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Pancreas Retransplant After Pancreas Graft Failure in Simultaneous Pancreas-kidney Transplants Is Associated With Better Kidney Graft Survival

Sandesh Parajuli, MD,[1] Annamalai Arunachalam, MD,[1] Kurtis J. Swanson, MD,[1] Fahad Aziz, MD,[1] Neetika Garg, MD,[1] Natalie Bath, MD,[2] Robert R. Redfield, MD,[2] Dixon Kaufman, MD, PhD,[2] Arjang Djamali, MD,[1,2] Jon Odorico, MD,[2] and Didier A. Mandelbrot, MD[1]

Background. Simultaneous pancreas-kidney (SPK) transplant is usually the best option for the diabetic end-stage renal disease patient. There is limited information about kidney graft outcomes in SPK recipients with isolated pancreas graft failure who do versus do not undergo pancreas retransplantation. **Methods.** Patients were divided into 2 groups based on whether they underwent pancreas retransplant (ReTx$^+$) or not (ReTx$^-$). Kidney graft function and survival were the primary endpoints. **Results.** One hundred and nine patients satisfied our selection criteria, 25 in ReTx$^+$ and 84 in ReTx$^-$. Mean interval from SPK to pancreas failure was significantly shorter in the ReTx$^+$ compared with the ReTx$^-$ group, 19.3 ± 36.7 versus 45.7 ± 47.0 months (P = 0.01), respectively. There was no significant difference in kidney graft follow-up post SPK between 2 groups (P = 0.48). At last follow-up, 15 of the 25 (60%) of the repeat pancreas graft had failed, with a mean graft survival among these failed pancreas graft of 2.6 ± 2.7 years, ranging from 0 to 8.1 years. Uncensored kidney graft failure was significantly lower in the ReTx$^+$ group compared with the ReTx$^-$ group, 44% versus 67% (P = 0.04). Death-censored kidney graft failure was also lower in the ReTx$^+$ group, 24% versus 48% (P = 0.04). The difference in patient survival did not reach statistical significance. In adjusted Cox regression analysis, rejection as a cause of pancreas failure was associated with increased risk of death-censored kidney graft failure, and pancreas retransplantation was associated with decreased risk of kidney graft failure. A similar pattern was seen after 1:1 matching for the interval between SPK and pancreas graft failure. **Conclusions.** Even though ReTx$^+$ patients accept the risks associated with repeat pancreas surgery, providers should consider this option in suitable otherwise healthy patients.

(*Transplantation Direct* 2019;5: e473; doi: 10.1097/TXD.0000000000000919. Published online 23 July, 2019.)

INTRODUCTION

Simultaneous pancreas-kidney (SPK) transplantation is often the best treatment option for diabetic end-stage renal disease patients.[1] SPK prolongs patient survival beyond the survival advantage associated with kidney transplantation alone.[2] The 5-year patient survival after SPK is 87% and 10-year patient survival is 70%, which is significantly better than the survival rates for patients with type 1 diabetes on maintenance dialysis who are on the transplant waiting list.[3,4] Even in a diabetic patient without uremia, pancreas transplantation alone has been associated with the reversal of diabetic nephropathy on biopsies after 10 years of normoglycemia.[5] With improvements in surgical technique, immunosuppression, and proper selection of recipients and donors, the half-life of SPK pancreatic

Received 29 May 2019. Revision received 6 June 2019.

Accepted 8 June 2019.

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

[2] Division of Transplant Surgery, University of Wisconsin School of Medicine and Public Health, Madison, WI.

The authors declare no conflicts of interest.

This work was supported by an unrestricted research grant from the Virginia Lee Cook Foundation.

The clinical and research activities being reported are consistent with the Principles of the Declaration of Istanbul as outlined in the Declaration of Istanbul on Organ Trafficking and Transplant Tourism.

S.P. participated in study concept, design, data collection, analysis, manuscript preparation, and editing. A.A., K.S., and N.G. performed data collection, manuscript preparation, and editing. F.A., N.G., R.R., D.K., and A.D. participated in manuscript preparation and editing. N.B. performed data collection and editing. J.O. participated in study concept, design, analysis, manuscript preparation, and editing.

D.M. and J.O. contributed equally to this study.

Correspondence: Sandesh Parajuli, MBBS, UW Medical Foundation Centennial Building 4175, 1685 Highland Avenue, Madison, WI 53705. (sparajuli@medicine.wisc.edu).

