

Selected Mildly Obese Donors Can Be Used Safely in Simultaneous Pancreas and Kidney Transplantation

Tarek Alhamad, MD, MS,^{1,2} Andrew F. Malone, MD,¹ Krista L. Lentine, MD, PhD,^{3,4} Daniel C. Brennan, MD,¹ Jason Wellen, MD,⁵ Su-Hsin Chang, PhD,⁶ and Harini A. Chakkerla, MD⁷

Background. Donor obesity, defined as donor body mass index (D-BMI) of 30 kg/m² or greater, has been associated with increased risk of technical failure and poor pancreas allograft outcomes. Many transplant centers establish a threshold of D-BMI of 30 kg/m² to decline donor offers for pancreas transplantation. However, no previous studies differentiate the impact of mild (D-BMI, 30-35 kg/m²) versus severe obesity (D-BMI, ≥35 kg/m²) on pancreas allograft outcomes. **Methods.** We examined Organ Procurement Transplant Network database records for 9916 simultaneous pancreas-kidney transplants (SPKT) performed between 2000 and 2013. We categorized donor body mass index (D-BMI) into 4 groups: 20 to 25 (n = 5724), 25 to 30 (n = 3303), 30 to 35 (n = 751), and 35 to 50 kg/m² (n = 138). Associations of D-BMI with pancreas and kidney allograft failure were assessed by multivariate Cox regression adjusted for recipient, donor, and transplant factors. **Results.** Compared with D-BMI 20 to 25 kg/m², only D-BMI 35 to 50 kg/m² was associated with significantly higher pancreas allograft [adjusted hazard ratio [aHR], 1.37; 95% confidence interval [CI], 1.04-1.79] and kidney allograft (aHR, 1.36; CI, 1.02-1.82) failure over the study period (13 years). Donor BMI 30 to 35 kg/m² did not impact pancreas allograft (aHR, 0.99; CI, 0.86-1.37) or kidney allograft (aHR, 0.98; CI, 0.84-1.15) failure. Similar patterns were noted at 3 months, and 1, 5, and 10 years posttransplant. **Conclusions.** These data support that pancreata from mildly obese donors (BMI, 30-35 kg/m²) can be safely used for transplantation, with comparable short-term and long-term outcomes as organs from lean donors. Consideration of pancreata from obese donors may decrease the pancreas discard rate.

(*Transplantation* 2016;00: 00–00)

Obesity has become an epidemic in the United States with more than one third of the adults obese as defined by body mass index (BMI) greater than or equal to 30 kg/m².^{1,2} Trends of obesity in transplant donors mirror the high prevalence of obesity in the general population. The adverse impact of donor obesity on transplantation outcomes among solid organ recipients is a growing concern. Among kidney transplant recipients, donor BMI (D-BMI) over 30 kg/m² has been associated with increased risk of delayed graft function (DGF),^{3,4} although conclusions regarding the impact

of donor obesity on kidney allograft failure have been conflicting.⁴⁻⁷ The data on the impact of donor obesity on pancreas transplant outcomes is limited. A single-center study between 1994 and 2001 found that 11% of 711 pancreas allografts were from obese donors (BMI >30 kg/m²) and that D-BMI greater than 30 kg/m² was associated with higher pancreas allograft failure compared with transplants from nonobese (BMI <25 kg/m²) donors. However, this study categorized all donors with BMI greater than 30 kg/m² in 1 group and did not explore possible differences in the

Received 11 January 2016. Revision received 15 April 2016.

Accepted 20 April 2016.

¹ Division of Nephrology, Department of Internal Medicine, Washington University School of Medicine, St. Louis, MO.

² Transplant Epidemiology Research Collaboration (TERC), Institute of Public Health, Washington University School of Medicine, St. Louis, MO.

³ Center for Transplantation Research, Saint Louis University School of Medicine, St. Louis, MO.

⁴ Division of Nephrology, Department of Internal Medicine, Saint Louis University School of Medicine, St. Louis, MO.

⁵ Department of Surgery, Washington University School of Medicine, St. Louis, MO.

⁶ Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, St. Louis, MO.

⁷ Division of Nephrology, Department of Medicine, Mayo Clinic, Phoenix, AZ.

The data reported here have been supplied by the United Network for Organ Sharing (UNOS) as the contractor for the Organ Procurement and Transplantation Network (OPTN). The interpretation and reporting of these data are the responsibility of the

author(s) and in no way should be seen as an official policy of or interpretation by the OPTN or the U.S. Government.

T.A. participated in study design, data acquisition, data analysis, interpretation, and writing of the article. A.M. participated in study design, interpretation, and writing of the article. K.L.L. participated in study design, interpretation, and writing of the article. D.C.B. participated in study design, interpretation, and writing of the article. J.W. participated in study design and writing of the article. S.-H.C. participated in data analysis and writing of the article. H.A.C. participated in study design, data acquisition, interpretation, and writing of the article.

Correspondence: Tarek Alhamad, MD, MS, Division of Nephrology, Washington University School of Medicine in St. Louis, 660 S. Euclid Avenue. CB: 8126. St. Louis, MO (talhamad@dom.wustl.edu).

