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Risk Factors for Early Post-transplant Weight Changes Among Simultaneous Pancreas-kidney Recipients and Impact on Outcomes

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Background. There are limited data about the risk factors for weight changes and the association of significant weight changes with graft and metabolic outcomes after simultaneous pancreas and kidney (SPK) transplantation. **Methods.** We included all SPK recipients with both allografts functioning for at least 6 mo post-transplant and categorized them based on the weight changes from baseline to 6 mo post-transplant. We analyzed risk factors for significant weight gain (SWG) and significant weight loss (SWL) over 6 mo post-transplant, as well as outcomes including pancreas uncensored graft failure, pancreas death-censored graft failure (DCGF), composite pancreas graft outcomes of DCGF, use of an antidiabetic agent, or hemoglobin A1C >6.5%, and kidney DCGF. **Results.** Of 280 SPK recipients, 153 (55%) experienced no significant weight change, 57 (20%) SWG, and 70 (25%) SWL. At 6 mo post-transplant, mean weight changes were 1.2% gain in the no significant weight change group, 13.4% gain in SWG, and 9.6% loss in the SWL groups. In multivariate analysis, the only factor associated with decreased risk for weight gain was older recipient age (aOR, 0.97; 95% confidence intervals, 0.95-0.99). Importantly, SWG or SWL were not associated with pancreas graft failure, P-DCGF, or K-DCGF. Interestingly in the adjusted model, SWG at 6 mo was associated with a lower risk for composite outcomes (HR, 0.35; 95% confidence intervals, 0.14-0.85). **Conclusions.** Forty-five percent of SPK recipients had significant weight changes by 6 mo post-transplant, but only 20% exhibited SWG. Likely because of proper management, weight changes were not associated with poor outcomes post-SPK transplant.

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INTRODUCTION

Many studies have demonstrated an increase in weight after abdominal solid organ transplantation.[1-5] Weight gain most commonly occurs during the first year and particularly within the first 6 mo after the transplant.[6] This weight gain is mainly associated with increased adipose tissue and visceral fat deposition leading to an increased risk of insulin resistance and the development of diabetes.[7] One prospective observational study that aimed to assess changes in body composition, lifestyle factors, and metabolic responses among living donor kidney transplant recipients, reported a significant increase in body weight, at 3- and 12-mo post-transplant (2.2 kg, $P = 0.03$ and 6.6 kg, $P < 0.0001$, respectively). The authors observed that the weight gain was due mainly to visceral and subcutaneous fat accumulation and was associated with the occurrence of insulin resistance.[7] Among abdominal solid organ transplant recipients, most of the studies about post-transplant weight gain are among kidney transplant recipients. On average kidney transplant recipients gain ~10% of their body weight during the first year of the transplant.[2,8,9]

There are many reasons why recipients of simultaneous pancreas and kidney (SPK) transplants might experience significant weight gain. After successful pancreas transplantation,

they would not need exogenous insulin therapy, which has been associated with weight gain.[10] As is the case after successful kidney transplantation, reversal of uremia, and the use of glucocorticoids, coupled with physical inactivity, removal of multiple dietary restriction increase the risk for weight gain.[11] Pancreas transplant recipients may experience higher rates of rejection, necessitating increased doses of corticosteroids. Furthermore, currently the T1D population undergoing SPK transplantation tends to be more obese at baseline than in years past.[12] Also, more patients with T2D and ESRD are undergoing SPK transplants, and higher C-peptide levels are associated with obesity and weight gain among the general population.[13] In this study, we examine risk factors for significant weight gain or significant weight loss among all SPK recipients at our center and determine whether weight gain or loss portends worse graft survival or metabolic functional outcomes.

MATERIALS AND METHODS

Population Selection and Study Design

We evaluated all adult SPK recipients, who underwent SPK transplants between January 1, 2012, and March 31, 2022, at the University of Wisconsin. The exclusion criteria consisted of patients who were <18 y of age at the time of the transplant, pancreas-after-kidney recipients, or pancreas transplant-alone recipients. Further, we excluded recipients who experienced graft failure of either kidney or pancreas within 6 mo post-transplant. We chose 6 mo post-transplant to assess weight changes, as by then most of the recipients would have been on a stable dose of steroids, have stable graft function, and have relatively stable post-transplant course. Further, we included only those with both functional grafts to minimize any confounding factors associated with either kidney or pancreas graft failure with weight changes. SPK recipients were categorized based on the weight changes at 6 mo compared with their pretransplant baseline weight. Significant weight gain (SWG) was defined as ≥7% weight gain from immediate pretransplant; significant weight loss (SWL) as ≥5% weight loss and all others as no significant weight change (NWC) at 6 mo post-transplant. Risk factors for SWG or SWL at 6 mo were analyzed. Additionally, pancreas uncensored graft failure, pancreas death-censored graft failure (P-DCGF), a composite outcome of P-DCGF, use of an antidiabetic agent or hemoglobin A1C (HbA1c) >6.5%; and Kidney DCGF (K-DCGF) were outcomes of interest. Further, we analyzed those outcomes of interest among recipients with T2DM only. Also, further, we analyzed outcomes based on the changes in the BMI categories by 6 mo. This study was approved by the University of Wisconsin School of Medicine and Public Health Institutional Review Board (IRB protocol number: 2014-1072). This study followed the Declaration of Helsinki. The clinical and research activities being reported were consistent with the Principles of the Declaration of Istanbul as outlined in "The Declaration of Istanbul on Organ Trafficking and Transplant Tourism."

P-DCGF was defined based on the current United Network for Organ Sharing criteria for pancreas graft failure, which include removal of the pancreas graft, reregistration for a pancreas transplant, registration for an islet transplant after receiving pancreas, or an insulin requirement that is ≥0.5 units/kg/d for 90 consecutive d.[14] K-DCGF was defined as initiating dialysis or retransplantation before the end of the data analysis. Recipients were followed till the end of data analysis in October 2023 or till the P-DCGF and K-DCGF or death.

Definitions of Significant Weight Gain and Significant Weight Loss

The definition of significant weight gain is not consistent in the literature, weight gain of 3% or 5% has also been used, but we chose the most commonly used conservative measure of ≥7% weight gain as significant weight gain.[15-20] Significant weight loss was defined as a weight loss of ≥5% from the pretransplant to 6 mo post-transplant, which is a commonly used definition in the literature.[21,22] Further, we defined change in BMI categories based on the World Health Organization's definition of weight: normal BMI as 18.5–24.9 kg/m^2, overweight as BMI ≥ 25–29.9 kg/m^2, and obesity as BMI ≥ 30 kg/m^2.[23] If the recipient's BMI remained the same BMI categories pretransplant, and at 6 mo post-transplant, we defined that as stayed the same, if it went up to the higher BMI grade, as increased, and to the lower BMI grade as decreased.

