Complications of pancreas transplantation in an initial experience of a transplant programme

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Introduction

Pancreas transplantation has been demonstrated to be a successful method for treating insulin-dependent diabetes mellitus (IDDM) by the increasing number of centres using this procedure. Usually, pancreas transplantation is combined with kidney transplantation in patients affected by IDDM and its resultant end-stage nephropathy. Solitary pancreas transplant is performed only in very few patients, and those selected are non-uraeemic diabetic patients with extremely labile metabolic control who, for this reason alone, experience a low quality of life.

Over the last few years, pancreas transplantation increased from ~500 transplants in 1990 to >1000 transplants performed in 1996. This is due to an increase in both patient and graft survival. In fact, from 1987–1996, 1 year patient and graft survival worldwide are respectively ~90% and 80% [1,2]. Several factors account for this improvement: the use of new immunosuppressive drugs, the technical refinements of the transplant procedure, a more accurate diagnosis of rejection together with new and less toxic antiviral, antifungal and antibacterial agents which are now used for prophylaxis and treatment of post-transplant infections. Nevertheless, pancreas transplantation still presents a high incidence of surgical complications. Moreover, at the beginning of any surgical experience, technical complications are more frequent. Therefore, in this study, we review the surgical complications of pancreas transplantation in our first 21 patients.

Patients and methods

Since 1991 in our centre (Institute of General Surgery IV, University of Padova), 21 pancreas transplantations were performed; patient demographics are shown in Table 1. Of 21 pancreas transplants performed, 19 were simultaneous kidney–pancreas transplantation (SPK), one was a pancreas transplant alone (PTA) and one was a pancreas after kidney (PAK) in a patient who underwent a SPK previously and lost pancreas function because of rejection. In 16 patients, transplantation was performed with the technique described by Sollinger [3], which consists of pancreateico-duodenal transplantation with bladder drainage (BD) of the exocrine secretion. The single PTA was also performed with this technique. In five other patients, enteric drainage (ED) of exocrine secretion was performed by a duodeno-jejunal anastomosis.

Through a median laparotomy, a pancreatic graft was placed into the iliac fossa with vascular end to side anastomosis to the external iliac vessels. In all patients, we elongated pancreatic arterial vessels (splenic and mesenteric arteries) with interposition of a Y iliac graft. On the other side, portal vein extension with an iliac venous graft was performed only in two cases. Duodenocysto- or duodenou-jejunal anastomosis was performed with a circular stapler. The kidney was positioned into the left iliac fossa, intraperitoneally, with vascular end to side anastomosis to external iliac vessels and ureterocystoanastomosis using the Lich–Gregoir technique.

For induction therapy, quadruple immunosuppressive therapy with cyclosporin, azathioprine, steroids and antilymphocyte globulin was given. In the remaining eight patients, mycophenolate mofetil was used instead of azathio-

Table 1. Patient demographics

<table>
<thead>
<tr>
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<th>Value</th>
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<tbody>
<tr>
<td>M:F</td>
<td>13:8</td>
</tr>
<tr>
<td>Average age</td>
<td>40 years (range 30–58)</td>
</tr>
<tr>
<td>SPK, PAK, PTA</td>
<td>19/3/1</td>
</tr>
<tr>
<td>Diabetic age</td>
<td>30 years (range 15–56)</td>
</tr>
<tr>
<td>Dialytic age</td>
<td>2.64 years (0.5–8)</td>
</tr>
<tr>
<td>HBsAg+</td>
<td>1</td>
</tr>
<tr>
<td>HCV+</td>
<td>2</td>
</tr>
<tr>
<td>HLA matching</td>
<td>any match</td>
</tr>
<tr>
<td>Cold ischaemia time: pancreas</td>
<td>8.9 h (range 6–12)</td>
</tr>
<tr>
<td></td>
<td>kidney</td>
</tr>
<tr>
<td></td>
<td>11.4 h (range 9–15)</td>
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</tbody>
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SPK, simultaneous pancreas–kidney transplant; PAK, pancreas after kidney transplant; PTA, pancreas transplant alone.
prine. Antithrombotic prophylaxis consisting of subcutaneous heparin during the post-operative period and an antiplatelet dose of oral acetylsalicylic acid was used as supportive therapy. Moreover, the patients received antibiotic prophylaxis with Imipenem-Cilastatin and Fluconazole, anti-pneumocystis prophylaxis with trimethoprim sulphamethoxazol and antiviral prophylaxis with Ganciclovir. Rejection episodes were treated with steroid pulses. Steroid-resistant rejections were treated with a 7-10 day course of antilymphocyte therapy and recycling of a steroid taper.

**Results**

One patient died in the post-operative period. This patient was a 49-year-old woman who underwent a SPK with BD of exocrine secretion. A duodenal leak, an *Escherichia coli* peritonitis and a very serious pancreatic, which required the pancreatic graft removal on the 40th post-operative day, complicated her post-operative course. A respiratory syncytial virus and an *Aspergillus fumigatus* pneumonia, which led to the patient’s death in spite of immunosuppression tapering and withdrawal, complicated the subsequent post-operative course.

In the post-operative period, we observed one vascular technical complication consisting of a vein thrombosis with pancreatic infarction, two duodenal leaks and one ureterocystoanastomotic leakage which was treated with insertion of urethral stent by cystoscopy.