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal's Web site (www.transplantjournal.com).

Copyright © 2016 Wolters Kluwer Health, Inc. All rights reserved.

ISSN: 0041-1337/16/0000-00

DOI: 10.1097/TP.0000000000001303

impact of mild (BMI, 30-35 kg/m²) versus severe donor obesity (BMI, >35 kg/m²) on pancreas allograft survival.⁸ Similarly, Stegal et al⁹ reviewed United Organ Network Sharing (UNOS) data between 2000 and 2003, and reported associations of D-BMI above 30 kg/m² (n=279) with a trend toward worse 3-year pancreas allograft survival when compared with D-BMI below 30 kg/m² (68.0% vs 77.9% at 3 years, *P* = 0.06) in the SPK setting. Similar to the previous study, all donors with BMI greater than 30 kg/m² were placed into 1 high-risk group.

Given existing knowledge gaps in the outcome implications of the severity of donor obesity, we examined the impact of donor BMI on pancreas and kidney allograft survival after SPKT considering the impact of 2 donor subgroups, mildly obese (D-BMI, 30-35 kg/m²) and very obese (D-BMI, ≥ 35 kg/m²) donors compared with nonobese donors.

MATERIALS AND METHODS

Study Population/Material

The study cohort was composed of all adult patients who received an SPKT between January 1, 2000, and December 31, 2013, based on the UNOS/Organ Procurement and Transplantation Network's (OPTN) database. We excluded previous organ transplant recipients and recipients of organs donated after cardiac death. The donor weight and height recorded at the time of procurement were used to calculate the D-BMI. Patients were categorized into 4 groups according to D-BMI: 20 to less than 25 kg/m², referred to as lean donors; 25 or greater to less than 30 kg/m², referred to as overweight donors; 30 or greater to less than 35 kg/m², referred to as mildly obese donors; 35 or greater to 50 kg/m², referred to as severely obese donors. The highest documented D-BMI was 50 kg/m² in the cohort. Donor BMI of 35 to 40 kg/m² (n = 111) and D-BMI of 40 to 50 kg/m² (n = 27) were combined due to small numbers.

Kidney allograft failure was defined as retransplantation, initiation of dialysis, or patient death. Pancreas allograft failure was defined as graft loss (as reported to UNOS) or patient death. Patient death was included as allograft loss regardless of the functional status of the kidney or the pancreas allograft at the time of death. The posttransplant mortality outcome included death from any cause. Delayed graft function of the kidney was defined as requirement for dialysis during the first postoperative week. Peak panel-reactive antibody (PRA) was calculated based on the higher PRA of class 1 or class 2 before transplantation. In addition to cold ischemia time, preservation time was defined as the sum of cold ischemia time and recipient warm ischemia time. We combined reported acute rejection episodes at discharge, 6 months, and 12 months into the definition of first-year acute rejection for the pancreas and kidney allografts, respectively.

The pancreas donor risk index (PDRI) is a risk index for 1-year pancreas survival that contains 10 donor factors and 1 transplant factor including donor age, sex, race, BMI, height, cause of death, preservation time, donation after cardiac death, and terminal creatinine and cold ischemia time.¹⁰ The PDRI was calculated only for donors with available donor factors and preservation time (no imputation was used). The PDRI was categorized in a similar manner to the original study except that we combined the first 2 categories into 1

group to correspond to the first quartile in our cohort, as: less than 1.16, 1.16 to 1.56, 1.57 to 2.11, and 2.12 or greater.

Statistical Methods

Patient characteristics were described using proportions for categorical variables, and means with standard deviations for continuous variables. Recipient and donor factors were compared among the 4 D-BMI groups using a χ^2 test for categorical variables and analysis of variance test or Kruskal-Wallis tests for continuous variables.

Kaplan-Meier analysis was used to estimate overall and D-BMI group-specific allograft and patient survival. The Log rank test was used to compare the statistical significance of differences in survival outcomes across D-BMI strata. Cox proportional hazards analysis including adjustment baseline donor and recipient characteristics were performed to examine independent associations of D-BMI on risks of kidney and pancreas allograft failure and patient mortality. Finally, multivariate logistic regression was used to examine the associations of D-BMI with pancreas as well as kidney acute rejection within 1 year posttransplant. All statistical analyses were performed using SAS statistical software (version 9.3, Cary, NC).

RESULTS

Baseline Characteristics of Study Cohort

The study cohort included 9916 SPKTs between January 2000 and December 2013. Among the SPKT donors, 58% were lean (D-BMI 20-25 kg/m², n = 5724), 33% were overweight (D-BMI 25-30 kg/m², n = 3303), 8% were mildly obese (D-BMI 30-35 kg/m², n = 751), and 1% were severely obese (D-BMI 35-50 kg/m², n = 138). Among 106 724 registered brain death donors, the rate of pancreas transplant from lean donors (D-BMI 20-25) was 27%, D-BMI 25-30 was 17.5%, mildly obese donors (D-BMI 30-35) was 9.3%, and from severely obese donors (D-BMI 35-50) was 4.1%. Recipient and transplant characteristics including age, BMI, sex, race, hypertension, length of dialysis, time on the wait list, HLA mismatches, peak PRA, induction, center volume (number of transplant per year), and preservation time were not statistically different across the D-BMI groups (Table 1). Severely obese donors were more likely to be women, to have a history of hypertension, and to have died from cerebral vascular accidents or anoxia. The lean donors were more likely to be younger (*P* = 0.01). Kidney allografts from both mildly (9.4%) and severely obese (10.45) donors were more likely to develop DGF than organs from lean donors (7.3%, *P* = 0.01). Comparisons of other baseline factors are described in Table 1.

