Whole-organ pancreas transplantation at Baylor Regional Transplant Institute: a chance to cure diabetes

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The success of pancreas transplantation has improved over the past several decades with advancements in surgical technique, immunosuppressive medicines, and immunologic testing. We retrospectively reviewed our experience with pancreas transplantation from 1995 to 2008. At the Baylor Regional Transplant Program, 151 pancreas transplants were performed in 147 patients: 135 were simultaneous pancreas-kidney transplants, 10 were pancreas transplants after kidney transplants, and 6 were pancreas transplants alone. Follow-up information was available for 138 patients. The 1-year acute cellular rejection rate was 31.6%; the 30-day surgical reexploration rate was 10%; and the technical failure rate was 5.3%. Five-year pancreas graft survival rates were 67% for simultaneous pancreas and kidney transplants and 50% for pancreas transplants after kidney transplants. These outcomes exceed expected results as calculated by the Scientific Registry of Transplant Recipients. In addition, the median time to transplant was 3.8 months, compared with a US median of 14.1 months. Pancreas transplantation is currently the closest thing to a cure for diabetes and should be given as an option for diabetic patients with or without end-stage renal disease.

The first pancreas transplant was performed by Lillehei more than 40 years ago (1). As with most transplants in that era, it was fraught with complications, both technical and immunologic. However, with the advancements in surgical technique, immunosuppressive medicines, and immunologic testing, the success of pancreas transplantation has improved in the current era (2–5). Studies have demonstrated improved length and quality of life, as well as improvements in neuropathy (6–12), nephropathy (13–15), and retinopathy (16–20) with a successful pancreas transplant. Whole-organ pancreas transplantation is the best possible cure for diabetes at this moment (5). Using data from 1995 to 2008, this report summarizes the pancreas transplantation experience of the Baylor Regional Transplant Institute (BRTI) in Dallas and Fort Worth, Texas.

METHODS

The charts of patients who received simultaneous pancreas-kidney transplantation (SPK), pancreas transplantation after kidney transplantation (PAK), or pancreas transplantation alone (PTA) were retrospectively reviewed. Long-term follow-up extended up to 15 years after pancreas transplant. Graft and patient survival, wait list time, length of stay in the hospital, acute rejection rates, and insulin-free allograft survival were reviewed.

Surgical technique

BRTI uses whole pancreaticoduodenal allografts, in which donor pancreas allografts are harvested with the duodenum intact. This technique, which was developed nearly 30 years ago, has improved surgeons' ability to drain the pancreas' exocrine secretions.

Two methods of exocrine secretion drainage are used about equally: bladder drainage and enteric drainage; neither method demonstrates significant benefits over the other (21–24). BRTI uses enteric drainage, which prevents loss of large volumes of bicarbonate-containing fluids and has lower rates of hematuria and recurrent urinary infections. In addition, the endocrine function of the pancreas can be delivered to the recipient's bloodstream either systemically, via the common iliac vein or inferior vena cava, or through the portal system, through connection to the superior mesenteric vein. BRTI uses the latter technique because it is more physiologic.

When pancreas transplant is performed either simultaneously with a kidney (SPK) or alone (PTA), the incision is made in the midline, and both organs are then implanted. The pancreas can be implanted in an intraabdominal or retroperitoneal position. The renal transplant is implanted in a retroperitoneal fashion on the opposite side of the pancreas transplant. PAK transplantation usually occurs when patients choose to have a kidney transplant before pancreas transplantation, either because they are listed for and receive a deceased donor kidney transplant first or have a living donor available for renal donation. In this situation, the patient usually has two incisions,

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one for the kidney transplant operation and another for the pancreas transplant.

Recipient criteria

All potential recipients of a pancreas transplant are evaluated and presented to the kidney and pancreas transplant selection committee. The guidelines listed in *Table 1* have to be met by individuals, whether they have diabetes type I or type II. Once patients have medical and financial approval, they are placed on the transplant waiting list for the organs for which they are approved. Some individuals who apply for pancreas transplant are not found to be suitable for various reasons and therefore are listed for renal transplantation alone.

Donors

Pancreas transplant allografts are allocated according to the guidelines of the United Network for Organ Sharing. Pancreas and renal allografts are retrieved from the deceased donor pool. Once suitable donor and recipient combinations are achieved, the immunological cross-match is performed.

RESULTS

In the BRTI program, 151 pancreas transplants were performed in 147 patients between 1995 and 2008: 135 were SPK, 10 were PAK, and 6 were PTA. Follow-up information was available for 138 patients; 9 patients were lost to follow-up or were followed at another center. The 1-year acute cellular rejection rate was 31.6%. Graft survival rates off insulin are shown in *Table 2.* The 30-day surgical reexploration rate was 10% (n = 15), and the technical failure rate was 5.3% (n = 8). Based on the most current data from the Scientific Registry of Transplant Recipients (25), the waiting time for SPK at BRTI rate was statistically shorter than the national rate. The median time to transplant was 3.8 months, compared with the regional median of 12.7 months and the US median of 14.1 months. Furthermore, Baylor All Saints had a median time to transplant of 1.9 months.

