Simultaneous Pancreas-Kidney Transplantation: Overview of the Ohio State Experience


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INTRODUCTION

Over 35 years ago, Lillehei and his colleagues reported on allotransplantation of the pancreas in humans. Since that time many advances have occurred in the field of transplantation. Currently pancreas transplantation has become a valid option in the surgical management of diabetes. Unfortunately, it is suitable for a limited number of diabetic patients and therefore its impact on the total number of diabetic patients is limited. In the United States diabetes is among the most common health problems. In the United States alone there are over 900,000 type I diabetic. Approximately 1100 pancreas transplants are performed each year which indicates that this procedure is being performed on a minority number of patients who lack the endocrine function of their native pancreas. Pancreas transplantation is done mostly in the setting of simultaneous pancreas-kidney. Over the years the surgical approach to pancreas transplantation has evolved from segmental transplantation to whole organ transplant. The drainage of exocrine function has also evolved from pancreatic duct injections to either bladder or bowel drainage. The venous drainage can be to the portal or systemic circulation. The advances in immunosuppressant medications have added more options to long term management of pancreas transplant recipients. In this paper we will review some of our single center experience with bladder exocrine drainage and systemic venous drainage for simultaneous combined pancreas-kidney transplantation.

DONOR SELECTION

Donor selection has remained a center specific preference with a tendency to underutilize the pancreas. Our donor selection criteria have been reported in the past. We follow the following guide lines in evaluating potential deceased donor: 1) No prior history of glucose intolerance, 2) age < 60 years, 3) a normal appearing pancreas at the time of the donor operation, 4) no evidence of pancreatic trauma. With time and experience we learned that hyperglycemia is not a good indicator for the quality of the organ. There are several factors that may lead to hyperglycemia in the donor. Stress of the trauma, the use of steroids, intravenous glucose, and thyrroxin cocktail are some of these factors. We currently evaluate organs from 55-60 years old donors. We rely on direct examination of the pancreas by the donor surgeon and overall quality of the donor. Most of pancreas transplants in our center are performed in the setting of simultaneous pancreas-kidney transplant (SPK). For this reason we have to consider the renal function as a factor in our decision making. The recent definition of extended criteria donor allowed us to use the kidney in a patient on the extended donor list and use the pancreas in a setting of isolated pancreas or pancreas after kidney transplantation. With the changes in
immunosuppressant medications, the outcome of isolated pancreas transplantation has improved significantly. Therefore, factoring these elements in the donor selection may increase the use of pancreas alone from such extended criteria donors.

RECIPIENT SELECTION

Recipient selection has remained unchanged for the most part. Diabetic patients are more prone to ischemic heart and peripheral vascular disease. Currently, the cardiovascular disease is usually the most limiting factor for recipients. Over time we have become more experienced in selecting recipients for SPK transplants. The waiting time is getting longer and sick patients may be better served with a living renal transplant followed by a pancreas transplant rather than waiting on dialysis for a simultaneous pancreas-kidney transplant. This has been reported by some programs. A thorough cardiac work up, with the assumption that the majority of these potential recipients may have coronary artery disease (CAD), is of vital importance. Several patients have been discovered to have silent coronary heart disease. These patients have undergone revascularization, either surgically or by interventional means. Other patients with non-correctable coronary heart disease either were found suitable for SPK or in some cases offered a kidney alone. Blindness and history of amputation are not considered contraindications at our center.

PROCEDURE

At our center all pancreatic donors were heart beating donors. The liver and pancreas are procured en bloc and separated on the back table. After flushing the pancreas with University of Wisconsin solution we inject amphotericin B in the duodenal segment and package the organ for transportation. All our recipients are performed via a midline incision. The pancreas is placed in the right iliac fossa and the kidney is placed in the left iliac fossa. Bladder drainage is performed in all patients. The entire procedure is intraabdominal. At the end of the procedure the kidney is placed in an extraperitoneal pocket that is dissected in the left iliac fossa to facilitate future biopsies. An arterial Y-graft is used regularly to construct the pancreas arterial supply on the back table (Fig. 1). We do not graft the portal vein. We actually believe that having a short portal vein is one of the reasons for having a low rate of pancreas thrombosis.

IMMUNOSUPPRESSION

Immunosuppressant medications have a major role in increasing the success rates of pancreas transplantation inside and outside the United States. With the introduction of cyclosporine in 1983, the survival of all solid organ transplants have improved. More recently the additions of Tacrolimus, mycophenolate mofetil, and microemulsion cyclosporine have given us more outcome options to select from to avoid some of the side effects without compromising the outcome. The recent introduction of rapamycin may help to propagate pancreas transplantation without steroid maintenance. We have always used antilymphocyte preparations for induction therapy. Our maintenance immunosuppression has been cyclosporine based at all times. We converted from traditional cyclosporine to microemulsion with its availability and from azathioprine to mycophenolate. Prednisone has been used until recently.

Fig. 1. Picture of a pancreatic allograft on the back table. In view are the short portal vein and the y-arterial graft.
when we switched to a steroid avoidance protocol with cyclosporine and rapamycin.