Pancreas Allograft Survival

No differences were observed in 1-, 5-, and 10-year pancreas survival comparing transplants from mildly obese versus the lean donors. However, pancreas allograft survival was inferior after transplants from severe obese compared with lean donors: 1-year survival, 77% versus 87%; 5-year survival, 62% versus 74%; and 10-year survival, 50% versus 56%, respectively (*P* = 0.03) (Figure 1).

After multivariate adjustment of recipient, donor, and transplant factors, mild donor obesity did not portend higher risk of pancreas graft failure (adjusted hazard ratio [aHR],

TABLE 1.
Recipient, donor, and transplant characteristics among SPKT recipients stratified according to D-BMI

	D-BMI 20-25 (n = 5724)	D-BMI 25-30 (n = 3303)	D-BMI 30-35 (n = 751)	D-BMI 35-50 (n = 138)	P
Recipient					
Age: mean ± SD, y	41.4 (8.6)	41.3 (8.5)	41.1 (8.6)	42.4 (8.9)	0.42
Sex					0.65
Female, %	38	38	36	36	
Race, %					0.74
White	73	72	72	71	
Black	16	16	17	17	
Hispanic	9	9	10	9	
Other	2	3	2	3	
BMI: mean ± SD	25 (4)	25.2 (4)	25.3 (4)	25.3 (4.6)	0.12
Length of dialysis, %					
Preemptive	20	19.3	18.4	24.6	0.11
≤2 y	36.6	32.3	36	39.9	
2-5 y	22.4	23.3	22.2	21.7	
>5 y	4.1	4.2	3.6	4.4	
Missing	21	20.9	19.8	9.4	
Waiting time for transplant, %					
≤1 y	61.6	60.9	64.5	71	0.13
1-3 y	33.1	33.4	30.9	23.2	
>3 y	5.4	5.7	4.5	5.8	
Delayed graft function, %	7.3	8.9	10.3	9.4	0.01
HLA mismatch, %					
0 Mismatch	1.6	1.5	1.9	1.5	0.43
1-2 Mismatches	3.9	4.8	4.1	5.8	
3-6 Mismatches	94.5	93.7	94	92.8	
Peak PRA, %					
0	59.9	60	60	63.8	0.58
1-20	24.6	24	24.6	27.5	
21-80	10.5	11.1	10.9	8	
81-100	3.3	3.3	4.1	0.7	
Missing	1.8	1.7	1.3	0	
Induction, %					
Thymoglobulin	21.3	21.8	21.4	23.2	0.84
IL2 receptor inhibitor	18.1	17.6	18.5	20.3	
Alemtuzumab	3.3	2.8	2.7	0.7	
Other	7.3	7.8	6.7	6.5	
No induction/missing	50	50.1	50.7	49.3	
Center volume, %					
<5 transplant per year	60	60	56	62	0.29
5-10 transplant per year	24	33	27	25	
≥10 transplant per year	16	17	17	13	
Donor					
Age: mean ± SD, y	25.5 (9.9)	28.2 (9.9)	28.3 (9.7)	28 (10.7)	0.01
Sex					
Female, %	30	29	35	57	0.01
Race, %					
White	67	65	66	68	0.29
Black	17	17	18	20	
Hispanic	13	15	14	11	
Other	3	3	2	1	
Hypertension, %	4.5	7.3	10.6	14.5	0.01
Terminal creatinine: mean ± SD, mg/dL	1 (0.8)	1.1 (0.7)	1.1 (0.6)	1 (0.4)	0.01
Primary cause of death, %					
Anoxia	12.1	11	11.7	15.2	0.01
CVA	16.8	19.2	19.6	26.1	
Head trauma/other	71.1	69.9	68.7	58.7	

Continued next page

TABLE 1. (Continued)

	D-BMI 20-25 (n = 5724)	D-BMI 25-30 (n = 3303)	D-BMI 30-35 (n = 751)	D-BMI 35-50 (n = 138)	P
Extended criteria donor, %	0.3	0.5	0.4	2.2	0.01
Organ sharing, %					
Local	88.4	88	87.8	84.8	0.06
Regional	8.3	7.9	8	7.3	
National	3.3	4.1	4.3	8	
Preservation Time (Donor CIT and Recipient WIT), %					
≤10 h	33.8	33.7	36.8	31.9	0.85
10-20 h	44.4	44.6	42.9	44.2	
>20 h	6.1	6.6	6.3	6.5	
Missing	15.7	15.1	14.1	17.4	
PDR categories, %					
0.6-1.15	69.4	52.9	32.1	14.9	0.01
1.16-1.56	20.4	28.7	38.6	43.9	
1.57-2.11	8.5	14	21.4	19.3	
≥2.12	1.8	4.5	(7.9)	21.9	
Secondary outcomes					
Pancreas rejection within first year, n (%)	8.5	8.9	10.1	6.5	0.37
Kidney rejection within first year, n (%)	10.3	11.3	11	14.5	0.25

CVA, cerebral vascular accidents.

