American Journal of Transplantation 2010; 10: 837–845
Wiley Periodicals Inc.

doi: 10.1111/j.1600-6143.2009.02996.x

Systematic Evaluation of Pancreas Allograft Quality, Outcomes and Geographic Variation in Utilization

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Pancreas allograft acceptance is markedly more selective than other solid organs. The number of pancreata recovered is insufficient to meet the demand for pancreas transplants (PTx), particularly for patients awaiting simultaneous kidney-pancreas (SPK) transplant. Development of a pancreas donor risk index (PDRI) to identify factors associated with an increased risk of allograft failure in the context of SPK, pancreas after kidney (PAK) or pancreas transplant alone (PTA), and to assess variation in allograft utilization by geography and center volume was undertaken. Retrospective analysis of all PTx performed from 2000 to 2006 (n = 9401) was performed using Cox regression controlling for donor and recipient characteristics. Ten donor variables and one transplant factor (ischemia time) were subsequently combined into the PDRI. Increased PDRI was associated with a significant, graded reduction in 1-year pancreas graft survival. Recipients of PTAs or PAKs whose organs came from donors with an elevated PDRI (1.57–2.11) experienced a lower rate of 1-year graft survival (77%) compared with SPK transplant recipients (88%). Pancreas allograft acceptance varied significantly by region particularly for PAK/PTA transplants ($p < 0.0001$). This analysis demonstrates the potential value of the PDRI to inform organ acceptance and potentially improve the utilization of higher risk organs in appropriate clinical settings.

Key words: Outcomes, pancreas transplantation, SRTR

Received 01 July 2009, revised 13 November 2009 and accepted for publication 01 December 2009

Introduction

Appropriate allograft selection is widely viewed as a key component to successful pancreatic transplantation (PTx) (1). Historically, fear of early graft loss from technical failure has resulted in very conservative organ acceptance practices. Unfortunately, the supply of high-quality, brain dead donors appears to be decreasing and consequently, there has been a reduction in the overall number of PTx performed, from a high of 1484 transplants in 2004 to 1331 in 2007, despite a significant waiting list of diabetic patients and data substantiating the value of PTx, particularly when combined with kidney transplantation (2).

Methods of systematic, quantitative assessment of donor quality have been developed for kidney (KDRI) (3) and liver (LDRI) donors (4). These donor risk indexes (DRIs) include factors which can be identified at the time of organ allocation that also predict the risk of early graft failure and are combined into a continuous scale. A DRI is derived from retrospective registry analyses that control for donor, recipient and transplant-related factors (such as HLA matching and cold ischemia time) and account for interactions leading to increased risk of graft loss.

PTx is performed in three distinct clinical scenarios: simultaneous kidney-pancreas (SPK) transplantation , pancreas after kidney (PAK) transplantation and pancreas transplant alone (PTA). Previous reports have demonstrated that the risk of allograft failure is higher in solitary PTx (PAK and PTA) versus SPK transplants. Since a DRI-like assessment has never been developed for pancreas transplantation, there are no prior data available to discern whether there is a differential effect of graft quality on transplant outcome as a function of the PTx type. Furthermore, unlike kidney transplantation in which certain recipient factors alone provide useful information as to when to use a high risk organ, there is no equivalent dataset to guide use of high-risk pancreas allografts for specific patient populations who might benefit from higher risk organs.

Previous reports have demonstrated substantial variation in the proportion of pancreas allografts that are recovered and transplanted as a function of region and organ procurement organization (OPO) practice (5). These differences may reflect center practice, local allocation systems which discourage the use of higher risk organs or variation in donor quality. A more precise characterization of the

degree of regional variation may be useful in examining current allocation practices to ensure that all appropriate and beneficial organs are utilized.

This paper describes the construction of a pancreas allograft PDRI based on data from SPK, PAK and PTA transplants. The PDRI was used to assess the differential impact of organ quality on PTx outcomes within each of the three clinical scenarios, and as a function of the type of transplant and recipient severity of illness. The PDRI was also used to examine the variation in organ recovery and transplantation practices within the United States.

Methods

Data source

Data from the Scientific Registry of Transplant Recipients were reviewed for all patients undergoing SPK (n = 6248), PTA (n = 780) or PAK (n = 2373) from January 1, 2000 to January 31, 2006. Demographic and transplant characteristics for recipients and donors were determined for all transplants (Table 1A and B). Graft failure was determined by center reporting on the pancreas follow-up forms and included patient death (Figure 1). All patients undergoing these transplants >18 years of age were included.

