Pancreas Transplantation From Pediatric Donors: A Single-Center Experience

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Background. Pancreas allografts from pediatric donors are considered less suitable due to the increased risk of surgical complications and reduced islet cell mass that may compromise function. **Methods.** All pancreatic transplants, procured from donors younger than 18 years, between January 2007 and March 2017, were included in the analysis. The grafts were subdivided into 3 groups by donor's weight: less than 30 kg, 30 to 60 kg, greater than 60 kg. Analysis of patient and graft survival was done between the groups, and subsequently between the pediatric cohort and the adult-donor control group. **Results.** Sixty-three pediatric-donor pancreas transplants were performed. The mean donor age and weight were of 12.10 ± 4.13 years and 47.8 ± 21.3 kg. Excellent metabolic control was achieved in 59 (93.65%) patients at the time of discharge and at a mean 5 year follow up, with the average hemoglobin A1c of 5.30 ± 0.61% and blood glucose level of 102.75 ± 20.70 mg/dL in those with a functioning graft. Nine graft losses were registered, of which one (1.6%) was due to arterial thrombosis. Eight (12.7%) patients experienced rejection. Overall graft survival and patient survival were of 85.7% and 92.1%, respectively, at a median follow-up of 37.07 months (minimum, 0.19 to maximum, 119.57). No differences among the 3 groups were identified. Long-term patient and allograft survival was comparable to that of the adult-donor pancreatic transplants. **Conclusions.** Pediatric-donor pancreas demonstrated excellent short-term outcomes with no surgical complications and promising long-term outcomes despite the smaller islet mass. Pancreata from pediatric donors should not be marginalized and can offset worsening organ shortage.

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According to the International Diabetes Federation, the overall annual increase in the incidence of type 1 diabetes (T1D) is approximately 3% to 4%.[1,2] In the United States, the peak age at diagnosis is approximately 14 years,[3] and 5% of adult-onset diabetes are diagnosed as T1D.[4] Incidence of T1D varies by age and geographical location, ranging from 4.9 per 100000 people in Austria to 61.7 per 100000 people in the United States.[3,5]

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Vascularized pancreas transplantation is a well-established treatment for patients with insulin-dependent diabetes mellitus to restore normal glucose levels and serum levels of glycosylated hemoglobin A1c (HbA1c).[6,7] Unfortunately, despite the implementation of the new pancreas allocation system in October 2014, the 2015 Annual Data Report reveals that pancreas utilization did not increase as expected while the waiting time for a pancreas transplant continues to rise. Currently, the percentage of active listings is approximately 65%, the highest since 2008.[8]

Use of pediatric organs for transplantation has been proposed as a strategy to increase pancreas donor pool and optimize donor utilization. Historically, pediatric donor pancreata were considered "less ideal" based on the presumed increased risk of surgical complications, in particular of thrombosis, and on the historical assumption that the reduced islet cell mass could compromise the graft function.[9-11] Despite some recent studies[12-15] that promote utilization of these organs, the Transplant Community appears to be skeptical of their outcomes and many Transplant Centers still reject a priori pediatric donors.

At the University of Illinois at Chicago, pancreas grafts procured from pediatric donors have been widely used since 2007. Hereby we report our experience and the short- and long-term transplant outcomes.

MATERIALS AND METHODS

This is a retrospective cohort analysis of all pancreas transplants performed from May 2007 through March 2017 at an

urban, academic medical center. This study was approved by the institutional review board protocol number 2014-0452.

Pediatric donors were further divided into 3 groups according to the donor weight: group 1, less than 30 kg; group 2, between 30 and 60 kg; and group 3, greater than 60 kg. The transplants from donors 18 years and older represented the adult control group for patient and allograft survivals. Primary objective was to compare allograft function at 5 years between the 3 pediatric donor allograft groups. Secondary outcomes included comparison of transplant surgery related complications and postoperative allograft function. Finally, patient and allograft survivals of the pediatric cohort were compared with the adult control.

Donor demographics, including sex, race, age, weight, cause of death, cytomegalovirus (CMV) status, and transplant type, were obtained from United Network for Organ Sharing. The following information on the donor's hospital course in the intensive care unit (ICU) were also included in the analysis: number of inotropic drugs needed, pancreatic function at the time of the procurement (fasting blood glucose [FBG], amylase), insulin requirement and steroid treatment.

Recipient demographics analyzed include gender, race, age, body mass index (BMI), previous transplants, CMV status, type of diabetes, panel-reactive antibody, and crossmatch results. The analysis of transplant parameters included length of surgery, cold ischemia time (CIT), estimated blood loss, blood transfusion during surgery and during hospitalization, exocrine drain management, length of stay, immunosuppressive therapy, anticoagulation prophylaxis, and antiviral therapy. Early postoperative surgical complications leading to reoperations were analyzed and compared between the pediatric groups.