0.99; confidence interval [CI], 0.86-1.37) compared with transplantation from lean donors, whereas severe obesity was associated with 37% higher risk of pancreas failure (aHR, 1.37; CI, 1.04-1.79) (Table 2). Recipient factors significantly associated with pancreas failure included black race, higher recipient BMI, higher PRA levels, kidney DGF,

and low transplant center volume. For the transplant center volume, centers that performed more than 10 SPKT per year had a lower risk for pancreas failure (aHR, 0.83; CI, 0.75-0.93), kidney failure (aHR, 0.88; CI, 0.78-0.98), and patient death (aHR, 0.86; CI, 0.74-1) compared with centers doing less than 5 SPKT per year (Table S1, SDC,

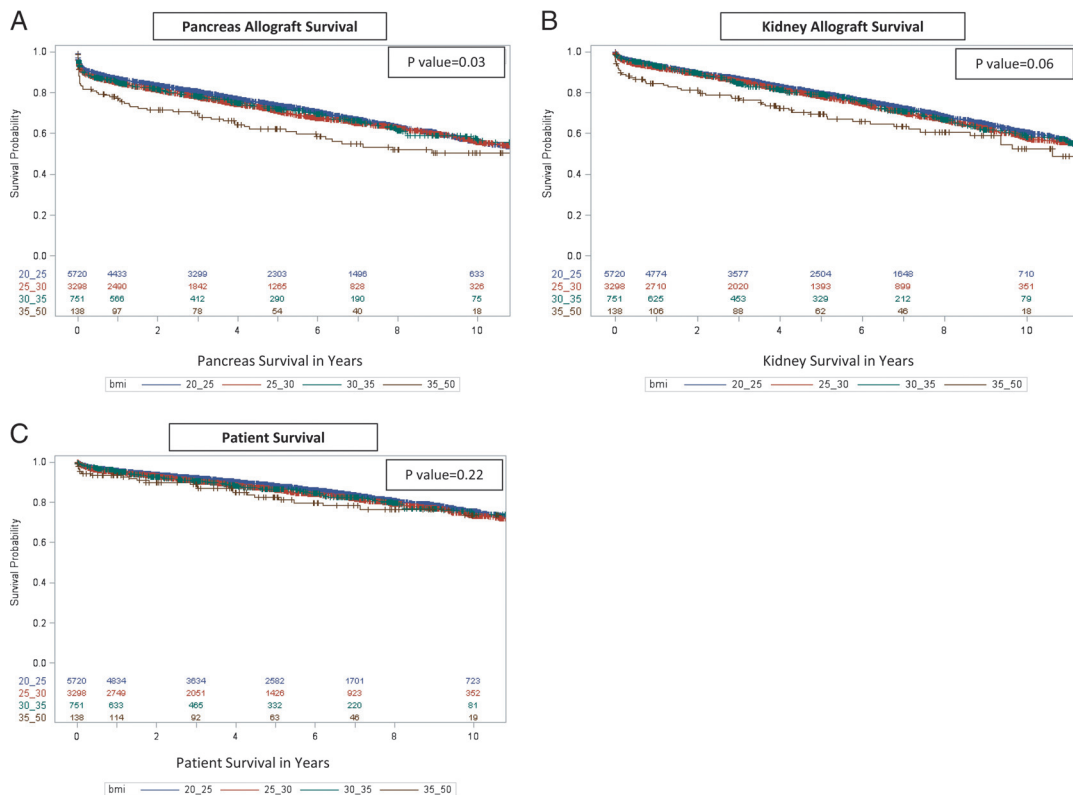


FIGURE 1. Kaplan-Meier pancreas, kidney, and patient survival probabilities among simultaneous pancreas and kidney transplantation recipients stratified according to donor body mass index.

TABLE 2.

Unadjusted and adjusted multivariate models for hazard of pancreas and kidney allograft failure stratified by donor body mass index

	Pancreas allograft failure				Kidney allograft failure			
	Unadjusted		Adjusted ^a		Unadjusted		Adjusted ^a	
Donor BMI	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
20-25 kg/m ²	Reference	—	Reference	—	Reference	—	Reference	—
25-30 kg/m ²	1.07 (0.99-1.16)	0.09	1.02 (0.94-1.11)	0.61	1.07 (0.98-1.16)	0.12	1.02 (0.93-1.11)	0.74
30-35 kg/m ²	1.05 (0.91-1.2)	0.49	0.99 (0.86-1.37)	0.85	1.06 (0.92-1.23)	0.43	0.98 (0.84-1.15)	0.82
35-50 kg/m ²	1.43 (1.1-1.86)	0.01	1.37 (1.04-1.79)	0.02	1.41 (1.07-1.87)	0.02	1.36 (1.02-1.82)	0.04
	Patient Death							
Donor BMI	Unadjusted		Adjusted ^a		Unadjusted		Adjusted ^a	
	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P	HR (95% CI)	P
20-25 kg/m ²	Reference	—	Reference	—				
25-30 kg/m ²	1.11 (0.99-1.24)	0.07	1.09 (0.97-1.22)	0.16				
30-35 kg/m ²	1.11 (0.91-1.35)	0.3	1.06 (0.87-1.29)	0.53				
35-50 kg/m ²	1.22 (0.82-1.82)	0.33	1.21 (0.8-1.82)	0.37				

