OPEN

Analysis of Individual Components of Frailty in Simultaneous Pancreas and Kidney, and Solitary Pancreas Transplant Recipients

Sandesh Parajuli, MD,[1,2] Jon Odorico, MD,[2,3] Isabel Breyer,[1] Emily Zona,[1] Fahad Aziz, MD,[1,2] Heather Lorden, RDN,[2,3] Jacqueline Garonzik-Wang, MD, PhD,[2,3] Dixon Kaufman, MD, PhD,[2,3] and Didier Mandelbrot, MD[1,2]

Backgrounds: It is not known which of the 5 components of the Fried frailty score have the most predictive value for outcomes in simultaneous pancreas-kidney transplant (SPK) and solitary pancreas transplant (SPT) recipients. **Methods:** In this study, we sought to investigate the association between pretransplant overall frailty and individual frailty components, with posttransplant outcomes among SPK and SPT recipients. Outcomes of interest were length of stay, kidney delayed graft function (K-DGF), readmission within 30 d after discharge, cardiovascular events, acute rejection, pancreas death-censored graft failure (DCGF), kidney DCGF, and death. **Results:** Of the individual frailty components among SPK (n = 113), only slow walk time was associated with an increased risk of mortality (adjusted odds ratio [aOR]: 4.99; $P = 0.03$). Among SPT (n = 49), higher sum frailty scores (coefficient correlation 0.29; $P = 0.04$) and weight loss (coefficient correlation = 0.30; $P = 0.03$) were associated with prolonged length of stay. Similarly, weight loss among SPT was associated with an increased risk of DCGF (aOR: 4.34; $P = 0.049$). Low grip strength was strongly associated with an increased risk of early readmission (aOR: 13.08; $P = 0.008$). **Conclusions:** We found that not all components of frailty contribute equally to predicting outcomes. Objective measurements of slow walk time, unintentional weight loss, and low grip strength were found to be associated with less optimal outcomes in pancreas transplant recipients. Targeted interventions may improve posttransplant outcomes. (Transplantation Direct 2023;9: e1523; doi: 10.1097/TXD.0000000000001523.)

Frailty prevalence among solid organ transplant candidates is higher than in the general population and is present at earlier ages.[1-5] Recently, frailty has received increasing attention in both medical and surgical fields as a physiologic syndrome that can be associated with numerous poor medical and surgical outcomes.[6-8] Although there is no gold-standard frailty definition, it has been operationally defined by Fried et al as meeting 3 of 5 phenotypic criteria indicating compromised energetics: low grip strength, low energy, slowed walking speed, low physical activity, and unintentional weight loss.[9-11] This is easy to measure in an outpatient setting, making it a powerful tool for risk stratification. Transplant programs use different tools and criteria to assess frailty among possible organ recipients. In 1 survey from the United States, among 133 kidney transplant programs that responded to the survey, McAdams-DeMarco et al[12] reported 19 different tools/criteria used by kidney transplant programs to assess for frailty before transplant. This variability likely exists among pancreas transplant programs too.

Pancreas transplant candidates may be at greater risk for frailty and uniquely susceptible to the downstream sequelae, in that these patients often have prolonged poorly controlled diabetes, in addition to other major medical comorbidities. They are also at greater risk for the long-term effects of diabetes, including chronic kidney disease (CKD) leading to end-stage kidney disease.[13,14] Diabetes and CKD are chronic, multiorgan systemic diseases that may be quite disabling.[15,16] Advanced CKD and comorbid conditions commonly associated with CKD, such as diabetes, anemia, and heart disease, may all further contribute to frailty.[17]

Received 24 May 2023. Revision received 9 June 2023.

Accepted 14 June 2023.

[1] Division of Nephrology, Department of Medicine, University of Wisconsin School of Medicine and Public Health, Madison, WI.

[2] UW Health Transplant Center.

[3] Division of Transplantation, Department of Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI.

The authors declare no conflicts of interest.

D.M. has received research funds from Virginia Lee Cook Foundation.

The data that support the findings of this study are available from the corresponding author upon reasonable request.

S.P. contributed in concept, data collection, design, analysis, and article preparation. J.O., F.A., H.L., J.G.-W., and D.K. contributed in article preparation and editing. I.B. and E.Z. contributed in data collection and editing. D.M. contributed in concept, article preparation, and editing.

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.transplantationdirect.com).

Correspondence: Sandesh Parajuli, MD, 4175 MFCB, 1685 Highland Ave, Madison, WI 53705. (sparajuli@medicine.wisc.edu).

ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000001523

Despite the potential benefit and knowledge gained from frailty assessment in pancreas transplant candidates, there is no consensus regarding the best tools to use to assess frailty, nor is it understood which individual component(s) of the frailty assessment are more or less predictive of various outcomes posttransplant. We assess frailty in all potential pancreas transplant recipients prospectively at the time of evaluation with a modified Fried frailty assessment, assessing 5 individual components: unintentional weight loss, self-reported exhaustion, low physical activity, walk time, and grip strength. Here, we examine the pretransplant frailty scores of our pancreas transplant recipients and their various posttransplant outcomes to determine which components of the modified Fried frailty assessment are most strongly associated with inferior posttransplant outcomes.

MATERIALS AND METHODS

Study Population

We studied all adult pancreas transplant recipients transplanted at the University of Wisconsin between February 2017 and October 2021, which had a pretransplant frailty assessment performed with a modified Fried frailty assessment. Because of the differences in the pathophysiological nature of the disease, we analyzed outcomes of interest among simultaneous pancreas-kidney (SPK) and solitary pancreas transplant (SPT) recipients separately. SPT was defined as recipients who have received pancreas-only transplants, regardless of previous transplant status. The only modification from the original Fried frailty assessment was that we substituted the Karnofsky Performance Status Scale[18] for the Minnesota Leisure Time Physical Activity Questionnaire (MLTPAQ).[19] This change was made because of the complexity and time required to obtain the MLTPAQ score, the fact that the Organ Procurement and Transplantation Network requires Karnofsky score collection, and the reported association between the Karnofsky score and transplant outcomes.[20]

Outcomes of Interest

The initial length of stay (LOS) after transplant, kidney delayed graft function (K-DGF), early readmission, any cardiovascular events, biopsy-proven pancreas rejection, pancreas death-censored graft failure (DCGF), death, and kidney DCGF were outcomes of interest among SPK recipients. Outcomes of interest were similar among SPT recipients except that K-DGF and kidney DCGF were not included.

LOS was the initial LOS after the transplant. We defined K-DGF as a need for dialysis within the first 7 d of kidney transplantation.[21] Any hospital admission requiring overnight hospital stay within 30 d of the initial posttransplant discharge was included as early readmission. Any cardiovascular (eg, congestive heart failure, acute coronary symptoms, abnormal heart rhythm, etc.) events requiring hospitalization before the end of the study or during an initial hospital stay for transplant were analyzed. All acute rejections were biopsy-proven. Pancreas DCGF was defined on the basis of the current United Network for Organ Sharing criteria for pancreas graft failure, which include removal of the pancreas graft, re-registration 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 days.[22] Kidney DCGF was defined as initiating dialysis or retransplantation before the end of the data analysis. All deaths were death with a functioning allograft.