Long-term graft function was defined as complete freedom from insulin and measured with serial determinations of HbA1c, FBG and C-peptide levels at 6 months and at years 1, 2, 3, 4, 5, and at the most recent follow-up. Graft loss was determined by the stable requirement of insulin treatment. Cause of graft loss was also analyzed.

During the initial study period, the preferred method of exocrine drain management changed from bladder drained to enteric drained pancreas for all pancreas transplants. Recipient procedure started with the full mobilization of the right colon. The final position of the pancreas was head-down with the portal vein to the inferior vena cava, just before the bifurcation and the "Y" graft to the common iliac artery on the right. This position allowed us to keep the portal vein the shortest possible. In some circumstances, to prevent kinking or obstruction, the portal vein had been shortened. When performing simultaneous pancreas-kidney (SPK) transplantation, the kidney was positioned on the left with vascular anastomosis to the external iliac vessels. Screening pancreas ultrasonography protocol was performed in all cases on day 1 and as needed (monitoring collection, vascular waveform) for the rest of the hospitalization.

In terms of medical management, the immunosuppression and prophylaxis protocols are standardized for all pancreas recipients. Induction therapy consists of rabbit antithymocyte globulin and methylprednisolone followed by a rapid, 5-day steroid taper. Maintenance therapy consists of mycophenolate and tacrolimus (10-15 ng/mL for the first 2 months, then 5-10 ng/mL thereafter). Institutional immunosuppression regimen did not change during the study period. All patients received antimicotic prophylaxis with fluconazole 200 mg during the first postoperative week. The antimicrobial prophylaxis included ampicillin/sulbactam and vancomycin. Cytomegalovirus prophylaxis included valganciclovir 450 mg daily for 6 months except those with negative CMV serology in both donor and recipient. In that case, 1 month of acyclovir was used for herpes simplex virus prophylaxis. The anticoagulation protocol consisted of low dose, straight rate heparin at 300 units per hour until patient could transition to an oral regimen. Oral prophylaxis consisted of aspirin-dipyridamole 25 mg/200 mg every 12 hours for 2 months, followed by lifelong 81-mg aspirin daily. No special consideration was given for pediatric versus adult donor pancreas recipients.

Descriptive and quantitative variables were compared between the 3 pediatric groups in a multivariate analysis. Patient and graft survivals at 5-year follow up were analyzed in the pediatric cohort and compared with the survival rates of the adult control group. In the multivariate analysis, donor age, donor weight, donor inotropic support in the ICU, transplant era, and type of transplant were studied as risk factors and HbA1c and FBG as predictive values of graft survival.

Statistics

Patient and graft survival rates were estimated using Kaplan-Meier curves and compared between groups using a log-rank test. Patients lost at the follow-up with functioning graft were included in this analysis. Visual binning was the statistical method used to obtain the 3 homogeneous weight groups. Continuous variables were reported as means ± standard deviation and compared between groups using analysis of variance test. Categorical variables were summarized as percentages and compared between groups using Fisher exact test. *P* values were calculated using 2-tailed tests and considered significant if less than 0.05. A multivariate Cox regression analysis was performed to assess the effect of different parameters on graft survival. Donor age, donor weight, donor inotropic support in ICU, type of pancreas transplant, transplant era, HbA1c level at 1 year, and blood glucose level at 1 year were taken into account. All analyses were performed using IBM SPSS statistical software version 23.0.

RESULTS

From May 2007 through March 2017, 138 pancreas transplants were performed. In this cohort, 63 (45.7%) were pediatric donor transplants that were further divided into group 1, less than 30 kg (n = 19); group 2, between 30 and 60 kg (n = 21); and group 3, greater than 60 kg (n = 23). Donor sex and race distribution are similar in the 3 pediatric groups, as seen in Table 1. The remaining 75 (54.3%) transplants from adult donors represented the control group.

Pediatric pancreas grafts were procured by the regional Organ Procurement Agency in 28 (44.4%) cases; the other 35 (55.6%) organs came from the other regions. Donor organ suitability was determined during the back-bench preparation because many organs were procured out of the region. Therefore, we relied on surgical expertise to perform final organ inspection at the time of the transplant. No vasculature diameter cutoff was applied either to the splenic artery or the portal vein. The mean age and weight of the donor were 12.10 ± 4.13 years and of 47.8 ± 21.3 kg, respectively. There were no specific donor selection criteria, no limit on patient weight and BMI, as long as the HbA1c was normal. Only

TABLE 1.