^a Adjusted for recipient age, sex, race, body mass index, dialysis vintage, wait list time, human leukocyte antigen mismatch, peak panel reactive antigen, induction, delayed graft function, and center volume, and for donor age, sex, race, hypertension, and terminal creatinine, cause of death, organ sharing, and pancreas preservation time (Table S1, SDC, <http://links.lww.com/TP/B300> for full regression results).

<http://links.lww.com/TP/B300>). Other donor factors associated with pancreas failure risk included increasing age, black race, cerebral vascular accident as a cause of death, and national sharing (compared with local) (Table S1, SDC, <http://links.lww.com/TP/B300>).

Further multivariate analyses were performed at different time points and showed that mild donor obesity did not increase the risk of pancreas graft failure at 3 months (aHR, 1.08; CI, 0.85-1.36), 1 year (aHR, 1.06; CI, 0.87-1.3), 5 years (aHR, 1.04; CI, 0.88-1.21), or 10 years (aHR, 0.98; CI, 0.56-1.14) compared with transplant from lean donors (Figure 2). In contrast, severe obesity (D-BMI group, 35-50 kg/m²) was associated with increased risk of pancreas graft failure at 3 months, 1 year, 5 years, and 10 years (Figure 2).

Kidney Allograft Survival

There was a strong trend toward worse kidney survival after SPKT from severely obese donors compared with other

D-BMI groups. The 1-, 5-, and 10-year kidney allograft survival rates after transplants from very obese donors were 84%, 70%, and 52%, respectively, compared with survival rates of 93%, 80%, and 61% after transplants from lean donors, respectively (P = 0.06). There were no significant differences in kidney graft survival after SPKT from mildly obese compared with lean donors (Figure 1).

After multivariate adjustment, and compared with the lean donor, there was no difference in kidney allograft survival in the mild obese donors (aHR, 0.98; CI, 0.84-1.15), whereas severe obese donors conferred a 36% higher risk of kidney allograft failure (aHR, 1.36; CI, 1.02-1.82) (Table 2). Other risk factors associated with kidney allograft failure are listed in Table S1 (SDC, <http://links.lww.com/TP/B300>).

Patient Survival

No significant differences were noted in patient survival across the D-BMI groups at 1-, 5-, and 10-year follow-up (Figure 1). After multivariate adjustment, mild obese donors

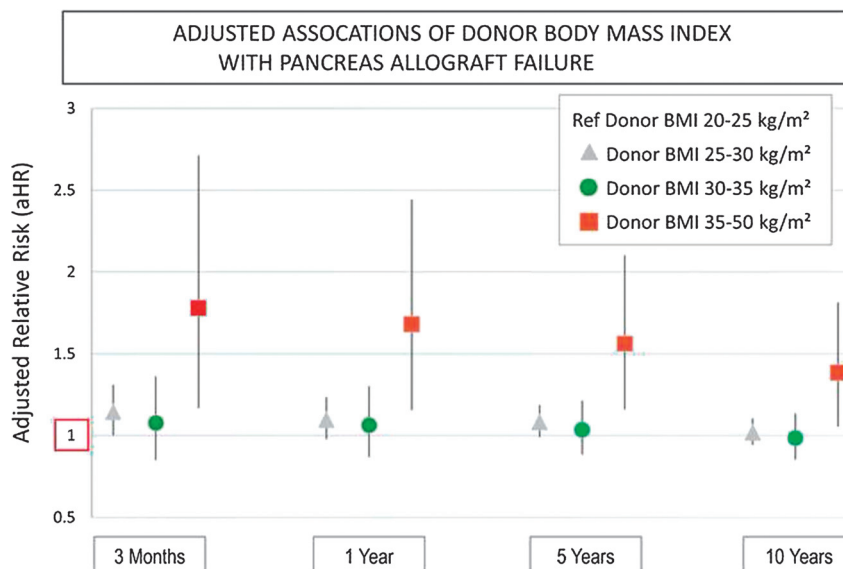


FIGURE 2. Association of donor body mass index and pancreas allograft failure at 3 months, 1 year, 5 years, and 10 years.

did not confer higher risk for patient death (aHR, 1.21; CI, 0.8-1.82) compared with lean donors (Table 2).

