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Simultaneous *en-bloc* pancreas and kidney transplantation from a small paediatric donor after circulatory death

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Abbreviations

SPKT simultaneous pancreas and kidney transplant

DCD declaration of circulatory death

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Abstract

Simultaneous pancreas and kidney transplantation (SPKT) is an effective treatment option for patients with type 1 diabetes and end stage renal disease. Increasing demands for organs for transplantation coupled with a rise in age and size of adult donors has led to greater utilization of paediatric donors, and with good outcomes. Nonetheless, there remains reticence amongst transplant surgeons to transplant pancreases from small paediatric donors despite the optimal characteristics and macroscopic features of the younger pancreas. We report a successful case of SPKT from a small paediatric donor and explore the aspects of potential concern that might have led some clinicians to decline these organs. We also discuss the measures taken to overcome potential obstacles to successful transplantation from this donor source, and the rationale behind them.

Introduction

Simultaneous pancreas and kidney transplantation (SPKT) is an effective treatment option for patients with type 1 diabetes and end stage renal disease.¹ Donor organ quality is directly related to transplantation outcomes; in pancreas transplantation, donor age and obesity are major determinants of successful transplantation.^{2,3} Increasing demands for organs for transplantation coupled with a rise in age and size of adult donors has led to greater utilization of paediatric donors, and with good outcomes.⁴⁻¹² Nonetheless, there remains reticence amongst transplant surgeons to transplant pancreases from small paediatric donors despite the optimal characteristics and macroscopic features of the younger pancreas. In some circles, small paediatric pancreas donors continue to be considered *marginal* due to concerns over insufficient pancreatic beta-cell mass to meet adult metabolic requirements¹³, size matching⁴ and the increased risk of thrombosis.¹⁴ Paediatric donation for liver, kidney and intestinal transplantation is common, not least because of the important consideration of matching the size of the donor to the recipient. The pancreas, however, is almost exclusively transplanted into adult recipients, and hence size matching is afforded an entirely different consideration.

We report a successful case of SPKT from a small paediatric donor and explore the aspects of potential concern that might have led some clinicians to decline these organs. We also discuss the measures taken to overcome potential obstacles to successful transplantation from this donor source, and the rationale behind them.

Case report

A 43-year-old female with complex type 1 diabetes (dialysis dependence, retinopathy and hypoglycaemia unawareness) was admitted for SPKT. She had a disease duration of 35 years and required 50-60 units of insulin a day. The donor was a 4-year-old female who was involved, as a pedestrian, in a road traffic collision at 40-50 miles per hour. The donor suffered a cardiac arrest and extensive cranial and thoraco-abdominal injuries which necessitated emergency laparotomy revealing distended small and large bowel loops, but no major visceral injuries. The donor was transferred to a regional trauma unit with a laparostomy (open abdomen) and vacuum dressing in situ. The patient suffered two further cardiac arrests prior to cessation of ventilation. Brain stem death could not be declared and, therefore, upon withdrawal of life sustaining treatment and declaration of circulatory death, a supra-rapid laparotomy and *en-bloc* organ procurement was performed with cold in-situ preservation using University of Wisconsin solution. The time from withdrawal of treatment to asystole was 7 minutes, and was followed by a further 10 minutes until cold preservation was commenced.

The weight and height of the donor and recipient were 16Kg/111cm and 64Kg/166cm respectively. HLA mis-match was 1:2:2. The organs had very good pre-donation function and were of macroscopically excellent quality (non-fatty, non-fibrotic). A joint decision was made by two experienced surgeons to accept and transplant the offered organs, one of whom also performed the organ procurement procedure. Via a modified Rutherford-Morrison incision the pancreas and single left kidney (1 artery, 1 vein, 1 ureter) were transplanted *en-bloc* into the extra-peritoneal right iliac fossa (*Figures 1*). An aortic patch containing the left renal artery, SMA and coeliac artery was anastomosed to the recipient's right common iliac artery. The left renal vein and portal vein were anastomosed consecutively to the recipient's common iliac vein, whilst the ureter was anastomosed to the bladder in the standard fashion. No anti-vasospasm therapy was applied. Reperfusion of the

organs was brisk and uniform. Finally, the peritoneum was breached to facilitate anastomosis of the duodenum to a loop of terminal ileum and thereafter both the transplanted pancreas and kidney were intra-peritonealised. The total ischaemic time was 17 hours and 42 minutes (re-warm ischaemia 73 minutes). Standard therapeutic anti-coagulation (weight adjusted intravenous heparin) and immunosuppression (Campath, Tacrolimus, Mycophenolate) regimens were followed post-operatively. However, a return to theatre to control active bleeding from the duodenal anastomosis mandated a change from therapeutic to prophylactic anti-coagulation regimens – this was complicated further by an upper limb deep vein thrombosis. At 8 months post-transplantation the patient had excellent dual graft function with normal blood glucose levels and a stable creatinine value of ~120 pmol/L.