Donor and recipient baseline characteristics

	Group 1 (<30 kg)	Group 2 (30-60 kg)	Group 3 (>60 kg)	Total	*P*
No. patients	19	21	23	63	
Donor weight (mean ± SD)	24.43 ± 3.71	42.47 ± 9.59	71.97 ± 9.09	47.8 ± 21.37	0.000*
Donor age (mean ± SD)	7.74 ± 1.99	11.9 ± 3.25	15.87 ± 1.93	12.10 ± 4.13	0.000*
Donor BMI (mean ± SD)	15.47 ± 1.74	19.32 ± 3.81	24.74 ± 3.30	20.13 ± 4.92	0.000*
Recipient age at transplant	41.32 ± 9.59	38.95 ± 9.16	42.43 ± 9.44	40.94 ± 9.36	0.464
Recipient BMI	27.04 ± 4.47	28.49 ± 5.23	26.36 ± 5.02	27.28 ± 4.93	0.358
Recipient sex					0.401
• Male (%)	12 (63.2%)	14 (66.7%)	11 (47.8%)	37 (58.7%)	
• Female (%)	7 (36.8%)	7 (33.3%)	12 (52.2%)	26 (41.3%)	
Donor sex					0.930
• Male (%)	15 (78.9%)	16 (76.2%)	17 (73.9%)	48 (76.2%)	
• Female (%)	4 (21.1%)	5 (23.8%)	6 (26.1%)	15 (23.8%)	
Recipient race					0.929
•African-American	6 (31.6%)	6 (28.6%)	9 (39.1%)	21 (33.3%)	
•Hispanic	4 (21.1%)	6 (28.6%)	5 (21.7%)	15 (23.8%)	
•White	8 (42.1%)	8 (38.1%)	9 (39.1%)	25 (39.7%)	
•Other	1 (5.3%)	1 (4.8%)	0	2 (3.2%)	
Donor race					0.180
•African-American	5 (26.3%)	4 (19%)	8 (34.8%)	17 (27%)	
•Hispanic	7 (36.8%)	4 (19%)	9 (39.1%)	20 (31.7%)	
•White	7 (36.8%)	13 (61.9%)	5 (21.7%)	25 (39.7%)	
• Other	0	0	1 (4.3%)	1 (1.6%)	
Recipient diabetes					0.510
•Type 1	17 (89.5%)	20 (95.2%)	22 (95.7%)	59 (93.7%)	
•Type 2	1 (5.3%)	1 (4.8%)	0	2 (3.2%)	
•Iatrogenic	1 (5.3%)	0	0	1 (1.6%)	
•Steroid-induced	0	0	1 (4.3%)	1 (1.6%)	
Cause of donor death					NA
•MVA, 1	5	6	9	20	
•Stroke, 2	3	2	0	5	
•Asthma attack, 3	3	4	1	8	
•Homicide/gunshot, 4	1	0	9	10	
•Other, 5	7	9	4	20	
DBD/DCD	18/1	20/1	23/0	61/2	NA
Recipient CMV status					NA
•Positive	14	11	17	42	
•Negative	5	10	5	20	
•Unknown	—	—	1	1	
Donor CMV status					NA
•Positive	12	5	16	33	
•Negative	7	16	7	30	
•Unknown	—	—	—	—	

in case of injury or hematoma in the pancreatic graft the organ was refused. Cold ischemia time over 20 hours was not considered a contraindication.

In the pediatric cohort, 28 (44.4%) transplants were SPK, 17 (27.0%) were pancreas alone transplant (PAT), 18 (28.6%) were pancreas after kidney (PAK) transplant, as seen in Table 2. Only 10 (15.8%) patients had bladder drained exocrine gland of the pancreas. Majority of recipients (93.7%) had T1D. There was no donor/recipient BMI or weight-matching criteria.

In the adult cohort, 38 (50.7 %) transplants were SPK. Twenty-one (28%) patients had bladder-drained exocrine gland of the pancreas. In the remaining 54 cases, drainage was enteric. All transplants were systemically drained. When comparing surgical technique and perioperative management, recipients of pediatric and adult pancreata were treated in the same way.

