Donation After Circulatory Arrest in Pancreas Transplantation: A Report of 10 Cases

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ABSTRACT

Introduction. Transplantation of pancreas allografts procured from donation after circulatory death (DCD) remains uncommon. This study reviews a series of pancreas transplants at a single center to assess the donor and recipient characteristics for DCD pancreas transplant and to compare clinical outcomes.

Methods. DCD procurement was performed with a 5-minute wait time from pronouncement of death to first incision. In 2 patients, tissue plasminogen activator was infused as a thrombolytic during the donor flush. All kidney grafts were placed on pulsatile perfusion.

Results. There were 606 deceased donor pancreas transplants, 596 standard donors and 10 DCD donors. Of the 10 DCD transplants, 6 were simultaneous pancreas-kidney and 4 were pancreas transplant alone. The average time from incision to aortic cannulation was less than 3 minutes. The median total ischemia time for the DCD grafts was 5.4 hours, compared with 8.0 hours for standard donors ($P = .15$). Median length of hospital stay was 7 days for both groups, and there were no episode of acute cellular rejection in the first year post-transplant for the DCD group (4.2 % for standard group, $P = .65$). There was no difference in early or late graft survival, with 100% graft survival in the DCD group up to 1 year post-transplant. Ten-year Kaplan-Meier analysis shows similar graft survival for the 2 groups ($P = .92$).

Conclusions. These results support the routine use of carefully selected DCD pancreas donors. There were no differences in graft function, postoperative complications, and early and late graft survival.

PANCREAS transplantation (PT) remains the treatment of choice for select candidates with diabetes, particularly type 1 and most commonly in association with a simultaneous kidney transplantation for end-stage diabetic nephropathy [1]. However, because the procedure carries potential risk for life-threatening complications after transplant, pancreata undergo strict selection criteria to minimize the risk-benefit ratio associated with the procedure [2,3]. Yet, like livers and kidneys, the supply of pancreata continues to fall further behind the demand, and this phenomenon can be traced back in part to the strict selection criteria that limit their use to roughly 20% of consented donors [4–9]. This ever-growing gap between the number of patients requiring transplants and the availability of suitable organs has spurred a search for ways to effectively increase the usable organ pool without sacrificing organ quality and increasing adverse events such as delayed graft function, technical complications, and graft rejection. One such method is increased utilization of the largely unused pool of donors who expire via cardiac or circulatory death. The use of these extended criteria organ donors has successfully increased the number of grafts available for transplantation [10,11]. In contrast to liver grafts, which show definitively that donation after circulatory death (DCD) livers may perform worse than deceased after brain death (DBD) donors [12], investigators have found similar functioning of DCD kidney grafts compared with standard grafts [13,14]. Pancreas transplants in particular have a limited but growing amount of data regarding the difference between DCD and DBD graft

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functioning. Transplantation of pancreas grafts procured from DCD donors has been reported but remains uncommon [10,11,15,16]. It has long been believed that due to the high sensitivity of the pancreas to ischemic insult, DCD pancreata should be avoided, and this belief is evident in the data [2,3,9,17–19]. Outcomes for these grafts are still not well described in the literature and few studies extend beyond 5-year follow-up. However, recent studies from Muthusamy et al [20], Qureshi et al [21], Shahrestani et al [13], and others [14,17] are demonstrating that with proper protocols, DCD graft function can be on par with that of DBD grafts at 5 years. This surprising trend is supported by our findings that extend to 10 years of follow-up.

This study reviews a series of pancreas transplants at a single center to assess the donor and recipient characteristics for DCD pancreas transplants and to compare clinical outcomes for these DCD and standard donors. Post-transplant clinical outcomes include post-transplant serum amylase and lipase, length of hospital stay, and short- and long-term graft survival.

MATERIALS AND METHODS

Study Population

The records of all pancreas transplants performed at a single center over a 13-year period from 2003 to 2016 were reviewed (606). There were 596 DBD pancreas transplants and 10 DCD pancreas transplants. A thrombolytic donor preflush protocol was introduced in July 2011. In 2 patients, tissue plasminogen activator was infused as a thrombolytic during the first liter of donor flush as described elsewhere [16]. Follow-up of the study population ranged from 6 months to 14 years.