Model development

A Cox regression model was fit using all available donor, recipient and transplant factors to assess the risks of graft failure at 1 year. The model was stratified by transplant type in order to allow differing failure rates for each type of PTx. A likelihood ratio test was performed to assess whether the coefficients differed by strata; a significant difference was not found ($p = 0.85$). In addition, several interactions between transplant type and clinically relevant donor and recipient characteristics were also examined. Significant interactions were found between transplant type and recipient age, and between PAK and cerebrovascular accident (CVA) as donor cause of death. The index of concordance for the final 1-year graft failure model was 0.67.

Recipient factors in the model included transplant type, age, race, sex, body mass index (BMI), panel reactive antibody (PRA), presence of peripheral vascular disease, primary payment type, albumin and previous transplant. Transplant specific factors included transplant center, duct management, degree of HLA matching, preservation time and transplant year.

Donor factors in the model included: age, sex, race, BMI, height, cause of death, donation after cardiac death (DCD) and serum creatinine. Additional donor variables were considered and excluded based on their lack of association with outcomes including: amylase, lipase, serum glutamic oxaloacetic transaminase (SGOT), serum glutamic pyruvic transaminase (SGPT), duration of downtime, time of flush solution, smoking, cocaine use, alcohol use, hypertension, sodium and viral serologies. However, the absence of associations with these factors may reflect incomplete data recording as well as existing clinical practice, which limits the use of organs with significantly abnormal laboratory values.

Determination of the DRI

Donor and transplant specific factors, including ischemia time, which were statistically significantly associated with graft failure in the survival model, were used to construct the DRI. The appropriate coefficients were then combined in an index such that the 'median' donor had a DRI of 1.0. Increasing DRI is associated with a higher risk of graft failure, so that the DRI can be interpreted as a risk ratio comparing the donor at hand with the median risk donor. The median donor is defined as male, 28 years of age, non-black, non-Asian, BMI of 24, height of 173 cm, non-CVA/stroke as the cause of death, pancreas preservation time of 12 h, non-DCD and serum creatinine less than 2.5 mg/dL. For the purpose of allocation and regional comparisons, cold ischemia time was fixed at 12 h for all donors.

Definition of high and median risk recipient

To determine the differential effect of organ quality in recipients of median and high risk, two recipient profiles were determined. The median risk recipient was 41 years old, BMI of 25, male, white, albumin 3.7 gm/dL, PRA = 0, private insurance, no prior PTx and enterically drained. The high risk recipient was defined as age >50, BMI >30, female, PRA = 20, with all other characteristics held constant.

Statistical analyses

All calculations were performed using SAS version 9.1.3 (SAS Institute Inc., Cary, NC). A p-value of 0.05 was considered significant and differences were assessed using parametric and nonparametric statistical tests as appropriate.

IRB approval

This project was approved by HRSA's SRTR project officer. HRSA has determined that this study satisfies the criteria for the IRB exemption described in the 'Public Benefit and Service Program' provisions of 45 CFR 46.101(b)(5) and HRSA Circular 03.

Results

The PDRI includes 10 donor and one transplant characteristic (Table 2). Donor factors include donor sex, age, black race, Asian race, BMI, cause of death, creatinine, height and DCD status. The transplant factors include pancreas preservation time and an interaction between PAK and the donor cause of death. Among the donor factors examined, age, BMI and DCD status appeared to have the greatest impact on risk. For example, increasing donor age from 28 to 45, holding all other factors constant, was associated with a 56% increase in risk (PDRI increases from 1.0 to 1.56). Similarly, a DCD donor was associated with a relative risk of graft failure of 1.39 compared to a brain dead donor.

Increasing PDRI was associated with a significant increase in graft loss within the first year posttransplant for all types of PTx (Figure 2). Among average risk recipients, there appeared to be a differential risk of graft loss associated with high PDRI organs that were used in solitary PTx as compared with SPKs (Tables 3 and 4). PTx in average risk recipients, using donors with a PDRI between 1.57 and 2.11, had a 1-year graft survival of 83% following SPK versus 77% for PAK or PTA. Those pancreas survival rates are consistent with the national averages published from SRTR analyses. The cause of failure appeared similar across PDRI categories for SPK recipients (Table 5B). In the isolated PTx recipients (PAK/PTA), however, there was a trend toward higher rates of technical early loss among recipients of high PDRI organs ($p = 0.08$) (Table 5A).