Causes of Pancreas Allograft Failure

Pancreas allograft failure were reported in 7.7% (n = 439) of the D-BMI 20 to 25 kg/m², 13.3% (n = 439) of the D-BMI 25 to 30 kg/m², 9.2% (n = 69) of the D-BMI 30 to 35 kg/m², and 13.8% (n = 19) of the D-BMI 35–50 kg/m² within the first 3 months. Overall, there were significant differences in the cause of allograft failure within 3 months posttransplant across D-BMI strata ($P < 0.001$, Figure 3). Distributions of allograft failure causes across D-BMI levels of 20 to 25, 25 to 30, 30 to 35, and 35 to 50 kg/m², respectively, included: vascular thrombosis, 59%, 61%, 54%, and 74%; infection, 7%, 6%, 7%, and 0%; bleeding, 2%, 3%, 0%, and 0%; anastomotic leak, 4%, 6%, 6%, and 0%; pancreatitis, 4%, 5%, 10%, and 5%; rejection, 6%, 5%, 10%, and 0%; primary nonfunction, 7%, 5%, 4%, and 5%; and unspecified, 12%, 10%, 9%, and 16%.

Rejection within 1 Year

Frequencies of pancreas and kidney acute rejection were similar among recipients of SPKT from the various D-BMI groups (Table 1). Compared with lean donors, mild obese (odds ratio [OR], 1.21; CI, 0.94-1.56) and severe obese donors (OR, 0.75; CI, 0.38-1.48) were not associated with higher risks of pancreas rejection. Similarly, compared with lean donors, mild obese (OR, 1.06; CI, 0.83-1.36) and severe obese donors (OR, 1.47; CI, 0.91-2.4) were not associated with higher risk of kidney rejection.

Pancreas Donor Risk Index

The D-BMI group 35 to 50 kg/m² had the highest percentage of PDRI (≥ 2.12 [21.9%]) and the lowest percentage of PDRI (0.6-1.15 [14.9%]) compared with the other D-BMI groups (Table 1). Among the lean donor BMI group, the 1-year pancreas allograft survival was 89%, 85%, 81%, and 81% across PDRI levels less than 1.16, 1.16-1.56, 1.57-2.11, and 2.11, respectively. Among the SPKT from severely obese donors, the 1-year pancreas allograft survival was 93%, 86%, 82%, and 72% across PDRI levels less than 1.16, 1.16-1.56, 1.57-2.11, and greater than 2.11, respectively (Figure 3).

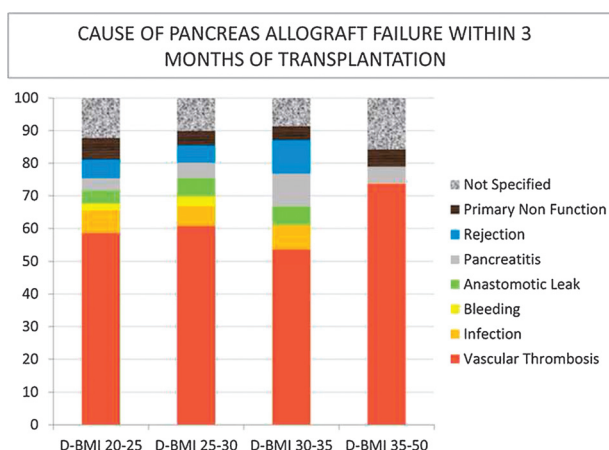


FIGURE 3. Causes of pancreas allograft failure within 3 months of transplantation.

Discussion

There is a general reluctance to procure organs for SPKT from obese donors (BMI over 30 kg/m²) due to concerns of suboptimal organ quality and inferior allograft survival. Prior studies have reported inferior pancreas allograft survival among donors with BMI greater than 30 kg/m².⁸⁻¹⁴ Many transplant centers, therefore, established a donor BMI of 30 kg/m² as a cutoff for accepting pancreata. However, these previous reports did not distinguish outcomes between mildly obese donors (BMI, 30-35 kg/m²) and severely obese (BMI, ≥ 35 kg/m²). In another single-center study that included all pancreas transplants (n = 308) between 2003 and 2009 examined the impact of obese donors (defined by donor BMI ≥ 30 kg/m²).¹⁵ The study concluded that pancreas transplant from donors with 30 kg/m² or greater can be accomplished with similar outcomes to the lean donors. However, this study included only 7 donors with BMI more than 35 kg/m² and did not perform multivariate analysis.¹⁵ We performed a more granular analysis of obese SPKT donors and demonstrate that organs procured from mildly obese donors (D-BMI 30–35 kg/m²) were not associated with higher risk of pancreas allograft failure or kidney allograft failure compared with the lean donors. In contrast, SPKT from severe obese donors was associated with 37% higher risk of pancreas allograft failure (aHR, 1.37; CI, 1.04-1.79) and 36% higher risk for kidney allograft failure (aHR, 1.36; CI, 1.02-1.82) compared with transplants from lean donors.

