REVIEW

Paediatric living donor liver transplantation

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Paediatric liver transplantation is a highly effective therapy for children with end-stage liver disease; 1-year survival rates currently exceed 90% and long-term survivors enjoy an almost-normal quality of life. Key to the success of paediatric liver transplantation has been the technical refinement to provide children with suitably sized grafts. Adult-to-paediatric living donor liver transplantation highlights this success and has been instrumental in decreasing waiting list mortality to less than 5%.

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Liver transplantation (LT) is the definitive treatment for children with end-stage liver disease (ESLD). The greatest limitation for LT is scarcity of deceased donor organs. This is particularly critical for smaller children (weighing <10 kg). Living donor liver transplantation (LDLT) has emerged over the last 2 decades as a viable alternative option, offering children definitive treatment, reducing their mortality while on the waiting list, and providing adequate long-term graft and patient survival.[1] Compared with the whole-size deceased donor graft, LDLT in children presents a greater technical challenge with a greater chance of complications. The shorter vascular pedicles, the orientation and the size mismatch between the vessels of graft and recipient can lead to multiple forms of vascular complications. Graft size can increase the technical challenge and even compromise abdominal wall closure. The presence of a cut surface can lead to bleeding and/or bile leakage, and the size of the bile duct along with its blood supply can compromise adequate biliary drainage. Here I comprehensively review paediatric LDLT and its most recent developments.

Indications

Indications for LT in children include:

- extrahepatic cholestasis, e.g. biliary atresia
- intrahepatic cholestasis, e.g. Alagille syndrome, and progressive familial intrahepatic cholestasis (PFIC) syndromes
- metabolic diseases such as Wilson's disease, alpha 1 antitrypsin deficiency, Crigler-Najjar syndrome, and other inborn errors of metabolism (tyrosinaemia, hyperoxaluria, organic acidaemias)
- fulminant hepatic failure
- primary liver tumours, e.g. hepatoblastoma and hepatocellular carcinoma (HCC).

Cholestatic liver diseases

Biliary atresia is the most common indication for LT in children. Typically, most of these children will have undergone a Kasai's procedure that has failed to establish bile flow, and transplantation is necessitated by the development of secondary biliary cirrhosis.

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Metabolic diseases

The group of metabolic diseases accounts for the second most common indication for LT. The metabolic diseases are divided into those associated with structural damage to the liver (Wilson's, alpha-1 antitrypsin) and those in which the liver is structurally normal and LT is required to replace a life-threatening enzyme deficiency (Crigler-Najjar syndrome, ornithine transcarbamylase deficiency, or hyperoxaluria type 1).

Liver tumours

Non-resectable hepatoblastoma is effectively treated with total hepatectomy and transplantation. HCC is often secondary to other metabolic conditions (e.g. tyrosinaemia) and, if contained within the liver, is also effectively treated with total hepatectomy and transplantation.[2]

Surgery

Thomas Starzl performed the first human LT in a 2-year-old child with biliary atresia 4 decades ago.[3] The patient died in the operating room of uncontrolled haemorrhaging. The evolution of paediatric LT has focused mainly on the refinement of its surgical techniques to counteract the critical shortage of deceased donor organs. This shortage is most profound for children, who require smaller grafts. Given the low number of paediatric donors, up to 50% of children would die while on the waiting list before receiving a transplant. To alleviate the lack of available organs for young recipients, reduced and then split deceased LTs were performed in the 1980s. The development of these techniques has almost eliminated waiting list mortality for children.[4] The scarcity of organs has been alleviated also in part by the development of LDLT programmes in various centres worldwide. Eighty per cent of the paediatric deaths caused by liver disease occur in children aged <2 years. LDLT offers several advantages over deceased donation, including: reduced time on the waiting list; procurement under optimal conditions from a healthy donor; a shorter cold ischaemia time; and elective scheduling of the operation.

