rejection and graft loss and should be addressed with every visit. The true ceiling for patient survival and graft longevity in pediatric LT recipients remains unknown. Some centers perform surveillance liver biopsies and have found increased hepatitis and fibrosis despite normal transaminases.[3] A unique aspect is that some children may develop operational tolerance and may be weaned off immunosuppressant.[4]

INDICATIONS FOR LIVER TRANSPLANT

LT in children should increase life expectancy and/or QOL. The indications for LT in children may be end-stage liver disease with significant synthetic dysfunction (acute or chronic), intractable portal hypertension, refractory ascites, coagulopathy, encephalopathy, variceal bleed, recurrent life-threatening episodes of cholangitis, spontaneous bacterial peritonitis, refractory pruritus, deforming xanthomas, failure to thrive despite maximal nutritional support, unresectable hepatic tumors, and certain metabolic diseases. The common disease processes leading to LT evaluation are listed in **Table 1**. The SRTR data show that the most common indication for pediatric LT is BA across all ages. This could be due to a late diagnosis, failed Kasai portoenterostomy, recurrent cholangitis, and progressive portal hypertension. The indications for LT change with the recipient's age. In the young population the common indications for LT are BA, metabolic disease, acute liver failure, and cholestasis. In the age group of 1 to 5 years, malignant liver tumors become the 4th indication for LT. In the population aged 11 to 17 years, noncholestatic cirrhosis is the most common cause for LT, followed by acute liver failure, metabolic disease, BA and cholestatic cirrhosis.

Indications for LT may change overtime. With earlier screening, diagnosis, and Kasai portoenterostomy, BA may decrease as the indication for LT. Only 16% of children with BA survive up to 2 years with their native liver if the total serum bilirubin measured 3 months following Kasai procedure is greater than 6 mg/dL, compared with 84% for those with a total bilirubin less than 2 mg/dL.[5] Parenteral nutrition-associated liver disease has decreased as an indication for LT, likely due to improved chronic total parenteral nutrition management and intestinal rehabilitation.[6] Metabolic diseases can lead to cirrhosis and be a risk factor for liver tumors (α-1 antitripsin deficiency, tyrosinemia, and Wilson disease) or acute liver failure. There are other metabolic diseases in which an LT replaces the defective enzyme and decreased associated morbidity (urea cycle defects, organic acidemias, and Crigler–Najjar syndrome type I). In some metabolic diseases the LT does not correct the enzyme deficiency in other organs beside the liver but is expected to improve QOL and decrease extrahepatic complications. There are some diseases in which an LT is needed to prevent progression of extrahepatic disease, such as primary hyperoxaluria type 1 and organic acidemias. There are a few