Among patients with >1 frailty assessment, the frailty assessment closest to the transplant was used for the analysis. Recipients were assigned 0 or 1 point for each component of frailty, with total frailty scores ranging between 0 and 5. The associations between each individual frailty score were analyzed. Recipients of multiorgan transplants except for SPK were excluded. Patients were followed up until their death, DCGF, or until the end of the study analysis on October 31, 2022. This study was approved by the University of Wisconsin Health Sciences Institutional Review Board (IRB protocol number: 2014-1072). This study was in adherence to 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." Because of the nature of the study, informed consent from study patients pertinent to this study was not obtained.

Frailty Assessment and Selection Criteria

Frailty assessment was performed by a certified clinical transplant dietitian during their pretransplant evaluation in the clinic as described before.[23] Briefly, the patients were assigned 0 or 1 point for each component of the modified Fried frailty assessment. Pancreas transplant candidates received 1 point each for unintentional weight loss ≥10 lb or 5% of the body weight, exhaustion ≥3 d/wk, <60% Karnofsky score for physical activity, slow gait speed based on height and gender cutoffs, and low grip strength based on gender and body mass index cutoffs. To overcome the potential impact of dialysis access on grip strength on the same side, grip strengths were measured in both hands and the greater of the 2 measurements was used for analysis. Patients on the waitlist were reevaluated every 1 to 2 y, including the frailty assessment. Higher-risk patients (eg, >65 y) or those considered to be at risk for the progression of frailty were assessed every year. Also, patients on the waiting list were reevaluated after major medical or surgical events.

Frailty assessment and scores were discussed during pretransplant selection meetings and considered one of the factors in deciding whether to approve or deny transplant listing. Pancreas transplant selection criteria were based on the physical, psychological, medical, or surgical conditions of the patients. Patients with diabetes for >10 y usually underwent cardiac catheterization before listing for transplant. Most patients underwent 2D echo, stress test, or both, based on their age and physical activity, as described before.[24] All potential recipients were extensively discussed at the multidisciplinary selection meeting before approving or declining rejecting their listing.

Surgical Technique

The technique was constant throughout the study period. All pancreas transplants were preserved with the University of Wisconsin solution. All pancreata were enterically drained via a side-to-side duodenojejunostomy.

Immunosuppression

Patients undergoing pancreas transplants 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 SPT or 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 on the basis of 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 posttransplant, 8 to 10 ng/mL from months 3 to 12, and 6 to 8 ng/mL after 1 y. Recipients of SPT were maintained at a higher tacrolimus trough goal of 9 to 12 for the entire posttransplant period unless complicated by infections or malignancy. The initial mycophenolate sodium dose was 720 mg po 3 times daily for 1 mo, or as long as tolerated, then twice daily thereafter. For patients in whom steroids were continued, prednisone was tapered to 10 mg daily by 8 wk posttransplant, with further taper determined by the managing provider. Patients undergoing early steroid withdrawal stopped steroids after postoperative day 4.

Pancreas Rejection Treatment

Most of the pancreas biopsy was done for the cause that is an unexplained rise 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 intravenous 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]

Posttransplant Follow-Up

After discharge from the patient's initial admission, patients are typically seen at posttransplant times of 3 wk, 6 wk, 3 mo, 6 mo, 9 mo, 12 mo, 18 mo, 24 mo, and then annually. We follow our transplant recipients at either the University Hospital or various outreach regional clinics at least once a year until graft failure, death, or the patient decides to transfer their care to a different provider. Patients with major health events posttransplant needing hospitalization are admitted to our hospital whenever possible. If patients are admitted to outside centers, all major health events are captured and documented in our master database. Therefore, it is unlikely any of the outcomes of interest would have been missed.

Statistical Analysis

Data were reported as mean ± SD or percentages. Categorical data were analyzed using the chi-square test. The Kruskal–Wallis test was used to analyze nonnormative data. Bivariable and multivariable logistic regression models were used to assess associations between sum frailty scores or each of the frailty components and the outcomes of interest. Because of the small sample size and fewer outcomes of interest, only a few clinically relevant variables were included in the multivariable regression model. Some of the significant 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

SPK Recipients

Patient Outcomes

A total of 113 SPK recipients fulfilled our selection criteria, and their baseline characteristics are shown in Table 1. The mean interval between the frailty assessment and the transplant was 6.7 ± 4.6 mo (Table 2). Fifty-seven recipients (50%) had a sum frailty score of 0. None had sum frailty scores of 4 or 5. The most prevalent component of frailty was low grip strength in 29% of the recipients, followed by self-reported exhaustion in 15% of the recipients.

Length of Stay

The median posttransplant LOS was 9 d, ranging from 5 to 121 da (Table 3). The sum frailty scores or individual components of Fried frailty were not significantly associated with LOS (Table 4). None of the recipients were sent to a skilled nursing facility or rehabilitation center at the initial posttransplant discharge.

TABLE 1.

Baseline clinical characteristics of SPK recipients

	Variables	
	Total number of recipients	113
Recipient factors	Male, n (%)	77 (68)
	Non-white, n (%)	35 (31)
	Age at transplant, y	47.7 ± 9.8
	Body mass index, kg/m^2	26.8 ± 3.5
	Previous transplant recipients, n (%)	5 (4)
	Preemptive kidney transplant, n (%)	23 (20)
Donor factors	Mean Kidney Donor Profile Index, %	24.7 ± 18.1
	Male, n (%)	76 (67)
	Non-white, n (%)	22 (20)
	Age at transplant, y	26.6 ± 11.2
	Body mass index, kg/m^2	23.3 ± 3.8
	Donation after circulatory death, n (%)	39 (35)
	Mean pancreas cold ischemia time, h	12.1 ± 4.1
	Cause of death, n (%)	
	Anoxia	49 (43)
	Cerebrovascular	12 (11)
	Trauma	47 (42)
	Other	5 (4)
Immunological risk and immunosuppressant	cPRA > 20%, n (%)	11 (10)
	Mean HLA mismatch	4.6 ± 1.1
	Induction immunosuppression, n (%)	
	Antithymocyte globulin	62 (55)
	Alemtuzumab	50 (44)
	Basiliximab	1 (1)
	Early steroid withdrawal, n (%)	7 (6)

cPRA, calculated panel reactive antibody; SPK, simultaneous pancreas-kidney.

TABLE 2.

