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Intestinal Transplantation at the University of Pittsburgh: Six-Year Experience

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INTESTINAL transplantation, with tacrolimus-based immunosuppression, has become a therapeutic option for patients with irreversible intestinal failure.[1-3] In this report we divide the last 6 years of development into three chronological phases to assess outcome and to analyze the developmental process of intestinal transplantation at the University of Pittsburgh.

MATERIALS AND METHODS

From May 1990 to August 1996, a total of 86 patients received intestinal grafts, either as an isolated graft (SB, n = 33), as a combined liver and intestinal graft (SB/L, n = 40), or as a composite of multivisceral organs (MV, n = 13). Donor and recipient procedures are described elsewhere.[4] The major indications for transplantation in children (n = 52) were gastroschisis (n = 13), vulvulus (n = 12), and intestinal atresia (n = 7), and the major indications for adults were splanchnic vascular thrombosis (n = 9), Crohn's disease (n = 8), and trauma (n = 6). Patients were divided into three chronological phases based on immunosuppressive, surgical, and donor/recipient selection strategies.

Phase 1 (n = 30) spans from May 1990 through October 1992; Phase 2 (n = 29) encompasses patients transplanted from November 1992 to December 1994; and Phase 3 includes patients from January 1995 to the present.

Postoperative immunosuppression consisted of tacrolimus, steroids, and prostaglandin E1 for all phases. Azathioprine, mycophenolate mofetil, cyclophosphamide, and/or bone marrow transplantation were added as immunosuppressive options in Phase 3. The colon was added to the intestinal graft for all patients in Phase 2. Donor CMV status was random in Phase 1 and for the first several cases of Phase 2, after which strong efforts were made to obtain CMV-seronegative donors. Recipient selection was random in Phases 1 and 2. In Phase 3, recipients were carefully selected. Patient and graft survival rates were determined using Kaplan-Meier, and the Log-Rank Test was used to compare survival curves. A P-value less than .05 was considered significant.

RESULTS

Overall actuarial patient and graft survival rates are 73% and 60% at 1 year, 58% and 50% at 2 years, and 45% and 37% at 5 years. Fig 1 shows patient and graft survival rates based on phase. One-year patient and graft survival was

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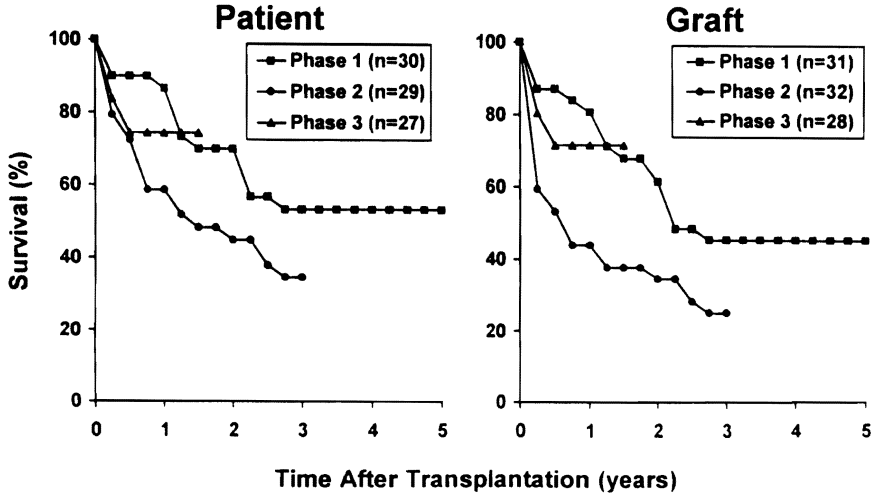

Fig 1. Life table representation of clinical intestinal transplantation patient and graft survival by phase of development.

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86.7% and 80.7% for Phase 1, 58.6% and 43.8% for Phase 2, and 74.4% and 71.5% for Phase 3. Three-year patient survival and graft survival rates were 53.3% and 45.2% for Phase 1 and 34.5% and 25% for Phase 2. Phase 1 graft survival was significantly better than Phase 2 graft survival. In Phase 1 the major causes of graft loss were rejection (n = 5), posttransplant lymphoproliferative disease (PTLD) (n = 4), and infection (n = 3). In Phase 2 the major causes of graft loss were rejection (n = 8), infection (n = 8), and PTLD (n = 6). While the ratios of graft loses were similar in both phases, CMV-associated graft loss was more prevalent in Phase 1 (n = 6) than in Phase 2 (n = 4). Most of the infections occurring during Phase 2 were secondary to bacteria or fungi, which were presumably related to the inclusion of the colon in the graft. Although the follow-up is short, most patients in Phase 3 lost their grafts to recipient mis-selection, or technical problems. Only two patients lost their grafts to rejection.

So far 13 patients in Phase 3 have received donor-derived simultaneous bone marrow transplantation. While 1-year survival of patients receiving bone marrow transplantation (83%) was better than for patients who did not receive bone marrow (66%), no statistical difference was seen.

DISCUSSION

Our 6-year struggle has highlighted the difficulty and complexity of intestinal transplantation. Although our efforts may have allowed intestinal transplantation to reach a new stage of development, further efforts need to be made to improve intestinal function and to prevent intestinal rejection. The colon was added to the intestinal graft in Phase 2 to try to lessen the problems associated with dysmotility, high stomal output, and intractable diarrhea. To overcome these recurring problems a trial of clonidine and nifedipine was started to try to reduce dysmotility of the intestinal grafts. Surgically we are trying to improve intestinal function by including the intestinal ganglion in the intestinal graft. While traditionally the intestinal ganglia were stripped from the graft vasculature to ease the anastomosis, we currently leave the ganglion intact, hoping to improve reinnervation of the graft. Although azathioprine, mycophenolate mofetil, and bone marrow transplantation have all reduced the incidence of rejection, the development of intestinal transplantation requires further improvement of immunosuppression or immunomodulation.

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