Selection Criteria for Simultaneous Pancreas-kidney Transplant

SPK selection criteria are based on physical, psychological, medical, and surgical aspects of the patient's condition and are similar for type 1 diabetes (T1DM) or type 2 diabetes (T2DM) candidates at our center. All patients with T2DM were on insulin pretransplant, with detectable fasting C-peptide levels of at least 0.5 ng/mL or more with minimal cardiac and other comorbidities. All potential recipients were extensively discussed in the multidisciplinary selection meeting before approving or disapproving their SPK candidacy. At no time during this series or currently in our program, there was a protocolized criterion for pretransplant C-peptide level to approve or disapprove SPK transplant eligibility among T2DM candidates. The cutoff for BMI among T1DM was <32 kg/m^2 and for T2DM was <35 kg/m^2. Contraindications for SPK transplantation parallel with other solid organ transplant criteria (cardiovascular disease, active infection, cancer, noncompliance, and poor social support).[24]

All potential recipients are evaluated by a transplant dietitian during their pretransplant evaluation in the ambulatory clinic. Recipients are also followed post-transplant by a transplant dietitian if significant weight changes were observed or based on the physician's discretion or the patient's request.

Simultaneous Pancreas-kidney Transplant Procedure

All pancreas transplants were accomplished using enteric drainage, side-to-side duodenojejunostomy to the proximal jejunum without Roux-en-Y, and systemic venous drainage to the proximal right common iliac vein or distal inferior vena cava. In most cases, the kidney was placed contralaterally to the left iliac vessels.

Immunosuppression

Patients undergoing pancreas transplantation received induction immunosuppression with a depleting agent (antithymocyte globulin or alemtuzumab) or a nondepleting agent (basiliximab) based on immunological risk factors.[25] Patients having pretransplant donor-specific antibodies, recipients of a

secondary SPK,[26] those experiencing previous pancreas graft failure because of rejection, and those patients in whom an early steroid withdrawal was planned, were more likely to receive depleting agents for induction. Patients were typically maintained on a triple immunosuppressive regimen, with tacrolimus, mycophenolate mofetil or mycophenolic acid, and steroids. Some patients underwent early steroid withdrawal based on clinical judgment and the patient's request. Doses and drug levels were individually adjusted based on the patient's clinical condition, including infection, malignancy, and rejection. Most SPK recipients were maintained on tacrolimus with a trough goal of 10 to 12 ng/mL in the first 3 mo post-transplant, 8 to 10 ng/mL from months 3 to 12, and 6 to 8 ng/mL after 1 y. For patients in whom steroids were continued, prednisone was tapered to 5 to 10 mg daily by 7 wks post-transplant, with further taper determined by the managing provider. Patients undergoing early steroid withdrawal stopped steroids after postoperative day 4.

Pancreas Rejection Treatment

The majority of pancreas graft rejection episodes were biopsy proven. Pancreas biopsies were primarily performed for unexplained increases in pancreatic enzymes. We also performed a pancreas biopsy for the detection of de novo donor-specific antibodies as described before.[27] Treatment of pancreas rejection was based on the type and severity of rejection and was graded by the Banff criteria.[28] Acute T–cell mediated rejection was treated with IV steroid pulse with or without antithymocyte globulin 6 to 12 mg/kg in 4 to 10 divided doses, whereas mixed rejection was treated with steroids, antithymocyte globulin, intravenous immunoglobulin, and plasmapheresis. Antibody-mediated rejection was treated with steroids, intravenous immunoglobulin, and plasmapheresis.[29]

Statistical Analysis

Continuous data were compared using Student's *t*-test or the Wilcoxon rank-sum test, as appropriate, whereas categorical data were analyzed using Fisher's exact test or chi-square test. *P* values ≤0.05 were considered statistically significant. Risk factors associated with SWG or SWL with reference to NWC were studied using univariate and multivariate regression analyses. Variables associated with outcomes at a *P* value ≤0.10 in univariate analysis were kept in the multivariate analysis. Outcomes of interest were also analyzed as unadjusted and adjusted logistic regression models. All variables from the baseline characteristics in Table 1 were included in the adjusted model. A box and whisker chart showing the distribution of weights at various timeframes post-transplants between 3 groups was presented, along with the percentage change in the weight at 6 mo. Outcomes of interest were also presented as a Kaplan-Meier survival analysis. All analyses were performed using the MedCalc Statistical Software version 16.4.3 (MedCalc Software, Ostend, Belgium; https://www.medcalc.org; 2016).

RESULTS

A total of 301 SPK were transplanted during the study period, and 280 were included in the study based on the aforementioned exclusion criteria. Excluded cases were as follows: 19 cases of pancreas graft failure (6 also had kidney graft failure) and 2 cases of kidney graft failure only (with functioning pancreas graft) within 6 mo post-transplant. Of these 280 SPK recipients, 153 (55%) were in the NWC group, 57 (20%) with SWG, and 70 (25%) with SWL (Table 1). There were no significant differences in pretransplant BMI across the groups, 26.6 ± 3.5 kg/m^2 in NWC, 26.3 ± 4.0 in SWG, and 26.4 ± 3.5 in SWL group ($P = 0.85$), as well as no significant differences in actual body weight. Recipients experiencing SWL had significantly lower pretransplant fasting C-peptide compared with other groups (mean 0.76 ± 1.86 ng/mL SWL group, 2.5 ± 3.4 ng/mL SWG, and 2.2 ± 3.5 ng/mL NWC, $P = 0.002$). Also, recipients with SWL had a significantly higher proportion of T1DM compared with other groups (84% SWL group, 60% SWH group, and 62% NWC; $P = 0.002$). All other donor, immunological, and recipient baseline characteristics were not significantly different across the groups.

In univariate analysis recipients of older age at the time of transplant and recipients of pre-emptive transplantation (without being on dialysis) were less likely to gain significant weight (Table 2). None of the factors were associated with significant weight gain. After adjustment of multiple variables with *P* value ≤0.1, the only variable associated with decreased risk for weight gain was recipients of older age (HR, 0.97; 95% confidence intervals (CI), 0.95-0.99; $P = 0.04$). Of note, pretransplant C-peptide level was not associated with increased risk for weight gain. Similarly in univariate analysis recipients with higher pretransplant C-peptide levels were less likely to have significant weight loss (Table 3), and recipients with T1DM were more likely to have significant weight loss. After adjustment for these variables along with variables with *P* value ≤0.1 in univariate analysis, none of the factors were significantly associated with weight loss in multivariate analysis.