In the pediatric donor cohort, excellent metabolic control was achieved in 59 (93.6%) patients at the time of discharge and at a mean 5 year follow-up with an average HgbA1c of 5.30 ± 0.61% and FBG level of 102.75 ± 20.70 mg/dL in those with functioning graft at last follow up. The relation between donor weight and long-term graft function was assessed by comparing mean 5-year HgbA1c values and

TABLE 2.
Surgical details

	Group 1 (<30 kg)	Group 2 (30-60 kg)	Group 3 (>60 kg)	Total	*P*
Transplant era					
•2007-2012	11	10	19	40	0.046
•2013-2017	8	11	4	23	
CIT (mean ± SD)	16 h 36 min ± 4 h 52 min	14 h 55 min ± 4 h 42 min	13 h 33 min ± 5 h 7 min	14 h 57 min ± 5 h 3 min	0.204
Length of surgery: mean ± SD, min	274.56 ± 65.3	311.43 ± 109.64	276 ± 64.94	288.43 ± 84.41	0.299
Estimated blood loss: mean ± SD, mL	228.57 ± 183.67	286.11 ± 258.28	280.95 ± 248.23	268.87 ± 233.54	0.759
Type of transplant					NA
PAT	5	5	7	17	
SPK	8	10	10	28	
PAK	6	6	6	18	

5-year FBG among the 3 weight groups. No statistically significant differences were observed between the 3 groups ($P = 0.468$ and $P = 0.138$ respectively). Nine graft losses were registered, of which only 1 was due to arterial thrombosis. Overall, 8 (12.7%) patients experienced allograft rejection, of which 5 (62.4%) led to graft loss, the other 3 (37.6%) were successfully treated with medical therapy.

Immunosuppressive Therapy, Antimicrobial, and Anticoagulation Prophylaxis

In the pediatric cohort, 60 (95.2%) patients received induction with daily rabbit antithymocyte globulin 1.5 mg/kg using ideal body weight on postoperative days (POD) 0 to 4. Two patients received interleukin-2 receptor antagonist (IL-2RAs) on PODs 0 and 4, and 1 patient received a single dose of alemtuzumab 30 mg on POD 0. No justification was recorded for protocol deviation. All patients received maintenance immunosuppression per protocol with tacrolimus in combination with mycophenolic acid and a rapid, 5-day steroid taper. Antimicrobial prophylaxis was per protocol in all patients.

In the pediatric cohort, 57 (90.5%) patients received postoperative anticoagulation with heparin until patient could transition to an oral regimen. In 2 cases, the heparin drip was held for high risk of bleeding and aspirin-dipyridamole started when the risk of bleed was minimal. One patient was known to have heparin-induced thrombocytopenia and he was treated with argatroban drip at 0.5 μg/kg per minute. Another patient was found to have heparin-induced thrombocytopenia postoperatively, so heparin was discontinued, and aspirin-dipyridamole was started. Two patients were receiving warfarin therapy before surgery and were restarted on warfarin instead of aspirin-dipyridamole. Only 1 patient on the conventional regimen developed an arterial thrombus. No arterial thrombi were observed in patients on alternative anticoagulation therapies.

Patient and Graft Survivals

Thirteen patients were lost to follow up in the pediatric-donor cohort 13 (20.6%) of 63. Overall patient survival was comparable among the 3 pediatric-donor groups (group 1, 94.7%; group 2, 95.2%; and group 3, 87%; $P = 0.966$) with a median follow-up of 37.07 months (Figure 1). Similar findings in patient survival were observed between the entire pediatric-donor cohort and the adult control group (pediatric, 92.1%; adult, 96.3%; $P = 0.58$) (Figure 2). Five deaths were observed among the pediatric-donor cohort during the 5-year follow up, and 4 deaths occurred with functioning graft.

Overall graft survival in the pediatric-donor cohort was 85.7%. There was no significant difference between the 3 pediatric donor groups (group 1, 89.5%; group 2, 76.2%; group 3, 91.3%; $P = 0.124$) (Figure 3). Moreover, no difference in graft survival was noted between the pediatric donor cohort versus the adult control group (85.7% vs 80%; $P = 0.753$) (Figure 4).

In the pediatric cohort, 9 (14.3%) patients lost their allograft (Table 3). No differences were observed in terms of cause of graft failure among pediatric-donor groups ($P = 0.3$). The main cause of pediatric allograft failure was acute cellular rejection that was observed in 5 (7.93%)