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ISSN: 2373-8731

DOI: 10.1097/TXD.0000000000000919

grafts has increased to over 14 years.[6] The majority of the improvement in long-term graft survival is attributed to the fewer early technical graft losses.[7] Of the various forms of pancreas transplantation, SPK has been associated with the best pancreatic graft survival.[8]

In one registry, data analysis of transplants between 1984 and 2009, the 5-year kidney graft survival among SPK recipients was 81% compared with 73% for pancreas graft survival.[9] Thus, some SPK recipients will have a functional kidney graft and failed pancreas graft, so may develop the complications associated with diabetes. However, data are limited about kidney graft outcomes in SPK recipients with isolated pancreas graft failure who do versus do not undergo pancreas retransplantation. Here, we present our experience with SPK recipients with a failed pancreas graft, comparing kidney graft outcomes based on whether or not they underwent pancreas retransplantation.

MATERIALS AND METHODS

Study Population and Design

This was a single-center cohort study of SPK recipients transplanted between 01/01/2000 and 12/31/2016 who experienced pancreas graft failure and retained kidney graft function. Those with simultaneous graft failure (within 30 days apart) or kidney graft failure before pancreas were excluded (Figure 1). Patients were divided into 2 groups based on whether they underwent pancreas retransplant ($ReTx^+$) or not ($ReTx^-$). Patients were excluded if the pancreas retransplant was in the form of repeat SPK. Kidney graft function and graft survival were the primary endpoints. This study was approved by the University of Wisconsin School of Medicine and Public Health Institutional Review Board.

Variables and Definitions

Clinical information on transplant recipients included age at the time of transplant, gender, race, types of transplant, induction immunosuppressive medication, cold ischemia time, kidney donor profile index, and human leukocyte antigen mismatch. We also included renal function at the time of pancreas graft failure. Pancreas allograft failure was defined based on 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, requirement for insulin that is ≥0.5 units/kg/day for 90 consecutive days or recipient death.[10] Kidney graft failure was defined as a return to dialysis, retransplantation, or patient death. Patient's last follow-up was censored at death or graft failure, for those who experienced it, or at last serum creatinine, among those with a functioning graft.

Surgical Technique

The technique was constant throughout the study period. All pancreas transplants were preserved with University of Wisconsin solution. There was enteric drainage of exocrine secretions and systemic venous drainage of endocrine secretions. No Roux-en-Y limb was performed. Most of the kidneys were placed on the left and pancreas on the right side, except in some cases the pancreas and kidney were placed ipsilaterally.

Pancreas retransplant was performed via midline incision as previously described.[11] Briefly, the vein of the pancreas was anastomosed to the distal inferior vena cava. An end-to-side anastomosis between the donor iliac Y-graft and right common iliac artery was the preferred technique for obtaining inflow. Similar to the primary SPK, enteric drainage was performed in all pancreas retransplants.

Pancreas Retransplant Selection

The indications for pancreas retransplant were similar to those for a primary SPK transplant, that is, uncontrolled diabetes with maximal medical therapy, diabetic complications, etc. However, there was no requirement for hypoglycemic unawareness, as patients have already assumed the risk of immunosuppression. A careful review of the cause for pancreas graft failure was done. In the setting of acute thrombosis, hypercoagulable workups were performed. Contraindications for retransplantation were likewise similar to primary transplant (cardiovascular disease, active infection, cancer, obesity/insulin resistance, compliance, and poor social support). During the evaluation for retransplantation, special attention was paid to the potential arterial and venous landing zones, available space for the graft, and the potential need for vascular conduit creation. We considered the cause and posttransplant interval from SPK to pancreas graft failure in evaluating patients for pancreas retransplant. Patients with SPK pancreas grafts that failed immediately due to the technical issues were

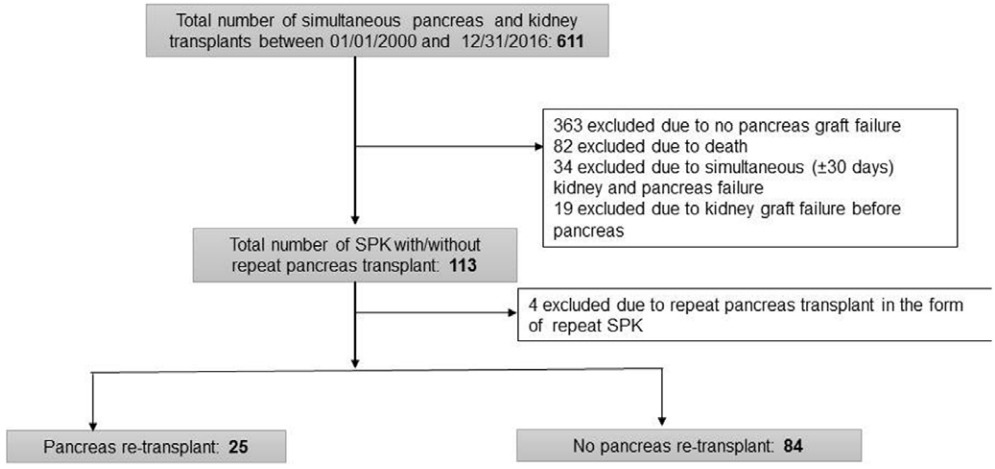

FIGURE 1. Study design among SPK recipients transplanted between 2000 and 2016. SPK, simultaneous pancreas-kidney.

more likely to undergo pancreas retransplant regardless of their kidney function.

