



Isolated Intestinal Versus Composite Visceral Allografts: Causes of Graft Failure

M.E. de Vera, J. Reyes, J. Demetris, G. Mazariegos, N. Schaefer, H. Vargas, G. Bond, T. Wu, J. Fung, T.E. Starzl, and K. Abu-Elmagd

ALTHOUGH tacrolimus-based immunosuppression has made clinical intestinal transplantation feasible, the risk of the requisite long-term high-dose treatment has inhibited the widespread use of these procedures.¹ Such a risk could be partially eliminated with safe adjustment of the current immunosuppressive management protocol according to the type of intestinal allograft.

MATERIALS AND METHODS

Between May 2, 1990 and May 4, 1999, 124 consecutive patients received a total of 130 intestinal allografts: 51 isolated intestine and 79 composite visceral grafts (62 liver \pm intestine and 17 multivisceral). Of these, 73 (59%) were children and 51 (41%) were adults. All grafts were cadaveric and ABO identical. No attempts were made to alter the graft immunologic tissue with irradiation, anti-lymphocyte preparations, or other modalities. HLA matching was random and crossmatch testing was positive in 18% of the grafts. The mean cold ischemia time was 8.7 ± 7 hours. Baseline immunosuppression was done with tacrolimus and steroids, and daclizumab was used as induction therapy in the last 17 grafts. A single dose of unmodified donor bone marrow cells (3 to 5×10^8 cells/kg body weight) was infused intravenously during the first 24 hours after transplantation in 26 recipients. Azathioprine or mycophenolate mofetil was given from the outset in selected cases. Steroid-resistant rejection was treated with OKT3. Details of the donor and recipient operations were previously published¹⁻⁴ and the same immunosuppressive protocol was used for both the isolated intestinal and composite visceral recipients as described elsewhere.^{1,4} Chi-square and Fisher Exact tests were used for statistical analysis.

RESULTS

With a median follow-up of 41 months (range 0 to 109), 71 grafts were lost with an overall incidence of 55%. Of these, 26 were isolated intestine and 45 were composite visceral grafts. Forty-four (62%) were lost during the first 12 postoperative months (early) at a median time of 57 days. The remaining 27 (38%) grafts were lost 13 to 85 months after transplantation (late) with a median time of 26 months. The overall leading causes of graft loss were opportunistic infection (44%) and refractory rejection (30%).

Refractory rejection occurred at a significantly ($P = .0007$) higher rate when comparing the isolated intestine (54%) with the composite visceral (16%) grafts. Such a difference was maintained at a statistically significant level during both the early (57% vs 20%) and late (50% vs 7%) postoperative follow-up period with P values of .014 and .023, respectively. Chronic rejection was histologically documented in the enterectomy specimen of nine (35%) isolated intestinal grafts with a higher frequency during the late postoperative period (50%) compared to the first year after transplantation (21%). There was only one example of chronic rejection (late) of both liver and intestine in a composite visceral allograft that was given to an adult recipient across a strong positive crossmatch.

Lethal infections, including posttransplant lymphoproliferative disorder (PTLD) and cytomegalovirus (CMV), developed at a significantly ($P = .03$) higher rate among the composite visceral recipients (53%) compared to patients who received isolated intestine (27%). Such a difference was more significant ($P = .007$) during the late postoperative period with a rate of 80% and 25%, respectively.

DISCUSSION

With a similar immunosuppressive management protocol, the isolated intestinal allografts were at a significantly higher risk of intractable rejection compared to the composite visceral allografts that contained liver. Equally important was the occurrence of uncontrollable rejection at a relatively high frequency beyond the first postoperative year after isolated intestinal transplantation. The documented high incidence of lethal infections among the composite allograft recipients reflects the complexity of the operative technique and perioperative management of these high-risk patients. However, the development of lethal infections at a relatively high rate long after transplantation might reflect the long-term complications of the unified immunosuppres-

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.

sive protocol that was adopted for these patients, particularly during the early phase of the study period.

In conclusion, isolated intestinal allografts are at a significantly higher risk for intractable acute and chronic rejection compared to the composite visceral grafts that contained liver. Until a better immunomodulation strategy is available, the current immunosuppressive regimen should be adjusted for each individual recipient and maintenance therapy should be kept at a relatively high level for the isolated intestinal recipients.

REFERENCES

1. Abu-Elmagd K, Todo S, Tzakis A, et al: J Am Coll Surg 179:385. 1994
2. Starzl TE, Todo S, Tzakis A, et al: Surg Gynecol Obstet 172:335. 1991
3. Casavilla A, Selby R, Abu-Elmagd K, et al: Ann Surg 216:605, 1992
4. Abu-Elmagd K, Reyes J, Todo S, et al: J Am Coll Surg 186:512. 1998

...
CA
2
To
U.S.
1
OF
2