There were no significant differences across the groups for post-transplant follow-up (Table 4). The absolute weight at various time frames among the groups are summarized in Figure 1 and Table 4. Also, the percentage changes in weight at 6 mo among the groups are summarized in Figure 2.

Analyzing outcomes of interest at the last follow-up, with reference to NWC, neither SWG nor SWL was associated with any outcome (pancreas-uncensored graft failure, P-DCGF, pancreas composite outcomes or K-DCGF) (Table 5). This was further confirmed by the Kaplan-Meier survival analysis curve for these same outcomes (Figure 3). After adjustment for multiple variables, interestingly SWG was associated with a lower risk for composite outcomes of either P-DCGF or need for an antidiabetic agent or last HbA1c >6.5% (aHR, 0.35; 95% CI, 0.14-0.85; $P = 0.02$). Also, there was no significant difference in patient survival among these groups either based on the absolute weight changes or changes in BMI categories by the Kaplan-Meier survival analysis curve (Figure 4A,B).

At the time of transplant out of 280 recipients, 109 (40%) were in the normal BMI range pretransplant, of these at 6 mo, 85 continued to have normal BMI, 24, gained weight to become overweight/obese (including 1 obese). Similarly, 118 (42%) were overweight pretransplant and by 6 mo, 73 remained overweight, 26 gained weight and became obese, and 17 lost weight and became normal BMI range. Likewise, 53 (19%) were obese at the time of transplant, 40 remained obese, and 13 lost weight and became overweight. At 6 mo, 198 (71%) were in the same BMI category, and 52 (19%) SPK recipients, BMI categories increased from normal to overweight/obese or overweight to obese. In 30 (11%), BMI went down from overweight/obese to normal/overweight.

TABLE 1.

Baseline characteristics

	Variables	No significant change	Weight gain	Weight loss	*P*
Donor factors	Mean age (y)	26.6 ± 11.8	28.3 ± 12.3	27.6 ± 14.2	0.67
	Male (%)	106 (69)	34 (60)	39 (56)	0.11
	Non-white (%)	18 (12)	9 (16)	15 (21)	0.17
	Mean body mass index (kg/m^2)	23.5 ± 3.8	23.4 ± 3.8	22.9 ± 3.9	0.60
	Cause of death: cardiovascular (%)	20 (13)	8 (14)	13 (19)	0.55
	Terminal serum creatinine (mg/dL)	0.87 ± 0.36	0.79 ± 0.40	0.86 ± 0.48	0.44
	Mean kidney donor profile index %	25.3 ± 18.5	27.2 ± 19.3	30.5 ± 21.8	0.18
	Donation after circulatory death (%)	45 (29)	8 (14)	16 (21)	0.07
	Pancreas donor risk index	1.24 ± 0.47	1.30 ± 0.46	1.31 ± 0.53	0.58
	Pancreas cold ischemia time (h)	12.7 ± 4.0	11.5 ± 3.7	12.3 ± 3.7	0.13
	Kidney cold ischemia time (h)	14.8 ± 4.1	13.4 ± 3.8	14.4 ± 4.2	0.09
Immunologic factors	cPRA >20% (%)	19 (12)	7 (11)	15 (21)	0.051
	Mean HLA mismatch (of 6)	4.5 ± 1.2	4.4 ± 1.2	4.3 ± 1.2	0.39
	Previous transplant (%)	11 (7.2)	3 (5)	3 (4)	0.67
Recipients factors	Mean age (y)	47.2 ± 10.3	43.3 ± 8.7	46.0 ± 9.5	**0.04**
	Male (%)	105 (69)	38 (67)	37 (53)	0.07
	Non-white (%)	36 (24)	16 (28)	13 (19)	0.45
	Mean weight at the time of transplant (kg)	78.3 ± 15.8	77.8 ± 14.8	77.6 ± 13.9	0.95
	Mean body mass index (kg/m^2)	26.6 ± 3.5	26.3 ± 4.0	26.4 ± 3.5	0.85
	Mean pretransplant C-peptide (ng/mL)	2.2 ± 3.5	2.5 ± 3.4	0.76 ± 1.86	**0.002**
	Diabetes type				**0.002**
	Type I	95 (62)	34 (60)	59 (84)	
	Type II/other	58 (38)	23 (40)	11 (16)	
	Induction Immunosuppression (%)				0.17
	Alemtuzumab	49 (32)	20 (35)	17 (24)	
	Anti-thymocyte globulin	59 (39)	22 (39)	38 (54)	
	Basiliximab	45 (29)	20 (35)	15 (21)	
	Early steroid withdrawal (%)	13 (9)	5 (9)	5 (7)	0.93
	Preemptive transplant (%)	36 (24)	5 (9)	15 (21)	0.06
	Kidney-delayed graft function (%)	16 (11)	7 (12)	6 (9)	0.79

The bold values indicates statistical significance with $P > 0.05$.

TABLE 2.

Variables associated with significant weight gain by 6 mo post-transplant

		Univariate			Multivariate		
	Variables	OR	95% CI	p	OR	95% CI	p
Donor factors	Age/y	1.01	0.99-1.03	0.43			
	Male	0.74	0.44-1.25	0.26			
	Non-white	1.27	0.62-2.59	0.51			
	Body mass index/kg/m^2	0.99	0.93-1.06	0.84			
	Cause of death: Cardiovascular	1.06	0.50-2.24	0.88			
	Terminal serum Creatinine (mg/dL)	0.65	0.30-1.37	0.25			
	Kidney donor profile index/%	1.0	0.99-1.01	0.57			
	Donation after circulatory death	0.48	0.29-1.02	*0.06*	0.52	0.25-1.11	0.09
	Pancreas Cold ischemia time/hrs	0.94	0.88-1.01	*0.08*	1.02	0.83-1.24	0.88
	Kidney Cold ischemia time/hrs	0.93	0.88-1.01	*0.06*	0.93	0.76-1.13	0.45
Immunologic factors	cPRA >20%	0.61	0.22-1.69	0.37			
	HLA mismatch per of 6	0.92	0.75-1.13	0.45			
	Pancreas or kidney rejection within 6 mo	0.97	0.39-2.42	0.94			
	Previous transplant	0.78	0.24-2.49	0.67			
Recipients factors	Age/y	0.97	0.94-0.99	**0.03**	0.97	0.95-0.99	**0.04**
	Male	0.94	0.54-1.63	0.82			
	Non-white	1.18	0.67-2.11	0.56			
	Weight/kg	0.99	0.98-1.02	0.88			
	Body mass index/kg/m^2	0.98	0.92-1.05	0.66			
	Pretransplant C-peptide/ng/mL	1.02	0.94-1.09	0.72			
	Diabetes type: type I vs other/unknown	0.92	0.55-1.58	0.78			
	Nondepleting induction agent	1.21	0.70-2.08	0.50			
	Early steroid withdrawal	1.03	0.41-2.57	0.96			
	Pre-emptive transplant	0.39	0.16-0.99	**0.04**	0.41	0.16-1.03	0.06
	Kidney-delayed graft function	1.13	0.52-2.51	0.75			

The bold values indicates statistical significance with $P > 0.05$.
95% CI, 95% confidence intervals; OR, odds ratio.

