Living Donor Intestinal Transplantation

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KEYWORDS

• Intestinal failure • Pediatric recipients • Living donor small bowel transplantation
• Combined living donor intestinal/liver transplantation

KEY POINTS

- Living donor intestinal transplantation is compatible for appropriate candidates with deceased donor transplant graft and patient survival.
- Wait-time mortality has increased the viability of this procedure.
- Combining living donor intestinal/liver transplantation in pediatric recipients with organ failure allows for the reduction in waiting time, which is a large factor in the mortality rate of candidates on the deceased waiting list.
- Identical twins or human leukocyte antigen (HLA)-identical siblings have a significant immunologic advantage.
- ABO incompatibility and cross-match–positive transplants have been completed with success.

INTRODUCTION

Intestinal failure is defined as insufficient functional gut mass needed for adequate digestion and absorption of nutrient and fluid requirements for maintenance of adult nutrition in adults and growth in children.[1] Most cases of intestinal failure are due to loss of the small bowel as a result of surgical resection and approximately 10% are due to functional defects of absorption or motility.[2] In the United States, it has been estimated that approximately 225,000 patients require enteral or parenteral nutrition[3] as a result of short-term and long-term impaired intestinal absorption, the cost of which has been estimated to vary from $75,000 to $250,000 a year.[4] Thankfully advances in total parenteral nutrition (TPN) pharmacology and central line technology have allowed a decreased risk with use, but chronic use continues to pose a risk to end-organ damage, intestinal epithelial atrophy, and infectious risk.[5,6] Failure of

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medical intestinal rehabilitation with associated liver disease or concurrent failure is the primary indication for intestinal transplantation.[7]

The existing large gap between the number of potential recipients and available deceased donors (DDs) for liver and kidney transplantation has justified the significant expansion of living donor (LD) programs for those organs. This situation does not exist for adult recipients of intestinal transplantation, as the donor supply largely exceeds the current needs. However, there is a role for LD intestinal transplantation (LDIT) for pediatric patients with concomitant intestinal and liver failure.

According to United Network for Organ Sharing (UNOS) data, children (<10 kg) represent most (almost 70%) of the candidates on the intestinal transplantation waiting list in the United States. Most of them are listed for combined liver and bowel transplantation and 25% of pediatric patients worldwide die on the waiting list for an intestinal transplant.[8] The UNOS data and European Data sets show that this subset of patients still has the highest mortality rate on the waiting list compared with all the other categories of solid organ transplantation.[9,10] Small bowel transplantation (SBT) provides effective therapy for these patients and others with chronic, irreversible intestinal failure affected by subsequent life-threatening complications of TPN.

LDIT potentially can provide advantages, compared with DDs, including better tissue compatibility, shorter cold ischemia time, ability to implement desensitization protocols, and better donor bowel preparation. Probably the biggest advantage is that intestinal transplantation from a LD donor is a planned procedure, which is done at the optimal time for the recipient. The outcomes from LDIT in published literature are similar to those from DDs, which confirm the viability of the procedure.[11,12]

EARLY ATTEMPTS AT LIVING DONOR INTESTINAL TRANSPLANTATION

The first clinical intestinal transplant from an LD was reported in 1971. Alican and colleagues[13] described the case of an 8-year-old boy with the resection of the small bowel from the ligament of Treitz to the ileocecal valve secondary to strangulation. The transplant was performed with approximately 3 feet of ileum from his mother. However, the recipient's procedure was complicated by thrombosis of the vena cava, and the allograft had to be subsequently removed on the ninth posttransplant day. It was a new case and surgical attempt to save a child's life, whose case was incompatible with life without a transplant.

With the introduction of cyclosporine, the landscape of solid organ transplantation was revolutionized. However, the use of cyclosporine did not have as much of a benefit in intestinal transplantation as it did for other transplanted solid organs. Intestinal grafts are very susceptible to rejection because of high concentration of lymphoid tissue; therefore, a high level of immune suppression is required to prevent rejection, which can lead to serious and life-threatening sepsis. In the cyclosporine era, only 2 intestinal transplants from LDs were reported by Deltz and colleagues,[14,15] with both recipients receiving a 60-cm segment of jejunum. The first recipient was a boy, 4 years of age, with volvulus, who received the graft from his mother; unfortunately, the graft was removed due to an intractable rejection. The second recipient was a 42-year-old woman with a subtotal small bowel resection secondary to the thrombotic occlusion of mesenteric veins. She was on full enteral intake 2 weeks postoperatively and was weaned off parenteral nutrition until 1990, when chronic rejection caused the loss of the graft function. At that point in time, it was the first successful living intestinal transplant with a long-term function of more than 2 years.

The 1990s provided the introduction of tacrolimus as an immunosuppressive agent that allowed intestinal transplantation to become a clinically viable procedure with