Pancreas and Kidney Transplantation

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Introduction

The availability of pancreas transplantation has markedly changed the options available for treatment of end-stage renal disease in type 1 diabetes. Since its introduction, pancreas transplantation has continued to change and outcomes have markedly improved, in part due to significant improvements in immunosuppression regimens. There is now substantial data suggesting benefits of improved glucose control with pancreas transplantation over kidney transplantation alone. The procedures available, outcomes, relative risks and benefits, and special considerations of this transplant population are reviewed next (see Table 1 for summary of outcomes).

Overview of the Procedures and Indications for Pancreas and Kidney Transplantation

There are four kinds of pancreas and kidney transplant procedures available to diabetes patients. Kidney transplant alone (KTA) is available for the treatment of end-stage renal disease of type 1 and type 2 diabetes, whereas pancreas transplant procedures are usually reserved for type 1 diabetes (Table 1). The distribution of pancreas transplants performed as reported to the United Network of Organ Sharing (UNOS) from 1997 to 2000 included the following (from the most to the least performed): simultaneous pancreas-kidney (SPK), pancreas after kidney transplantation (PAK), pancreas transplant alone (PTA), and other (pancreas + with at least one organ other than kidney [eg, pancreas-liver, pancreas-kidney-liver, pancreas-intestinal-kidney, pancreas-intestinal-liver, pancreas-intestinal-liver-kidney, pancreas-heart, or pancreas-heart-kidney]) [1•]. Although most pancreas transplant recipients are 21 to 45 years of age, the frequency of those transplanted over the age of 45 continues to increase.

Kidney transplant alone

The KTA procedure is used for the management of end-stage renal disease of type 2 or type 1 diabetes, particularly when a living related kidney transplant is planned. Usually, a single kidney is transplanted and the native kidneys of the recipient are left in place. One-year graft survival rates are 88% versus 93% for cadaveric versus living related donor, respectively, whereas 1-year patient survival rates are 92% versus 96%, respectively.

Simultaneous pancreas-kidney transplantation

The SPK transplantation procedure is the most common pancreas transplant procedure performed, representing 82% of the more than 10,000 pancreas transplants reported to the UNOS between 1987 and 2000 [1•]. SPK transplantation has the best 1-year pancreas graft survival rate (82%), which reflects the mean survival of all reporting institutions, but a number of centers report even higher (> 90%) 1-year pancreas graft survival rates [3]. One-year patient (95%) and kidney (92%) survival rates are comparable with those reported for KTA.

In this procedure, a pancreas and kidney are transplanted simultaneously. Both organs are usually from the

Kidney transplantation is preferred over dialysis for management of end-stage renal disease complicating type 1 or type 2 diabetes, for those who are eligible. Simultaneous pancreas-kidney (SPK) or pancreas after kidney transplantation (PAK) is an important alternative to kidney transplantation alone for type 1 diabetes patients if the patient is able to withstand the additional risks of these procedures, because of the benefits of glucose control on other diabetic complications. Pancreas transplantation alone (PTA) is most useful for the treatment of debilitating, frequent hypoglycemia complicating type 1 diabetes, if renal function is adequate. One-year pancreas graft survival is best after SPK (82%) but has significantly improved after both PAK (74%) and PTA (76%). The 1-year kidney graft and patient survival rates after SPK are similar to kidney transplantation alone.

Pancreas transplantation normalizes glucose beyond what can be achieved with insulin therapy and has been shown to decrease progression of or improve most, if not all, diabetic end-organ complications using current immunosuppression regimens. However, the diabetologist and endocrinologist should remain involved in the care of the pancreas or kidney transplant recipient for treatment of vascular disease risk factors such as dyslipidemia, surveillance of other diabetic complications including foot ulcers, surveillance and treatment of bone loss, and management of hyperglycemia if it recurs.
same donor, but simultaneous donor pancreas and living related kidney transplantation have also been reported [4].

The recipient usually has type 1 diabetes, but approximately 3% of all pancreas transplant recipients are reported to have type 2 diabetes [1]. The role of this procedure to treat diabetes caused primarily by insulin resistance (type 2), which requires the use of agents that further exacerbate their underlying disease, is unclear.

The exocrine duct is either drained into the bladder using a small “button” of duodenal tissue (bladder drainage [BD]) or into the bowel (enteric drainage [ED]). Loss of sodium bicarbonate-rich exocrine effluent with BD can result in volume depletion and metabolic acidosis, requiring conversion to ED at a later time. However, consequences of leak after ED can be far more serious with risk of abdominal sepsis. When pancreas transplantation was first being developed, BD was used exclusively, but now 63% of SPK procedures employ ED from the outset. One-year graft survival rates are comparable between operations using BD and ED, as reported to the pancreas transplant registry (85% vs 81%) [1].

The venous effluent of the pancreas graft is either placed into the systemic or the portal circulation, depending on the preference of the surgeon or the size or accessibility of the available vessels. Although portal drainage is considered more physiologic, significant, objective benefits of using portal over systemic venous drainage have not yet been demonstrated. Thus, most pancreas transplant recipients still receive systemic venous drainage (79%), which remains technically feasible in more individuals [1].

Pancreas after kidney transplantation
The PAK is the second most common pancreas graft procedure, with increasing incidence over time. It includes 1% of all pancreas transplants reported to the UNOS from 1987 to 2000, and 18% of those reported in 1999 to 2000 [1]. A kidney is transplanted from one donor, followed by a pancreas transplant from a second unrelated donor. The use of a living related kidney for the initial procedure followed by an unrelated pancreas transplant allows more individuals to receive both pancreas and kidney grafts, because the list for kidney allografts is greater than for pancreas grafts. The 1-year pancreas graft survival rate for this procedure has improved significantly in the last 5 years, but remains less (74%) than after SPK. BD remains in greater use than ED (60% vs 40%) and is associated with a better 1-year graft survival (76% vs 69%). PAK has the highest retransplant rate (27% vs 15% for PTA or 1% for SPK) [1].

Pancreas transplant alone
The PTA procedure entails transplantation of a whole pancreas graft with no history of kidney transplantation and no intent of an immediate kidney transplant procedure. PTA is most likely to be used for the treatment of frequent, severe hypoglycemia events complicating type 1 diabetes, but has been used in the treatment of severe nephrotic syndrome when the creatinine clearance remains near normal or rarely for other severe, nonrenal diabetic complications. The recipient has to have adequate renal function, usually a creatinine clearance of greater than 70 mL/min, or rapid decline in renal function may occur, especially with cyclosporine. BD remains more common than ED (60% compared to 40%) with this procedure, because the pancreas graft is more accessible for surveillance biopsies and urine amylase can then be used to diagnose early rejection, which can be difficult to detect in the absence of a kidney graft. In this category, 1-year pancreas graft survival is greater with BD than ED (81% vs 68%). Overall 1-year pancreas graft survival rate has improved in this category (76%) and is similar to PAK, but remains less than SPK [1].

Benefits of Pancreas and Kidney Transplantation
Retinopathy, nephropathy, and neuropathy
The microvascular complications of diabetes are directly linked to glucose concentration [5]. Thus, normalizing glucose after successful pancreas transplantation as is reported consistently [6] might be expected to stabilize or reverse microvascular complications. Pancreas transplant candidates have had diabetes for 20 to 25 years on average prior to considering transplant surgery, so many have had laser surgery for retinopathy. This damage cannot be reversed. However, recent studies suggest that retinopathy may improve 3 years after SPK and the need for further laser