Indications and results of pancreatic transplantation: the Oslo experience 1983–1990

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Summary. The Norwegian pancreas transplantation programme was initiated in June 1983. By November 1990, a total of 77 pancreatic transplantations had been performed, 63 simultaneously with a renal transplant. Five patients received pancreatic grafts after previous renal grafting while nine non-uraemic diabetic patients received pancreatic grafts only. In April 1988, the surgical technique was changed from duct-occluded segmental pancreas to whole pancreas grafting with duodenocystostomy. In recipients of *combined* grafts from the first group (segmental pancreatic grafts), the 1- and 5-year survival rates were 96% and 90% for the patients, 84% and 69% for renal grafts and 66% and 45% for pancreatic grafts. In the second group (whole pancreatic grafts with duodenocystostomy), the 6-month and 2-year survival rates were 87% at both intervals for the patients, 87% and 75% for both grafts. However, even though the bladder drainage technique allows isolated pancreas graft rejection to be diagnosed, the results of *isolated* pancreas grafting were not improved by this technique, and most of these grafts were lost in therapy-resistant graft rejection.

Key words: Pancreas transplantation – Diabetes – Duodenocystostomy – Glucose control

Introduction

Even though pancreatic transplantation has taken the step from being experimental medicine to becoming an accepted clinical procedure, the indications and type of surgical technique are still debated. In Norway, the first pancreatic transplantation was performed in June 1983.

The pancreas was transplanted simultaneously with a renal graft and this soon became the standard treatment for uraemic diabetic patients provided no living donor was available. Later, the indication for pancreas transplantation was extended to include diabetic patients with a functioning renal graft and non-uraemic diabetic patients with extremely labile blood glucose.

The results of pancreatic transplantation by two different techniques and for various indications are presented.

Subjects and methods

Patients. Between June 1983 and November 1990, a total of 77 pancreas transplantations were performed in 75 patients. Sixty-three patients received pancreatic grafts simultaneously with a renal graft from the same cadaveric donor. Since 1984, pancreas transplantation alone has been performed in nine carefully selected non-uraemic patients with extreme difficulty in obtaining satisfactory metabolic control by other types of treatment, including insulin pen and insulin pump. Since 1988 pancreas transplantations have been performed in five patients with a functioning renal transplant. Two of these were pancreas retransplants. Patient characteristics are given in Table 1.

Table 1. Recipients of pancreatic grafts, June 1983–November 1990. Patient characteristics at the time of transplantation

Patient category	Sex male/female	Mean age (years)	Diabetes duration (years)
A	46/17	39 (24–55)	24 (7–41)
B	2/3	36 (31–45)	26 (18–39)
C	3/6	35 (18–52)	15 (9–22)

A=recipients of combined grafts

B=recipients of pancreas after kidney

C=Recipients of pancreas only

Selection criteria. Until 1988, practically all uraemic diabetic patients who did not have a suitable living related donor were offered combined renal/pancreatic transplantation, without regard to the severity of the diabetic complications. Of the first 46 recipients, ten were blind, two had a history of myocardial infarction, five had symptomatic coronary heart disease, six had experienced one or more cerebrovascular insults. One 55-year-old recipient who had an amputated foot, also had a coronary by-pass operation performed before transplantation.

Since 1988, most patients with symptomatic coronary heart disease, gangrene or a history of cerebrovascular insult have been excluded from the combined transplantation.

Organ harvesting. All grafts were harvested from cadaveric donors (age 5–55) after in situ perfusion with Euro-Collins (63 donors) or UW-solution (14 donors). Multi-organ harvesting (including liver and heart) was performed in about 80% of the donors.

Transplant technique. Segmental, duct-occluded pancreatic grafts (n=53) were used until 1988. The pancreatic duct was occluded with neoprene. Whole pancreas grafts with pancreaticoduodenocystostomy (n=24) have been used since April 1988.

Post-operative treatment. Thrombosis prophylaxis was given with dextran 70 for 1–2 weeks and was then changed to acetylsalicylic acid, 300–500 mg/day. Parenteral nutrition and urinary bladder drainage was maintained for 1 week.

Immunosuppression. Triple immunosuppressive therapy has been used for the majority of recipients. Rejection episodes were primarily treated with methylprednisolone. Steroid resistant rejection were treated with antithymocyte globulin(ATG, Fresenius) or Orthoclone OKT-3.

