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The Stockholm experience with pancreatic transplantation using enteric exocrine diversion

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Summary. Between April 1974 and June 1990, 128 pancreatic transplantations were performed. Of these 117 were with pancreatico-enterostomy. In four consecutive series of combined transplantations in uraemic diabetic patients the 1-year graft survival rate have successively improved (27%, 65%, 68% and 73%). In three similar series of single pancreatic transplantations the results also improved but still remained inferior (0%, 33% and 33%). In a series of combined transplantations performed in pre-uraemic diabetic patients the 1-year actuarial graft survival rate was only 25%. The results with pancreatic transplantation with pancreatico-enterostomy are now satisfactory. However, immunological loss graft function still constitute a major problem in the non- or pre-uraemic recipients. The metabolic control in patients with functioning grafts is normal or near-normal in the majority of patients followed for at least 1 year.

Key words: Pancreatic transplantation-Human-Enteric diversion.

Introduction

The results of pancreatic transplantation in the treatment of severe Type 1 (insulin-dependent) diabetes mellitus have recently shown a marked improvement. However, there is as yet no standard surgical procedure for pancreatic transplantation.

The most physiological technique is drainage of the exocrine secretion of the graft into the patient's bowel. When a pancreatic transplant program was initiated in Stockholm in 1974 we elected to drain the exocrine secretion into the patient's bowel by creating a pancreatico-enteric anastomosis (Groth et al. 1980). Initially this technique was associated with a high incidence of pancreatic fistulas. However, with refinements in the surgical technique and with the use of a pancreatic duct catheter for temporary protection of the pancreatico-enteric anastomosis the results became satisfactory. Furthermore, when pancreatico-duodenal grafts were introduced in 1988 the pancreatico-enteric anastomosis was replaced by a simple bowel-to-bowel anastomosis and the risk of enteric leakage has been more or less eliminated. We used enteric exocrine diversion in 117 of 128 pancreatic transplantations performed between April 1974 and June 1990. This report describes our experience with these transplantations.

Subjects and methods

Between April 1974 and June 1990, 128 pancreatic transplantations were performed at Huddinge Hospital. In four of the very early cases the pancreatic duct was simply ligated (Groth et al. 1976) and in seven transplantations performed between 1983 and 1984 the exocrine diversion was made to the patient's stomach (Tydén et al. 1985). These cases will not be discussed further.

Patients. Of the 107 diabetic patients, 10 underwent a second transplantation after the first had failed. All recipients suffered from Type 1 diabetes of long duration. Most of the transplantations were performed on uraemic diabetic patients; in 68 instances a combined renal and pancreatic transplantation was performed and in six instances the pancreatic transplantation was performed in a patient already having a renal graft. A further eight combined renal and pancreatic transplantations were performed in eight pre-uraemic recipients (mean creatinine 192 μmol/l; range 164-250 μmol/l). In 31 instances single pancreatic transplantations were performed in 26 non- or pre-uraemic diabetic patients. The indications included hyperlabile diabetes with or without defective hormonal counterregulation (five patients), severe progressive angiopathy (one patient), rapidly progressing retinopathy (two patients), severe neuropathy (two patients) and pre-uraemic nephropathy (16 patients). In four patients scheduled for a combined renal and pancreatic transplantation, severe preservation damage of the pancreas was revealed following revascularization of the pancreatic graft and the grafts were removed peroperatively. Consequently, these cases are included in the single pancreas transplant group.

Surgical technique. In the recipients the graft artery and the graft portal vein were anastomosed end-to-side to the iliac vessels. In the first five cases a simple end-to-end

pancreatico-Roux-en-Y loop enterostomy was created. In the following five transplantations a ducto-enterostomy was performed instead. All these grafts were placed extraperitoneally. However, because of technical problems with this technique, end-to-end pancreatico-enterostomy was reintroduced in 1981, but with some important modifications (Groth et al. 1982). Since then all grafts have been placed intraperitoneally. The cut end of the segmental grafts or the duodenum of pancreatico-duodenal grafts have mostly been anastomosed to a jejunal Roux-en-Y loop. However, in the most recent 18 cases with pancreatico-duodenal grafts the anastomosis was a simple side-to-side anastomosis between the donor duodenum and the recipient jejunum without the use of a Roux-en-Y loop. A catheter has been inserted into the pancreatic duct and then taken through the wall of the Roux-en-Y loop or the proximal part of the jejunum and brought out through a stab wound in the abdominal wall. By so doing we have temporarily exteriorized the pancreatic secretions, thus allowing the anastomosis to heal without being exposed to the digestive forces of the pancreatic exocrine secretion and also making the pancreatic secretions accessible for post-operative monitoring. The ductal catheter was removed 3-4 weeks after transplantation by simply pulling it out. Following this, the pancreatic secretions emptied into the recipient bowel.