Table 1: Donor and recipient characteristics of pancreas transplants (1/1/2000–12/31/2006)

			Transplant type					
	All (n = 9401)		KP (n = 6248)		PAK (n= 2373)		PTA (n = 780)	
	n	%	n	%	n	%	n	%
(A) Donor charaterstics								
Donor gender male	6331	67.3	4226	67.64	1600	67.4	505	64.7
Donor race	6751	71.8	4408	70.55	1765	74.4	578	74.1
White								
Black or African American	1235	13.1	894	14.31	257	10.8	84	10.8
Hispanic/Latino	1193	12.7	797	12.76	301	12.7	95	12.2
Other	86	0.9	52	0.83	18	0.8	16	2.0
Donor cause of death								
Anoxia	833	8.9	537	8.59	214	9.0	82	10.5
Cerebrovascular/stroke	1958	20.8	1271	20.34	517	21.8	170	21.8
Head trauma	6366	67.7	4271	68.36	1588	66.9	507	65.0
CNS tumor	64	0.7	44	0.7	13	0.6	7	0.9
Other	178	1.9	125	2	40	1.7	13	1.7
DCD	128	1.4	87	1.39	22	0.9	19	2.4
Donor SCr >2.5	162	1.7	66	1.06	75	3.2	21	2.7
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Donor age	9401	26.3 (10.8)	6248	26.5 (10.8)	2373	25.7 (10.5)	780	26 (10.9)
Donor BMI	9391	24 (4.2)	6243	24 (4.1)	2368	24.1 (4.1)	780	24.2 (4.3)
Donor's height (cm)	9398	172.6 (11.7)	6246	172.7 (11.7)	2372	172.4 (11.8)	780	172.1 (11.9)
Donor's weight (kg)	9401	72.1 (15.9)	6248	72.1 (15.8)	2373	72.1 (16)	780	72.1 (16.1)
Donor serum amylase	9222	133.7 (234.8)	6122	133 (239.8)	2338	134.1 (222.8)	762	138.6 (229.9)
Donor serum lipase	8896	75 (141.5)	5918	77.4 (142.4)	2254	66.1 (123.8)	724	82.9 (180.1)
Donor serum creatinine	9372	1.05 (0.89)	6229	1 (0.9)	2366	1.1 (0.9)	777	1.1 (1)
(B) Recipient charaterstics								
Recipient gender male	5459	58.1	3793	60.71	1352	57.0	314	40.3
Recipient race	7613	81.0	4811	77	2051	86.4	751	96.3
White								
Black or African American	1032	11.0	850	13.6	171	7.2	11	1.4
Asian	71	0.8	57	0.91	13	0.6	1	0.1
Other	74	0.8	56	0.9	15	0.6	3	0.4
Candidate PVD	693	7.4	435	6.96	217	9.1	41	5.3
Recipient previous PA transplant	720	7.7	98	1.57	538	22.7	84	10.8
Recipient peak PRA								
0–9	7518	80.0	5075	81.23	1832	77.2	611	78.3
10–80	1513	16.1	943	15.09	445	18.8	125	16.0
80–100	351	3.7	217	3.47	90	3.8	44	5.6
Recipient primary payment private	4830	51.4	3021	48.35	1180	49.7	629	80.6
Duct management noncystostomy	1820	19.4	945	15.12	605	25.5	270	34.6
	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)	N	Mean (SD)
Recipient age	9401	41.1 (8.2)	6248	40.9 (8.3)	2373	41.7 (7.7)	780	40.7 (9.6)
Recipient BMI	8291	25 (4.2)	5513	24.8 (4.1)	2072	25.2 (4.3)	706	25.5 (4.3)
Recipient's height (cm)	8541	170.3 (10.4)	5677	170.8 (10.5)	2131	169.7 (10.1)	733	168.4 (10.2)
Recipient's weight (kg)	8762	72.8 (15.3)	5810	72.7 (15.2)	2214	72.9 (15.2)	738	72.7 (15.8)
Recipient years since DM onset	8314	26.8 (8.3)	5500	26.5 (8)	2088	28.3 (7.8)	726	25.3 (10.9)
Pancreas preservation time	7415	13.6 (5.8)	4902	13.1 (5.7)	1883	14.1 (5.9)	630	15.4 (5.7)

Nationally, there was a significant difference between the PDRI of pancreata recovered but not transplanted (PDRI interquartile range of 1.03– 2.02) and accepted (PDRI interquartile range of 0.84–1.32) for transplantation ($p < 0.001$). There was no significant difference in the PDRI of organs used for SPK transplants (median = 1.01) compared to that used in isolated PAK/PTA transplants (median = 0.99) ($p = 0.09$). Interestingly, despite the ongoing need for organs, the use of marginal pancreas donors appears to be declining nationally. In 2000, the 75th percentile PDRI was 1.38 for transplants that decreased to 1.31 in 2006. The majority of this decline occurred in the PAK/PTA transplants in which the 75th percentile PDRI decreased from 1.43 to 1.25 ($p < 0.001$ for trend), while there was