Frailty assessment of SPK recipients

Variables	
Mean interval from frailty assessment to transplant, mo	6.7 ± 4.6
Sum frailty scores, n (%)	
0	57 (50)
1	39 (35)
2	14 (12)
3	3 (3)
Unintentional weight loss, n (%)	
0	100 (89)
1	13 (12)
Self-reported exhaustion, n (%)	
0	96 (85)
1	17 (15)
Low physical activity (Karnofsky <60%), n (%)	
0	111 (98)
1	2 (2)
Walk time, n (%)	
0	102 (90)
1	11 (10)
Low handgrip strength, n (%)	
0	80 (71)
1	33 (29)

SPK, simultaneous pancreas-kidney.

TABLE 3.

Length of hospital stay after SPK transplants

Sum frailty scores	n	Minimum	25th percentile	Median	75th percentile	Maximum	*P*
0	57	5	7	9	11	41	0.94
1	39	5	8	9	13	121	
2	14	7	8	8.5	10	13	
3	3	7	7.5	9	9.75	10	

SPK, simultaneous pancreas-kidney.

TABLE 4.

Length of stay outcome of SPK recipients correlated with frailty measures

	Coefficient correlation (95% CI)
Sum frailty scores	0.01 (–0.17 to 0.20; *P* = 0.88)
Weight loss	–0.10 (–0.28 to 0.08; *P* = 0.27)
Exhaustion	0.02 (–0.17 to 0.20; *P* = 0.84)
Karnofsky	0 (–0.19 to 0.18; *P* = 0.97)
Walk time	–0.03 (–0.22 to 0.15; *P* = 0.73)
Grip strength	0.10 (–0.08 to 0.28; *P* = 0.28)

SPK, simultaneous pancreas-kidney.

Outcomes Based on the Sum Frailty Scores

A total of 96 (85%) patients had a sum frailty score of <2, and the remaining 17 (15%) had a sum frailty score of ≥2 (Table 5). Compared with those with a sum frailty score <2, having a score ≥2 was not significantly associated with any of the 7 outcomes of interest (kidney DGF, early readmission, cardiovascular events, pancreas rejection, pancreas DCGF, death, and kidney DCGF), either in unadjusted or adjusted models.

TABLE 5.

Association based on the sum frailty score after SPK transplants

	Sum ≥2 vs <2	
	OR (unadjusted)	OR (adjusted[a])
Kidney DGF	0.29 (0.04-2.23; *P* = 0.23)	0.29 (0.04-2.26; *P* = 0.24)
Early readmission	1.07 (0.47-2.43; *P* = 0.87)	0.82 (0.34-1.97; *P* = 0.66)
Cardiovascular events	1.99 (0.66-6.02; *P* = 0.22)	1.38 (0.41-4.65; *P* = 0.61)
Pancreas rejection	0.38 (0.05-2.99; *P* = 0.36)	0.13 (0.01-1.45; *P* = 0.09)
Pancreas death-censored graft failure	0.80 (0.09-6.51; *P* = 0.84)	0.92 (0.10-8.78; *P* = 0.94)
Death	1.92 (0.49-7.58; *P* = 0.34)	1.88 (0.45-7.79; *P* = 0.38)
Kidney death-censored graft failure	1.27 (0.26-6.26; *P* = 0.76)	0.63 (0.09-4.23; *P* = 0.64)

[a]Adjusted for recipient's age, recipient's sex, recipient's BMI, and kidney DGF. For DGF as outcomes of interest, DGF was not included.
BMI, body mass index; DGF, delayed graft function; OR, odds ratio; SPK, simultaneous pancreas-kidney.

Various Outcomes

In an unadjusted model, slow walk time was significantly associated with an increased risk of patient mortality (odds ratio [OR]: 4.82; 95% confidence interval [CI], 1.20-19.46; *P* = 0.03; Table 6). This was further confirmed with Kaplan–Meier analysis (Figure 1). Even after adjusting for multiple characteristics (recipient's age, sex, body mass index, and kidney DGF), slow walk time was associated with increased risk for mortality (adjusted OR [aOR]: 4.99; 95% CI, 1.16-21.48; *P* = 0.03).

Only exhaustion was associated with increased risk for kidney DCGF in unadjusted analysis (OR: 4.53; 95% CI, 1.06-19.35; *P* = 0.04), but this was no longer statistically significant after adjustment for various other characteristics (aOR: 2.71; 95% CI, 0.53-13.83; *P* = 0.23).

A total of 18 SPK recipients (16%) had kidney DGF. None of the 5 variables of frailty assessment were associated with kidney DGF, either in the unadjusted or adjusted model.

A total of 39 patients (34.5%) had early readmission within 30 d of posttransplant discharge, with the common indication for admission being fever in 11 recipients, gastrointestinal symptoms (nausea, vomiting, diarrhea, abdominal pain) in 10 recipients, and acute kidney injury in 3 recipients. Other indications for readmission included electrolyte abnormalities, hypotension, intra-abdominal fluid collection, etc. None of the 5 variables of frailty assessment were associated with early readmission either in the unadjusted or adjusted model.

A total of 15 SPK recipients (13.3%) had cardiovascular events needing hospitalization. The most common indications were hypertensive urgency/emergency in 7 recipients, congestive heart failure with pulmonary edema in 3 recipients, and the remaining had various other events including demand ischemia, cardiac rhythm abnormalities, etc. None of the 5 variables of frailty assessment were associated with cardiovascular events either in the unadjusted or adjusted model.

Similarly, none of the individual variables of frailty assessment were associated with pancreas rejection or pancreas DCGF either in the unadjusted or adjusted model. Also, longer pancreas cold ischemia time was not significantly associated with an increased risk of pancreas DCGF in the unadjusted model (hazard ratio [HR]: 1.12, 95% CI, 0.94-1.32; *P* = 0.20).

TABLE 6.

