Liver Transplantation in Children: Update 2010

Binita M. Kamath, MBBChir, MRCP[a,b,*], Kim M. Olthoff, MD[c,d,e]

KEYWORDS

• Pediatric liver transplant • Liver disease
• Recipient • Donor

Pediatric liver transplantation is one of the most successful solid organ transplants.[1] According to the US Organ Procurement and Transplantation Network (OPTN)/Scientific Registry of Transplant Recipients (SRTR) data, the 1-year patient survival rate is 83% to 91%, depending on the age at transplant.[2] Five-year patient survival is also excellent, ranging from 82% to 84%. The number of pediatric liver transplants per year has remained steady in the last 10 years, averaging approximately 600 annually. Almost 12,000 pediatric liver transplants have been performed in the United States. The Studies in Pediatric Liver Transplantation (SPLIT) group is another important source of data regarding pediatric liver transplantation in North America. This group now represents 46 pediatric liver transplant centers across America and Canada and reflects the results of programs with a strong pediatric emphasis. This database has yielded valuable analyses on many of the issues surrounding pediatric liver transplantation. SPLIT survival data mirrors OPTN/SRTR results. The most recent review of the SPLIT database reveals patient survival rates of 91.4% and 86.5%, at 1 and 5 years following liver transplantation, respectively (R. Anand, personal communication, 2009).

Pediatric liver transplant recipients represent an important target population for primary care health professionals as well as transplant practitioners. With improving patient and graft survival, new concerns now face health care professionals caring for the transplant community, namely the long-term complications of immunosuppressive therapy and the potential for withdrawal of immunosuppression,

[a] Department of Pediatrics, University of Toronto, 27 King's College Circle, Toronto, ON M5S 1A1, Canada
[b] Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada
[c] Department of Surgery, University of Pennsylvania, 3451 Walnut Street, Philadelphia, PA 19104, USA
[d] Transplant Center, The Children's Hospital of Philadelphia, 34th Civic Center Boulevard, Philadelphia, PA 19104, USA
[e] Liver Transplant Program, Penn Transplant Institute, 2 Dulles, 3400 Spruce Street, Philadelphia, PA 19104, USA
* Corresponding author. Division of Gastroenterology, Hepatology and Nutrition, The Hospital for Sick Children, 555 University Avenue, Toronto, ON M5G 1X8, Canada.
E-mail address: binita.kamath@sickkids.ca.

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transplant recipients' quality of life, and the persistent shortage of donor organs leading to morbidity and mortality on the waiting list. These issues require constant collaboration between pediatricians, transplant hepatologists, transplant surgeons, nurses, dieticians, social workers, psychologists, and other supporting services.

HISTORICAL NOTES

Thomas E. Starzl performed the first liver transplantation in 1963 in a 3-year-old child with biliary atresia and thus pioneered a heroic journey through surgical refinement and improved immune suppression.[3] Although this first child died because of surgical difficulties and coagulopathy, Dr Starzl persisted and in the late 1960s performed another 8 pediatric liver transplants of which all the children survived surgery. Unfortunately, initial survival rates were poor because of inadequate immune suppression. The advent of cyclosporine A in 1978 transformed the field and dramatically improved rejection rates and outcomes. By 1983 pediatric liver transplantation was deemed the standard of care for hepatic failure or end-stage liver disease.[4] However, small infants had continued poor outcomes because of the technical challenges of creating and maintaining patent vascular anastomoses and waitlist mortality caused by the extreme shortage of appropriately sized small donors. The late 1980s was a period of surgical innovations that included reduced-sized grafts from adult deceased donors, split liver deceased donor grafts, and then live donor liver transplantation. These technical variants significantly reduced the waiting list mortality in children. In 2002 the implementation of the pediatric end-stage liver disease (PELD) and model for end-stage liver disease (MELD) scores designated priority for organ allocation to the sickest patients, rather than to those with the longest wait time, as had previously been the case. In addition, the PELD system conferred special status and protection to pediatric organs and recipients. Thus, in a mere 50 years this field has evolved from experimental conception to a successful, widespread, therapeutic strategy that benefits hundreds of children a year.

INDICATIONS FOR LISTING

There are 4 broad listing indications for evaluation and listing for pediatric liver transplantation (**Table 1**). The primary indication is the onset of life-threatening complications secondary to hepatic failure or chronic end-stage liver disease. Progressive primary liver disease refractory to maximal medical management is also an indication for liver transplantation, before the development of life-threatening complications. A smaller number of liver transplants are performed for metabolic disease, in which liver replacement is curative, and for unresectable primary liver tumors.

Chronic liver disease may lead to listing for liver transplantation either with a sudden deterioration, the so-called acute-on-chronic presentation, or with the progression of chronic disease leading to complications secondary to decompensation. Biliary atresia is the most common chronic disease leading to transplantation in children. The determination of the severity of liver disease requires an assessment of the life-sustaining functions of the liver. The major functions of the liver can be grouped into 4 general categories, namely protein synthesis (including clotting factors), bile formation and excretion, metabolic functions (including glucose homeostasis) and hemodynamic function (management of portal blood flow). A patient with chronic liver disease who has clinically significant abnormalities in 2 or more areas will likely benefit from liver transplantation. Children with only 1 area of dysfunction may be well sustained with medical therapies, although a severe abnormality in 1 area may still require