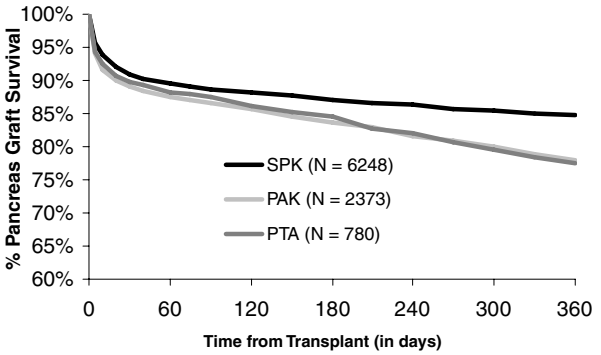

Figure 1: Kaplan–Meier survival analysis of pancreas allograft survival following simultaneous kidney-pancreas transplant (SPK), pancreas after kidney transplant (PAK) and pancreas transplant alone (PTA) among patients transplanted between 2000 and 2006. Allograft survival is adjusted for donor, recipient and transplant characteristics.

minimal difference in the SPK transplants—1.36–1.33 ($p = 0.29$ for trend).

Examining the most recent 2.5 years of our cohort (July 2004–December 2006), several UNOS regions were identified as being aggressive in their utilization of pancreas allografts (Table 6). The 75th percentile of PDRI of all types of PTx performed in regions 7 (1.47; $p < 0.001$ vs. national), 10 (1.44; $p < 0.001$ vs. national), 9 (1.37; $p = 0.34$ vs. national) and 1 (1.36; $p = 0.13$ vs. national) were all above the national 75th percentile of 1.30. By comparison, region 6 had the lowest 75th percentile PDRI (1.14; $p = 0.07$ vs. national). Differences by region were even greater in the utilization of allografts for SPK. The most aggressive region had a 75th percentile PDRI of 1.50 ($p < 0.001$ vs. national) compared to a PDRI of 1.05 ($p = 0.007$ vs. national) in the least aggressive region. Overall utilization of pancreas donors with PDRI of 1.16–1.56 varied from a high of 83% in region 10 to a low of 38% in region 1.

Utilization of higher risk PTx allografts was also correlated with center activity (Table 6). The 75th percentile PDRI among centers performing less than 10 PTx over 2.5 years was 1.19 for SPK transplants and 1.21 for solitary (PAK/PTA) transplants. For centers performing >40 transplants in 2.5 years, the 75th percentile PDRI was 1.42 for SPKs ($p < 0.01$ vs. national average) and 1.33 for solitary PTx ($p =$ NS compared with national average).

Discussion

The PDRI is a measure of allograft quality that predicts the risk of allograft failure at 1 year. The PDRI can be calculated from donor and transplant characteristics that are available at the time of organ offer and may potentially guide organ acceptance and allocation decisions. Furthermore, it appears that for recipients with median characteristics there is a differential effect of PDRI as a function of transplant type, in that graft outcome is worse for solitary PTx than SPK for poor quality organs. Furthermore, potentially useable allografts appear not to have been transplanted in regions without higher volume, aggressive PTx centers.

Prior retrospective analyses have identified a number of donor and transplant related factors which appear to be correlated with worse outcome following pancreas transplantation. Technical failure, defined as early graft loss due to nonimmune related factors (such as venous thrombosis), is responsible for the vast majority of pancreas graft loss within the first year posttransplant (6). Retrospective analyses from the University of Minnesota found that the overall rate of graft loss due to technical failure at a mean follow-up of 45 months ranged from 30.6% for SPK to 37.9% for PTA. The most common causes of technical failure were thrombosis (52%), infection (19%), pancreatitis

Table 2: Summary of pancreas DRI

Donor characteristics	Reference donor (DRI = 1.00)	Change factor value to	DRI
Gender	Male	Female	0.87
Age	28	45	1.56
Black race	No	Yes	1.27
Asian race	No	Yes	1.17
BMI	24	30	1.17
Height (cm)	173	190	0.9
Cause of death: CVA/stroke	No	Yes	1.23
Cause of death: CVA/stroke in PAK	No	Yes	0.93
Pancreas preservation time (h)	12	20	1.13
DCD	No	Yes	1.39
SCr > 2.5	No	Yes	1.22

Equation: pDRI = exp(–0.13792 × I [Female Donor])–0.034455 × I[Donor Age <20] × [Donor Age –20] + 0.026149 × [Donor Age –28] + 0.19490 × I [Donor Creatinine >2.5] + 0.23951 × I[Donor Black Race] + 0.15711 × I[Donor Asian Race] − 0.000986347 × [Donor BMI −24] + 0.033274 × I[Donor BMI >25] × [Donor BMI − 25] −.006073879 × (Donor Height −173) + 0.21018 × I [Donor COD CVA] −0.28137 × I [Donor COD CVA for PAK txp] + 0.014678 × [Preservation Time −12] + 0.33172 × I [DCD])

