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Pancreas-Kidney Transplantation: Complications and Readmissions in 9-Years of Follow-up

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ABSTRACT

Over 9 years, we have performed 93 simultaneous pancreas-kidney transplants (SPKT). The morbidity of this procedure is high compared with kidney transplantation alone; readmissions are frequent and costs are higher. Herein we have presented the complications during follow-up of these 93 patients. Their mean age was 34 ± 6 years and prior dialysis time was 32 ± 25 months. The median hospital stay on the first admission for the transplant procedure was 22 days, including 2 days in the intensive care unit. Bleeding, thrombosis, and infection were the most frequent reasons for prolonged hospitalization. Thirty patients underwent ≥1 surgical reinterventions. Incidence of acute rejection episodes was 11.8%. After discharge, 74.2% of the patients had 197 readmission episodes with infection being the main cause, urinary tract infections, the most frequent; however, systemic viral and fungal infections required the longest readmission periods. The need for surgical interventions, graft dysfunction, and vascular problems were the remaining causes of readmission. At the end of follow-up, 87 patients were alive, 86 with well-functioning kidneys and 74 with normal functioning pancreata. Global survival rates for patient, kidney, and pancreas were 96%, 95%, and 81% at 1-year; 93%, 90%, and 79% at 5-years; and 93%, 90% and 79% at 9-years. Although pancreas–kidney transplant patients are complex presenting many management difficulties, our overall results represent a positive stimulus for diabetic patients.

Simultaneous pancreas–kidney transplantation (SPKT) display greater morbidity, length of admission, and number of complications when compared to kidney transplantation alone (KTA), leading to higher costs. However, SPKT remains the best treatment option for good long-term results among type 1 diabetic patients with chronic kidney failure. A recently published review of 1000 SPKT from a single center[1] reinforced this position statement of the American Diabetes Association. We have presented herein the results of our SPKT program, including the rate and type of complications, causes of surgical reinterventions, and readmission episodes after the initial discharge.

PATIENTS AND METHODS

From May 2000 to May 2009, we performed 93 SPKT always using enteric diversion and vascular anastomoses to the systemic circulation. Immunosuppression included antithymocyte globulin (ATG) tacrolimus, mycophenolate mofetil (MMF), and steroids. After the 6th month, it was our policy to progressively taper steroids to complete withdrawal whenever possible. Infection prophylaxis comprised vancomycin, fluconazole, and a third-generation cephalosporin in the first days, with contrimoxazole and valgancyclovir thereafter. We also prescribed aspirin and low-molecular-weight heparin as soon as possible after surgery, if there were no bleeding complications.

RESULTS

The mean age of the 93 patients was 34 ± 6 years with a 23 ± 5.5 years, duration of diabetes. They had been on dialysis for 32 ± 25 months excepting 4 who were grafted preemptively. Twenty patients had no HLA match with the donor. Their

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mean insulin daily dose and HbA1c before transplantation were 39 ± 12 U and 8.5 ± 1.7%, respectively. Insulin administration was stopped at 1.3 ± 2.8 days after transplantation. A subset of 19% of subjects needed transient dialysis. An acute rejection episode was detected in 11 patients (11.8%). It involved both grafts in 3 cases; only the kidney in 6; and only the pancreas in 2. In all but 1, who had repeated episodes, the initial rejection episode was efficiently treated. The median hospital stay on the first admission for transplant surgery was 22 days (range, 9–46), including 2 days in the intensive care unit (range, 1–88). In 13 cases, residence in the intensive care was ≥4 days. The initial reasons for the prolonged stay were bleeding (n = 9), pancreatic leak/infection (n = 3), or thrombosis (n = 1). Eleven of 13 patients needed ≥1 reoperations, 2 resulting in pancreas loss, 1 in kidney loss, and 2 in death.

When we examined all patients who needed ≥1 surgical reinterventions (even with shorter stay in the intensive care unit) we noted 30 patients (32.2%), namely the 11 above mentioned and 19 other subjects who mostly experienced infections or bleeding (Table 1).

After the initial discharge, 197 readmissions occurred among 69/93 patients (74.2%), who required 1–11 episodes/patient during the 3.7 ± 2.5 years follow-up period (range, 0.2–9.1). The incidence of readmissions was greater in the first year (57.4%). Infection was the main reason for hospitalization, followed by surgical interventions, graft dysfunction, and vascular problems (Table 2). The etiology of infectious episodes (n = 121), was most frequently urinary tract origin (55.4%; n = 67 episodes); followed by digestive (10.7%, n = 13 episodes); respiratory (6.6%; n = 8 episodes, 2 tuberculosis); viral (5.8%; n = 7) namely cytomegalovirus disease (n = 6) or Epstcin-Barr virus (EBV) (n = 1); graft related; intra-abdominal infection (5.8%; n = 7); and systemic fungal (3.3%; n = 3 including, 2 aspergillosis and 1 candidemia. The longest admissions (>30 days) were noted in the 3 cases of fungal infections and in the EBV case.

At the end of follow-up, 10 kidney grafts had failed due to thrombosis (n = 3), rejection (n = 3; 1 repeated acute 1 late acute, and 1 chronic rejection), sepsis (n = 2), and death with functioning grafts (n = 2). The losses due to rejection occurred from 2.5 to 7 years after transplantation. Four of these 10 patients were retransplanted; 3 are still functioning and 1 lost due to patient death. At our last evaluation, the 86 patients with functioning kidneys displayed a mean serum creatinine value of 1.12 ± 0.30 mg/dL; creatinine clearance of 79.6 ± 26.4 mL/min and urinary protein excretion = 0.3 ± 0.27 g/da. Steroids were totally withdrawn in >80% of patients.

