Segmental Duct-Obstructed Pancreas Grafts Versus Pancreaticoduodenal Grafts With Enteric Diversion

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Between January 1985 and September 1987, we performed a prospective comparative study between segmental-pancreas transplantation with duct obstruction by neoprene (n = 17) and pancreaticoduodenal transplantation with enteric diversion to a Roux-en-Y intestinal loop (n = 14). All recipients had insulin-dependent diabetes. The immunosuppressive protocol consisted of low doses of the steroids cyclosporin A and azathioprine. Mean follow-up was 16.5 mo for the enteric-diversion group and 13.5 mo for duct-obstructed groups. Two-year patient and pancreas- and kidney-graft actuarial survival rates were 92.9, 75.5, and 74.2%, respectively, in the former group and 92.3, 58.4, and 63.7%, respectively, in the latter group (NS). Five whole-organ grafts were lost (3 vascular thromboses, 1 pancreatitis, 1 rejection), and four segmental grafts were lost (2 vascular thromboses, 1 bleeding, 1 patient's death with functional graft). More surgical complications occurred in the recipients of whole-organ grafts and were often related to the intestinal anastomosis. A satisfactory blood glucose control was observed at 3 mo and 1 yr in both groups. Provocative tests showed higher and prompter insulin secretion in patients with whole-organ grafts. In patients with segmental grafts, the response was lower and delayed with a general tendency to impaired glucose tolerance. A marked hyperinsulinemia after meals was observed in whole-organ graft recipients. Slight nocturnal hyperinsulinemia was observed in both groups. At 1 yr, glycosylated hemoglobin was normal in both groups. The absence of a significant difference between the two groups, in terms of survival and graft function, and the lower surgical complication rate seen with segmental grafts have made us return to neoprene-injected segmental grafts. *Diabetes* 38 (Suppl. 1):16–17, 1989

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The choice of the best surgical technique for the handling of pancreatic juice in pancreas transplantation and the choice of the mass of pancreatic tissue to be grafted are still unsolved problems in pancreas transplantation. Data presented in the last *Pancreas Transplantation Registry Report* (1) do not show significant differences in graft survival between the three techniques of exocrine-secretion management of pancreas grafts (enteric drainage, urinary drainage, duct obstruction). Also, similar results have been reported comparing segmental- and whole-pancreas grafts.

From the start of our clinical experience in pancreas transplantation in November 1976, we have promoted a technique of segmental-pancreas transplantation with neoprene duct obstruction, and most of our pancreases were grafted according to this technique. With the possible changes in long-term graft function in mind, we recently evaluated whole-organ transplantation with enteric drainage of the pancreatic juice. Between January 1985 and September 1987, we performed a comparative study between these two methods.

MATERIALS AND METHODS

Starting in January 1985, 29 insulin-dependent diabetic patients randomly received either a segmental duct-obstructed (DO) pancreas graft (17 patients) according to the technique previously described (2) or a whole-pancreas graft with enteric diversion (ED) of pancreatic exocrine secretion in a Roux-en-Y loop (14 patients). Data concerning patient population are shown in Table 1. Twenty-seven patients were submitted to a simultaneous pancreaticorenal transplantation. Two patients received a second pancreas transplant alone (1 DO, 1 ED). These 2 patients had a well-functioning kidney transplant. All grafts were harvested from cadaveric donors.

Immunosuppressive treatment included cyclosporin A (3 mg · kg^{-1} · day^{-1} i.v. then 6–8 mg · kg^{-1} · day^{-1} orally); prednisone (0.25 mg · kg^{-1} · day^{-1} i.v. then 5–10 mg/day

TABLE 1
General data on patient population submitted to pancreaticorenal transplantation

	Segmental pancreas	Whole pancreas
Patients (*n*)	17	14
Follow-up (mo)*	11.6 ± 2.1	13.8 ± 2.8
Age* (yr)	39.8 ± 6.8	33.5 ± 6.6
Diabetes duration* (yr)	25.9 ± 6.5	29.6 ± 3.5
Dialysis (%)	94	86
Dialysis duration* (yr)	14.1 ± 6.7	9.2 ± 5.3
Retinopathy (%)	100	93
Blindness (%)	13	14
Peripheral macroangiopathy (%)	35	28
Cardiopathy (%)	44	21
Neuropathy (%)	100	100

*Values are means ± SE.

orally); azathioprine (2–3 mg · kg^{-1} · day^{-1} i.v. then 1 mg · kg^{-1} · day^{-1} orally); and antilymphocyte globulin (ALG) for treatment of early rejection only. Two patients (1 DO, 1 ED) received the ALG during the first 2 wk as part of a new immunosuppressive protocol.