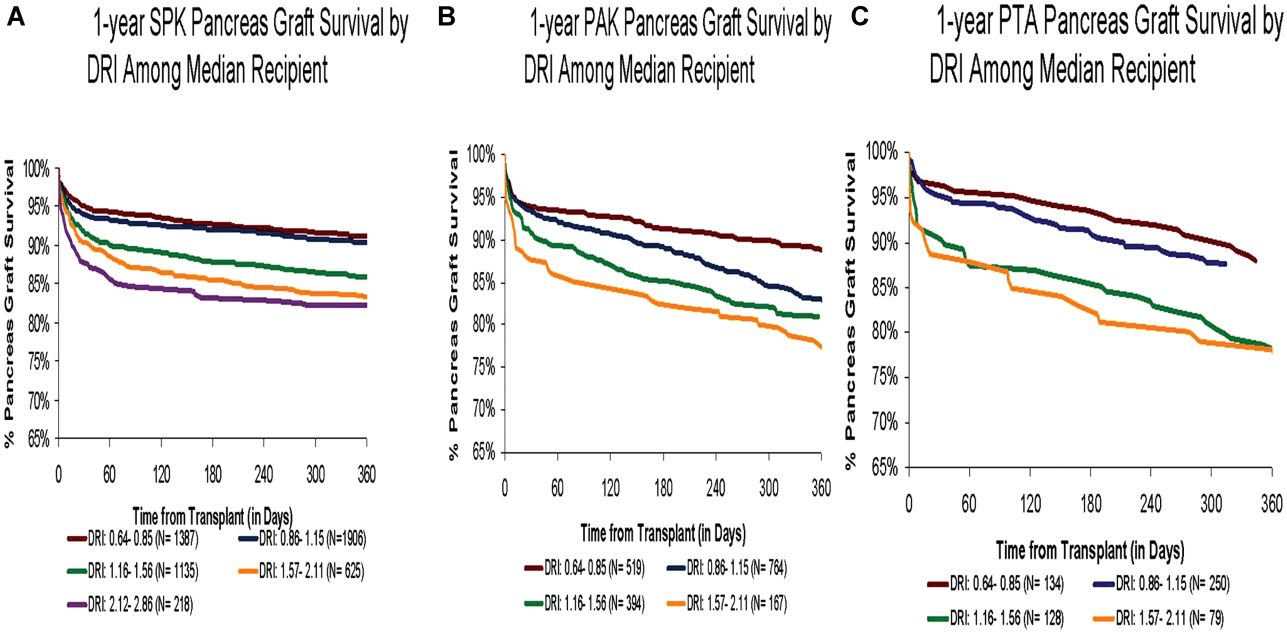

Figure 2: (A) Adjusted 1-year graft survival following simultaneous kidney-pancreas (SPK) transplant as a function of the pancreas donor risk index (PDRI). Curves shown reflect expect survival for an average recipient (41 years old, BMI = 25, male, white, albumin 3.7 gm/Dl PRA = 0, private insurance, no prior PTx and enterically drained) transplanted with pancreata from each PDRI strata. (B) Adjusted 1-year graft survival following pancreas after kidney (PAK) transplant as a function of the pancreas donor risk index (PDRI). Curves shown reflect expect survival for an average recipient (41 years old, BMI = 25, male, white, albumin 3.7 gm/Dl PRA = 0, private insurance, no prior PTx and enterically drained) transplanted with pancreata from each PDRI strata. (C) Adjusted 1-year graft survival following pancreas transplant alone (PTA) as a function of the pancreas donor risk index (PDRI). Curves shown reflect expect survival for an average recipient (41 years old, BMI = 25, male, white, albumin 3.7 gm/Dl PRA = 0, private insurance, no prior PTx and enterically drained) transplanted with pancreata from each PDRI strata.

(20%) and intestinal leak (6.5%). A number of donor factors were found to correlate with technical failure, including increased BMI (> 30 kg/m^2), prolonged preservation time (> 24 h) and nontrauma death. Interestingly, neither age of the donor nor type of transplant (SPK vs. PAK/PTA) correlated with graft loss.

The use of older donors for SPK transplants has been recently examined using UNOS registry data and survival modeling (7). Salvalaggio et al. found a higher rate of graft loss in SPK recipients associated with donors > 45 years of age compared to younger donors. At 5 years, the death-censored pancreas graft survival in SPK recipients using younger donors was 80.1% versus 71.3% for older donors; patient survival was similar with 5-year survival rates of 84.5% for young donors and 81.0% for older donors. By comparison, the 5-year survival rate of patients wait-listed for SPKs was only 45.4%. In this analysis, acceptance of an older donor organ rather than remaining on the waiting list was associated with improved survival if the expected wait for a young donor exceeded 1.5 years. Median waiting time for a young donor in the United States was approximately 547 days. However, there was substantial regional variation in the percentage of patients receiving a young donor SPK in this time, from a low of 11.1% in Region 1 to 69% in Region 3. Thus, the authors conclude that the benefit (and thus utilization) of older donors is likely to vary by regional allocation practice and donor supply. The