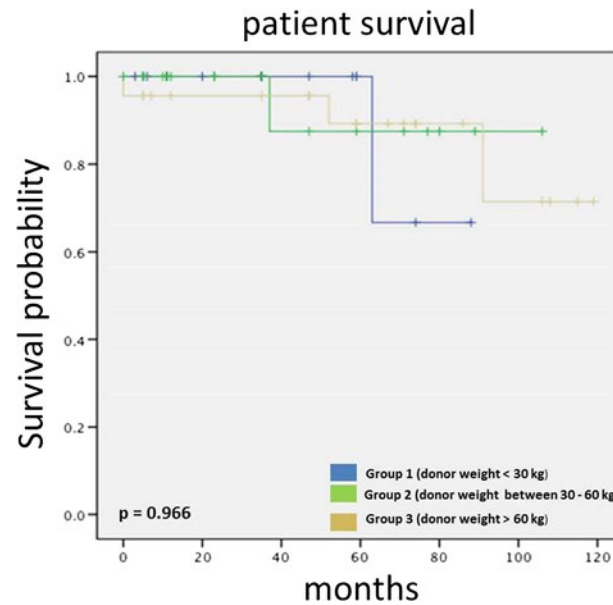

FIGURE 1. Patient survival by donor weight groups.

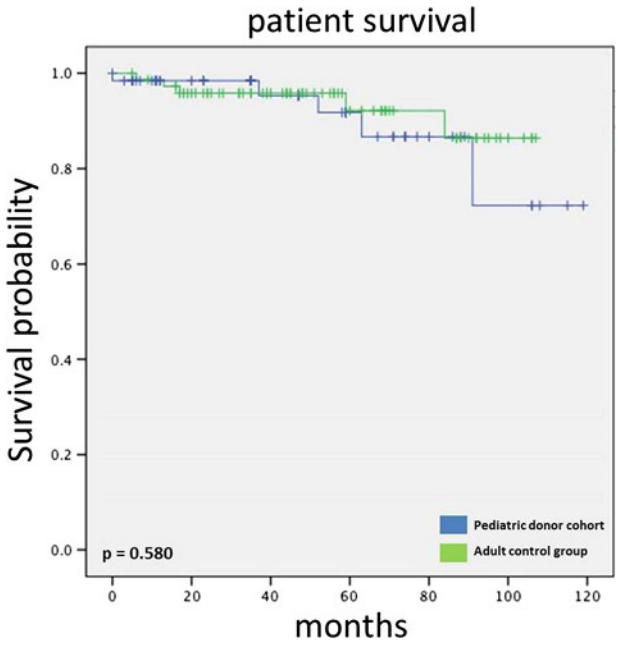

FIGURE 2. Patient survival pediatric donor cohort versus adult donor control.

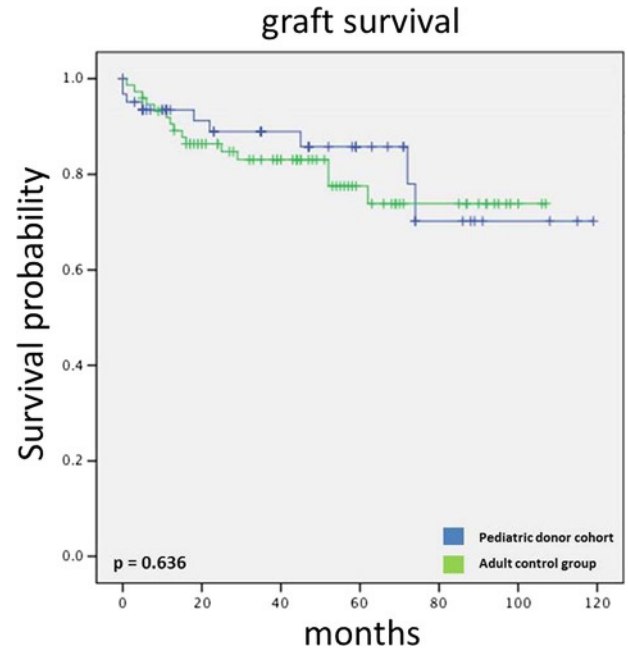

FIGURE 4. Allograft survival pediatric donor cohort versus adult donor control.

patients. One patient required graft pancreatectomy because of intestinal anastomotic leak. As previously mentioned, arterial thrombosis of the graft was observed only in 1 patient in group 2 of the pediatric-donor cohort, showing no statistical correlation with donor weight ($P = 0.36$). Among other causes of graft loss, 1 patient required insulin treatment since discharge for unknown reasons and a third patient underwent graft removal on POD 9 for the rupture of a mycotic pseudoaneurysm of the arterial graft.

In the pediatric-donor cohort, overall reoperation rate was 19%. In 12 cases, reoperation was necessary during the transplant hospital stay: 3 graft removals previously mentioned (arterial thrombosis, anastomotic leak, and mycotic pseudoaneurysm); 4 patients underwent relaparotomy due to hematoma evacuation; and 3 required abdominal washout and drainage of peripancreatic abscesses. Two patients experienced small-bowel obstruction and underwent small-bowel resection and reanastomosis. No statistical differences were observed in reoperation rate between the 3 pediatric groups ($P = 0.519$).