In all DCD donors life support was withdrawn either in the operating room or nearby area. Heparin (300 IU/kg) was administered systematically at the time of withdrawal of life support according to the local donor hospital policies. After withdrawing life support, vital signs and oxygenation saturations were recorded. Organ procurement began 5 minutes after declaration of circulatory death by the declaring physician. The distal aorta was cannulated and flushed with preservation solution, and the infrarenal inferior vena cava was vented for exsanguination. The average time from incision to aortic cannulation was less than 3 minutes. A midline sternotomy was then made, the thoracic aorta was clamped, and the inferior vena cava was divided in the thoracic cavity. Ice-slush was placed on the abdominal organs and 3 to 4 L of cold histidine-tryptophan-ketoglutarate or University of Wisconsin solution was flushed through the aorta. Pancreas allografts were rapidly removed after completion of the aortic flush en bloc with the liver. The pancreata were then separated from the livers on the back table [22]. Special care is required to avoid damage to vital structures during DCD donor organ procurement. Aberrant arterial vasculature is particularly vulnerable because dissection is performed in a cold field without blood flow or pulses evident to assist in identification of the vascular anatomy. All kidneys at our center are preserved with pulsatile perfusion until implantation.

Recipient Operation

Back table preparation of the DCD pancreas is identical to that of a standard donor and is described in detail elsewhere [23]. Briefly, a splenectomy is performed, the proximal donor duodenal staple line is oversewn with interrupted seromuscular stitches, the mesenteric staple is oversewn with a running horizontal mattress stitch, and the donor superior mesenteric and splenic arteries are reconstructed using a donor iliac artery Y graft.

The transplant operation was performed through a midline incision. The pancreas was routinely positioned with the tail toward the pelvis and the head and duodenum oriented superiorly to facilitate the enteric anastomosis. Systemic venous drainage was performed to the right common iliac vein or to the vena cava. Arterial perfusion of the allograft was routinely established from the right common iliac artery, although on rare occasions where this vessel was found to be diseased or had been the site for arterial anastomosis for a prior transplant, the inflow would be established either from the aorta or the left common iliac artery. All pancreas allografts were drained enterically using a stapled technique as described elsewhere [24]. In cases of simultaneous pancreas and kidney transplantation (SPK), the allografts were positioned ipsilaterally as described elsewhere [25]. Total ischemia times were defined as the time from cardiac arrest of the donor patient to reperfusion in the recipient patient for DCD grafts. For DBD grafts, total ischemia times are defined as the time from cross-clamping of the thoracic aorta until reperfusion in the recipient. This includes both warm and cold ischemia times.

The induction immunosuppression protocol consisted of 5 doses of rabbit antithymocyte globulin (1 mg/kg/dose) and maintenance with tacrolimus (target trough 6–8 ng/mL), sirolimus (target trough 3–6 ng/mL). For pancreas transplantation alone (PTA), mycophenolate mofetil (500 mg orally twice a day) was also included as part of the maintenance regimen. Steroids were exclusively used as a premedication for rabbit antithymocyte globulin and were discontinued following induction in all recipients. As of October 2007, due to the higher incidence of chronic immunologic graft loss in the PTA population, we have also added a single dose of rituximab (150 mg/m^2) as well on postoperative day 1. All recipients received routine perioperative antibiotics, prophylaxis against cytomegalovirus with oral valganciclovir and prophylaxis against *Pneumocystis jiroveci* pneumonia with trimethoprim and sulfamethoxazole, unless contraindicated. Systemic anticoagulation was not routinely used unless the patient had a specific history of a coagulation disorder.

Post-transplant graft injury was assessed using measured laboratory values including peak serum amylase and lipase levels. Early graft loss was assessed by 7- and 90-day graft loss, and long-term graft survival was assessed using the Kaplan-Meier method with log-rank analysis (10 years).

Standard statistical testing was conducted with commercially available software. The comparisons were performed with analysis of variance for numerical data and the χ^2 test for categorical data. Survival rates were estimated with the Kaplan-Meier method. A P value less than .05 was considered to be significant. The retrospective analysis of data from the transplant research database at our center was reviewed and approved by the institutional review board of the Indiana University School of Medicine.

RESULTS

Donor and Recipient Characteristics

Donor and recipient demographics are summarized in Table 1. Among the 10 DCD donors, 5 had their cause of death listed as anoxia, 4 were traumatic brain injury, and 1 was a cerebrovascular accident. There were no statistically significant differences in donor demographics between the DBD and DCD donors including gender, race, age, body mass index (BMI), and location of graft (local or not local). There were also no significant differences between standard