Table 3: Unadjusted 1-year pancreas allograft survival by DRI and transplant type

	SPK		PAK		PTA	
DRI group	Adjusted% graft survival	95% Confidence limits	Adjusted% graft survival	95% Confidence limits	Adjusted% graft survival	95% Confidence limits
0.64–0.85	88	(87, 90)	84	(81, 87)	84	(76, 89)
0.86–1.15	87	(86, 89)	77	(73, 79)	82	(77, 87)
1.16–1.56	82	(79, 84)	75	(70, 79)	70	(61, 77)
1.57–2.11	78	(75, 81)	69	(61, 75)	68	(57, 77)
2.12–2.86	77	(70, 82)	67	(46, 81)		

Table 4: Adjusted 1-year pancreas allograft survival by DRI and transplant type. Adjusted for recipient characteristics (median/mode recipient)

	SPK		PAK		PTA	
DRI group	Adjusted% graft survival	95% Confidence limits	Adjusted% graft survival	95% Confidence limits	Adjusted% graft survival	95% Confidence limits
0.64–0.85	91	(89, 93)	89	(86, 92)	88	(83, 93)
0.86–1.15	90	(89, 92)	83	(80, 86)	88	(84, 92)
1.16–1.56	86	(83, 88)	81	(77, 85)	78	(71, 86)
1.57–2.11	83	(80, 87)	77	(71, 84)	77	(69, 86)
2.12–2.86	82	(77, 87)	—	(—,—)	—	(—,—)

successful use of older donors has also been considered in single center experiences. Data from Wake Forest Medical Center demonstrated no difference in pancreas allograft survival at 29 months between conventional donors (80% vs. 79%) and extended donors (age <10 or >45) (8). In contrast, strong associations between donor age and graft survival were observed in the current and previous registry analyses; this discrepancy may be related to center selection and management practices that permit the successful use of pancreata from older donors as well as the greater number of cases available for analysis.

The other source of potential expansion of the donor pool, donation after cardiac death, has also been critically examined in small series and registry analyses. Early experience from the University of Wisconsin using DCD donors for SPKs demonstrated excellent pancreas allograft survival in DCD donors, despite a higher incidence of delayed graft function in the renal allograft (9,10). Registry analysis from transplants performed between 1993 and 2003 confirmed a growing use of DCD organs. However, by the end of 2003, only 0.1% of all PTxs were from DCDs. Our analysis of the SRTR database reveals that DCDs now represent 3.4% of all pancreas donors, demonstrating a growing comfort with this source of donor organs. In the previous analysis of registry data through 2002, there were no significant differences in pancreas allograft survival at 1, 3 or 5 years between DCD donor organs (92%, 82% and 74%, respectively) and DBD donors (86%, 77% and 70%, respectively). Acceptance of DCD organs is generally limited to donors with extubation and flush times of less than 30 min while donor demographic characteristics (age, sex, BMI) did not differ between the DCD and DBD population. However, we observed a marginally significant risk associated with DCD PTx (HR $= 1.39$, $p = 0.10$). Thus, the comparable unadjusted survival between DCD and DBD transplants noted in single center studies is likely a consequence of more careful selection of pancreata from DCD donors and may change as experience grows and organ selection criteria expand.

Expansion of the pool of available organs for SPK transplantation is crucial to meet demand for transplant and to keep waiting times for the uremic, diabetic patients to a minimum (11,12). Evaluation of the benefit of kidney transplantation using the metric of incremental life years from transplant has confirmed the value of SPK transplantation (13). When compared to the expected waiting list survival, SPK transplantation was associated with the greatest increase in expected life years from among all types of renal transplants. As demonstrated by Salvalaggio et al., the high waiting list mortality and long waiting time justifies the

Table 5: One-year cause of pancreas graft failure for (A) PTA/PAK and (B) SPK recipients

