ELSEVIER

The Miami Experience With Almost 100 Multivisceral Transplants

A.G. Tzakis, T. Kato, S. Nishida, D.M. Levi, W. DeFaria, G. Selvaggi, D. Weppler, J. Moon, J.R. Madariaga, A.I. David, J.J. Gaynor, J. Thompson, E. Hernandez, S. Tuteja, P. Tryphonopoulos, and P. Ruiz

ABSTRACT

We report our experience with 98 patients who received primary multivisceral transplantations. Three eras can be distinguished based on the evolution of technique, immunosuppression, and monitoring: August 1994 to December 1997 (first era); January 1998 to December 2000 (second era); and January 2001 to present (third era). Sixteen patients were transplanted during the first era, 18 during the second era, and 64 during the third era. Fifty-three patients are alive with a median follow-up of 37.5 months (range: 1 to 116 months). The leading cause of mortality was infection ($n = 17$), followed by rejection ($n = 6$). Seven patients required retransplantation and five of them subsequently died. The estimated 3-year survival was 25% ± 11% for era 1; 44% ± 12% for era 2; and 58% ± 7% for era 3. Additionally, 45.3% (29/64) of patients in the third era never developed rejection versus 23.5% (8/34) of patients in the first two eras combined. The percentage of patients who developed a moderate or severe rejection was significantly less in the third era compared with the first two eras combined, 31.6% (20/64) versus 67.6% (23/34). A comparison of the hazard rate of developing severe rejection showed a protective effect of the multivisceral graft ($P = .0001$). In conclusion, multivisceral transplantation is indicated for patients with short bowel syndrome and extended abdominal catastrophies. Evolution in surgical techniques, immunosuppression, and monitoring have improved patient survival, which is now similar to that of other complex solid organ transplants.

Multivisceral transplantation is the simultaneous transplantation of the stomach, pancreaticoduodenal complex, and intestine with (MVTx) or without (modified multivisceral, MMVTx) the liver.

METHODS

Herein we have presented all patients who received primary MVTxs in our program. Three eras were distinguished based on the evolution of technique, immunosuppression, and monitoring: August 1994 to December 1997 (first era); January 1998 to December 2000 (second era); and January 2001 to present (third era).

Maintenance immunosuppression was based on tacrolimus (Prograf, Fujisawa Pharmaceuticals, Deerfield, IL, USA). In the first era we aimed at 12-hour trough tacrolimus levels of 15 to 20 ng/mL. When daclizumab (Zenapax, Roche Pharmaceuticals, Nutley, NJ, USA) was used for induction,[1] the target levels were decreased to 10 to 15 ng/mL (second and third eras), and when alemtuzumab (Campath-1H [C1H], Berlex Laboratories, Montville, NJ, USA) was used,[2] they were further decreased to 5 to 10 ng/mL (third era). Steroids (methylprednisolone; Solumedrol, Pharmacia and Upjohn Co, Kalamazoo, MI, USA), were used in all cases except with C1H induction. In the second and third eras, we performed frequent protocol endoscopies and introduced the routine use of the magnifying endoscope for all but the smallest recipients (<2 years of age).[3]

RESULTS

One hundred patients received a primary multivisceral transplant (MTX) between December 1994 and April 2005.

From the Departments of Surgery (A.G.T., T.K., S.N., D.M.L., W.D., G.S., D.W., J.M., J.R.M., A.I.D., J.J.G., S.T., P.T.), Pediatrics (J.T.), Medicine (E.H.), and Pathology (P.R.), University of Miami Miller School of Medicine, Miami, Florida, USA.

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Address reprint requests to Andreas G. Tzakis, MD, PhD, Department of Surgery, University of Miami Miller School of Medicine, Highland Professional Building, 1801 NW 9th Ave, Suite 511, Miami, FL 33136. E-mail: atzakis@med.miami.edu

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Herein we have presented the results of 98 patients who have a minimum follow-up of 1 month, 65% of whom were children. Transplanted organs included the small intestine and pancreas in all cases, and the stomach in 96/98 cases. Other organs included in the transplant procedure were the liver ($n = 83$); large intestine ($n = 29$); one ($n = 6$) or two ($n = 6$) kidneys; and the spleen ($n = 32$). A composite graft of abdominal wall was used for abdominal closure in five patients.