Technical failure remains a major issue in pancreas transplantation affecting 7% to 22% of recipients.^{11,16,17} Most common causes of technical failure are allograft thrombosis, allograft pancreatitis, intra-abdominal infections, leaks, and bleeding. A recent single-center study reported that donor BMI of 30 kg/m² or greater had a strong trend of association with technical failure (defined within 3 months of transplantation) (aHR, 1.6; CI, 0.95-2.68; $P=0.076$) in the full model of multivariate analysis.¹¹ In the reduced model, a significant association (aHR, 1.87; CI, 1.21-2.88) was reported. However, similar to previous reports, all donors with BMI of 30 kg/m² or greater were categorized in 1 group. In our results, use of mildly obese donor was not associated with increased risk of pancreas graft failure at 3 months (Figure 2). It is worthwhile to note that severe obesity (D-BMI, 35-50 kg/m²) had its major impact on graft failure shortly after transplantation, which is likely attributed to technical failure (Figure 1A). In examining the causes of allograft failure within the first 3 months, 74% of failures in the D-BMI of 35 to 50 kg/m² were attributed to allograft thrombosis versus 53% in the D-BMI 30 to 35 kg/m². The D-BMI 30 to 35 kg/m² had a higher rate of graft failure secondary to pancreatitis and rejection. However, further analysis showed that mild obesity and severe obesity are not associated with higher risk of rejection within 1 year. Overall, 12% of causes were not specified, which makes conclusions of some specific reasons of failure are difficult to interpret especially in the setting of a small group of failure in the severely obese donors (n = 19).

The PDRI was developed to predict pancreas graft failure at 1 year.¹⁰ It is interpreted as a risk ratio comparing the particular donor to a median risk donor. With respect to donor BMI, the reference donor (PDRI = 1.00) had a BMI of 24 kg/m².¹⁰ In our cohort and as expected, the higher the

1 year pancreas allograft survival in the D-BMI group 20-25 kg/m² and 30-35 kg/m² by PDRI

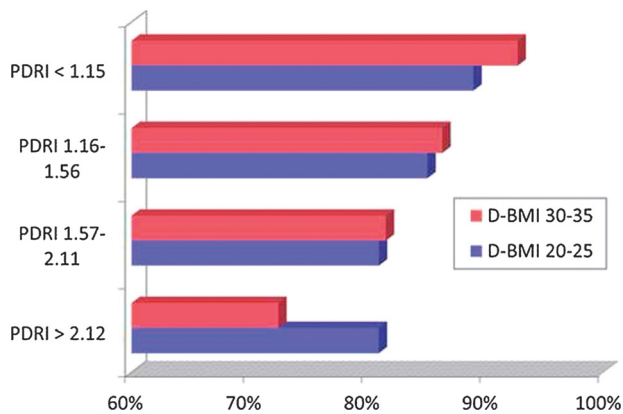


FIGURE 4. One-year pancreas allograft survival in the D-BMI group 20 to 25 kg/m² and 30 to 35 kg/m² stratified according to the PDRI groups.

D-BMI, the higher was the PDRI. Overall, pancreas allograft survivals at 1 year in the D-BMI group 20 to 25 kg/m² and 30 to 35 kg/m² were similar except that we observed a 9% decrease in pancreas graft survival when PDRI is more than 2.11 (Figure 4). Although not significant, but being more cautious is warranted when considering these donors with high PDRI.

The volume of pancreas transplant procedures performed at a center has been previously reported to impact pancreas allograft survival.¹⁸ In the multivariate model adjusting for center volume, we demonstrated that centers performing more than 10 SPKT per year had a lower risk for pancreas failure (aHR, 0.83; CI, 0.75-0.93), kidney failure (aHR, 0.88; CI, 0.78-0.98), and patient death (aHR, 0.86; CI, 0.74-1) compared with centers doing less than 5 SPKT per year. Pancreas transplantation remains a technically challenging procedure and increase in surgical expertise and establishing a well-developed pancreas multidisciplinary team would contribute to better outcomes. Our results should not replace visual inspection of pancreas organ by transplant surgeon, but to encourage not declining organs solely based on the status of mildly obese donor (when the PDRI is not higher than 2.12). Clinical judgment of other donor risk factors and use of PDRI would be always encouraged.

Pancreas has the highest discard rate among solid organ transplants, and this has increased over the last decade from 18% in 1998 to 28% in 2011.¹⁹ In the same time, recent SRTR/OPTN annual report indicates that the percentage of patients waiting more than 5 years for SPK increased from 4.5% in 2004 to 8.6% in 2014.²⁰ Similarly, the percentage of highly sensitized patients in the waiting list for SPK (calculated panel reactive antibody, 98-100%) has doubled from 5% in 2004 to 9.9% in 2014.²⁰ Expanding the donor pool by considering mildly obese donors will create new chances and increase the opportunities for pancreas transplantation of highly sensitized patients and possibly decrease the waiting time.

The approval of the United States Federal food and Drug Administration (FDA) of islet cell transplantation may increase the use of pancreas organs from mildly obese donor, which may result in a greater competition of utilizing these organs.