In the adult group, 14 (18.7%) patients lost their allograft. No differences were observed in terms of cause of graft failure among pediatric and adult groups ($P = 0.49$). The main cause of adult allograft failure was acute cellular rejection that was observed in 12 (16%) patients. Arterial thrombosis of the graft was observed in 2 patients.

Overall reoperation rate was 16% (12 cases). One graft removal for arterial thrombosis, 2 anastomotic leaks, 8 patients underwent relaparotomy due to hematoma evacuation or abdominal washout and drainage of peripancreatic abscesses. One patient experienced a deep abdominal wall-wound abscess and fascial dehiscence requiring reoperation for drainage, debridement of the wound, and wound V.A.C. placement.

No statistical differences were observed in reoperation rate between the pediatric group and the adult one ($P = 0.95$). When considering the major surgical complications (arterial thrombosis, anastomotic leak, and hematoma evacuation-abdominal washout), no statistical significances were found (see Table 4).

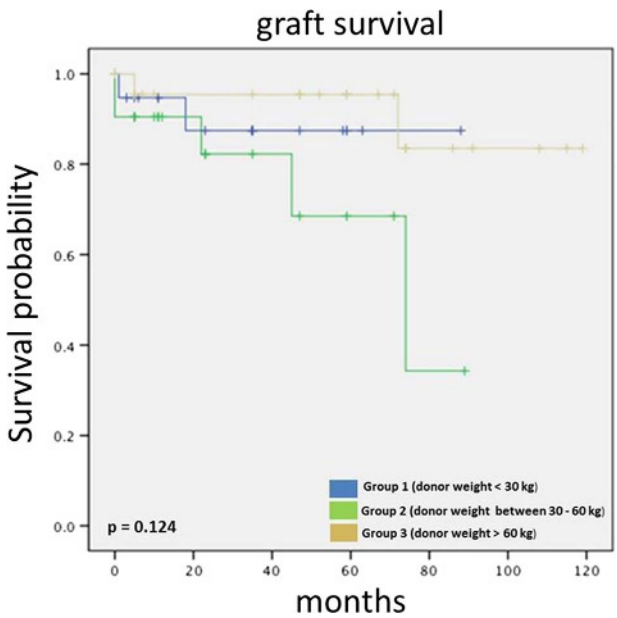

FIGURE 3. Pediatric donor allograft survival by donor weight groups.

Cox Regression Analysis

Donor weight had no significant influence on graft survival (hazard ratio [HR], 0.985; 95% confidence interval [CI], 0.953-1.017; $P = 0.358$). As shown in Table 5, HbA1c level at 1 year (HR, 2.637; 95% CI, 1.162-5.983; $P = 0.02$) and, most prominently, blood glucose level at 1 year (HR, 1.034; 95% CI, 1.013-1.056; $P = 0.001$) had a statistically significant effect on graft survival. High Hb1Ac and blood

TABLE 3.
Graft outcomes

	Group 1 (<30 kg)	Group 2 (30-60 kg)	Group 3 (>60 kg)	Total	*P*
Median follow-up: minimum-maximum, mo	—	—	—	37.07 0.19-119.57	NA
At 5 y					
• FBS: mean ± SD, mg/dL	114.5 ± 33.4	98.67 ± 3.51	100.08 ± 18.43	102.75 ± 20.69	0.468
• HbA1c mean ± SD	5.35 ± 0.26	4.67 ± 0.60	5.43 ± 0.62	5.30 ± 0.61	0.138
Vascular thrombosis	—	1	—	1	0.362
Acute rejections	2	1	5	8	0.345
Graft loss	2	5	2	9	0.307
• Arterial thrombosis	—	1	—	1	0.362
• Anastomotic leak	1	—	—	1	0.340
					0.345
• Acute rejection	1	2	2	5	
• Insulin from discharge	—	1	—	1	NA
• Other[a]	—	1	—	1	NA
Death	1	1	3	5	
Death with functioning graft	1	—	3	4	

[a] Infected arterial graft and mycotic rupture with need of emergent pancreatectomy.

glucose levels, measured at 1 year after transplant, were both strongly related with the probability of graft loss.