Immunosuppression and Prophylaxis

Patients undergoing pancreas transplant received induction immunosuppression with a depleting agent (anti-thymocyte globulin or alemtuzumab) or non-depleting agent (basiliximab) based on immunological risk factors.[12] Patients with pretransplant donor-specific antibodies, repeat SPK, previous pancreas graft failure due to rejection, or planned for early steroid withdrawal were more likely to receive depleting agents for induction. Patients were typically maintained on a triple immunosuppressive regimen, with a calcineurin inhibitor (usually tacrolimus), antiproliferative agent (usually mycophenolate mofetil or mycophenolic acid), and steroids. Some patients had 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 10–12 ng/mL in first 3 months posttransplant, 8–10 ng/mL from month 3 to 12, and 6–8 ng/mL after 1 year. The initial mycophenolate sodium dose was 720 mg by mouth 3 times daily for 1 month, then twice daily after that. Prednisone was tapered to 10 mg daily by 8 weeks posttransplant, with further taper determined by the managing provider. Patients undergoing early steroid withdrawal stopped steroids after postoperative day 4.

In patients at high risk (donor positive/recipient negative) or intermediate (recipient positive) risk for cytomegalovirus (CMV) infection, prophylaxis with valganciclovir was used for 6 months. In those at low risk for CMV infection (donor negative/recipient negative), only acyclovir was given, for prophylaxis of herpes infection. All patients also received fluconazole for 1 month and sulfamethoxazole-trimethoprim for 1 year as prophylaxis.

Statistical Analysis

Continuous data were compared using Student *t*-test or the Wilcoxon Rank Sum test, when appropriate, while categorical data were analyzed using Fisher exact test or the chi-squared test, when appropriate. Uncensored and death-censored graft failure were analyzed using Kaplan-Meier analyses. *P*-values <0.05 were considered statistically significant. Risk factors associated with death-censored kidney graft failure were studied using univariate and multivariate stepwise Cox regression analyses. All variables in Table 1 were analyzed in univariate analysis and variables with *P*-value <0.05 in univariate were analyzed in multivariate.

RESULTS

A total of 611 SPK transplants were performed during the study period, of which 109 met our selection criteria. There were 25 in ReTx$^+$ group and 84 in ReTx$^-$ group (Figure 1).

Baseline characteristics are shown in Table 1. Cold ischemia time for kidney, the interval from SPK to pancreas graft failure, thrombosis as the cause of pancreas graft failure, and pancreas graft failure within 90 days of SPK were significantly different between groups. Both groups had similar other baseline characteristics, including a renal function at the time of pancreas graft failure. The causes of pancreas graft failure in the ReTX$^+$ group were graft thrombosis 11 (44%), rejection 3 (12%), anastomotic enzyme leak 4 (16%), and various other reasons (pancreatitis, insulin resistance, etiology unknown) 7 (28%). In the ReTX$^-$ group, rejection was the most common cause of pancreas graft failure in 25 (30%) patients, 12 (14%) had graft thrombosis, 11 (13%) had insulin resistance,

TABLE 1.

Baseline characteristics

Variables	Pancreas ReTx$^+$ (n = 25)	Pancreas ReTx$^-$ (n = 84)	*P*
Males	19 (76%)	56 (67%)	0.38
Mean age at time of transplant, y	39.8 ± 8.3	39.7 ± 7.6	0.92
Caucasian	23 (92%)	77 (92%)	0.96
Types of transplant			0.39
DBD	20 (80%)	73 (87%)	
DCD	5 (20%)	11 (23%)	
Induction immunosuppression			0.06
IL-2 receptor antibodies (basiliximab or daclizumab)	12 (48%)	52 (62%)	
Alemtuzumab	9 (36%)	30 (36%)	
Anti-thymocyte globulin	4 (16%)	2 (2%)	
Mean KDPI (%)	30 ± 23	31 ± 23	0.86
Mean cold ischemia time (pancreas), h	15.3 ± 4.1	13.7 ± 4.2	0.08
Mean cold ischemia time (kidney), h	16.5 ± 4.4	14.6 ± 4.3	0.04
Mean HLA mismatch (out of 6)	4.6 ± 1.0	4.5 ± 1.2	0.55
Mean interval from SPK to pancreas failure, mo	19.3 ± 36.7	45.7 ± 47.0	0.01
Graft thrombosis as a cause of pancreas graft failure	11 (44%)	12 (14%)	0.001
Rejection as a cause of pancreas graft failure	3 (12%)	25 (30%)	0.08
Pancreas graft failure within 90 days of SPK	16 (64%)	21 (25%)	<0.001
Mean interval from pancreas failure to pancreas retransplant, mo	15.4 ± 12.5	NA	
Serum creatinine at time of pancreas failure (mg/dL)	2.4 ± 2.1	2.0 ± 1.2	0.29
eGFR at time of pancreas failure	44.5 ± 28.0	48.2 ± 24.5	0.52