Analyzing outcomes of interest at the last follow-up, with reference to no change in BMI categories, either increased or decreased BMI categories were not associated with outcomes of interest (Figure 5A-D).

Further, 87 (31%) were SPK recipients with T2DM among the entire cohort. Of these 87 recipients, 55 (63%) were in the NWC group, 21 (24%) with SWG, and 11 (13%) with SWL. Analyzing outcomes of interest at the last follow-up, with reference to NWC, neither SWG nor SWL was associated with any outcome (pancreas-uncensored graft failure, P-DCGF, pancreas composite outcomes, or K-DCGF) (Table 6). After adjustment for multiple variables, SWG was associated with a lower risk for composite outcomes of either P-DCGF or need for an antidiabetic agent or last HbA1c >6.5% (aHR, 0.01; 95% CI, 0.001-0.63; $P = 0.03$), which was a similar pattern to that observed in the entire cohort, whereas SWL was associated with increased risk for composite outcomes among T2D recipients (aHR, 8.28; 95% CI, 1.28-53.60; $P = 0.02$).

DISCUSSION

In this large cohort of 280 SPK recipients, only 20% had significant weight gain at 6 mo post-transplant, whereas 25% had significant weight loss. Some of the presumed variables including pretransplant weight and BMI, pretransplant C-peptide levels, and early steroid withdrawal were not associated with either significant weight gain or weight loss. Recipients who had significant weight loss at 6 mo gained some weight at various time frames; however, their weight at the last follow-up was only slightly above their pretransplant weight, by a mean of 0.37%. In contrast, those without significant weight change or with significant weight gain continued to gain weight throughout the course. With reference to no significant absolute weight changes or changes in BMI categories, neither weight gain nor weight loss was associated with better or worse graft outcomes. We acknowledge that substantial weight gain after SPK transplantation is not ideal and can have other health consequences despite the nonassociation with graft failure and post-transplant composite poor glycemic control, and patient survival outcomes.

Systemic venous drainage of the transplanted pancreas leads to hyperinsulinemia because of the direct drainage of insulin into the peripheral circulation, bypassing the hepatic extraction, that naturally occurs upon insulin secretion from the native pancreas.[30] The specific mechanisms by which hyperinsulinemia affects adiposity remain understudied though some of the proposed mechanisms include the promotion of lipogenesis through stimulation of fatty acid uptake and triglyceride synthesis, along with the inhibition of lipolysis.[31] Therefore, hyperinsulinemia may have a direct effect on fatty acid metabolism and weight gain.[32] It is well understood that insulin is a strong stimulator of lipid transport into adipocytes, adipocyte differentiation, and an effective inhibitor of lipolysis.[33] Thus, it is possible that hyperinsulinemia post-transplant contributes to early weight gain. Another hypothesis for the weight gain observed following enterically drained pancreas transplants is the correction or over-correction of undiagnosed pretransplant pancreatic exocrine insufficiency, leading to increased

TABLE 3.

Variables associated with significant weight loss by 6 mo post-transplant

		Univariate			Multivariate		
	Variables	OR	95% CI	*P*	OR	95% CI	*P*
Donor factors	Age/y	1.01	0.99-1.02	0.68			
	Male	0.68	0.42-1.08	0.11			
	Non-White	1.57	0.89-2.78	0.12			
	Body mass index/kg/m^2	0.97	0.92-1.04	0.40			
	Cause of death: Cardiovascular	1.31	0.72-2.40	0.38			
	Terminal serum Creatinine (mg/dL)	0.98	0.55-1.77	0.95			
	Kidney donor profile index/%	1.0	0.99-1.02	0.13			
	Donation after circulatory death	0.79	0.45-1.37	0.40			
	Pancreas Cold ischemia time/h	0.98	0.93-1.04	0.57			
	Kidney cold ischemia time/h	0.98	0.93-1.04	0.56			
Immunologic factors	cPRA > 20%	1.52	0.86-2.68	0.15			
	HLA mismatch per of 6	0.91	0.75-1.09	0.29			
	Pancreas or kidney rejection within 6 mo	0.69	0.25-1.89	0.47			
	Previous transplant	0.67	0.21-2.13	0.49			
Recipients factors	Age/y	0.99	0.97-1.01	0.48			
	Male	0.64	0.40-1.02	*0.06*	0.77	0.48-1.26	0.30
	Non-white	0.81	0.44-1.48	0.49			
	Weight/kg	1.0	0.98-1.01	0.80			
	Body mass index/kg/m^2	0.99	0.92-1.06	0.73			
	Pretransplant C-peptide/ng/mL	0.83	0.72-0.96	**0.01**	0.88	0.74-1.05	0.17
	Diabetes type						
	Type I vs Other/unknown	2.4	1.26-4.57	**0.008**	1.38	0.58-3.29	0.47
	Non-depleting induction agent	0.74	0.42-1.31	0.30			
	Early steroid withdrawal	0.88	0.35-2.18	0.78			
	Pre-emptive transplant	0.92	0.52-1.63	0.77			
	Kidney-delayed graft function	0.86	0.37-1.98	0.72			

The bold values indicates statistical significance with $P > 0.05$.
95% CI, 95% confidence intervals; OR, odds ratio.

TABLE 4.

