Long-Term Outcomes of Pancreas After Kidney Transplantation in Small Centers: Is It Justified?

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ABSTRACT

Background. Currently, the long-term advantages of having a pancreas transplantation (PT) are debated, particularly in patients receiving pancreas after kidney (PAK) allografts. The United Network for Organ Sharing (UNOS) requires that a transplant center perform a minimum number of PT per year to remain an active PT center. The long-term outcomes and challenges of PAK in small pancreas transplant centers are not well studied.

Methods. In this retrospective analysis, we report short- and long-term outcomes in a small center performing 2–9 PT annually.

Results. Forty-eight PT (25 simultaneous pancreas and kidney transplantation [SPK], 23 PAK) were performed in our center. Donor and recipient demographics were similar in both groups. All suitable local donors were used for SPK. All organs for PAK transplantation were imported from other UNOS regions. Mean follow-up was 61 ± 46 and 74 ± 46 months for SPK and PAK, respectively. Patient and graft survival rates were similar in SPK and PAK groups and better than the reported national average. Four patients (11%) died (1 due to trauma, 1 brain lymphoma, 1 ruptured aneurysm; and 1 unknown cause). Two patients (4%; 1 SPK, 1 PAK) lost their grafts because of thrombosis on postoperative days 3 and 5 in 2002. No graft thrombosis occurred since 2002. Seven patients (15%) required reoperation (4 for bleeding, 2 anastomotic leaks, 1 small bowel perforation). Two patients (4%) developed post-transplantation lymphoproliferative disease. Five patients (11%) experienced cytomegalovirus antigenemia which responded well to antiviral therapy.

Conclusions. Compared with outcomes for diabetic patients on dialysis, current SPK and PAK short- and long-term results are favorable even in a small PT center. Therefore, unless there is a contraindication, PT should be offered to all type 1 diabetic patients with end-stage renal disease at the time of kidney transplantation or afterward.

DIABETES MELLITUS (DM) is a devastating disease. Diabetes is the number one cause of kidney failure and blindness in Western countries. Compared with the general population, patients with diabetes have a 25-fold increased rate of of blindness, a 17-fold greater rate of renal failure, 5 times the rate of amputation, and twice the incidence of heart disease. After 20 years of diabetes, nearly one-half of patients will be blind, have end-stage renal disease (ESRD), and/or have a major sensory/motor neurologic disturbance. Pancreas transplantation (PT) offers a return to euglycemia that may prevent some of the severe complications of diabetes [1–4]. It remains debatable whether PT provides long-term benefits to patients with diabetes, particularly in pancreas after kidney transplantations (PAK) [5–7]. Furthermore, the outcomes of PT in small centers performing <10 PT procedures per year

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have not been well studied. Therefore, in the present retrospective analysis, we report our outcomes of PT in a small center performing <10 transplantations per year. We also analyze the outcomes after PAK procedures and compare them with simultaneous pancreas and kidney transplantations (SPK).

METHODS

The medical records of all PT from July 2001 to July 2013 were reviewed. Forty-five PT (25 SPK and 23 PAK) were identified and included in this study. Surgical technique was previously described [8].

Immunosuppression

SPK patients received 3 doses of rabbit antithymocyte globulin (rATG, 1–1.5 mg/kg) and PAK patients were given 4–5 doses of rATG (1–1.5 mg/kg). Maintenance immunosuppression consisted of tacrolimus, mycophenolate mofetil (MMF), or enteric-coated mycophenolic acid (MPA) and steroids. Tacrolimus was started on postoperative day (POD) 1. Target tacrolimus trough levels were 10–15 ng/mL for the 1st 3 months, 7–10 ng/mL for the 1st year, and 5–7 ng/mL thereafter. One gram MMF was administered intravenously every 12 hours beginning immediately after surgery. Patients were switched to oral MMF when their bowel function returned. Patients were instructed to take full-dose MMF (2 g daily or its equivalent of MPA) unless not tolerated. Steroids were given as follows: 250 mg intravenously before surgery; 125 mg intravenously on POD 1; 30 mg prednisone orally begun on POD 2; followed by weekly dose reductions to achieve a maintenance dose of 5 mg/d by 1 month.