DISCUSSION

Pancreas transplantation is a successful treatment for type 1 diabetic patients that restores insulin independence.[6,7,16] The number of currently available "ideal" pancreas donors is not sufficient to meet the increasing demand on the pancreas transplant waiting list worldwide.[16,17] Despite that, strict criteria for pancreas donor eligibility persist. The ideal donor age for pancreas transplantation is between 10 and 40 years with an ideal weight between 30 and 80 kg.[14] In the past, some authors[9,18-20] have supported the use of pancreas grafts procured from pediatric donors to increase the donor pool, but limited data are available regarding their use in adult recipients. For this reason, transplant surgeons remain skeptical about utilization of pediatric donors and are more inclined to reject pediatric grafts a priori. Thus, there is still no consensus about donor age and weight limits in pancreas transplantation.[12] The main concerns with using pediatric grafts are focused on the high risk of incidence of surgical complications—in particular, thrombosis—because of the small dimensions of the graft vessels[21,22] and poor functional outcome due to the reduced islet cell mass.[9,14,18]

An analysis of Organ Procurement and Transplantation Network data demonstrated[23] that the use of "extra small donors" (donor, <20 kg) is associated low risk of technical complications (6.5%). Similar low rate of complications (10.2%; leak/graft thrombosis) was reported by Fernandez et al[12] in the largest study demonstrating utilization of pediatric donors for SPK. Illanes et al[15] published a case series of 6 SPK and 2 pancreas transplant alone using pediatric donors weighing less than 28 kg with excellent results: no thrombosis, fistula, or pancreatitis were observed. In our experience, the incidence of thrombosis was 1.6%, and no statistical correlation with donor weight was identified. Moreover, the use of pediatric grafts was not associated with increase in technical difficulty. Rate of reoperation was low at 19% with no statistical differences between the 3 donor weight groups. Based on this evidence, allograft thrombosis should not be considered an impediment to the use of the pediatric allograft.

Illanes et al[15] underlined the importance that the small donors chosen for transplantation had laboratory values within normal limits and that there were no administered inotropic or vasoactive drugs during their ICU stay. They also pointed out the positive impact brief CIT had on transplant outcome; in their study, CIT did not exceed 7 hours. In our experience, mean CIT was about twice as long (14 hours

TABLE 4.
Comparison on surgical complication: pediatric vs adults

Surgical complications	Adult cohort (n=63)	Pediatric cohort (n=75)	x^2	*P*
Arterial thrombosis	2	1	0.1876	0.66
Anastomotic leak	2	3	0.4305	0.51
Hematoma evacuation—abdominal washout	8	7	0.007	0.93
Total	12	11	0.078	0.78

TABLE 5.
Multivariate cox regression

Variables	HR	95% CI	Std. error	*P*
Donor age	0.918	0.778-1.082	0.084	0.306
Donor weight	0.985	0.953-1.017	0.017	0.358
Donor inotropic support in ICU	0.889	0.510-1.547	0.283	0.677
Type of transplant (PAT vs others)	1.374	0.284-6.641	0.804	0.692
Transplant era	1.014	0.186-5.530	0.866	0.988
HbA1c level 1 y	2.637	1.162-5.983	0.418	0.020
Blood glucose level 1 y	1.034	1.013-1.056	0.011	0.001

57 minutes ± 5 hours 3 minutes) and mean donor amylase was of 123.8 ± 145.3 units/L, accepting sometimes donors with values over 800 units/L. Inotropic drugs during donor's ICU stay were used in 57 (90.5%) of the pediatric donors; however, in the Cox regression analysis, this was not associated with worst graft outcome ($P = 0.677$).

Historically, the low islet mass volume of pediatric pancreata has been considered the other great impediment to their utilization.[10,11] This is due to the assumption of a mismatch between secretion of insulin by pediatric β-cell mass and the physiologic demands of adult recipients, resulting in poorer long-term β-cell function. Recent studies have shown that β cells from younger individuals have superior regulation of insulin secretion compared with those from older individuals.[24] Adding value to this theory, authors have demonstrated that age was the primary donor characteristic influencing pancreas graft function, showing that pancreata harvested from donors older than 45 years were associated with an increased risk of losing glycemic control and premature loss of graft function.[25,26]

Additionally, considering that β cell mass is directly correlated to body mass,[24] some authors suggest avoiding the choice of recipients with high metabolic requirements, selecting those with lower weights to maximize islet mass function.[12,18] Sampaio et al[27] reported that recipient obesity was associated with inferior outcomes in pancreas and kidney transplantation, confirming that a weight discrepancy between recipient and donor is associated with worse graft outcome. The strategy of reducing that discrepancy can potentially improve the outcomes of pancreas allografts procured from pediatric donors. In this cohort, no effort was made to match donor and recipient age or weight. Despite this, excellent metabolic control was achieved in 59 (93.7%) cases at the time of discharge. At a median follow-up of 37.07 months, the average HbA1c was 5.30 ± 0.61% with mean blood glucose level of 102.75 ± 20.70 mg/dL in those with functioning allograft. Donor age or weight was not associated with poor glycemic control or worse graft outcomes.