Comparison of various outcomes

Characteristics	No significant weight change	Significant weight gain	Significant weight loss	*P*
Mean follow-up post-SPK (mo)	71.4 ± 32.0	80.1 ± 32.9	71.7 ± 33.6	0.21
Pancreas rejection within 6 mo post-transplant (%)	6 (4)	4 (7)	2 (3)	0.49
Kidney rejection within 6 mo post-transplant (%)	9 (6)	1 (2)	2 (3)	0.33
Either the pancreas or kidney rejection within 6 mo (%)	14 (9)	5 (9)	4 (6)	0.68
Mean weight at 6 mo (kg)	79.2 ± 16.2	88.2 ± 16.9	70.0 ± 12.5	**<0.001**
Mean weight change in % at 6 mo	1.2 ± 3.3	13.4 ± 5.0	-9.6 ± 3.5	**<0.001**
Mean weight at 12 mo (kg)	82.3 ± 18.8	90.7 ± 18.0	75.0 ± 13.8	**<0.001**
Mean weight change in % at 12 mo	4.7 ± 8.9	16.8 ± 9.6	-3.3 ± 8.8	**<0.001**
Mean weight at 2 y (kg)	84.9 ± 20.0	90.5 ± 18.7	77.6 ± 15.4	**0.002**
Mean weight change in % at 2 y	7.4 ± 11.4	17.9 ± 11.1	0.73 ± 12.4	**<0.001**
Mean weight at 3 y (kg)	86.6 ± 21.0	91.8 ± 19.4	76.4 ± 14.0	**0.001**
Mean weight change in % 3 y	9.2 ± 12.3	18.8 ± 12.6	-0.2 ± 13.9	**<0.001**
Mean weight at last follow-up (kg)	87.1 ± 22.2	88.7 ± 20.6	77.5 ± 15.3	**0.002**
Mean weight change in % at last follow-up	11.2 ± 17.9	14.6 ± 17.4	0.37 ± 13.4	**<0.001**
Mean HbA1c among those with graft survival (g/dL)	5.7 ± 0.9	5.5 ± 0.6	5.6 ± 0.6	0.54
HbA1c > 6.5 %	14 (9.2)	2 (4)	4 (6)	0.27
On antidiabetic agents (%)	11 (7)	0	3 (4)	0.08
Mean serum creatinine at last follow-up with graft survival (mg/dL)	1.32 ± 0.67	1.25 ± 0.54	1.22 ± 0.31	0.50
Mean serum eGFR at last follow-up (mL/m^2)	67.6 ± 22.9	70.2 ± 20.9	65.8 ± 17.8	0.58
Pancreas uncensored graft failure (%)	24 (16)	10 (18)	18 (26)	0.20
Pancreas death-censored graft failure (%)	14 (9)	6 (11)	9 (13)	0.70

The bold values indicates statistical significance with $P > 0.05$.
eGFR, estimated glomerular filtration rate; HbA1c, hemoglobin A1C; SPK, simultaneous pancreas and kidney.

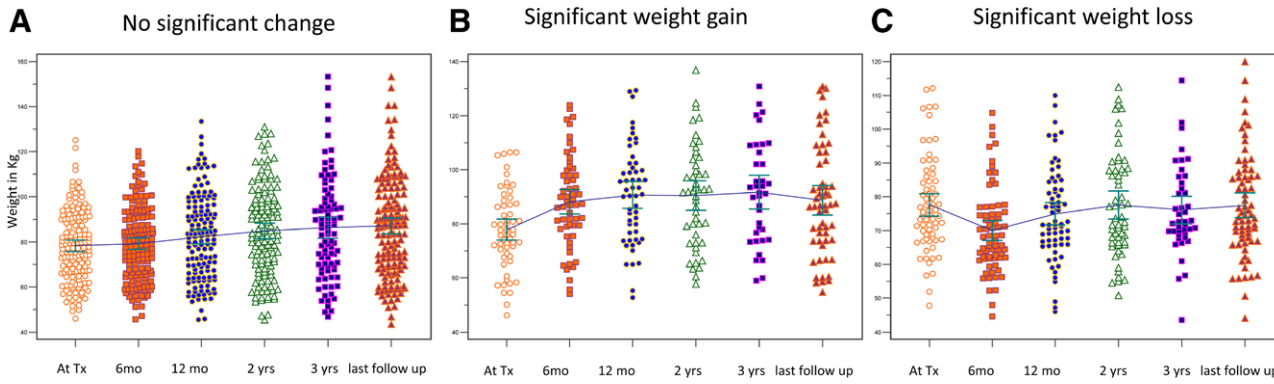

FIGURE 1. Absolute weight at various times post-transplantation across the 3 groups.

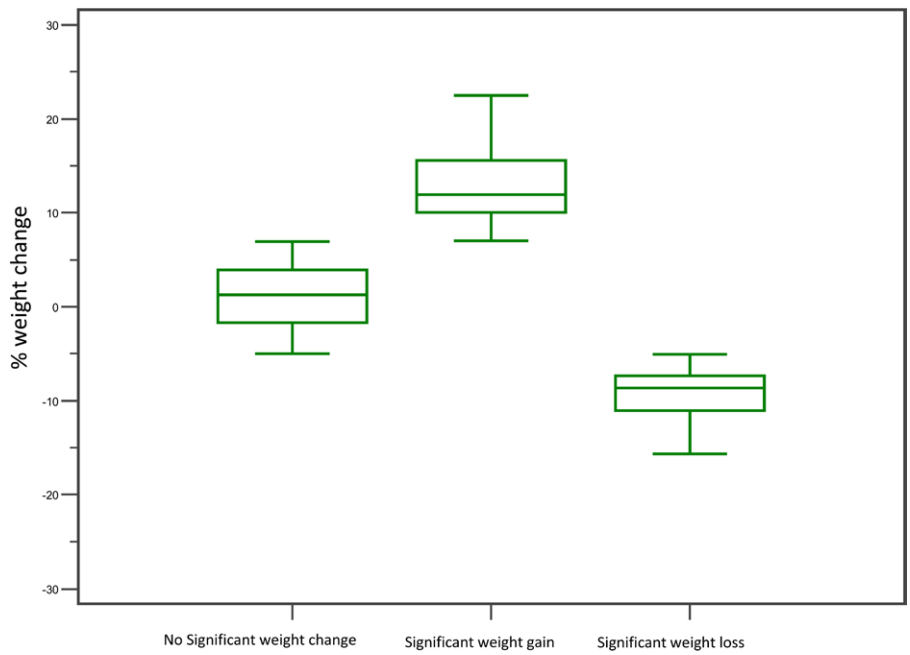

FIGURE 2. Percentage change in weight at 6 mo post-transplantation across the 3 groups.

TABLE 5.