Association with outcomes after SPK transplants

Outcomes	Variables	OR (unadjusted)	OR (adjusted[a])
Kidney DGF (n=18; 16%)	Weight loss	0.58 (0.08-4.39; $P = 0.60$)	0.55 (0.07-4.42; $P = 0.57$)
	Exhaustion	0.42 (0.06-3.15; $P = 0.40$)	0.41 (0.05-3.12; $P = 0.39$)
	Karnofsky	1.67 (0.22-12.78; $P = 0.62$)	1.78 (0.23-13.88; $P = 0.58$)
	Walk time	0.62 (0.08-4.66; $P = 0.61$)	0.64 (0.08-4.97; $P = 0.67$)
	Grip strength	0.85 (0.30-2.38; $P = 0.76$)	0.84 (0.29-2.39; $P = 0.75$)
Early readmission (n=39; 34.5%)	Weight loss	1.28 (0.50-3.34; $P = 0.61$)	0.83 (0.29-2.32; $P = 0.72$)
	Exhaustion	2.12 (0.96-4.68; $P = 0.06$)	1.67 (0.71-3.89; $P = 0.24$)
	Karnofsky	–	–
	Walk time	0.98 (0.30-3.22; $P = 0.98$)	0.76 (0.23-2.56; $P = 0.66$)
	Grip strength	1.35 (0.70-2.58; $P = 0.37$)	1.35 (0.69-2.63; $P = 0.38$)
CV events (n=15; 13.3%)	Weight loss	0.86 (0.18-4.15; $P = 0.86$)	0.38 (0.07-2.20; $P = 0.28$)
	Exhaustion	2.98 (0.79-11.15; $P = 0.10$)	2.66 (0.56-12.64; $P = 0.22$)
	Karnofsky	2.46 (0.30-19.81; $P = 0.40$)	4.60 (0.52-40.45; $P = 0.17$)
	Walk time	2.60 (0.57-11.94; $P = 0.22$)	1.78 (0.36-8.85; $P = 0.48$)
	Grip strength	1.29 (0.45-3.72; $P = 0.63$)	1.26 (0.40-3.95; $P = 0.69$)
Pancreas rejection (n=13; 11.5%)	Weight loss	0.60 (0.08-4.81; $P = 0.63$)	0.16 (0.02-1.64; $P = 0.12$)
	Exhaustion	1.43 (0.31-6.62; $P = 0.64$)	0.66 (0.12-3.76; $P = 0.64$)
	Karnofsky	–	–
	Walk time	1.99 (0.43-9.15; $P = 0.37$)	1.95 (0.39-9.65; $P = 0.41$)
	Grip strength	1.18 (0.38-3.72; $P = 0.77$)	1.09 (0.31-3.85; $P = 0.90$)
Pancreas DCGF (n=8; 7%)	Weight loss	–	–
	Exhaustion	2.11 (0.42-10.48; $P = 0.36$)	2.15 (0.39-11.05; $P = 0.38$)
	Karnofsky	–	–
	Walk time	–	–
	Grip strength	0.35 (0.04-2.80; $P = 0.32$)	0.41 (0.05-3.50; $P = 0.4$
Death (n=10; 8.9%)	Weight loss	1.66 (0.34-8.22; $P = 0.53$)	2.11 (0.34-13.08; $P = 0.42$)
	Exhaustion	0.84 (0.10-6.76; $P = 0.84$)	0.87 (0.10-7.67; $P = 0.90$)
	Karnofsky	–	–
	Walk time	**4.82 (1.20-19.46; $P = 0.03$)**	**4.99 (1.16-21.48; $P = 0.03$)**
	Grip strength	1.92 (0.54-6.77; $P = 0.32$)	1.97 (0.53-7.30; $P = 0.31$)
Kidney DCGF (n=9; 8%)	Weight loss	0.88 (0.10-7.47; $P = 0.88$)	0.34 (0.03-3.67; $P = 0.37$)
	Exhaustion	**4.53 (1.06-19.35; $P = 0.04$)**	2.71 (0.53-13.83; $P = 0.23$)
	Karnofsky	–	–
	Walk time	1.49 (0.18-12.24; $P = 0.70$)	1.07 (0.12-9.49; $P = 0.95$)
	Grip strength	0.91 (0.22-3.82; $P = 0.90$)	0.69 (0.15-3.16; $P = 0.64$)

[a]Adjusted for recipient's age, recipient's sex, recipient's BMI, and kidney DGF. For DGF as outcomes of interest, DGF was not included.
Bold *P* signifies $P < 0.05$ and statistical significance.
BMI, body mass index; CV, cardiovascular; DCGF, death-censored graft failure; DGF, delayed graft function; OR, odds ratio; SPK, simultaneous pancreas-kidney.

SPT Recipients

A total of 49 SPT recipients fulfilled our selection criteria, 39 were primary pancreas transplant alone recipients, 6 had previous pancreas transplant alone, 2 had previous SPK transplant, and 1 each was a previous kidney and islet recipient.

Patient Outcomes

The baseline characteristics of the 49 SPT recipients are shown in Table 7. The mean interval between the frailty assessment and the transplant was 6.59 ± 4.6 mo (Table 8). 33 (67%) had a sum frailty score of 0. None had sum frailty scores of ≥3. The most prevalent component of frailty was unintentional weight loss in 22% of the recipients. None had a Karnofsky score of 1.

Length of Stay

The median posttransplant LOS was 7 d, ranging from 1 to 19 d (Table 9). One recipient died on day 1 because of cardiac arrest, producing a LOS of 1 d. Higher sum frailty scores (coefficient correlation [*r*] 0.29; 95 % CI, 0.006-0.53; $P = 0.04$) and weight loss (r=0.30; 95% CI, 0.02-0.53; $P = 0.03$) were associated with prolonged LOS (Table 10). None of the recipients were sent to a skilled nursing facility or rehabilitation center at the initial posttransplant discharge.

Outcomes Based on the Sum Frailty Scores

A total of 33 recipients (67%) had a sum frailty score of 0, and the remaining 16 (33%) had sum frailty scores of ≥1 (Table 11). Compared with those with a sum frailty score of 0, having a score ≥1 was not associated with any of the 5 outcomes of interest (early readmission, cardiovascular events, pancreas rejection, pancreas DCGF, and death), either in unadjusted or adjusted models.

Various Outcomes

A total of 16 recipients (32.7%) had early readmission within 30 d of posttransplant discharge, with the most common indications for admission being fever in 8 recipients, and gastrointestinal symptoms (pancreatitis, abdominal pain, diarrhea) in 4 recipients (Table 12). Various other indications included incisional drainage

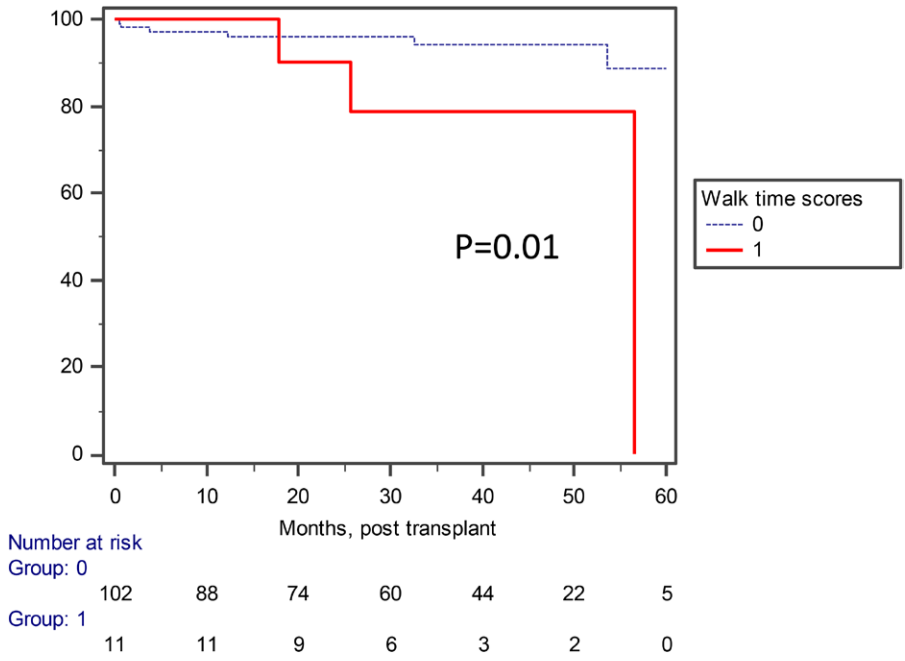

FIGURE 1. Patient survival probability is significantly low among simultaneous pancreas and kidney recipients with slow walk time (P = 0.01)