Twenty-one patients lost their pancreas grafts due to late rejection (n = 2, >2 years after the transplant); thrombosis (n = 9); bleeding (n = 3); pancreatic leak/infection (n = 5) or patient death (n = 2). Four were retransplanted with a solitary pancreas, 3 of which are functioning, whereas 1 was lost due to noncompliance with immunosuppression and subsequent pancreas rejection. The 74 patients with functioning pancreas grafts show mean fasting glucose values of 80 ± 9.4 mg/dL HbA1c of 4.8 ± 0.4%, and C-peptide of 3.06 ± 1.46 ng/mL.

Six patients succumbed due to sepsis in the first 3 months (n = 2); invasive aspergillosis (n = 1); stroke (n = 1); myocardial infarction (n = 1); or unknown cause (n = 1). The acturial survival rates at 1, 5, and 9 years were 81%, 79%, and 79% for the pancreas graft; 95%, 90%, and 90% for the kidney graft, and 96%, 93%, and 93% for the patients, respectively.

Table 1. Complications Leading to Relaparatomy: Causes for the First Surgical Reintervention (n = 30 Patients)

Infection	9*
Bleeding	10*
Thrombosis - Px	5
Thrombosis - Kx	3
Intestinal occlusion	2
Urinary fistula	1

One to 12 reinterventions/patient.
*Four of these evolved to pancreas thrombosis.
Px, pancreas; Kx, kidney.

DISCUSSION

Our results reflect the complexity of SPKT. We observed the same causes for surgical reinterventions—infection, bleeding, and enzyme leak—as previously reported for enteric-drained patients.[1] The total length of hospital stay and intensive care residence were directly related to the presence of important complications: patients reoperated due to thrombosis, bleeding, pancreatic leak, or infection; or even patients without surgical reinterventions but who displayed relevant bleeding or infection. These patients also had an increased rate of graft loss and death. Intra-abdominal infection is a well-known risk factor for graft and patient loss;[2] pancreas thrombosis, for pancreas loss.[2]

The registered reoperation rate of 32.2% SPKT (n = 30) was similar to that observed in other series.[3] It eventuated in graft pancreatectomy in approximately half of these patients (17/30 patients) with an 18% incidence among all patients, which is similar to the experience of other centers.[3] Relaparotomy had been considered to be a risk factor for pancreas graft survival.[3] Not only the pancreas graft may be at risk when surgical complications occur, but also patient survival and a significant financial impact.[4]

The literature shows a reduction in patient survival during the first 3 months after a pancreas transplant compared with subjects a waiting a transplant. However, thereafter it reverses with transplanted patients performing better at 1 year.[5]

The EUROSPK study[6] reported a much higher 44.8% rejection rate than that in our study (11.8%), but we continued steroids for ≥6 months after transplantation, which may in part explain the difference. Four of our patients lost their grafts due to rejection: 1 pancreas and kidney loss, 2 kidney losses, and 1 sole pancreas loss. In all

Table 2. Causes of Readmission After First Discharge: Readmission Causes: 197 Episodes (in 69 from the Global 93 Patients, 74.2%)

Vascular (6.1%): 12 episodes in 8/93 patients (8.6%)	Cardiovascular	3	1 death	
	Cerebrovascular	1	1 death	
	Peripheral vascular	4		
Dysfunction Tx (8.1%): 16 episodes in 13/93 patients (14%)	With rejection	7	4 pancreas	3 kidney
	Without rejection	6		
Surgical (13.2%): 26 episodes in 22/93 patients (23.7%)	Ocular	4		
	Abdominal	8		
	Urinary	4		
	Others	10		
Infecction (61.4%): 121 episodes in 52/93 patients (55.9%)	Urinary (n = 67), digestive (n = 13), respiratory (n = 8), systemic viral (n = 7), systemic fungal (n = 4), others			

4, it was a late occurrence (>2 years after the transplant); early rejection episodes were all controlled. Only 1 of these subjects died due to a myocardial infarction at 6 months after failure of both grafts while on dialysis. However, pancreas rejection and consequent loss have been reported to decrease patient survival.[6] Also kidney rejection has been associated with reduced patient survival among SPKT patients.[2] This was not our experience, possibly due to the low rejection rate.

After the initial discharge, three quarters of our SPKT had to be hospitalized at ≥1 times, namely 197 episodes or 2 episodes/patient, which is similar to other published data.[7] Infection was the main cause. Not surprisingly, the urinary tract was a frequent site, as in other series.[7,8] After the initial transplantation admission, infection remains an important morbidity factor during patients follow-up. Surgical procedures were the second cause for readmission, as we included all cases: namely ocular, orthopedic, urinary (ureteral stenosis principally), and abdominal surgeries (wound related, intestinal occlusion, peripancreatic collections, etc). Graft dysfunction was the third cause for readmission (8.1%; n = 13 episodes), among half of which we established a diagnosis of an acute rejection episode (n = 7). Late rejections were more difficult to resolve: 4 patients lost their grafts. Vascular complications were not common; the 8 affected patients included 4 who suffered cardiovascular or cerebrovascular episodes leading to death in 2 cases.

We considered our survival rates to be good and not inferior to those presented by other similar[2] or larger series[1] at 1 year[2] and in the longer term.[1] In fact, our 9-year survival data—93% patient, 90% kidney, and 79% pancreas—were good when compared with other published 10-year results.[1]

Two important recently published papers have concluded that SPKT provides a significant extension to patient life,[1] namely 10 years longer than that of KTA from a deceased donors.[5] Our perception is that SPKT patients are really difficult to manage not only in the early period, but also in follow-up. Complications are frequent; costs are high and directly related to the complication rate. However it is satisfactory to observe good results among these patients.

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