
Summation Addresses

Vascularized Pancreas Transplantation

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What can pancreas transplantation accomplish? Can it stabilize, prevent, or even reverse the devastating secondary complications of diabetes, and does it have the capacity to lengthen life span? Obviously, the answers to these questions are not fully known, but it appears from some of the presentations of the First International Congress on Pancreatic and Islet Transplantation that we have reason to be encouraged; successful pancreas transplantation has the capacity to normalize carbohydrate metabolism, to remove the patient from insulin dependency, and to improve the patient's well-being. Surgical transplantation of the pancreas by primary vascular union, a procedure that takes ~3 h, might be compared with coronary artery-bypass grafting for angina, which also improves the patient's well-being. However, pancreas transplantation might have a more therapeutic rationale than coronary-bypass grafting in that at least some of the underlying complications of diabetes might be prevented, whereas in coronary-bypass grafting, the underlying process is not altered.

Professor F.C. Goetz (Univ. of Minnesota, Minneapolis, MN) showed that long-term successful pancreas transplantation is the only way to convert glycosylated hemoglobin to a completely normal level on a long-term basis. Any type of rigid insulin therapy was unable to produce a glycosylated hemoglobin level within the normal range. Goetz presented a preuremic patient of Prof. D.E.R. Sutherland (Univ. of Minnesota) who received a pancreas transplant in 1977 at the University of Minnesota and has been insulin independent since then. A pretransplant kidney biopsy showed an increased mesangial volume. A kidney biopsy obtained in 1980, 3 yr after transplantation, demonstrated a significant decrease in mesangial volume. Sutherland also showed a

decrease in mesangial volume in native kidney biopsies of seven preuremic patients who had pancreas transplants functioning for >2 yr. In addition, the Stockholm group has compared patients who had received combined kidney-pancreas transplants with diabetic patients who received kidney transplants only. Three years later, kidney biopsies from patients who had received only a kidney transplant revealed early glomerulopathy, but no glomerular abnormalities were noted in the patients receiving both organs. The Munich group presented evidence of improvement in peripheral neuropathy in their patients, with an increase in the motor nerve conduction velocities after successful pancreas transplantation; this result was also confirmed by Sutherland, whose patients developed a significant increase in nerve conduction velocities.

PATIENTS

Several reports were presented, in both the plenary and poster sessions, regarding improvement in patients' well-being. From a subjective point of view, gastroenteropathy, neuropathy, and patient's quality of life improved significantly. However, Dr. R.P. Robertson (Univ. of Minnesota) showed that retinopathy, once established, became progressive and was not different from the progression of retinopathy noticed in nontransplanted diabetic patients. Professor R. Landgraf (Univ. of Munich, Munich, FRG) showed some striking data regarding improved blood flow and oxygenation in peripheral small vessels in the feet after successful pancreas transplantation.

Regarding selection of patients for pancreas transplantation, the surgeons generally agreed that patients who were eligible for a kidney transplant and in the good-risk category, without significant coronary artery disease, should receive a simultaneous pancreas transplant. Results of this operation in terms of pancreas-graft success rates at 1 and 2 yr with quadruple immunosuppressive therapy were quite impressive in the major centers in Europe and in the United States. Data presented by the Wisconsin group demonstrated graft success rates >80% in patients receiving a kidney-pancreas transplant, whereas graft success rates in the patients re-

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ceiving only a pancreas were $\leq 50\%$. Nevertheless, the consensus was that the appropriately selected post-kidney-transplant patient should be eligible for a pancreas transplant.

GRAFT REJECTION

Many investigators believe that the advantage of the simultaneous kidney-pancreas transplantation is simply that the serum creatinine is a more precise monitor of rejection than any existing marker for pancreas-graft rejection. Thus, treatment of pancreas rejection would occur when kidney rejection occurred.

Concerning other parameters for the diagnosis of rejection, the Stockholm group presented some interesting data on pancreatic juice cytology, which could be measured up to 5 wk, i.e., when the catheter from the duct of Wirsung was removed. Also, this group reported one or two new promising serum markers, one a pancreas-specific protein, the other anionic trypsin. Magnetic resonance imagery was shown in several pictures by Dr. W.T.C. Yuh (Univ. of Iowa Hospitals and Clinics, Iowa City) to confirm rejection. Radionuclide scanning and serum and urine interleukin 2 levels may be useful in the future. Currently, however, urinary amylase seems to be the most reliable indicator of pancreas rejection, although it is probably not as precise an indicator of rejection as serum creatinine is for kidney rejection.

SURGICAL PROCEDURES

Surgical procedures were discussed throughout the meeting. Briefly, most of the major European centers, with the exception of the Stockholm group, continue to use the distal pancreas segment. Advantages of this technique are that it lends itself to combined liver and pancreas removal. The American centers continue to use the whole organ with duodenal segment, which is the Starzl modification of the original Lillihei procedure. The duodenal segment can either be attached to the bladder or to the jejunum in a side-to-side

fashion or be attached, as in the Stockholm program, to a Roux-en-Y limb. If the intestinal anastomosis is chosen, the surgeon should consider leaving a catheter in the duct of Wirsung to measure pancreatic juice amylase and cytology for the 1st mo. However, results were essentially the same regardless of the surgical procedure used.

IMMUNOSUPPRESSION

Immunosuppression was covered in several sessions. Most groups are using a modification of quadruple-drug therapy, with polyclonal anti-T-lymphocyte antibody induction along with low-dose cyclosporin, Imuran (Burroughs Wellcome, Research Triangle Park, NC), and prednisone. Before completion of the course of polyclonal antibody therapy, cyclosporin doses were raised to appropriate levels, and steroids were rapidly tapered. Throughout the discussions, several presenters emphasized that treatment of rejection should probably be initiated with monoclonal antibody therapy rather than a 3-day trial of steroids.

GRAFT STORAGE

Data were presented from the Wisconsin group emphasizing the enormous capability of the University of Wisconsin storage solution in extending graft storage times. The Minnesota group was able to preserve organs with a silica gel-fractionated protein for >24 h. Because the registry data showed a beneficial effect of matching, an increase in cold storage should enable prospective matching of donor-recipient combinations.

CONCLUSION

The major remaining challenge in pancreas transplantation is the development of a more precise method of determining rejection early enough to permit successful treatment. As a corollary, the most effective strategy will be to prevent the occurrence of rejection.