Results

The series has been divided into five groups based on the period when the patients were treated (1974-1980; 1981-1983; 1984-1985; 1986-1987; 1988-1990). As shown in Table 1 considerable improvements in the overall results have occurred with time. When the series is divided into different patient categories, it is obvious that the best results have been obtained in uraemic diabetic recipients of combined renal and pancreatic grafts from the same donor. In the latest series of combined transplantations the 1-year patient and pancreatic survival rates are 82% and 73%. With single pancreatic transplantation in non-uraemic recipients, the results have also improved, but only from poor to intermediate. In the first part of the segmental graft series the graft losses because of pancreatic fistula were approximately 13%. This figure was reduced to 1% in the latest part of this series. With the use of pancreatico-duodenal grafts, there has been only one case of enteric leakage and this was not from the anastomosis but from the closed end of the duodenal segment.

Table 1. Results using pancreatic transplantation with enteric exocrine drainage in Stockholm, 1974-1990

	n	1-year patient survival	n	1-year graft survival
All cases				
1974-80	5	80%	8	0%
1981-83	16	81%	16	25%
1984-85	24	83%	25	52%
1986-87	38	95%	43	49%
1988-90	24	87%	25	49%
Combined renal and pancreatic transplantation in uraemic diabetic patients				
1974-80	0	0%	0	0%
1981-83	15	80%	15	27%
1984-85	20	90%	20	65%
1986-87	21	100%	22	68%
1988-90	11	82%	11	73%
Combined renal and pancreatic transplantation in pre-uraemic patients				
1987-88	7	100%	8	25%
Single pancreatic transplantations in non- or pre-uraemic diabetic patients				
1974-85	7	71%	10	0%
1986-87	13	85%	15	33%
1988-90	6	83%	6	33%
Pancreatic transplantation after kidney transplantation				
1974-87	4	75%	6	17%

Discussion

The optimal handling of the exocrine secretion in pancreatic transplantation has been much debated. As already mentioned, several techniques other than enteric drainage have been used to handle the exocrine secretion of the pancreatic graft. One reason for this was the high incidence of exocrine fistulas and infections encountered with enteric drainage in the early cases. Today most groups favour exocrine drainage to the recipient's bladder, as advocated by Sollinger et al. (1985). With such drainage the risk of bacterial contamination is reduced. Moreover, monitoring of the amylase excretion from the pancreatic graft, as reflected by the amylase level in the patient's urine, has been found useful in the diagnosis of rejection. However, some characteristic disadvantages with the bladder drainage technique have also emerged. These include urinary tract pathology and chronic metabolic acidosis, secondary to the loss of the alkaline pancreatic secretions via the bladder (Nghiem et al. 1987; Munda et al. 1987).

Diversion of the exocrine secretions to the bowel is obviously the most physiological technique. Initially the results with this technique were poor, but with refinements in the surgical procedure and with the application of a pancreatic duct catheter for temporary protection of the pancreatico-enteric anastomosis the incidence of exocrine leakage was greatly reduced (Groth et

al. 1982; Tydén et al. 1987). With the use of pancreatico-duodenal grafts the anastomosis needed for enteric drainage has been reduced to a simple bowel-to-bowel anastomosis and the risk of enteric leakage has been more or less eliminated. Indeed, in the present series of pancreatico-duodenal transplantations the entero-enterostomy anastomosis was considered to be so safe that the usual Roux-en-Y loop was omitted after the first seven cases, and in the latest 18 cases the duodenum was simply anastomosed side-to-side to the jejunum (Tydén et al. 1990). Although the enteric anastomosis was considered safe, a pancreatic duct catheter was used to divert the exocrine secretion to the exterior for the first few weeks. This permits monitoring of the pure pancreatic secretion. The amylase content and the cytology of the exteriorized juice are important markers for pancreatic graft rejection episodes (Brattström et al. 1987; Reinholt et al. 1988). This is of special importance when the pancreas alone is transplanted. In patients who receive simultaneous renal and pancreatic grafts the diagnosis of rejection can usually be based on renal markers. When the ductal catheter has been removed the diagnosis of rejection in the patients with a pancreatic graft alone must, however, rely on serum markers. We have shown that serum levels of pancreas specific protein (procarboxypeptidase B) (Fernstad et al. 1989) and anodal trypsin (Brattström et al. 1989) have a high correlation with inflammatory events in the pancreatic graft. However, these findings require further confirmation.

Most groups, including our own, have performed mostly pancreatic transplantation as a procedure ancillary to renal transplantation in diabetic patients with end-stage renal disease. By so doing we largely circumvent the question as to whether it is justifiable to expose the diabetic patient to a surgical procedure which is to be followed by chronic immunosuppression. The recent marked improvement in the results of combined renal and pancreatic transplantation has, however, made us decide to offer pancreatic transplantation also to non-uraemic diabetic patients. Further support for this change in policy has been provided by the finding that the vascular lesions in the diabetic patient with end-stage renal disease are not reversed, and perhaps not even halted, by pancreatic transplantation (Solders et al. 1987; Ramsay et al. 1988), a finding probably explicable by the fact that the secondary lesions in these patients are too far advanced to be affected. At present, however, the results with pancreatic transplantation alone are similar to those obtained with combined transplantation a few years ago. Graft function is lost for various reasons, including some of the well-known technical complications. Moreover, chronic rejection, which is uncommon in recipients of combined grafts in uraemic recipients, is responsible for most of the single pancreatic graft failures (Tydén et al. 1990). Apparently this procedure also requires a learning phase.

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