Table 1. Guidelines for pancreas transplantation at Baylor Regional Transplant Institute

Variable	Simultaneous pancreas and kidney transplantation	Pancreas transplantation after kidney transplantation	Pancreas transplantation alone
Diabetes type	Type I or II	Type I or II	Type I only
Medical clearance	General workup	General workup	General workup
Cardiac clearance	Cardiac catheterization	Cardiac catheterization	Cardiac catheterization
Vascular clearance	As indicated	As indicated	As indicated
Renal clearance	<20	>60	>60
C-peptide	<10	<10	Nondetectible
Hemoglobin A_{1c} (if type II)	<6.5	<6.5	n/a
Insulin requirement (if type II)	<1 U/kg/day*	<1 U/kg/day*	n/a
Body mass index (kg/m^2)	<30	<30	<30
Flow cytometry cross-match	T cell –, B cell +/– with PRA = 0	T cell –, B cell –/– with PRA = 0	T cell –, B cell –/+ with PRA = 0
Age* (yrs)	18–55	18–55	18–55
Other	Nonsmoker	Nonsmoker	Nonsmoker

*Age is relative.

Table 2. Rates of graft survival for different types of transplants at Baylor Regional Transplant Institute

Transplant procedure	Graft	Graft survival (years)				
		1	3	5	10	13
Simultaneous pancreas kidney	Kidney	96%	90%	83%	78%	72%
Simultaneous pancreas kidney	Pancreas	88%	78%	67%	56%	56%
Pancreas after kidney	Pancreas	66%	50%	50%	N/A	N/A
Kidney alone (in patients with diabetes mellitus)	Kidney	92%	83%	71%	46%	41%
Kidney alone (in patients without diabetes mellitus)	Kidney	95%	86%	78%	62%	58%

DISCUSSION

The recent developments in surgical and immunosuppressive techniques have allowed pancreas transplantation to develop into an effective treatment to halt the progression of diabetes in selected individuals (2–25). According to the International Pancreas Transplant Registry (2), larger-volume pancreas centers also perform better and have better outcomes. BRTI is a high-volume center, performing 20 to 30 pancreas transplants yearly. The results presented here exceed the expected outcomes as calculated by the Scientific Registry of Transplant Recipients, based on several different factors.

The pancreas transplant team consists of many individuals. Though the BRTI group is skilled in liver and kidney transplantation, the pancreas transplant procedure is confined to a core group. Their experience includes pancreas donor management and acceptance, surgical pancreas transplantation techniques, postoperative management, and immunosuppressive

management. Additionally, medical management by transplant nephrologists experienced in the care of pancreas transplant recipients is part of our team approach. Transplant nurses familiar with pancreas transplantation are also a vital part of the team.

Another factor in BRTI's success with pancreas transplantation is its immunosuppression regimens. Studies in the mid 1990s demonstrated significantly better outcomes with the use of antibody induction to minimize rejection rates and immunologic graft loss. Prior to the induction era, first-year graft loss rates exceeded 20% due to rejection. These rates have been minimized, though rejection can still occur. The common agents used are antithymocyte globulin and the antibody to the IL-2 receptor. Additionally, studies have shown that tacrolimus is the immunosuppressant drug of choice for pancreas transplantation. A variety of successful immunosuppressive protocols are available, all of which include antibody use (5).

Patient selection is critical. Although strict criteria have been established, they are used mainly as guidelines and are reinforced by the kidney/pancreas transplant selection committee. The most common postoperative complication in diabetics is cardiac related (5), and therefore little variation is allowed. The immediate postoperative cardiac complication rate at BRTI in the past 10 years is minimal due to established selection criteria.

Surgical complications occur in our patients, as do pancreas and/or kidney graft loss. As with all transplants, this operation is not without risks (26, 27). The current state of the operation has yielded improved patient survival, improved graft survival, low wound infection rates, shorter hospitalization, and less intraoperative blood transfusion rates compared with only a few years ago. Additionally, with the techniques currently used, accessibility to the pancreas allograft by noninvasive and invasive techniques has become much easier for posttransplant monitoring.

Finally, the waiting list times for pancreas transplantation are shorter than expected, despite an increasing number of listings across the nation (25). Frequently, diabetics who qualify for SPK will receive transplants sooner than diabetics waiting for a kidney alone. This is akin to preemptive renal transplant for chronic kidney disease patients. The better outcomes are likely due to a healthier recipient population. Also, among diabetic patients, renal graft survival is superior in SPK and PAK patients than in patients with kidney transplants alone, even living-donor kidney transplants.

Successful pancreas transplantation at BRTI has rapidly become a recognized mode of effectively stopping the progression of diabetes. This transplant is currently the closest thing to a cure for diabetes and therefore should be given as an option for diabetic patients with or without end-stage renal disease. Islet cell transplantation, also available through BRTI (28), is a nonsurgical means of acquiring allo beta-islets and has a separate list of indications similar to that for patients being considered for PTA. The outcomes of pancreas transplant at BRTI exceed governmental standards, which further adds to the success and well-being of the patients being transplanted.

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