The numbers of transplanted patients during the first era was 16; during the second era, 18 under Zenapax induction; and during the third era, 64. Among the 50 children who were transplanted during this last era, 36 received induction with Zenapax and 14 with C1H. All 14 adults who were transplanted during the third era received C1H.

Patient Survival, Graft Survival, Cause of Death

Fifty-three patients were alive at a median follow-up of 37.5 months (range: 1 to 116 months). The leading causes of mortality were infection ($n = 17$) and rejection ($n = 6$). Seven patients required retransplantation and five of them subsequently died.

A comparison of patient survival by era indicated a more favorable outcome with the more recent era. Estimated survivals at 1 and 3 years were 44% ± 12% and 25% ± 11% for era 1 ($n = 16$); 56% ± 12% and 44% ± 12% for era 2 ($n = 18$); and 73% ± 6% and 58% ± 7% for era 3 ($n = 64$). A multivariate analysis of death due to nonrejection revealed three variables with a significantly unfavorable prognostic value: (1) transplantation during the first era; (2) patient hospital-bound pretransplant; and (3) pediatric patient who received C1H induction.

Intestinal Rejections

There was a greater freedom from rejection in the third era. In fact, 45.3% (29/64) of patients in the third era never developed rejection versus 23.5% (8/34) of patients in the first two eras combined. The percentage of patients who developed a moderate or severe rejection was significantly less in the third era compared with the first two eras combined: 31.6% (20/64) versus 67.6% (23/34). Survival for patients who had no rejection versus mild or moderate rejection was similar. Survival following severe rejection was significantly poorer than survival with other grades of rejection. A comparison of the hazard rate of developing severe rejection showed a protective effect of a multivisceral graft ($P = .0001$): less than one tenth (7/98) of multivisceral transplant patients (with or without liver) developed severe rejection compared with approximately one third (29/91) of nonmultivisceral intestinal transplant patients (ie, isolated intestine or liver-intestine). Among 115 patients who received a liver graft, the hazard rate of developing severe rejection was significantly higher among patients who received a combined liver-intestinal transplant compared with those who received a multivisceral transplant (9/32 vs 4/83, $P = .0001$). There were no significant differences in the nonrejection mortalities.

DISCUSSION

Rejection of the intestinal graft is the litmus test of multivisceral transplantation. Survival improved at the same time as the incidence and severity of rejections declined. It is now similar to the overall results of other complex solid organ transplants. The use of tacrolimus has been instrumental,[4,5] as has the use of antilymphocyte globulins to improved survival.[4,6] Frequent protocol biopsies, particularly with the use of the magnifying endoscope, have been also critical for the timely, accurate diagnosis of rejection. They also help to avoid overtreatment.

Our study indicated that the multivisceral graft confers protection of the intestinal component from severe rejection as also predicted by previous studies.[7] Contrary to previous studies, our results failed to show a protective effect of the liver on the incidence of severe rejection.[4,8]

In the third era we used multivisceral transplantation as the procedure of choice for small children with extensive abdominal pathologies. The native organs, which could have been conceivably preserved, are frequently affected by the underlying pathology, the prior surgical manipulations, the dense adhesions, the chronic intestinal obstruction, and the portal hypertension. When preserved they necessitate a portocaval shunt, which can be precarious. Their retention forces the new viscera to a paratopic position. By comparison, the multivisceral transplant contains healthy organs, is orthotopic, and carries a smaller risk of technical imperfections. It does not require backbench alterations, which could endanger its tiny vascular network. If the findings reported herein stand the test of time, the added risk from the addition of the stomach and pancreaticoduodenal complex is small.

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