Donor selection

The typical living donor is a parent or first-degree relative of compatible bloodtype and aged between 18 and 55 years. The donor undergoes thorough medical and psychological evaluation, after which detailed imaging (computed tomography or magnetic resonance imaging) is performed to evaluate the potential graft size, as well as vascular and biliary anatomy. In general, children are well served by receiving a left lateral segment graft. Donor safety is the over-riding concern and has been excellent after left lateral segmentectomy, with a usually quoted donor mortality of 0.02 - 0.05% (a risk approaching that of donating a kidney).[5]

The first LDLT, in which segments 2 and 3 were procured from the mother and transplanted into a child with biliary atresia, was reported in 1988.[6] The procurement usually involves removing the left lateral segment along with the left branch of the portal vein, left hepatic artery and left hepatic vein. The recipient operation is similar to that of implantation of a cadaveric split left graft; the inferior vena cava (IVC) is preserved, the left hepatic vein is anastomosed to the recipient IVC, and the left portal vein of the graft is anastomosed to the main portal vein in the recipient. The arterial anastomosis is slightly more difficult as only the left hepatic artery is available; this is usually anastomosed to the recipient common hepatic artery. The biliary anastomosis is technically difficult because it is performed at the level of the right or left hepatic duct. Biliary reconstruction is more commonly in the form of a Roux-en-Y, due to the size mismatch and the anatomical position and orientation conferred by the size of the graft.

Biliary atresia leading to cirrhosis is by far the most common cause of ESLD in the paediatric population, accounting for over 50% of the indications for LT.[7] The portal vein in this subset of patients is typically hypo-plastic and narrow, as a result of recurrent cholangitis and previous Kasai's portoenterostomy. This usually means that the portal vein needs to be dissected back to the splenoportal junction and may require the use of vein grafts.[8] The artery, however, is usually unexpectedly larger for the size of the child, making the arterial anastomosis relatively straightforward. Because children with biliary atresia have usually had prior abdominal surgery, operative blood loss and the risk of enterotomies are higher. Furthermore, there may be associated cardiac and intestinal anomalies that need to be known prior to transplantation so that the best post-operative care can be rendered.[9]

LDLT for the paediatric recipient, especially in smaller children, has led to the development of new surgical techniques to increase the donor pool. Almost all of these techniques use the left lateral segment (segments 2 and 3) for transplantation, but even this graft could be too large for children weighing <10 kg. Monosegment LT appears to be a satisfactory option for infants weighing <10 kg. Either segment 2 or 3 can be transplanted with satisfactory results in very small children.[10]

LDLT has been widely debated from a societal and ethical point of view and has become an accepted procedure worldwide, especially for paediatric recipients.[11,12] Donor mortality and morbidity rates are low following left lateral segment donation, and recipient survival rates are between 80% and 90% at 1 year post-transplantation in experienced centres.[13]

Post-operative complications

Primary non-functioning of the liver following transplantation, although rare, is a devastating complication and needs to be recognised early to allow appropriate management and re-transplantation to be offered. Similarly, hepatic artery thrombosis usually also leads to massive hepatic necrosis and allograft failure also necessitating retransplantation.[14] If identified early, arterial reconstruction can be attempted with variable results. Portal vein thrombosis usually does not result in graft loss, but needs to be corrected by thrombectomy and anastomotic revision when detected in the early post-transplant period.[15] Left lateral segment grafts in particular are associated with an increased risk of problems with the hepatic venous anastomosis, and can sometimes result in acute Budd-Chiari syndrome; these may be avoided by attention to technique.

Biliary complications occur in 10 - 20% of paediatric LDLT recipients; bile leaks from the cut surface of the liver or the anastomosis are the most common. Drainage is usually required. Cut surface leaks are mostly self-limiting and can be managed conservatively while anastomotic leaks may require re-operation and anastomotic revision. Later on, anastomotic strictures can occur and are usually managed by percutaneous means and occasionally by revision of the anastomosis.

Conclusion

LDLT has been widely debated from a societal and ethical context, and has become an accepted procedure worldwide, especially for paediatric recipients. Donor mortality and morbidity rates are low following left lateral segment donation, and recipient survival rates are between 80% and 90% at 1 year post transplantation in experienced centres. The good survival rates following LDLT allow transplantation to take place before the onset of life-threatening complications and severe nutritional failure.

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