Risk for outcomes by last follow-up among the entire cohort of both T1D and T2D recipients

		Unadjusted			Adjusted[a]		
Complications		**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
Pancreases uncensored graft failure	No weight changes	Ref	Ref	Ref	Ref	Ref	Ref
	Weight gain	0.90	0.43-1.90	0.79	0.55	0.24-1.24	0.15
	Weight loss	1.52	0.82-2.82	0.18	1.06	0.52-2.17	0.87
Pancreas DCGF	No weight changes	Ref	Ref	Ref	Ref	Ref	Ref
	Weight gain	0.92	0.35-2.41	0.87	0.46	0.15-1.44	0.18
	Weight loss	1.25	0.54-2.92	0.60	1.14	0.41-3.12	0.80
Pancreas composite outcomes	No weight changes	Ref	Ref	Ref	Ref	Ref	Ref
	Weight gain	0.61	0.28-1.34	0.22	0.35	0.14-0.85	**0.02**
	Weight loss	0.88	0.45-1.71	0.71	0.90	0.42-1.95	0.79
Kidney DCGF	No weight changes	Ref	Ref	Ref	Ref	Ref	Ref
	Weight gain	0.94	0.36-2.45	0.89	0.55	0.17-1.73	0.31
	Weight loss	0.99	0.39-2.46	0.97	1.49	0.52-4.24	0.46

[a] Adjusted for: Donor:age, sex, race, BMI, cause of death, terminal serum creatinine, donation after circulatory death donor, pancreas cold time, kidney cold time, cPRA, HLA mismatch, previous transplant. Recipient: age, sex, race, weight, pretransplant C-peptide level, types of diabetes, depleting induction, early steroid withdrawal, pre-emptive transplant, and kidney-delayed graft function. The bold value indicates statistical significance with $P < 0.05$.

95% CI, 95% confidence interval; BMI, body mass index; DCGF, death-censored graft failure; HR, hazard ratio.

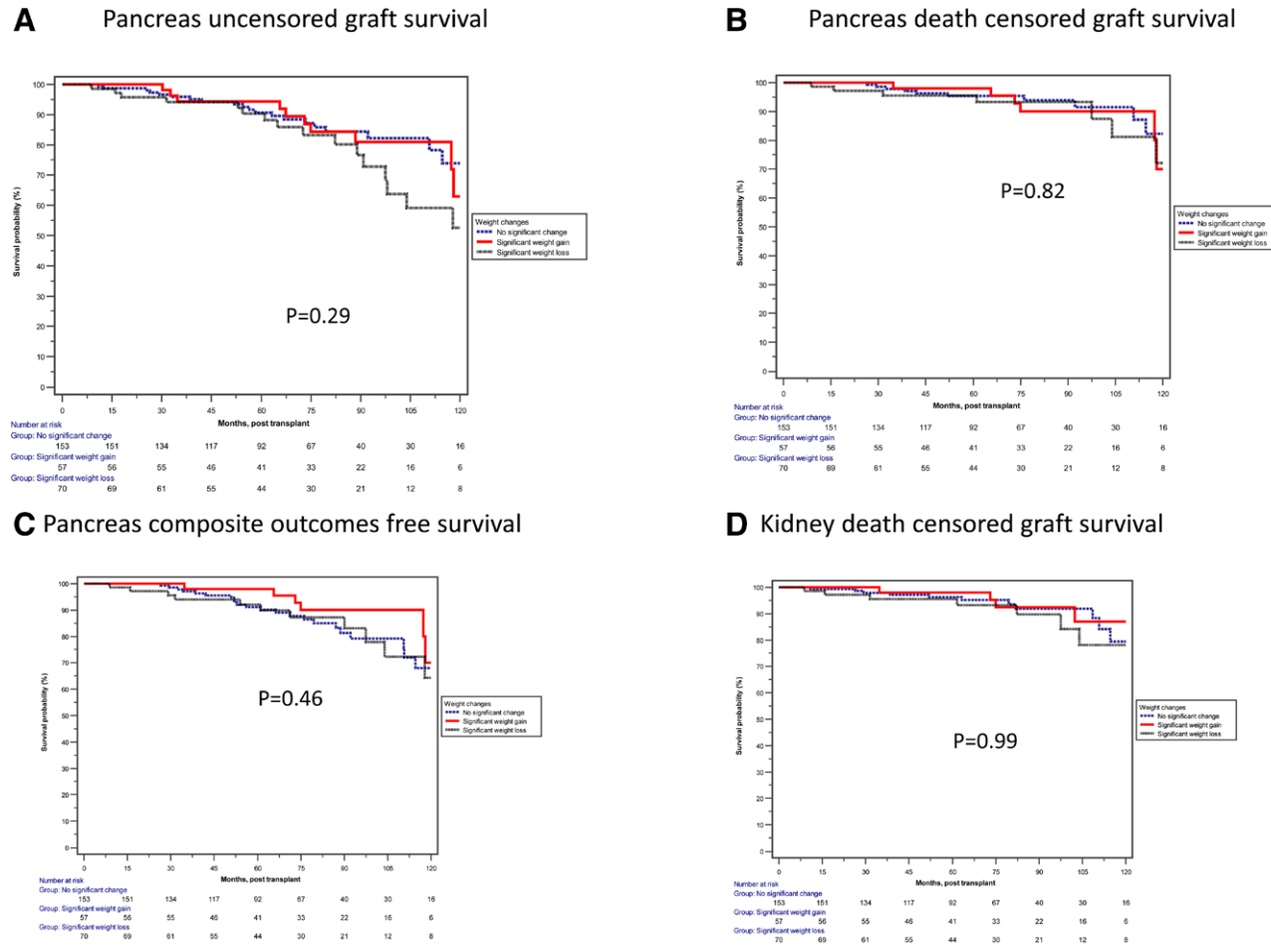

FIGURE 3. No significant difference across the 3 groups in terms of pancreas uncensored graft survival (A, $P=0.29$), pancreas death-censored graft survival (B, $P=0.82$), pancreas composite outcomes (C, $P=0.46$), or kidney death-censored graft survival (D, $P=0.99$), based on the absolute weight changes.