		Among failures not resulting in death n (%)		Among all failures	Among all Tx within 1 years – n (%) failed				Total
DRI Group	n Txps	Tech.	Immuno.	n (%) due to death	Due to death	Tech.	Immuno.	Unknown	n (%) failure
(A) PTA/PAK recipients									
		42 (58)	31 (42)	15 (15)	15 (2)	42 (6)	31 (5)	15 (2)	103 (16)
0.86–1.15	1014	94 (59)	66 (41)	32 (14)	32 (3)	94 (9)	66 (7)	31 (3)	223 (22)
1.16–1.56	522	60 (60)	40 (40)	14 (10)	14 (3)	60 (11)	40 (8)	25 (5)	139 (27)
1.57–2.11	246	40 (74)	14 (26)	9 (12)	9 (4)	40 (16)	14 (6)	14 (6)	77 (31)
2.12–2.86	57	6 (–)	5 (–)	1 (–)	1 (–)	6 (–)	5 (–)	3 (–)	15 (–)
(B) SAK recipients									
		77 (79)	21 (21)	36 (23)	36 (3)	77 (6)	21 (2)	26 (2)	160 (12)
0.86–1.15	1906	123 (78)	34 (22)	66 (27)	66 (4)	123 (6)	34 (2)	19 (1)	242 (13)
1.16–1.56	1135	90 (74)	31(26)	51 (25)	51 (4)	90 (8)	31 (3)	34 (3)	206 (18)
1.57–2.11	625	68 (77)	20 (23)	30 (22)	30 (5)	68 (11)	20 (3)	17 (3)	135 (22)
2.12–2.86	218	21 (68)	10 (32)	9 (18)	9 (4)	21 (10)	10 (5)	11 (5)	51 (23)

Table 6: Utilization: Summary of pancreas DRI by region, transplant type and center size (pancreas transplants from 6/30/2004 to 12/31/2006). Transplant-related characteristics (such as pancreas preservation time and donor CVA for PAK) were not used to compute the DRI for the purpose of evaluating utilization

					Transplant type							
					PAK/PTA				SPK			
	DRI percentiles				DRI percentiles				DRI percentiles			
All	N	25th	50th	75th	N	25th	50th	75th	N	25th	50th	75th
All	3375	0.84	1.00	1.3	1134	0.83	0.99	1.27	2241	0.84	1.01	1.31
Region												
1	121	0.85	1.07	1.36	90	0.83	1.03	1.36	31	0.94	1.13	1.41
2	458	0.85	1.03	1.27	174	0.8	0.98	1.17	284	0.89	1.05	1.35
3	403	0.84	0.98	1.23	58	0.82	0.95	1.1	345	0.84	0.99	1.27
4	156	0.81	0.93	1.19	34	0.84	0.96	1.03	122	0.81	0.93	1.22
5	487	0.83	0.95	1.18	117	0.83	0.92	1.08	370	0.83	0.96	1.21
6	95	0.85	0.91	1.14	15	0.89	1.19	1.38	80	0.84	0.91	1.05
7	670	0.85	1.08	1.47	312	0.85	1.05	1.46	358	0.86	1.09	1.5
8	129	0.82	0.92	1.17	24	0.87	1	1.23	105	0.81	0.91	1.15
9	97	0.86	1.02	1.37	41	0.84	0.97	1.21	56	0.88	1.08	1.4
10	444	0.85	1.05	1.44	179	0.84	1.07	1.5	265	0.85	1.03	1.42
11	315	0.82	0.98	1.19	90	0.82	0.93	1.07	225	0.82	1.01	1.22
Transplant type												
SPK	2241	0.84	1.01	1.31	—	—	—	—	—	0.84	1.01	1.31
PAK	857	0.83	0.98	1.28	—	0.83	0.98	1.28	2	—	—	—
PTA	277	0.84	0.99	1.24	—	0.84	0.99	1.24	0	—	—	—
Center size (per last 2.5 years)												
<10	233	0.82	0.94	1.19	66	0.82	0.92	1.21	167	0.82	0.95	1.19
10–19	569	0.83	0.96	1.23	157	0.82	1	1.25	412	0.83	0.96	1.23
20–29	486	0.83	0.97	1.23	147	0.82	0.97	1.24	339	0.83	0.98	1.22
30–39	282	0.83	0.97	1.2	78	0.81	0.95	1.12	204	0.84	0.99	1.21
>40	1805	0.85	1.03	1.39	686	0.84	1	1.33	1119	0.86	1.05	1.42

potential increased risk of the use of marginal organs in this population if the pancreas allograft survival rates can be maintained (7).

The use of pancreas allografts for solitary transplants (PTA and PAK) has been far more controversial. In a national registry analysis, Ventstrom et al. suggested that survival was actually reduced in patients who received PTA compared to those patients who remain on the waiting list (14). These findings were challenged by Gruessner et al. who examined a more contemporary cohort and found no detrimental effect of PTx on survival (15). However, they also did not demonstrate a mortality benefit. It should be noted that 1-year patient survival rates in PTA recipients are the highest of any solid organ transplant group. Furthermore, pancreas transplantation provides dramatic improvements in quality of life (16). Other benefits of PTx, including the reduction in end organ complications, have been extrapolated from the Diabetes Control and Complications trial, but have not been definitively proven in the PTA and PAK population (17). However, given the limited long-term success of islet transplantation and lack of good prospective studies, only whole organ PTx can truly result in sustained euglycemia without significant hypoglycemia.