This is the first study to our knowledge differentiating the impact of mildly obese (BMI, 30-35 kg/m²) and severely obese (BMI, >35 kg/m²) donors on allograft and patient survival after SPK transplantation. Some of the limitations of the study include inherent concerns of analyzing registry data with missing data. To reduce the impact of missing data, we created a “missing” category for the variables. Additionally, variables including patient compliance, center-specific delivery of care were not captured in the available data. We were not able to directly measure hyperselection for pancreas organs, but we included all relevant donor and recipient factors in the national registry study in the multivariate analysis model to reduce its impact. We also examined 1-year pancreas survival according to PDRI and found that worse outcome should be expected if the PDRI greater than 2.12. The possibility of uncaptured complications in the OPTN is another limitation. Lastly, we lacked sufficient sample size and statistical power to further assess gradations in risk with donor BMI 35 kg/m² or greater. We examined center-reported pancreas graft failure as part of available outcome measures and reporting practices may vary across centers. It is only recently that UNOS has suggested offering at standardized criteria defining pancreas failure to include: recipient's transplanted pancreas is removed, recipient reregisters for a pancreas, recipient registers for an islet transplant after receiving a pancreas transplant, recipient's total insulin use is greater than or equal to 0.5 units/kg per day for a consecutive 90 days or recipient dies (OPTN policy 1.2 definitions; effective upon implementation and notice to members).²¹

CONCLUSIONS

Given the increasing prevalence of diabetes mellitus and the growing need for pancreata for SPKT among patients with end stage renal disease secondary to diabetes, there is an increasing need for identifying optimal pancreata for transplantation. Our examination of the impact of the degree of donor obesity on outcomes after SPKT suggests that D-BMI between 30 and 35 kg/m² does not increase the risk of pancreas allograft failure. Consideration of SPKT from mildly obese donors may increase the donor pool and decreases waiting times.

REFERENCES

- Ogden CL, Carroll MD, Kit BK, et al. Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA*. 2014;311:806–814.
- Lentine KL, Delos Santos R, Axelrod D, et al. Obesity and kidney transplant candidates: how big is too big for transplantation? *Am J Nephrol*. 2012;36:575–586.
- Weissenbacher A, Jara M, Ulmer H, et al. Recipient and donor body mass index as important risk factors for delayed kidney graft function. *Transplantation*. 2012;93:524–529.
- Gore J, Pham P, Danovitch G, et al. Obesity and outcome following renal transplantation. *Am J Transplant*. 2006;6:357–363.
- Kasiskie BL, Snyder JJ, Gilbertson D. Inadequate donor size in cadaver kidney transplantation. *Am J Nephrol*. 2002;13:2152–2159.
- Ortiz J, Gregg A, Wen X, et al. Impact of donor obesity and donation after cardiac death on outcomes after kidney transplantation. *Clin Transplant*. 2012;26:E284–E292.
- Reese PP, Feldman HL, Asch DA, et al. Short-term outcomes for obese live kidney donors and their recipients. *Transplantation*. 2009;88:662–671.
- Humar A, Ramcharan T, Kandaswamy R, et al. The impact of donor obesity on outcomes after cadaver pancreas transplants. *Am J Transplant*. 2004;4:605–610.
- Stegall MD, Dean PG, Sung R, et al. The rationale for the new deceased donor pancreas allocation schema. *Transplantation*. 2007;83(9):1156–1161.

10. Axelrod DA, Sung RS, Meyer KH, et al. Systematic evaluation of pancreas allograft quality, outcomes and geographic variation in utilization. *Am J Transplant.* 2010;10:837–845.
11. Finger EB, Radosevich DM, Dunn TB, et al. A composite risk model for predicting technical failure in pancreas transplantation. *Am J Transplant.* 2013;13:1840–1849.
12. Sousa MG, Linhares MM, Gonzalez AM, et al. Multivariate analysis of risk factors for early loss of pancreas grafts among simultaneous pancreas-kidney transplants. *Transplant Proc.* 2010;42:547–551.
13. Sousa MG, Linhares MM, Salzedas-Netto AA, et al. Risk factors of pancreatic graft loss and death of receptor after simultaneous pancreas/kidney transplantation. *Transplant Proc.* 2014;46:1827–1835.
14. Hilling DE, Baranski AG, Haasnoot A, et al. Contribution of donor and recipient characteristics to short- and long-term pancreas graft survival. *Ann Transplant.* 2012;17:28–38.
15. Fridell JA, Mangus RS, Taber TE, et al. Growth of a nation part I: impact of organ donor obesity on whole-organ pancreas transplantation. *Clin Transplant.* 2011;25:E225–E232.
16. Humar A, Ramcharan T, Kandaswamy R, et al. Technical failures after pancreas transplants: why grafts fail and the risk factors—a multivariate analysis. *Transplantation.* 2004 ;78:1188–92.
17. Norman SP, Kommareddi M, Ojo AO, et al. Early pancreas graft failure is associated with inferior late clinical outcomes after simultaneous kidney-pancreas transplantation. *Transplantation.* 2011;92:796–801.
18. Mandal AK, Drew N, Lapidus JA. The effect of center volume on pancreas transplant outcomes. *Surgery.* 2004;136:225–231.
19. Kandaswamy R, Stock PG, Skeans MA, et al. OPTN/SRTR 2011 Annual Data Report: pancreas. *Am J Transplant.* 2013;13(Suppl 1):47–72.
20. Kandaswamy R, Skeans MA, Gustafson SK, et al. Pancreas. *Am J Transplant.* 2016;16:47–68.
21. Changes UP. OPTN/UNOS Policy 1. Administrative Rules and Definitions. Definition of Pancreas Graft Failure (approved, pending implementation). http://optn.transplant.hrsa.gov/media/1211/policy_notice_07-2015.pdf. Published July 1st, 2015. Accessed January 7, 2016.