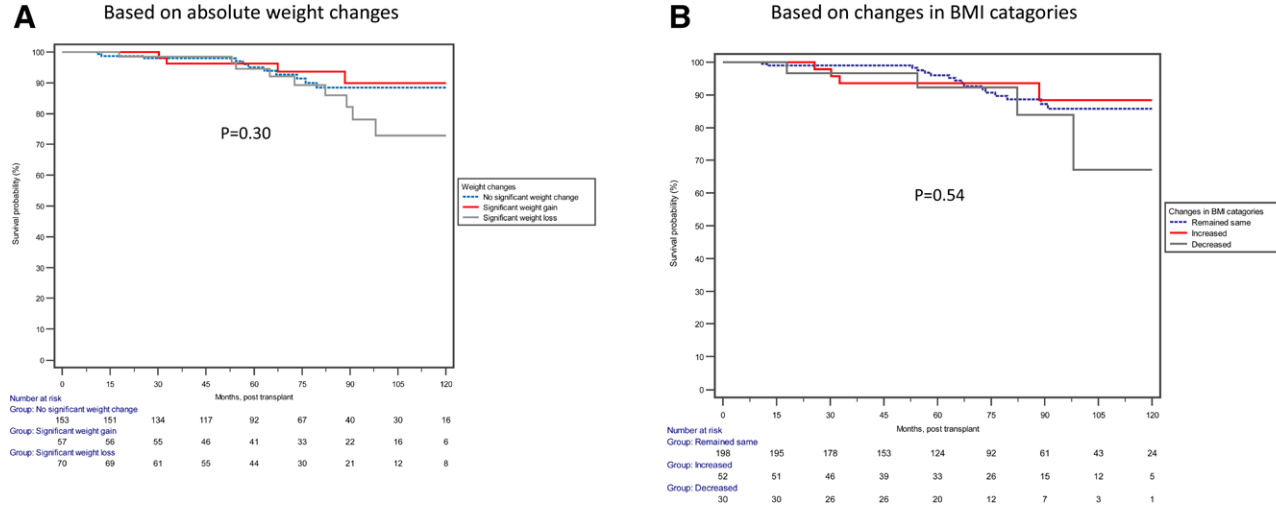

FIGURE 4. No significant difference across the 3 groups regarding patient survival based on absolute weight change (A, $P=0.30$) or BMI categories (B, $P=0.54$).

gastrointestinal absorption of fat and nutrients leading to weight gain.[34] However, one study that formally measured exocrine function after pancreas transplantation by measuring fecal elastase-1 levels did not demonstrate a correlation between weight gain and fecal elastase-1 levels.[35] This same study also did not find any association between pretransplant C-peptide levels and weight gain.[35] The present study similarly found no association between pretransplant C-peptide levels

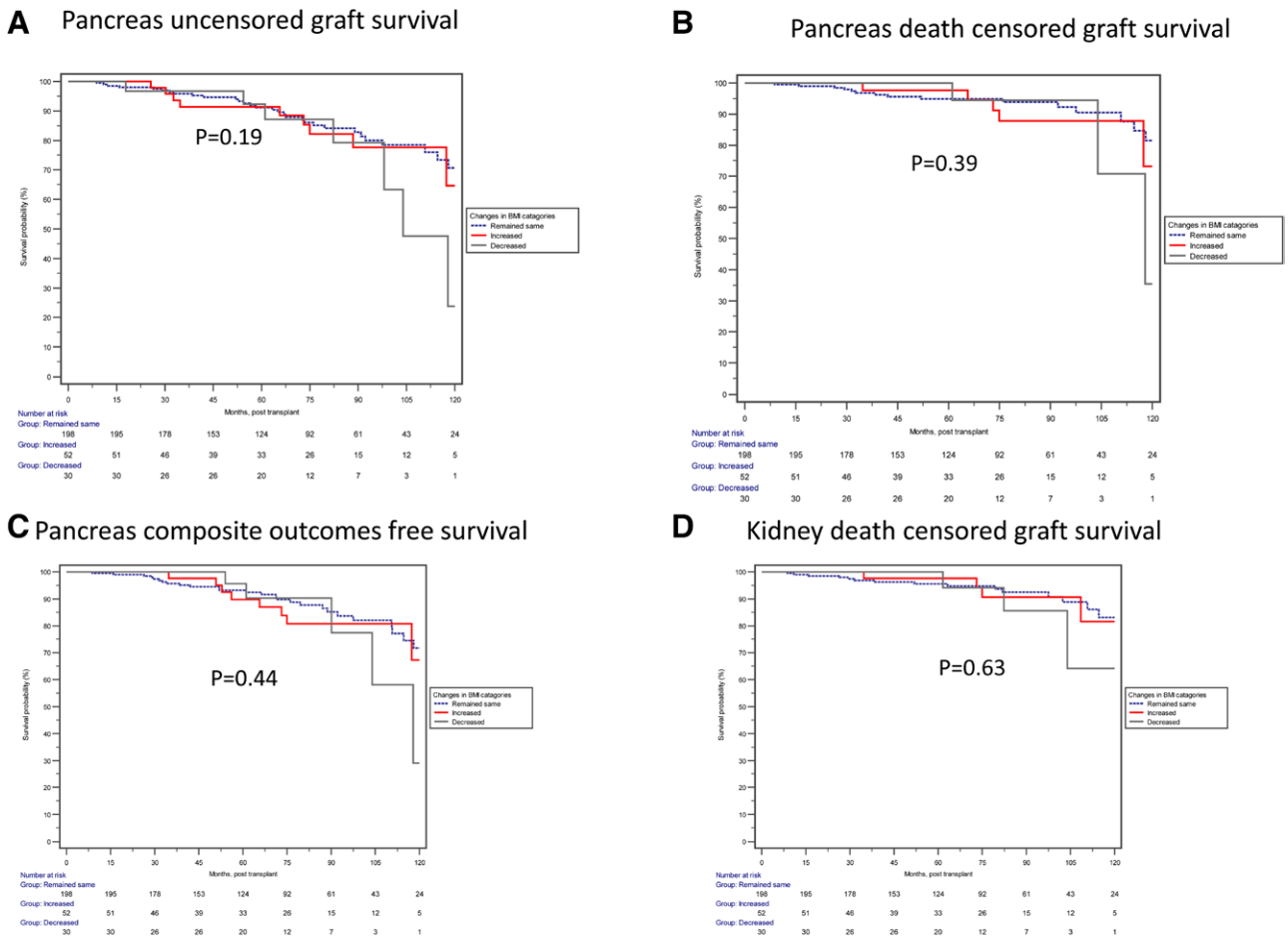

FIGURE 5. No significant difference across the 3 groups in terms of pancreas uncensored graft survival (A, $P=0.19$), pancreas death-censored graft survival (B, $P=0.39$), pancreas composite outcomes (C, $P=0.44$), or kidney death-censored graft survival (D, $P=0.63$), based on the changes in BMI categories.

TABLE 6.