Results

With the exception of two grafts that never functioned, all pancreatic grafts obtained primary good function leading to normoglycaemia within a few hours. Two kidneys had delayed function. In the course of the first 3 months, rejection episodes were experienced by 95% of the recipients of segmental grafts and by all 24 recipients of pancreaticoduodenal transplants. While most rejection in the first group (segmental grafts) could be reversed by methylprednisolone, all rejections in recipients of pancreaticoduodenal grafts proved to be steroid resistant.

Patient survival

All recipients of sequential pancreas after kidney and recipients of pancreas only were alive 1 year after the transplantation. Four recipients of combined grafts died within 3 months after the transplantation, all with functioning pancreatic grafts. The cause of death was myocardial infarction in two patients (both in the first group), cytomegalovirus infection in one, and fungal sepsis in one (both in the second group). The patient survival in the two groups is shown in Figure 1.

Fig.1. Cumulative patient survival in recipients of combined grafts 1983–88 (—) and 1988–90 (···)

Pancreas graft survival

Of nine patients receiving pancreatic grafts only, three were insulin-independent for more than 1 year (one patient died with a functioning graft after 5 years). Six grafts lost function 1 week to 6 months post-transplant.

All five pancreatic grafts transplanted after a previous renal graft, were lost in chronic rejection within the first 6 months. Pancreas graft survival rates in recipients of combined grafts are shown in Figure 2 for the two techniques respectively.

Fig.2. Cumulative pancreas graft survival in recipients of combined grafts 1983–88 (—) and 1988–90 (···)

Renal graft survival

The cumulative renal graft survival is shown in Figure 3.

Fig.3. Cumulative renal graft survival in recipients of combined grafts 1983–88 (—) and 1988–90 (...+...)

Discussion

Thanks to improved surgical techniques and more effective immunosuppressive treatment, the results of pancreas transplantation have improved substantially in recent years and now approach or equal those of other organ transplants (Sollinger et al.1988; Sutherland and Moudry-Munns 1990). This only holds true if the pancreas is transplanted simultaneously with a kidney. In accordance with results reported from the International Pancreas Transplant Registry (Sutherland and Moudry-Munns 1990) our results of sequential pancreas after kidney and pancreas transplantation alone are significantly less successful. Even though the bladder drainage technique may facilitate diagnosis of pancreatic graft rejection by monitoring urinary amylase excretion, a large percentage of these grafts are lost in irreversible rejection. However, in recipients of combined renal and pancreatic grafts, the change from duct-occluded segmental to bladder drained whole pancreas grafts improved the 2-year pancreas graft survival from 50% to 75% in our patients. This may partly also be the result of better means of organ preservation and safer immunosuppressive therapy. The unsatisfactory results obtained in non-uraemic patients have again led us at present to restrict pancreas transplantation to uraemic diabetics and to perform simultaneous pancreatic and renal transplantation in these patients.

As reported by others (Mellert et al. 1990), the frequency of rejection episodes are significantly higher in recipients of combined grafts than in recipients of renal grafts only. Furthermore, a considerable percentage of the rejections are steroid resistant. However, most of them are successfully reversed by monoclonal or polyclonal antibodies. In our series of 17 combined pancreaticoduodenal

and renal transplants, only one pancreas was lost in rejection. The intensified immunosuppression may, on the other hand, impose an increased risk for the patient.

Even though the morbidity following combined transplantation may be higher than after renal transplant alone, the combined transplant does not increase the per- or post-operative mortality (Brekke et al. 1990). Long-term follow-up studies seem to indicate that a functioning pancreatic graft enhances the long-term survival of the simultaneously transplanted kidney and improves the life expectancy (Abendroth et al 1990, Brekke et al. 1990) and quality of life (Nakache et al.1989) of the recipient.

Based on experience with a total of 77 pancreatic transplantations it is concluded that the probability of pancreatic graft survival now approaches that of the renal graft, provided the pancreas is transplanted simultaneously with a kidney. Furthermore, preliminary results of long-term studies suggest improved survival and enriched quality of life for patients with a functioning pancreatic transplant. These results imply that combined renal and pancreatic transplantation should be the treatment of choice for the uraemic diabetic patient, provided this treatment is given before advanced extrarenal diabetic complications have developed.

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