



2139

The Long-Term Efficacy of Multivisceral Transplantation

J.R. Madariaga, J. Reyes, G. Mazariegos, J.J. Fung, T.E. Starzl, and K. Abu-Elmagd

UNDER tacrolimus-based immunosuppression, long-term rehabilitation has become achievable with intestinal transplantation.¹ Herein, we report our 9-year experience with multivisceral transplantation for patients with diffuse irreversible gastrointestinal diseases.

MATERIALS AND METHODS

Between May 2, 1990 and August 18, 1999, a total of 135 intestinal transplants were performed at our center. Of these, 18 (13%) were multivisceral, which included stomach, duodenum, pancreas, and intestine. The liver was part of the graft in all but three cases and donor colon was included in 10 (56%). Nine were adults and 10 were females. Of the 18 grafts, 15 were primary, and the indications for transplantation were dysmotility syndrome (35%), splanchnic thrombosis (24%), gut neoplasm (18%), and others (24%). Before transplantation, mean (\pm SD) bilirubin was 11 ± 16 mg/dL and mean number of abdominal operations was 2.2 ± 1.2 , and most patients received TPN for a mean period of 29 ± 19 months.

All donors were cadaveric and ABO identical with random HLA match, and no attempts were made to immunomodulate the graft. Lymphocytotoxic crossmatch was positive in two (11%) patients, and 44% of the donors were cytomegalovirus (CMV) positive. The mean cold ischemia time was 8.5 ± 1.7 hours, and the operative time was 13.8 ± 3.3 hours. The details of the donor and recipient operations have been described elsewhere.^{2,3} Tacrolimus and steroids were the baseline immunosuppression for all patients. Imuran or Cellcept were used from the outset as a third drug in selected cases. Cytoxan or Daclizumab were used as induction therapy for a few cases. Unmodified donor bone marrow cells were infused perioperatively as a single dose (3 to 5×10^8 cell/kg body weight) in three (17%) recipients. The postoperative management protocol was described elsewhere,^{1,4} and follow-up was to October 30, 1999 with a minimum of 3 and maximum of 98 months.

RESULTS

Using the Kaplan-Meier method, the actuarial patient and graft survival rates were 54% and 42% at 1 and 5 years, respectively. The survival rates were similar between adults and children. The leading causes of patient death and graft loss were microbial/viral infections (54%), posttransplant lymphoproliferative disease (PTLD) (38%), and rejection (8%). The lethal infections were CMV ($n = 1$), adenovirus ($n = 1$), fungal ($n = 2$), bacterial ($n = 1$), and de novo C-hepatitis ($n = 1$). Inclusion of the colon was associated with high (90%) mortality.

With a mean follow-up of 30 months, the incidence of allograft rejection was 66% for intestine, 27% for liver, 20% for colon, 11% for stomach, and 11% for pancreas. OKT3 was used to treat steroid-resistant rejection in 39% of recipients. There was no single example of vascular or chronic rejection.

The major morbid events were CMV disease (35%), PTLD (47%), and graft-versus-host disease (GVHD) (6%). With equal frequency of CMV disease among adults and children, PTLD occurred at a higher rate among the pediatric recipients. The diagnosis of GVHD was unequivocal in only one adult recipient that evolved to chronic disease. Of the 18 grafts, 12 (67%) were fully functioning and recipients were completely off total parenteral nutrition (TPN) at the time of patient death or last follow-up. All of the current survivors are free of TPN with full enteric nutritional autonomy with four recipients beyond the 3-year milestone after transplantation.

DISCUSSION

Multivisceral transplantation has become a viable rescue therapy for patients with diffuse irreversible gastrointestinal diseases. The most common indications in adults were total occlusion of the splanchnic circulation, particularly of the portomesenteric system associated with liver failure, and/or intractable intestinal variceal bleeding. Dysmotility and malabsorption syndromes were more common indications among the pediatric patients. The type of graft was tailored according to the need of each individual recipient.

Compared to isolated intestinal allografts, the incidence of refractory rejection was lower and the rate of lethal infections, particularly PTLD, was higher among the multivisceral recipients.¹ The failure to achieve higher survival rates could be related to the complexity of this unique population and our early learning experience. However, the immunobiologic effect of massive donor organ transplantation could be another contributing risk factor. In conclusion, multivisceral transplantation is associated with satisfactory long-term survival outcome and should be

From the Thomas E. Starzl Transplantation Institute, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania, USA.

Address reprint requests to Dr Kareem Abu-Elmagd, Thomas E. Starzl Transplantation Institute, Fourth Floor Falk Clinic, 3601 Fifth Avenue, Pittsburgh, PA 15213. E-mail: kae@med.pitt.edu.

selectively considered as a rescue therapy for patients with extensive gastrointestinal diseases.

REFERENCES

1. Abu-Elmagd K, Reyes J, Todo S, et al: J Am Coll Surg 186:512, 1998
2. Starzl TE, Todo S, Tzakis A, et al: Surg Gynecol Obstet 172:335, 1991
3. Todo S, Tzakis A, Abu-Elmagd K, et al: Transplantation 59:234, 1995
4. Abu-Elmagd K, Todo S, Tzakis A, et al: J Am Coll Surg 179:385, 1994