Prophylaxis

Antimicrobial prophylaxis with 500 mg ciprofloxacin twice daily was given to all patients for 4–5 days. All patients received valgancyclovir and trimethoprim/sulfamethoxazole for cytomegalovirus (CMV) and *Pneumocystis carinii* pneumonia prophylaxis, respectively, for 3 months starting at POD 2. CMV-seronegative recipients of kidneys from CMV-seropositive donors received valgancyclovir prophylaxis for 6 months.

All patients were examined daily during their immediate post-transplantation hospitalization. After discharge, they were seen in clinic twice weekly for the 1st month, once weekly during the 2nd month, and every other week in the 3rd month. Afterward, patients continued to be seen in clinic at least biannually. Complete blood counts, urinalysis, and urine cultures were routinely obtained during each postoperative visit.

Anticoagulation

All patients received 5,000 units of heparin before vascular clamping and continued on a heparin drip for 3–4 days. The aim was to keep partial thromboplastin time between 45 and 60 seconds. On POD 4–5, all patients received 81 mg oral acetylsalicylate daily and continued indefinitely unless contraindicated.

In addition, all patients received 300 μg octreotide intravenously every 8 hours for 2–3 days; then it was tapered to subcutaneously for 1–2 days and then discontinued. All patients also received 500 mg vitamin C intravenously for 5 days as an antioxidant.

After discharge, all patients were seen and carefully examined twice weekly for the 1st month, then once a week for the 2nd month, and every other week for the 3rd month. After 3 months, patients were seen bimonthly for the 1st year, and comprehensive laboratory testing was performed every month for the 1st year. All patients were seen in our clinic 3–4 times per year after the first year.

Statistics

Demographic and nonparametric outcome variables were assessed with the use of chi-square or Fisher exact analysis. Unpaired Student *t* test was used for comparison of parametric data. Kaplan-Meier estimation was used to study time to graft loss and rejection-free rates. A .05 level of nominal significance was used in all testing.

RESULTS

Patient and donor demographics are presented in Table 1. The Kaplan-Meier curves for patient and graft survival are shown in Figs 1 and 2. In comparison, Fig 3 shows national graft survival (online Scientific Registry of Transplant Recipients data). In 2002, 2 patients (4%; 1 SPK, 1 PAK) lost their grafts because of thrombosis on PODs 3 and 5, respectively. No graft thrombosis occurred since 2002. Seven patients (15%) required reoperation (4 for bleeding, 2 anastomotic leaks, 1 small bowel perforation). Two patients (4%) developed post-transplantation lymphoproliferative disease. Five patients (11%) experienced CMV antigenemia which responded well to antiviral therapy. No patient died because of surgical complications. One patient experienced acute cellular rejection 14 months after transplantation and was treated with rATG. Eight patients experienced perioperative increase in their serum amylase and lipase without any symptom of pancreatitis. All chemical pancreatitis resolved with conservative therapy.

DISCUSSION

Since the first PT in 1966 at the University of Minnesota, PT surgery is still considered to be a very complicated procedure [9]. Therefore, compared with kidney and even liver transplantation, fewer centers offer PT to their diabetic patients [10]. In 2008, only 126 of 258 (49%) transplant centers in the United States reported performing ≥1 PT [2].

Table 1. Donor and Recipient Demographics

	SPK (n = 25)	PAK (n = 23)	P Value
Recipient age (y), mean ± SD [range]	45 ± 6 [31–57]	41 ± 7 [30–50]	.08
Donor age (y), mean ± SD [range]	22 [7–45]	20.8 [10–42]	.7
Female (%)	31	25	.6
Nonwhite (%)	12.5	9	.7
CIT (h), mean [range]	13.6 [9–24]	16.3 [10–22]	.01
Imported from other DSAs (%)	8	100	<.00001
HLA MM, mean ± SD	4.5 ± 1.3	3.9 ± 1.4	.1
DR MM, mean ± SD	1.5 ± 0.5	1.2 ± 0.6	.1
PRA >30%	3	1	.3
CMV D+ to R−	4	3	.7

Abbreviations: CIT, cold ischemia time; DSA, donor-specific areas; MM, mismatch; PRA, panel reactive antibody; CMV, cytomegalovirus; D, donor; R, recipient.