**PATIENTS AND GRAFT OUTCOME**

Experience with simultaneous pancreas-kidney transplantation is spreading widely but rather slowly compared to kidney and liver transplantation. It is being performed in chronically ill patients who have been suffering from diabetes on the average of 22 years. These patients are known to have coronary artery disease, retinopathy, autonomic neuropathy and micro and macrovascular disease which lead to major resource utilization. For the above reasons and others, pancreas transplantation is being performed mostly in the United States. The Ohio State University transplantation program launched pancreas transplantation in 1985. Initially we elected to perform sequential pancreas transplants in recipients of kidney transplants, and subsequently expanded to simultaneous pancreas-kidney transplants. From our initial experience, the simultaneous procedure became the procedure of choice for patients with type-1 diabetes and end stage renal disease. Our program has experience with about 600 cases of simultaneous pancreas-kidney transplants over a period of 15 years. During this long period the advances in the different aspects of transplantation have lead to increase in patient survival as has been reported by others. In our entire experience the one and 10 year patient survivals are 94% and 62% respectively (Fig. 2). This has been achieved with a decrease in the incidence of acute rejection and without increase in the incidence of viral infections (Fig. 3). The pancreatic graft one and ten year survival is 83%, and 50% respectively (Fig. 4). The renal graft one and ten year survival is 86%, and 50% respectively (Fig. 5).

Coronary artery disease is common among the potential recipients of pancreas transplant. Therefore we reviewed our outcome in SPK transplant recipients with coronary artery disease. We observed that transplanting patients after correcting CAD with surgery or stent placement is feasible with acceptable patient and graft survival. With this approach we continued to accept patients with treatable coronary artery disease and adequate cardiac reserve. In a different review, we examined the impact of the loss of either the kidney or the pancreas on the patient and the other organ. We also observed that the loss of the renal graft has a major negative impact on patient survival. On the other hand the loss of the pancreas had no impact on patient survival. In the same study, we observed that the loss of one organ has a major impact on the loss of the other organ. Death with a functioning graft remained to be the most common cause of graft loss in our experience. Obesity also was found to be a negative risk factor for patient survivals in our hands. Overall results of SPK transplantation have been

![Fig. 2. Kaplan-Meier curve of overall patient survival for SPK transplant recipients (N=598).](image)

![Fig. 3. Incidence of acute rejection in recipients of SPK recipients at Ohio State University during different induction regimens. ALG=Minnisota antilymphocyte globulin, OKT3/AZA=OKT3 and azathioprin, OKT3/Cellcept=OKT3 and Mycophenolate mofetil, Simulect=Basiliximab, and CellCept, TMC/Rapa=Rabbit thymoglobulin and Sirolimus with steroid avoidance.](image)
is becoming more frequent in the last few years. Some programs prefer a living donor kidney transplantation followed by deceased donor pancreas transplantation especially. It is clear that diabetic patients with end stage renal disease have lower survival compared to patients who received renal allografts and those receiving an SPK transplant do better then those getting a kidney alone.

ENTERIC CONVERSION

Bladder drainage of the exocrine function of the pancreatic allograft was the most commonly used method in the past. Enteric conversion is a major controversial issue regarding the drainage of exocrine function of the transplanted pancreas. It has been predicted that 20-25% of the recipients will need enteric conversion within three years. Therefore most of the pancreas transplant programs have changed to enteric drainage as the primary technique for exocrine function. Our center has continued to perform bladder drainage in all patients. In our experience the enteric conversion remained about 10%, even with more liberal use of this procedure. The indications for enteric conversion are mostly related to urologic complications. Late urine leak and chronic hematuria are the two most common indications. Recurrent urinary tract infections have resulted in few cases of enteric conversions (Fig. 6). In a recent review of 540 patients performed at our center with a mean of 5 years of follow up we

acceptable in most centers. Recently simultaneous deceased donor pancreas and living renal transplantation has been reported as another option for treatment of diabetic patients with end stage renal disease. However, this procedure is not widely spread and the short and long term results are not well understood.

One of the advances in recent years is the ability to obtain percutaneous pancreas biopsy with high level of safety. Atwell et al. reported 96% of adequate biopsy specimen with this technique. With these advances and longer waiting time pancreas after kidney transplantation

![Fig. 4. Kaplan-Meier curve of overall pancreas graft survival for SPK transplant recipients (N=598).](image1)

![Fig. 5. Kaplan-Meier curve of overall renal graft survival for SPK transplant recipients (N=598).](image2)

![Fig. 6. Indications for enteric conversion in recipients of simultaneous pancreas-kidney transplants.](image3)
have converted only 53 recipients. The immediate postoperative complications such as urine leaks are extremely uncommon and when they occur are easy to treat, usually with simple Foley catheter drainage. Some reports show an increased incidence of intrabdominal infections with primary enteric drainage. There are intermittent reports of early leaks with enteric drainage, accompanied by significant morbidity and associated mortality. 22 For all the above reasons we continued to perform bladder drainage, especially to provide patient safety.

CONCLUSION

At Ohio State University SPK is the most common setting for pancreas transplantation. Over the years and with more experience we have become more liberal with donor and recipient selection. This has not compromised the long term patient, kidney or pancreas survival. Bladder drainage has remained our drainage procedure of choice in all patients. This has been accomplished with very low, acceptable rate of enteric conversion. With advances in immunosuppression, the acute rejection rate has decreased without an increase in viral infections.

REFERENCES

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