Risk for outcomes by last follow-up among SPK recipients with T2DM

		Unadjusted			Adjusted[a]		
Complications		**HR**	**95% CI**	***P***	**HR**	**95% CI**	***P***
Pancreases uncensored graft failure	No weight changes	Ref	Ref	Ref	Ref	Ref	Ref
	Weight gain	0.89	0.18-4.42	0.89	1.38	0.17-11.26	0.76
	Weight loss	0.96	0.11-7.99	0.97	0.62	0.06-6.72	0.69
Pancreas DCGF	No weight changes	Ref	Ref	Ref	Ref	Ref	Ref
	Weight gain	–	–	–	–	–	–
	Weight loss	2.78	0.25-30.90	0.41	2.06	0.06-67.80	0.68
Pancreas composite outcomes	No weight changes	Ref	Ref	Ref	Ref	Ref	Ref
	Weight gain	0.29	0.06-1.47	0.14	0.01	0.001-0.63	**0.03**
	Weight loss	0.63	0.11-3.65	0.61	8.28	1.27-53.6	**0.02**
Kidney DCGF	No weight changes	Ref	Ref	Ref	Ref	Ref	Ref
	Weight gain	2.27	0.17-28.49	0.54	–	–	–
	Weight loss	–	–	–	–	–	–

[a]Adjusted for: Donor: BMI. Recipient: age, sex, race, BMI, pretransplant C-peptide level, early steroid withdrawal.
The bold values indicates statistical significance with $P > 0.05$.
95% CI, 95% confidence interval; BMI, body mass index; DCGF, death-censored graft failure; HR, hazard ratio; SPK, simultaneous pancreas and kidney; T2DM, type 2 diabetes.

and weight gain. However, in another study among 37 pancreas transplant recipients, Torabi et al report rapid weight gain post pancreas transplant among patients with elevated pretransplant C-peptides.[36] Aligning with the study by Torabi et al, Gurram et al observed that recipients with pretransplant C-peptide levels ≥2.0 ng/mL had inferior post-transplant outcomes including weight gain.[37] Some patients after resolution of their renal failure report a dramatically increased appetite.

In others, significant postoperative infections and reoperations may severely limit early weight gain or even promote weight loss that requires a prolonged period to normalize. The degree of steroid use has been implicated in weight gain post-transplant; however, in the present study, the proportion of patients undergoing early steroid withdrawal was similar in the 3 weight groups and the occurrence of rejection in the first 6 mo, necessitating higher steroid doses, was not associated with weight gain. Summarizing existing data here and in the literature, it is not possible to specifically attribute one particular factor or cause of weight gain that may occur following SPK transplantation, though this appears to only affect a subset of patients in the modern era.

Listing and transplant of SPK among patients with T2DM are on the rise. According to the Scientific Registry of Transplant Recipients 2022 annual data report, 23.2% of adult candidates on the waiting list for pancreas transplants were T2DM compared with 7.8% in 2011.[12] This has led to changes in the baseline characteristics of potential candidates, including a rise in the proportion of candidates with obesity with BMI >30 kg/m^2 from 18.3% in 2011 to 23.2% in 2022, as being overweight or obese are highly prevalent in this population.[12] According to the Centers for Disease Control and Prevention National Diabetes Statistics Report (2017–2020 data), 62.8% of US adults aged 18 y or older diagnosed with diabetes were obese (ie, BMI ≥ 30 kg/m^2).[38] However, despite the high prevalence of obesity in the T2DM population, many studies have found similar outcomes of SPK in patients with T1DM and T2DM, including composite outcomes and PTDM.[39,40] In this study, we report the type of diabetes not to be associated with outcomes of interest as outcomes were similar among recipients with T2DM and the entire cohort.

Weight gain is a known common post-transplant complication for all solid organ transplant recipients. Approximately 50% of patients gain weight after kidney transplantation, mainly within the first year of transplant.[3] It is estimated that 20% to 30% of kidney transplant recipients, 30% to 40% of liver transplant recipients, >45% of lung transplant recipients, and 38% to 48% of heart transplant recipients are obese.[41] However, there is limited information about weight changes among SPK recipients. In this study, we report 45% of SPK recipients exhibit significant weight changes, but by 6 mo post-transplant, the proportion of recipients with SWL is higher than the proportion with SWG. However, even these recipients with SWL at 6 mo continue to gain weight later and have detrimental composite outcomes compared with those with NWC. Early weight loss may be because of catabolic effects of early post-transplant surgical recovery, ileus, fever, readmissions, and so on, despite relatively uncomplicated courses.

Similar to previously published studies, we did not observe an increased incidence of graft failure associated with weight gain.[5] In fact and surprisingly, we found significant weight gain by 6 mo was associated with a lower risk of developing the composite outcome including the development of post-transplant diabetes, compared with no weight change by 6 mo. We do not presently have an explanation for this surprising finding.

In this cohort of 280 SPK recipients, 25% had significant weight loss by 6 mo post-transplant. The incidence of weight loss that was observed in SPK recipients in the present study was similar to that observed in pancreas recipients, which we had previously reported.[20] There are certain hypotheses about weight loss among pancreas transplant recipients including independence from exogenous insulin, decreased frequent carbohydrate intake previously utilized to avoid hypoglycemia unawareness, and the presence of gastroparesis.[20] To the best of our knowledge, there are no data about the risk factors and effect of weight loss among SPK recipients.

This study has the expected limitations of a single-center observational study, reflecting our specific population and clinical approach. Our findings are reflective of the practices at our center, and this should be factored into the interpretation. Also, we assessed risk factors and outcomes based on weight changes by 6 mo post-SPK transplant, outcomes could have been different if different post-transplant time frames had been chosen. Also, the proportion of early steroid withdrawal was low in this study, as it was not common practice until the recent past. Incidence and outcomes could be different if the steroid-sparing protocol had been utilized more consistently. However, this substantial data set with more granular data provides useful information for estimating risks and outcomes. Also, to the best of our knowledge, this study is the largest of its kind, from a single center in the modern era with consistent surgical techniques and maintenance immunosuppressive agents.

In summary, the early incidence of significant weight gain and weight loss is highly prevalent among SPK recipients; 45% of SPK recipients had significant weight changes by 6 mo post-transplant. Pretransplant C-peptide, which is also the marker of insulin secretion/resistance, was not associated with weight changes post-transplant. Likely because of proper management, weight changes were not associated with poor outcomes post-SPK transplant. Even those with early SWL by 6 mo continue to gain weight later; thus, education, medications, or behavioral modification designed to maintain weight in these patients may help prevent future detrimental outcomes. As this is an observational study, without intervention, although it may not have an immediate practical implementation; however, it will help educate the providers and patients about the incidence of weight changes after transplant. SPK recipients are a unique patient population among solid organ transplants, who have stringent selection criteria. However immediate weight changes at 6 mo did not have detrimental outcomes in these relatively healthy recipients. In the future, if there is some relaxation in the selection criteria to receive SPK transplants, weight changes may impact the outcomes.

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