TABLE 7.
Baseline clinical characteristics of SPT recipients

	Variables	
	Total number of recipients	49
Recipient factors	Male, n (%)	22 (45)
	Non-white, n (%)	2 (4)
	Age at transplant, y	48.4 ± 9.7
	Body mass index, kg/m^2	27.6 ± 3.6
	Previous transplant recipients, n (%)	10 (20)
Donor factors	Male, n (%)	32 (65)
	Non-white, n (%)	16 (33)
	Age at transplant, y	5 (10)
	Body mass index, kg/m^2	23.2 ± 4.5
	Donation after circulatory death, n (%)	5 (10)
	Mean pancreas cold ischemia time, h	12.5 ± 3.9
	Cause of death, n (%)	
	Anoxia	23 (47)
	Cerebrovascular	5 (10)
	Trauma	19 (39)
	Other	2 (4)
Immunological risk and immunosuppressant	cPRA > 20%, n (%)	16 (33)
	Mean HLA mismatch	4.6 ± 1.3
	Induction immunosuppression, n (%)	
	Antithymocyte globulin	29 (59)
	Alemtuzumab	20 (41)
	Early steroid withdrawal (%)	8 (16)

BMI, body mass index; cPRA, calculated panel reactive antibody; DGF, delayed graft function; SPT, solitary pancreas transplant.

TABLE 8.
Frailty assessment of SPT recipients

Variables	
Mean interval from frailty assessment to transplant, mo	6.59 ± 4.6
Sum frailty scores, n (%)	
0	33 (67)
1	15 (31)
2	1 (2)
Unintentional weight loss, n (%)	
0	38 (78)
1	11(22)
Self-reported exhaustion, n (%)	
0	46 (94)
1	3 (6)
Low physical activity (Karnofsky <60%), n (%)	
0	49 (100)
1	0
Walk time, n (%)	
0	48 (98)
1	1 (2)
Low handgrip strength, n (%)	
0	46 (94)
1	3 (6)

SPT, solitary pancreas transplant.

and rejection. In an unadjusted model, low grip strength was significantly associated with an increased risk of early readmission (OR: 11.09; 95% CI, 2.64-46.67; P = 0.001). This was further confirmed with the Kaplan–Meier analysis (Figure 2). Even after adjusting for multiple characteristics (recipient's age, sex, body mass index, and donor's body mass index), low grip strength was associated with an increased risk for early readmission (aOR: 13.08; 95% CI, 2.91-58.71; P = 0.008).

In an unadjusted model, weight loss was significantly associated with an increased risk of pancreas DCGF (OR: 4.47; 95% CI, 1.11-17.99; P = 0.03). This was further confirmed with the Kaplan–Meier analysis (Figure 3). Even after adjusting for multiple characteristics (recipient's age, sex, and donor's body mass index), weight loss was associated with an increased risk of pancreas DCGF (aOR: 4.34; 95% CI, 1.01-18.81; P = 0.049). Likewise, longer pancreas cold ischemia time was not significantly associated with an increased risk of pancreas DCGF in the unadjusted model (HR: 0.99, 95% CI, 0.83-1.19; P = 0.93).

A total of 4 SPT recipients (8.2%) had cardiovascular events needing hospitalization. The indications were cardiac arrest,

TABLE 9.

Length of hospital stay after SPTs

Sum frailty scores	n	Minimum	25th percentile	Median	75th percentile	Maximum	*P*
0	33	6	6	7	8	11	**0.009**
1	15	1	7.25	10	10.75	19	
2	1	4	4	4	4	4	

SPT, solitary pancreas transplant.

TABLE 10.

Length of stay outcome of SPT recipients correlated with frailty measures

	Coefficient correlation (95% CI)
Sum frailty scores	**0.29 (0.006-0.53; *P* = 0.04)**
Weight loss	**0.30 (0.02-0.53; *P* = 0.03)**
Exhaustion	0.11 (–0.18 to 0.39; *P* = 0.45)
Karnofsky	–
Walk time	0.07 (–0.22 to 0.34; *P* = 0.65)
Grip strength	–0.11 (–0.38 to 0.18; *P* = 0.45)

CI, confidence interval; SPT, solitary pancreas transplant.

TABLE 11.

Association based on the sum frailty score after SPT transplants

	Sum ≥ 1 vs 0	
	OR (unadjusted)	OR (adjusted[a])
Early readmission	1.38 (0.51-3.78; *P* = 0.53)	1.30 (0.40-4.20; *P* = 0.66)
Cardiovascular events	5.64 (0.58-54.61; *P* = 0.13)	6.95 (0.61-78.55; *P* = 0.12)
Pancreas rejection	1.41 (0.44-4.55; *P* = 0.56)	0.97 (0.23-4.18; *P* = 0.97)
Pancreas death-censored graft failure	1.26 (0.30-5.29; *P* = 0.75)	1.06 (0.22-5.02; *P* = 0.52)
Death	–	–

[a]Adjusted for recipient's age, recipient's sex, and donor's BMI.
BMI, body mass index; OR, odds ratio; SPT, solitary pancreas transplant.

intraventricular thrombosis, and demand ischemia. None of the 5 variables of frailty assessment were associated with cardiovascular events either in the unadjusted or adjusted model.

Similarly, none of the 5 variables of frailty assessment were associated with pancreas rejection or death either in an unadjusted or adjusted model.

All Pancreas Transplant Recipients

When looking at outcomes among all pancreas transplant recipients (SPK and SPT), only a higher sum frailty score was associated with longer LOS (r=0.16; 95% CI, 0.002-0.30; P = 0.046; **Table S1, SDC,** http://links.lww.com/TXD/A559). None of the other outcomes were significantly associated with individual variables of frailty assessment (**Table S2, SDC,** http://links.lww.com/TXD/A559).