The findings of this study, that pancreas allograft failure differs according to transplant type, should inform clinical decision making and allocation. The effect of changing donor characteristics can increase the relative risk of graft failure significantly and represented an absolute decrease in organ survival of greater than 10% at 1 year for the highest risk organs (Table 4). Use of donors with higher PDRI is appropriate and beneficial in the context of an SPK transplant versus a solitary PTx. Organs used for SPK transplantation have been demonstrated to have overall better survival and reduced graft loss even at higher PDRIs. PTA and PAK that use organs from relatively higher PDRI donors are associated with a slightly higher early technical failure rate contributing to early graft loss. Our data suggests this risk may be exacerbated by poor organ quality. Thus, high PDRI organs should be employed with greater caution in this population.

Equally important is the finding of significant differences in organ utilization across the nation as a function of center activity and waiting times. Concern over excess wastage of viable pancreas allografts has been voiced by several authors over the past several years. Stratta, Kaper and Krieger have all documented the underutilization of pancreas allografts nationally and in particular DSAs (5,18,19). This

practice reduces the number of organs recovered per donor and reduces access to life-saving SPK transplants. In part, this practice may be the result of caps on SPKs as a result of kidney payback obligations. It appears reasonable to limit the exportation of solitary pancreata from relatively high-risk donors when they could be used successfully as a local SPK transplant. As kidney sharing is often limited, many pancreata which could be used for a local SPK are discarded if allocated out of region for a PTA or PAK. Similar variation in utilization has also been observed in the Eurotransplant network (20). In their experience, organ acceptance can be predicted as a function of Pancreas Suitability Score (PASS). The PASS is a composite score including age, BMI, intensive care unit stay, history of cardiacarrest, elevated sodium, amylase, lipase and vasopressor requirement. However, unlike the PDRI, the PASS has not been correlated with graft outcome overall, nor in specific transplant types. It is therefore unclear whether these factors represent valid reasons for declining an offered organ.

The PDRI is subject to the limitations of all registry analyses and should be viewed as a work in progress. The donor factors here represent only those that are currently collected through the OPTN and are subject to reporting variation and a lack of retrospective validation. As such, other potentially important variables including donor surgeon experience, donor length of hospital stay, flush volume, vasopressor utilization and appearance of the gland were not included. However, an extensive list of variables was examined and excluded based on statistical analysis including type of preservation solution and donor amylase. Because PTx surgeons remain conservative, the allografts available for evaluation through the PDRI are already a highly selected group, perhaps excluded based on these factors. Therefore, the predictive value of these factors may not be captured given the limited number of high-risks grafts that have been previously utilized.

The PDRI does include cold ischemia time as an important component of the index. While this is not strictly a donor characteristic, it is driven by the location of the donor and the intrinsic limitation of travel time. Recipient surgeons can generally estimate logistical factors and incorporate them into the organ acceptance decision. It is also important to note that for applications and analyses where the CIT is not yet known or not relevant, the PDRI can be calculated using the same equation without CIT data without any loss of utility. Under these circumstances, the CIT term in the equation can be eliminated or set to the reference value such that the contribution of the CIT term to the PDRI calculation is zero. Thus, utilization of the PDRI is possible in either allocation algorithms or simply for communication of pure donor risk at the time of organ offer. In fact, use of the liver and kidney DRI equations, both of which technically include CIT, are being considered for these purposes by the OPTN. For the allocation and regional variation analyses in this study, the ischemia time was held constant at 12 h, allowing an accurate reflection of region variability.

The PDRI is also a complex interaction of multiple variables. However, with the readily accessible technology available through the OPTN, we anticipate that the PDRI could be easily calculated and provided to clinicians at the time of a specific donor offer. Equally important, patients can be apprised of the potential impact of donor quality on the balance between waiting time and risk of graft failure.

In summary, the PDRI was used to assess the differential impact of organ quality on PTx outcomes within a particular clinical scenario (SPK, PAK and PTA), between the groups and according to recipient severity of illness. The PDRI predicted PTx graft outcome using data available at the time of the organ offer. Increased PDRI was associated with a significant, graded reduction in 1-year pancreas graft survival. PDRI is a useful measure of graft quality and demonstrates the potential value to inform organ acceptance, understand opportunities to enhance efficiency of the organ allocation process, and potentially improve the utilization of higher risk organs in appropriate clinical settings.

Acknowledgment

Funding Sources: The Scientific Registry of Transplant Recipients is funded by contract number 234-2005-37009C from the Health Resources and Services Administration, U.S. Department of Health and Human Services. The views expressed herein are those of the authors and not necessarily those of the U.S. Government.

Human Subjects Statement: This study was approved by HRSA's SRTR project officer. HRSA has determined that this study satisfies the criteria for the IRB exemption described in the Public Benefit and Service Program_ provisions of 45 CFR 46.101(b)(5) and HRSA Circular 03.

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