Discussion

Transplantation of kidneys from paediatric donors into adult recipients is a well-established technique with successful outcomes, even from very small donors.¹⁵⁻¹⁸ In recent years, the technical feasibility of pancreas transplantation from paediatric donors has also been demonstrated.⁴⁻¹⁴ Yet, reports from small donors are few in number, and may reflect ongoing concerns within the pancreas transplant community regarding the use of such donors. Low blood flow and venous pressures in the recipients' central venous system predispose donor pancreases, especially organs with small calibre portal veins, to venous stasis and hence the risk of thrombosis. Meanwhile, the multiple anastomoses required to reconstruct the donor pancreas arterial vasculature increases the risk of stenosis, especially in smaller vessels. To overcome this, transplantation of the pancreas and kidney from small donors has largely been performed *en bloc*.^{4,11} In some instances, dual kidneys have been transplanted along with the pancreas, meaning that only a single aortic conduit and caval outflow was required.¹¹ Other techniques, such as the *piggy-back*, anastomosed the reconstructed pancreas onto the aorto-caval conduits which were, themselves, anastomosed to the recipient.¹²

However, the published *en bloc* techniques have their limitations.^{4,6, 12} First, the transplantation of dual kidneys from a young donor with excellent function, precludes another recipient from receiving a potentially excellent kidney graft. Paediatric donors are in short supply, especially for paediatric recipients, and hence there is an argument against promoting dual kidney transplants from these

donors. Our technique enabled the maximum number of recipients to benefit from the donor. Second, the portal vein requires its own anastomosis irrespective of whether this is to a donor conduit or to the recipient's native vein. Separate anastomoses for the portal vein and renal vein means that, in the event of a loss of the pancreas graft secondary to a portal vein thrombus, the viability of the kidney graft would not be compromised. This is because a thrombus from a separate and more proximal portal vein anastomoses would propagate cranially, and a transplant pancreatectomy could be performed without disrupting the venous anastomosis from the kidney. Finally, the single arterial anastomosis of the aortic conduit (containing the coeliac axis, superior mesenteric artery and left renal artery) minimised the potential risks from disrupted perfusion, bleeding, stenosis, and pseudoaneurysm.

In this reported case, organ donation followed the declaration of circulatory death (DCD); this is standard practice in the UK for such a young donor.¹⁸ Other reported cases of small paediatric pancreas donation have followed the diagnosis of brain death.^{5,7} This distinction is important because the additional hypoxic insult experienced during the warm ischaemic time associated with DCD donation drives a more time-critical retrieval and transplantation process. Measures to reduce both warm and cold ischaemic time, such as eliminating unnecessary and complex vascular anastomoses, are likely to play a significant role in improving outcomes.

Donor pancreas mass poorly correlates with post-transplantation graft function, and islet cell yield from very small donors may result in excellent metabolic function in adult recipients^{4,10}. SPKT from paediatric donors are reported to have superior long-term outcomes compared with adult donors.^{5,10}

At 5 years follow up, mean (SD) glucose levels and HbA1c levels were lower in recipients of paediatric donors (85.3 ± 13 mg/dL, respectively) vs adult donors (Glucose: $85.3 [13]$ mg/dL vs $95.1 [29]$ mg/dL, $p = 0.001$. Hb A1c: $5.5 [1.0]$ % vs $5.9 [3.5]$ %, $p = 0.010$).⁵ Moreover, Krieger *et al* found no significant difference in graft survival when “non-ideal” donors (including paediatric donors) were utilised compared with grafts from “ideal” adult donors and supported the further expansion of the pancreas donor pool to include these groups.⁸ Biglarnia *et al* demonstrated successful utilisation of very small paediatric donors (age 1.5-26 months, weight 4-15kg) and achieved excellent graft function, despite presumed graft immaturity and high recipient/donor weight ratio.¹⁴ Historical concerns that paediatric pancreases are suboptimal, because of a presumption that lower islet mass

from paediatric donors are incapable of meeting the metabolic requirements of adult recipients are unfounded.^{5,10}

It has been demonstrated that infant pancreases are a rich source of islet cells.¹⁹ It has also been suggested that due to reduced exposure of paediatric islet cells to environmental and genetic stressors, paediatric pancreases are more resilient to the hypoxic stress following transplantation, and have an increased replicative capacity compared to adult donors.⁵ The adaptive capability of very small paediatric pancreases has been demonstrated, with recipient computed tomographic scans identifying somatic growth of up to 140% over a median follow up of 750 days.¹⁴ Furthermore, paediatric β cells have superior insulin secretory regulation compared to adult cells, possibly due to the reduction of intracellular ATP concentration associated with advancing age.²⁰ Despite this, paediatric donors continue to be underutilised for pancreas transplantation because of an inaccurate assumption over insufficient levels of islet cell mass.

In conclusion, pancreas transplantation from small paediatric donors after circulatory death is both safe and efficacious. Our reported technique facilitates the maximum utilisation of all organs for transplantation whilst minimising the risks associated with excessively complex vascular reconstruction. Continued characterisation of this source of high quality organs as *marginal* is inappropriate.

Disclosure

The authors of this manuscript have no conflicts of interest to disclose as described by the *American Journal of Transplantation*.

Figure Legends

Figure 1: En-bloc pancreas and kidney graft prior to transplantation. A – Aortic patch; D – Duodenum; LK – Left kidney; LRV – Left renal vein; PV – Portal vein; U - ureter

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Figure 1

En-bloc pancreas and kidney graft prior to transplantation.

A – Aortic patch; D – Duodenum; LK – Left kidney; LRV – Left renal vein; PV – Portal vein; U - ureter