DISCUSSION

In this large, single-center series of 113 SPK recipients and 49 SPT recipients who underwent pretransplant frailty assessment using a modified Fried frailty assessment tool, we report various outcomes associated with individual components of frailty. Although the association between frailty and poor transplant outcomes in various other solid organ transplant recipients has been previously described, this study provides novel detail about the contribution of individual components of frailty to those outcomes among pancreas transplant recipients. Among the 5 components, we found low grip strength to be the most prevalent among SPK recipients, whereas slow walk time was associated with an increased risk of mortality. Among SPT recipients, unintentional weight loss was most prevalent and was associated with an increased risk of pancreas DCGF, along with prolonged LOS. Also, low grip strength was associated with an increased risk of early readmission. Finally, higher sum frailty scores were associated with prolonged LOS among SPT recipients. None of the frailty components were predictive of acute rejection or cardiovascular events. Among the frailty assessment components, self-reported exhaustion and Karnofsky score were the least predictive of any of our outcomes of interest.

Several studies have shown that patients with diabetes are more likely to be frail than those without diabetes.[30-32] The pathophysiology of diabetes leading to frailty is multifactorial including insulin resistance worsening the intramyocellular fatty-acid metabolites caused by reduced mitochondrial activity, loss of skeletal muscle mass, and function leading to sarcopenia and frailty.[32-34] Also, multiorgan subclinical complications associated with diabetes may accumulate, leading to frailty.[35] In addition, sarcopenia is highly prevalent among patients with CKD or end-stage renal disease.[36,37] With all these factors, it is not unusual for patients with diabetes and CKD to be frail.

Among kidney-only transplant recipients, multiple studies have defined the physical frailty phenotype as a score ≥3 and have found associated poor outcomes, including increased risk of DGF and early readmission.[38,39] Similar to our previous report among kidney-only recipients,[23] low grip strength was more prevalent among SPK recipients, whereas it was not prevalent (only in 6%) among SPT recipients, indicating a complex interaction between diabetes and CKD leading to muscle weakness.

Compared with other abdominal transplants, pancreas transplants historically have the highest incidence of complications, which may lead to graft failure.[40] However, in the more recent era, improvements in patient selection, surgical techniques, perioperative care, and immunosuppressive agent tailoring have improved outcomes of both SPK and SPT.[40,41] Proper selection of patients and appropriate management of possible complications may limit the risk of graft loss and improve the short- and long-term outcomes of both the pancreas graft and the patient. Also, historically, pancreas transplantation was considered appropriate primarily only among patients with chronic CKD with insulin-dependent type 1 diabetes. However, more recently, pancreas transplantation has been extended to patients with CKD and type 2 diabetes who meet the United Network for Organ Sharing criteria for listing.[42,43] In addition, there has been some loosening over time of criteria for recipient age cutoffs. In 2016, almost one fourth of pancreas recipients were aged >50 y at the time of transplant, and these recipients had similar patient survival compared with younger recipients.[44,45] Given all these factors, tools to predict early and late complications among pancreas transplant recipients, beginning with the pretransplant evaluation

TABLE 12.

Association with outcomes after SPT transplants

Outcomes	Variables	OR (unadjusted)	OR (adjusted[a])
Early readmission (n=16; 32.7%)	Weight loss	1.19 (0.37-3.78; $P = 0.77$)	0.65 (0.16-2.54; $P = 0.53$)
	Exhaustion	0.53 (0.07-4.12; $P = 0.54$)	1.01 (0.13-8.12; $P = 0.99$)
	Karnofsky	–	–
	Walk time	0.88 (0.11-7.29; $P = 0.91$)	0.97 (0.09-9.66; $P = 0.98$)
	Grip strength	**11.09 (2.64-46.67; $P = 0.001$)**	**13.08 (2.91-58.71; $P = 0.008$)**
CV events (n = 4; 8.2%)	Weight loss	4.29 (0.60-30.62; $P = 0.15$)	4.65 (0.54-39.91; $P = 0.16$)
	Exhaustion	–	–
	Karnofsky	–	–
	Walk time	–	–
	Grip strength	9.62 (0.86-107.1; $P = 0.07$)	10.32 (0.89-121.29; $P = 0.06$)
Pancreas rejection (n=12; 24.5%)	Weight loss	1.34 (0.36-5.05; $P = 0.66$)	1.05 (0.21-5.19; $P = 0.95$)
	Exhaustion	1.64 (0.35-7.77; $P = 0.53$)	1.88 (0.32-10.90; $P = 0.48$)
	Karnofsky	–	
	Walk time	0.99 (0.12-8.59; $P = 0.99$)	0.53 (0.05-5.39; $P = 0.59$)
	Grip strength	–	–
Pancreas DCGF (n=8; 16.3%)	Weight loss	**4.47 (1.11-17.99; $P = 0.03$)**	**4.34 (1.01-18.81; $P = 0.049$)**
	Exhaustion	–	–
	Karnofsky	–	–
	Walk time	–	–
	Grip strength	2.93 (0.36-23.96; $P = 0.31$)	3.26 (0.39-27.21; $P = 0.28$)
Death (n=3; 6.1%)	Weight loss	8.58 (0.77-95.0 $P = 0.08$)	---
	Exhaustion	4.41 (0.36-54.04; $P = 0.25$)	1.32 (0.06-33.21; $P = 0.86$)
	Karnofsky	–	–
	Walk time	–	–
	Grip strength	–	–

[a]Adjusted for recipient's age, recipient's sex, and donor's BMI.
BMI, body mass index; CV, cardiovascular; DCGF, death-censored graft failure; OR, odds ratio; SPT, solitary pancreas transplant.

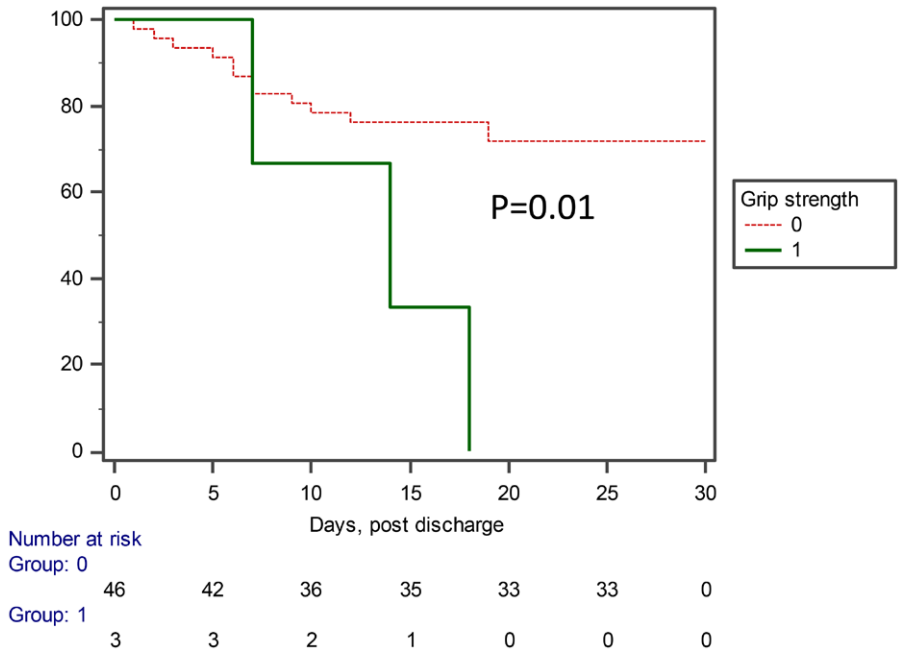

FIGURE 2. Free of early readmission probability is significantly low among solitary pancreas transplant recipients with low grip strength ($P = 0.01$)

phase, are warranted. For that, frailty assessment could be a valuable tool. However, substantial differences in content validity, feasibility in clinical settings, and predictive ability of various frailty assessment tools make it difficult to choose a single best scale. Choosing a highly predictive scale that is less cumbersome and easy to use in clinical practice may be helpful. Based on our findings, slow walk time may be important while assessing frailty among SPK recipients, while low grip strength and weight loss may be important to predict poor outcomes among SPT recipients.