In 14 of 16 patients with duodenocystoanastomosis, we observed episodes of haematuria; three patients were treated with a cystoscopic diathermy coagulation. In four patients, a peri-pancreatic fluid collection was observed. They were treated with surgical drainage. In another patient, we drained a lymphocele, which appeared 6 weeks after transplantation.

Among delayed surgical complications, we observed five laparoceles, and three of them were surgically corrected. Five patients with BD of exocrine secretion presented some reflux pancreatitis episodes from 1 to 18 months after transplantation, which in four patients resolved after bladder catheterization. In three cases, BD was converted to ED, because of frequent reflux pancreatitis associated with urinary tract infection (one patient), urethritis with urethral stenosis (one patient) and serious vulvitis with urethritis and metabolic acidosis (one patient). In two patients, cholelithiasis developed, which needed laparoscopic cholecystectomy.

From an immunological point of view, in 13 patients there was at least one acute rejection; in seven patients the rejection was steroid resistant, and was treated with monoclonal antibodies in six patients and antilymphocyte globulin in one patient. Regarding long-term results, 18 patients are alive at present. Besides the patient described above, two patients who were HbsAg+ and HCV+ died because of hepatic failure due to an acute hepatitis 33 and 43 months respectively after transplantation. In both cases, the function of the two grafts was effective at the moment of death.

Finally another two patients lost renal function due to acute rejection; in fact their pancreases are still in good working order.

**Discussion**

In our experience, we recorded one post-operative death. In this patient, even if the actual cause of death was a respiratory syncytial virus and *Aspergillus* pneumonia, the first complication observed was a surgical one. In fact, we believe that the duodenal leak, which was diagnosed after only a few days, and the very serious pancreatitis caused a progressive debilitation of the patient. This event opened up the way for pulmonary aspergillosis to take hold. In fact, the association between multiple post-operative surgical complications and aspergillosis is well known.

As far as pancreatic exocrine secretion drainage is concerned, in 16 patients we performed a BD. This technique is the most frequently used in the world. According to the International Pancreas Transplant Registry [2], at the end of 1996, BD was used for the majority of pancreas transplants. However, ED has recently increased in popularity and, from 1994 to 1996, this drainage technique was carried out in 15% of US patients. In SPK results for 1994–1996, BD and ED were comparable, with 1 year graft survival rates of 82 and 77% respectively.

BD is preferred because it permits pancreas monitoring by 24 h amylasuria as an indicator of rejection. However, even in centres with vast experience, BD is burdened with several urological complications observed in ~50% of transplanted patients [4], such as haematuria, reflux pancreatitis, recurrent urinary infections, urethritis with urethral stenosis or rupture and metabolic acidosis. This high incidence of urological complications and the improvement of results of the ED technique [5,6] led us to choose this technique in five transplantations. In these patients, we preferred a side to side duodenocolon anastomosis, without utilizing a Roux ansa. Also, in three patients, we converted BD to a ED as frequently suggested [7,8]. It is a simple intervention, which is recommended when urological complications do not resolve after an adequate period of conservative therapy [8]. The presence of peripancreatic fluid collections represents another complication, which is observed in ~20% of transplanted patients, as shown in other medical literature [9] as well as in our experience. Several causes can be responsible for these collections, such as pancreatic or duodenal segmental fistula, haematoma, pancreatic phlegmon, lymphocele, pseudocyst or urinoma. The therapy is based on the use of hormones similar to somatostatin or, more often, on percutaneous or surgical drainage. In 30% of cases, these collections become infected and this eventually explained the necessity for organ transplantation [9]. Duodenal leakage and vascular complications are other complications frequently observed in pancreas transplantation.
In other institutes with a wide experience of the use of BD, duodenal leakage presents an incidence of 15% [10], while leakage with ED has been observed in only 3% of cases [5]. Some authors [11], in order to reduce the frequency of this complication when BD of exocrine secretion is performed, suggested a reinforcement of the duodenocystoanastomosis by winding of lateral umbilical ligaments. In every case, intraperitoneal positioning of the organ, compared with extraperitoneal, reduces the gravity of fistulas because the pancreatic juice can be partly absorbed by the peritoneum [12].

As regards vascular complications, they represent one of the most serious problems of pancreas transplantation. Thrombosis occurs during the first week after transplantation with a 12–20% frequency [13] and it can be arterial or, more frequently, venous. In order to prevent the thrombosis, almost all centres utilize anticoagulant therapy with dextran, warfarin or heparin. Since these drugs could cause bleeding, some authors suggest the use of aspirin only [10]. In our case, the use of subcutaneous heparin and acetylsalicylic acid in anti-aggregating doses for 20 days after transplantation did not cause any thrombosis, except in one patient. In this patient, there could have been an intimal lesion of the portal vein due to the cannulation of the inferior mesenteric vein during organ harvesting.

Conclusions

Even in our small experience, despite morbidity, pancreas transplantation is a relatively safe method of treating IDDM. It can be performed with improving success, enhancing quality of life and offering an opportunity to reduce the incidence of secondary diabetic complications.

References

2. IPTR—International Pancreas Transplant Registry. *Newsletter* 1997; 9