Metabolic control of diabetes was tested by performing an oral glucose tolerance test (OGTT), a circadian glycemic and insulinemic profile, and an evaluation of glycosylated hemoglobin levels, 3 mo and then every 6 mo posttransplantation.

RESULTS

One-year patient, pancreas, and kidney actuarial survival rates were 92.8, 71.4, and 92.3%, respectively, for the ED group and 93.3, 69, and 74.5%, respectively, for the DO group. At 2 yr, patient survival remained unchanged; pancreas and kidney survival rates were 58.4 and 63.9%, respectively, for the ED group and 69 and 63.5%, respectively, for the DO group (NS). The main causes of loss of pancreas grafts were early vascular thrombosis (5 grafts, 2 in DO group and 3 in ED group) and rejection (3 grafts, 1 lost at 8 mo in patient from DO group who had irreversible kidney rejection 2 mo after transplantation). Two irreversible rejections occurred in the ED group. In one patient the pancreas was lost 34 mo after transplantation, and the kidney was lost because of rejection at 20 mo. In the other patient, both organs were rejected 14 mo after transplantation. One patient in the DO group died with a functioning graft 5 mo after transplantation (necrosing enteritis), and two transplantectomies were necessary: one for a major postoperative bleeding in the DO group and the other for an extensive pancreatic necrosis that was probably due to a prolonged cold ischemia in the ED group. Twelve DO (71%) and 8 ED (57%) pancreas grafts are still functioning; all these patients, with the exception of one, are insulin independent. This one exception had a DO graft that required insulin therapy (30% of pretransplant dose) despite a preserved C-peptide secretion.

Complications requiring iterative surgery were more frequent in the ED group: one enteric leakage, two small-bowel occlusions, one postoperative bleeding, and two wound dehiscences were observed in the ED group. In the DO group, only one wound dehiscence and one postoperative bleeding occurred.

The circadian profiles showed good glycemic control in both groups. However, higher postprandial insulinemic peak and more evident fasting hyperinsulinemia were observed in the ED group. A slight hyperinsulinemia during the night was also present in the DO group.

The OGTT showed a better glucose tolerance in the patients of the ED group than those of the DO group 3 mo and 1 yr posttransplantation. In the latter group, smaller and more retarded insulinemic peak was observed at 3 mo, and slight deterioration in glucose tolerance was seen after 1 yr. Seven patients of each group had a pancreas survival >1 yr; all seven patients of the ED group showed a normal OGTT at 3 and 12 mo posttransplantation. In the DO group at 3 mo, four patients had a normal glucose tolerance, two had an impaired glucose tolerance, and one had a diabetic response. In the DO group at 1 yr, 6 patients had an impaired glucose tolerance, and one patient presented a diabetic response (OGGT interpreted according to the WHO committee criteria; 3). Despite these differences, the mean glycemic control at 1 yr was nearly the same in the two groups of patients, with mean (±SE) fasting glycemic and insulinemic levels of 4.93 ± 0.3 mM and 10.7 ± 0.8 μU/ml, respectively, in the DO group and 4.97 ± 0.14 mM and 16.7 ± 2.7 μU/ml, respectively, in the ED group.

The similar glycemic control was confirmed by the glycosylated hemoglobin levels: 7.27 ± 0.32% in the DO group vs. 7.01 ± 0.32% in the ED group at 1 yr.

DISCUSSION

No significant differences were observed in patient and pancreas survival between whole- and segmental-pancreas transplantations. This is in agreement with the *Pancreas Transplantation Registry Report* (1) and previously reported results (4).

The causes of graft loss (vascular thrombosis, rejection) were comparable in the two groups of patients. Surgical complications appeared to be more frequent in the ED group and were mainly related to intestinal anastomosis. The relatively high incidence of wound dehiscences was due to the poor healing in diabetic immunosuppressed patients and to the use of absorbable sutures, a practice that has now been abandoned.

The mean glycemic control was good in the short and long term in both groups of patients, despite the alterations in insulin secretion observed in the DO group, probably because of the lesser mass of β-cells.

The absence of significant differences between the two groups in terms of survival and graft function and the lower rate of surgical complication observed in the DO group led us to stop the comparative study in September 1987 and to switch back to the technique of duct obstruction. Metabolic studies of the two groups have been continued to obtain long-term data.

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