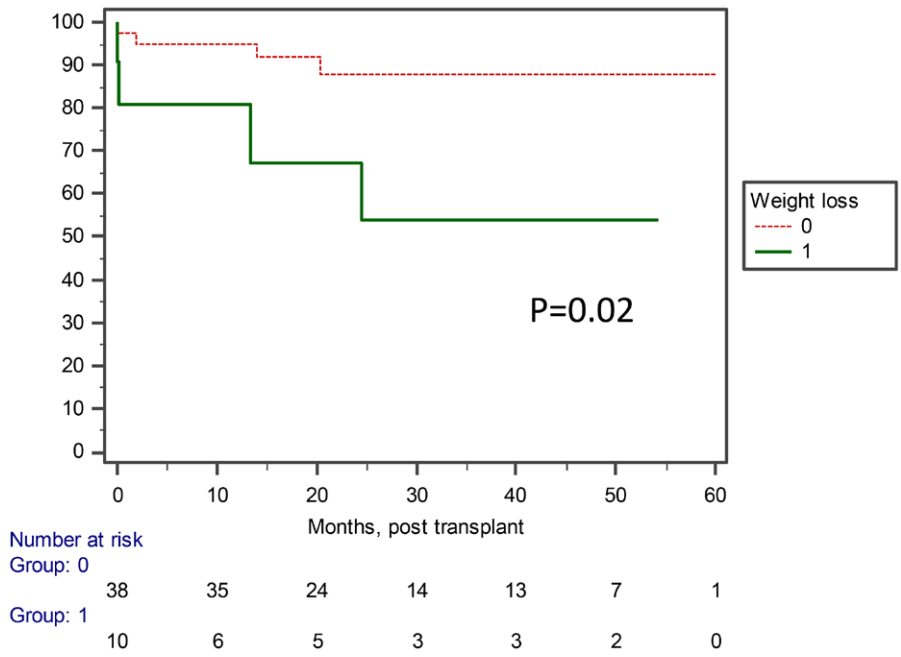

FIGURE 3. Free of pancreas death-censored graft survival probability is significantly low among solitary pancreas transplant recipients with weight loss (P = 0.02)

This study has the expected limitations of a single-center observational study, reflecting our specific population and clinical approach. Our findings are reflective of our specific practices, and this should be factored into the interpretation. To characterize the physical frailty phenotype, we incorporated the Karnofsky Performance Scale, instead of MLTPAQ. MLTPAQ could have different outcomes when analyzed individually. Likely because of stringent selection criteria among pancreas transplant recipients and frailty assessment and scores weighing heavily while selecting or declining for transplant, none of the pancreas recipients had high pretransplant frailty scores. Therefore, outcomes based on the sum frailty score of <3 vs ≥3, which is typically used to define frailty based on the Fried phenotype, were not reflected in our population. Also, not all US centers use the Fried frailty assessment. We were also not able to identify how many potential candidates were denied for pancreas transplant exclusively because of high frailty scores. However, this substantial data set with more granular data than are generally available in registries provides a useful basis for estimating risks and outcomes. Another potential advantage of our single-center data is that they reflect a more homogeneous clinical approach to patient selection, surgical technique, and medical management, in contrast to registry data involving multiple centers. Also, to the best of our knowledge, this is the first study assessing various outcomes among pancreas transplant recipients based on each component of the modified Fried Frailty assessment.

In summary, we found that not all components of frailty contribute equally to predicting outcomes. When accepting or denying patients for listing based on the frailty assessment, frailty components should be considered both individually and as a sum, with particular relevance given to the objective measurements of weight loss, walk time, and grip strength. Similarly, the correlation between frailty components and outcomes could vary based on the types of organ transplant recipients, as we found different outcomes among SPK and SPT recipients in this study, and among the kidney transplant recipients as described before.[23] Also, we believe this finding may be useful to transplant centers if they plan to implement a frailty assessment of potential pancreas transplant recipients but have limited resources and wish to focus on the objective measures of weight loss, walk time, and grip strength.

REFERENCES

1. Parsons RF, Tantisattamo E, Cheungpasitporn W, et al. Comprehensive review: frailty in pancreas transplant candidates and recipients. *Clin Transplant.* 2023;37:e14899.
2. Parajuli S, Aziz F, Garg N, et al. Frailty in pancreas transplantation. *Transplantation.* 2021;105:1685–1694.
3. Haugen CE, Chu NM, Ying H, et al. Frailty and access to kidney transplantation. *Clin J Am Soc Nephrol.* 2019;14:576–582.
4. Van Jacobs AC. Frailty assessment in patients with liver cirrhosis. *Clin Liver Dis (Hoboken).* 2019;14:121–125.
5. Jha SR, Hannu MK, Chang S, et al. The prevalence and prognostic significance of frailty in patients with advanced heart failure referred for heart transplantation. *Transplantation.* 2016;100:429–436.
6. Kojima G, Liljas AEM, Iliffe S. Frailty syndrome: implications and challenges for health care policy. *Risk Manag Healthc Policy.* 2019;12:23–30.
7. Kobashigawa J, Dadhania D, Bhorade S, et al. Report from the American Society of Transplantation on frailty in solid organ transplantation. *Am J Transplant.* 2019;19:984–994.
8. Walston J, Robinson TN, Zieman S, et al. Integrating frailty research into the medical specialties—report from a U13 conference. *J Am Geriatr Soc.* 2017;65:2134–2139.
9. Dolenc E, Rotar-Pavlič D. Frailty assessment scales for the elderly and their application in primary care: a systematic literature review. *Zdravstveno Varstvo.* 2019;58:91–100.
10. Fried LP, Tangen CM, Walston J, et al; Cardiovascular Health Study Collaborative Research Group. Frailty in older adults: evidence for a phenotype. *J Gerontol A Biol Sci Med Sci.* 2001;56:M146–M156.
11. Xue QL. The frailty syndrome: definition and natural history. *Clin Geriatr Med.* 2011;27:1–15.
12. McAdams-DeMarco MA, Van Pilsum Rasmussen SE, Chu NM, et al; AST Kidney Pancreas Community of Practice Workgroup. Perceptions and practices regarding frailty in kidney transplantation: results of a national survey. *Transplantation.* 2020;104:349–356.

