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Intestinal Transplantation in 31 Adults

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DURING the last 5 years, intestinal transplantation has become a feasible therapeutic option for patients who have irreversible intestinal failure under tacrolimus (FK 506)-based immunosuppression.[1-3] Although there was no mortality in adults during the first 2 years after initiation of our intestinal transplantation program, survival rates worsened rapidly over the last 3 years. In this article, we analyze the main contributing factors for the deterioration of patient and graft outcome after adult intestinal transplantation.

MATERIALS AND METHODS

From May 1990 to September 1995, 33 intestinal transplantations have been performed in 31 adult patients with a mean age of 33.7 years (19 to 58 years). Sixteen patients received isolated intestinal transplantation (small bowel transplantation [SBT]), 9 received combined liver/SBT, and 6 received multivisceral transplantation (MVT). Eleven recipients received a portion of the colon as a part of their intestinal graft. In the most recent three patients, donor bone marrow was infused at the time of transplantation in an attempt to augment microchimerism. The major indication for transplantation was intestinal failure resulting from splanchnic vascular thrombosis (n = 9), Crohn's disease (n = 7), trauma (n = 5), desmoid tumor (n = 4), adhesion (n = 2), and others (n = 4). Donor and recipient procedures are described elsewhere.[4] Postoperative immunosuppression was with tacrolimus (FK 506), steroids, and in selected cases azathioprine.

Intestinal allograft rejection was monitored using clinical, endoscopic, and histopathologic parameters. Acute graft rejection was treated either by augmenting FK 506 therapy, steroid bolus, steroid recycle, or OKT3 based on the severity of the rejection episode. Recovery of intestinal graft function was assessed primarily by serial gastrointestinal (GI) radiographs, FK 506 oral pharmacokinetics, and D-xylose absorption test.[5]

Kaplan-Meier and log rank tests were used for statistical analysis of survival. Statistical significance was achieved if the P value was less than .05.

RESULTS

Fourteen of 31 recipients (42%) are currently alive 1 to 62 months after intestinal transplantation. Actuarial patient and graft survival were 73% and 60% at 1 year, 59% and 44% at 2 years, and 39% and 29% at 4 years, respectively. The main causes of death were sepsis or multiorgan system failure (n = 5), pneumonia or adult respiratory distress syndrome (ARDS) (n = 5), hepatitis C (n = 2), other infections (n = 2), and posttransplant lymphoproliferative disorder (n = 1). The major causes of graft failure were acute rejection (n = 5), cytomegalovirus (CMV) infection (n = 3), ARDS or pneumonia (n = 3), chronic rejection (n = 2), and hepatitis C (n = 2).

Survival was analyzed by type of intestinal transplantation. Four-year patient and graft survival were 27% and 13% in isolated intestinal transplantation, 45% and 45% in combined liver/SBT, and 50% and 43% in MVT. Although no statistical differences were found among each group, primary small bowel grafts tended to have lower survival rates than primary liver/SBT and MVT grafts. Of special note, graft loss from CMV and rejection were only found in the isolated small bowel recipients.

A total of seven primary grafts were removed in isolated intestinal recipients. The reasons for graft removal were acute rejection (n = 4), chronic rejection (n = 1), CMV infection (n = 1), and pneumonia (n = 1). Of seven patients, three are alive on total parenteral nutrition (TPN), two died, and two underwent retransplantation but died eventually.

Cytomegalovirus infection was a significant problem, especially for patients receiving an isolated intestinal graft. Fourteen recipients (45%) developed CMV disease. Patients who received CMV-seropositive intestinal grafts had significantly worse patient survival than those who received CMV-seronegative grafts (P = .047). Four-year actuarial patient survival of the patients receiving CMV-seronegative was 57% compared with 17% 4-year survival of patients receiving CMV-seropositive grafts. Persistent CMV disease was found more frequently in isolated intestinal transplantation recipients.

The inclusion of the colon in the intestinal graft also contributed to the worsening graft outcome. Two-year actuarial patient survival rates of the patients receiving intestinal grafts with and without colon were 36% and 73%, respectively (P = .055). Two-year actuarial graft survival rates of the patients receiving intestinal grafts with and without colon were 25% and 54%, respectively (P = .042).

Of eight patients who are alive and at home with functioning grafts, seven (85%) are completely free from TPN and enjoy an unrestricted oral diet. One patient requires partial TPN at night because of rapid motility of GI tract.

DISCUSSION

The worsening outcome over the past 5 years demanded that new strategies be developed to overcome the complexities of intestinal transplantation. The survival analysis from 31 adult recipients shows the risk of CMV seropositive donor and the inclusion of the colon. The high incidence of persistent CMV enteritis in adult isolated intestinal recipients seems to be the major contributing factor to the worse

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graft survival after isolated intestinal transplantation compared with the other procedures. We believe that the outcome after transplantation can be significantly improved by avoiding CMV-seropositive grafts, excluding the donor colon from the intestinal graft, avoiding extremely difficult cases, and by adding other immunosuppressive drugs (such as cyclophosphamide or mycophenolate mofetil) in combination with FK 506.[6] Also, long-term survival could be improved by enhancing graft acceptance by infusion of donor bone marrow to augment microchimerism, although it is too early to assess the results.

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