Indeed, pediatric pancreata should be considered a promising resource for transplantation. Few retrospective studies have analyzed pancreas transplant outcomes[12-15] from pediatric donors and compared them with adult donor allografts. The outcomes from these studies showed no difference in survival between pediatric and adult-donor recipients, including up to 10 years of long-term follow-up.[12,13] A previously published registry analysis shows better 10-year patient and graft survivals with pediatric allografts compared with adult grafts (patient, 70% vs 68% and graft, 54% vs 51%, $P = 0.001$).[23] Fernandez et al[12] presented the optimal results of 142 SPK from pediatric donors after 10-years of follow-up with a patient survival rate of 85% and graft survival rate of 72%. Van der Werf et al[19] reported that excellent early function and graft survival were achieved in 17 patients who received pediatric organs from donors between 4 and 10 years of age. Similarly, Krieger et al[14] demonstrated excellent pancreas and kidney graft survival rates in 24 recipients of donor organs from donors younger than 10 years. Socci et al[13] described a series of SPK and pancreas transplant alone from pediatric donors with a patient survival rate of 94.12% and a pancreas graft survival of 63.35% at 9 years. Moreover, these studies demonstrated better graft survival in the pediatric donor group.[12-15]

The multivariate analysis of our study confirms that there is no significant difference when graft survival is compared with donor age and donor weight ($P = 0.306$ and $P = 0.358$, respectively). The same holds true when the comparison is evaluated between graft outcome and donor sex ($P = 0.816$). Examining the surgical era (era 1, 2007-2012 vs era 2, 2013-2017), a mild risk is identified in being transplanted in the era 2007 to 2012 but with no statistical difference ($P = 0.988$). This difference can be attributed to the improvement in the surgical expertise of the transplant team over the years. Specifically, during the early study period, the operative practice at our center changed to predominately enteric drained pancreas transplant. In terms of medical management, during the same time, low-dose, fixed rate heparin infusion was added in the immediate postoperative period in addition to the historical anticoagulation with oral, twice-daily aspirin-dipyridamole that was initiated before discharge. Immunosuppression regimen remained unchanged in this study period, and no adjustment was done based on the pediatric nature of our donors.

It is well known that PAT carries a higher risk of rejection compared with SPK or PAK transplantations.[28,29] In our study, no differences were observed between the occurrence of rejection and donor weight ($P = 0.345$). Among the 8 (12.7%) cases of acute cellular rejections, 2 were PAT, 3 SPK, and 3 PAK. Rejection was successfully treated in 5 of 8 cases. All 3 cases of cellular rejection in PAK led to graft loss. The Cox regression shows trend toward worst graft survival in PAT recipients but with no statistical significance ($P = 0.692$). A significant correlation was identified with worsening allograft survival and hyperglycemia and elevated HbA1c at 1 year ($P = 0.001$ and $P = 0.020$, respectively).

To the best of our knowledge, we are presenting the second largest cohort of pancreas transplants using pediatric donors younger than 18 years. Our study of 63 pancreas transplants with grafts procured from pediatric donors demonstrated excellent short-term outcomes. The rate of surgical complications was comparable with adult cohort despite small anatomy and promising long-term outcomes despite the smaller islet mass. The patient and allograft outcomes in the pediatric donor transplants were comparable with those of pancreatic transplants procured from adult donors. Donor weight did not impact overall patient and graft survivals ($P = 0.966$ and $P = 0.124$ respectively). Moreover, when we examine the patient and graft survival rates of the recipients who received pediatric donor allografts with the ones of the adult control group, overall graft survival ($P = 0.753$), and overall patient survival ($P = 0.58$) were comparable.

Although this study illustrates that pediatric donors can be used for pancreas transplantation, there are several limitations of this analysis. First, this is a retrospective analysis with a small sample size. Larger patient population would validate observed trends. Moreover, all the patients were transplanted over a long-time frame (from 2007 to 2017) during which changes have been introduced to the surgical technique of the transplant team. However, the consistency of our medical management can be considered a strength of this study.

In conclusion, the use of pediatric donors resulted in excellent short- and long-term outcomes, with few surgical complications and patient and graft survival that mimicked adult donor transplants. Our results demonstrate that outcomes of pediatric donor pancreas are noninferior to the

adult donor outcomes. Pediatric donors remain underused for pancreas transplantation but should no longer be considered "nonideal." Their increased utilization will offset the growing organ shortage. The finding of this study should encourage transplant surgeons to use pediatric donors more frequently, making it no more a brave deed but a safe, standard procedure.

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