13. Chao CT, Wang J, Huang JW, et al. Frailty predicts an increased risk of end-stage renal disease with risk competition by mortality among 165,461 diabetic kidney disease patients. *Aging Dis.* 2019;10:1270–1281.
14. Lee JS, Auyeung TW, Leung J, et al. The effect of diabetes mellitus on age-associated lean mass loss in 3153 older adults. *Diabet Med.* 2010;27:1366–1371.
15. Perkisas S, Vandewoude M. Where frailty meets diabetes. *Diabetes Metab Res Rev.* 2016;32:261–267.
16. Hruska KA, Choi ET, Memon I, et al. Cardiovascular risk in chronic kidney disease (CKD): the CKD-mineral bone disorder (CKD-MBD). *Pediatr Nephrol.* 2010;25:769–778.
17. Kim JC, Kalantar-Zadeh K, Kopple JD. Frailty and protein-energy wasting in elderly patients with end stage kidney disease. *J Am Soc Nephrol.* 2013;24:337–351.
18. Crooks V, Waller S, Smith T, et al. The use of the Karnofsky Performance Scale in determining outcomes and risk in geriatric outpatients. *J Gerontol.* 1991;46:M139–M144.
19. Richardson MT, Leon AS, Jacobs DR, Jr, et al. Comprehensive evaluation of the Minnesota leisure time physical activity questionnaire. *J Clin Epidemiol.* 1994;47:271–281.
20. Bui K, Kilambi V, Rodrigue JR, et al. Patient functional status at transplant and its impact on posttransplant survival of adult deceased-donor kidney recipients. *Transplantation.* 2019;103:1051–1063.
21. Siedlecki A, Irish W, Brennan DC. Delayed graft function in the kidney transplant. *Am J Transplant.* 2011;11:2279–2296.
22. Definition of Pancreas Graft Failure: Pancreas Committee June, 2015. Available at https://transplantpro.org/wp-content/uploads/sites/3/Definition-of-Pancreas-Graft-Failure.pdf. Accessed February 11, 2023.
23. Parajuli S, Astor BC, Lorden HM, et al. Analysis of individual components of frailty: pre-transplant grip strength is the strongest predictor of post kidney transplant outcomes. *Clin Transplant.* 2022;36:e14827.
24. Aziz F, Dhingra R, Anders M, et al. Non-obstructive coronary angiogram findings prior to kidney transplantation do not predict post-transplant cardiac events. *Clin Nephrol.* 2020;94:273–280.
25. Aziz F, Parajuli S, Kaufman D, et al. Induction in pancreas transplantation: T-cell depletion versus IL-2 receptor blockade. *Transplant Direct.* 2022;8:e1402.
26. Niederhaus SV, Leverson GE, Lorentzen DF, et al. Acute cellular and antibody-mediated rejection of the pancreas allograft: incidence, risk factors and outcomes. *Am J Transplant.* 2013;13:2945–2955.
27. Parajuli S, Mandelbrot D, Odorico J. Utility of protocol pancreas biopsies for de novo donor-specific antibodies. *Transplant Direct.* 2022;8:e1287.
28. Drachenberg CB, Odorico J, Demetris AJ, et al. Banff schema for grading pancreas allograft rejection: working proposal by a multi-disciplinary international consensus panel. *Am J Transplant.* 2008;8:1237–1249.
29. Aziz F, Parajuli S, Uddin S, et al. How should pancreas transplant rejection be treated? *Transplantation.* 2019;103:1928–1934.
30. Jang HC. Sarcopenia, frailty, and diabetes in older adults. *Diabetes Metab J.* 2016;40:182–189.
31. Hubbard RE, Andrew MK, Fallah N, et al. Comparison of the prognostic importance of diagnosed diabetes, co-morbidity and frailty in older people. *Diabet Med.* 2010;27:603–606.
32. Kalyani RR, Corriere M, Ferrucci L. Age-related and disease-related muscle loss: the effect of diabetes, obesity, and other diseases. *Lancet Diabetes Endocrinol.* 2014;2:819–829.
33. Krentz AJ, Viljoen A, Sinclair A. Insulin resistance: a risk marker for disease and disability in the older person. *Diabet Med.* 2013;30:535–548.
34. Park SW, Goodpaster BH, Strotmeyer ES, et al; Health, Aging, and Body Composition Study. Accelerated loss of skeletal muscle strength in older adults with type 2 diabetes: the health, aging, and body composition study. *Diabetes Care.* 2007;30:1507–1512.
35. Yoon SJ, Kim KI. Frailty and disability in diabetes. *Ann Geriatr Med Res.* 2019;23:165–169.
36. Rao M, Jaber BL, Balakrishnan VS. Chronic kidney disease and acquired mitochondrial myopathy. *Curr Opin Nephrol Hypertens.* 2018;27:113–120.
37. McBride MJ, Foley KP, D'Souza DM, et al. The NLRP3 inflammasome contributes to sarcopenia and lower muscle glycolytic potential in old mice. *Am J Physiol Endocrinol Metab.* 2017;313:E222–E232.
38. Garonzik-Wang JM, Govindan P, Grinnan JW, et al. Frailty and delayed graft function in kidney transplant recipients. *Arch Surg.* 2012;147:190–193.
39. McAdams-DeMarco MA, Law A, Salter ML, et al. Frailty and early hospital readmission after kidney transplantation. *Am J Transplant.* 2013;13:2091–2095.
40. Humar A, Kandaswamy R, Granger D, et al. Decreased surgical risks of pancreas transplantation in the modern era. *Ann Surg.* 2000;231:269–275.
41. Gruessner AC, Sutherland DE. Pancreas transplant outcomes for United States (US) cases as reported to the United Network for Organ Sharing (UNOS) and the International Pancreas Transplant Registry (IPTR). *Clin Transpl.* 2008;45:299–315.
42. Pham PH, Stalter LN, Martinez EJ, et al. Single center results of simultaneous pancreas-kidney transplantation in patients with type 2 diabetes. *Am J Transplant.* 2021;21:2810–2823.
43. Parajuli S, Mandelbrot D, Aufhauser D, et al. Higher fasting pre-transplant C-peptide levels in type 2 diabetics undergoing simultaneous pancreas-kidney transplantation are associated with posttransplant pancreatic graft dysfunction. *Transplantation.* 2023;107:e109–e121.
44. Scalea JR, Redfield RR, 3rd, Arpali E, et al. Pancreas transplantation in older patients is safe, but patient selection is paramount. *Transpl Int.* 2016;29:810–818.
45. Kandaswamy R, Stock PG, Gustafson SK, et al. OPTN/SRTR 2016 annual data report: pancreas. *Am J Transplant.* 2018;18:114–171.