DBD, donation after brain death; DCD, donation after circulatory death; eGFR, estimated glomerular filtration rate; HLA, human leukocyte antigen; KDPI, kidney donor profile index; ReTx$^+$, underwent pancreas retransplant; ReTx$^-$, did not undergo pancreas retransplant; SPK, simultaneous pancreas-kidney.

TABLE 2.
Outcomes

Variables	Pancreas ReTx+	Pancreas ReTx−	*P*
Mean kidney graft follow-up post SPK, y	9.2 ± 5.2	8.3 ± 4.8	0.48
Mean interval from pancreas failure to last follow-up, y	7.6 ± 4.9	4.6 ± 3.9	0.002
Last serum creatinine, mg/dL	1.4 ± 0.3 (n = 14)	1.5 ± 0.7 (n = 28)	0.25
Last eGFR	55.5 ± 17.8	55.3 ± 22.6	0.97
Uncensored kidney graft failure	11 (44%)	56 (67%)	0.04
Death-censored kidney graft failure	6 (24%)	40 (48%)	0.04

eGFR, estimated glomerular filtration rate; ReTx+, underwent pancreas retransplant; ReTx-, did not undergo pancreas retransplant; SPK, simultaneous pancreas-kidney.

5 (6%) had pancreatic anastomotic enzyme leak or bleeding, 4 (5%) had graft failure due to infections, and the remaining 27 (32%) had various other reasons, including poor initial graft function and unknown cause. The 1-year pancreas graft survival among 109 SPK recipients was 55%. A total of 38 recipients had biopsy-proven acute rejection of kidney, 3 (12%) were in ReTx+ group, and 35 (42%) in the ReTx− group during the study period.

The mean posttransplant kidney follow-up was 9.2 ± 5.2 years in the ReTx+ group and 8.3 ± 4.8 years in the ReTx− group (Table 2). The mean interval from pancreas graft failure to last follow-up was significantly longer in the ReTx+ group, 7.6 ± 4.9 years compared with 4.6 ± 3.9 years in ReTx− (P = 0.002). There was a significantly lower percentage of kidney graft failure (uncensored) in ReTx+ group compared with the ReTx−. Death-censored graft failure was also significantly lower in ReTx+ group (P = 0.04). This trend was found in Kaplan-Meier analysis for both death-censored (Figure 2) and uncensored kidney graft survival. However, patient survival was not significantly different (Figure 3). The 1-year pancreas graft survival among 25 recipients with pancreas retransplant was 84%, which was slightly lower than the primary SPK recipient's 1-year pancreas graft survival of 89% (P = 0.70).

Since there was a significant difference between ReTx+ and ReTx− groups in that patients with early pancreas graft failure were more likely to get a pancreas retransplant, we matched 1:1 for this variable and repeated the outcome analysis. None of the baseline characteristics, except for the kidney cold ischemia time, were significantly different between the groups (Table 3). The Kaplan-Meier survival curves showed a significant difference in both the uncensored and death-censored kidney graft survival between the groups, similar to what was found without matching (Figure 4).

In univariate analysis (Table 4), pancreas retransplant (hazard ratio [HR] 0.31; 95% confidence intervals [CI], 0.13-0.73; P = 0.007) and pancreas graft failure within 90 days (HR 0.47; 95% CI, 0.24-0.92; P = 0.03) were associated with a decreased risk of death-censored kidney graft failure. Rejection as a cause of pancreas graft failure (HR 2.42; 95% CI, 1.31-4.48; P = 0.005) was associated with increased risk of death-censored kidney graft failure. However, after adjustment for those variables, only rejection as a cause of pancreas graft failure (HR 2.17; 95% CI, 1.12-4.19; P = 0.02) was associated with the increased risk of graft failure, and pancreas retransplant (HR 0.34; 95% CI, 0.13-0.81; P = 0.02) was associated with decreased risk of death-censored kidney graft failure.

Of the 25 patients with repeat pancreas grafts, 15 had pancreas graft failure at last follow-up, with mean graft survival among these failed graft of 2.6 ± 2.7 years ranging from 0 to 8.1 years. Eleven had death-censored graft failure (4 due to thrombosis, 2 due to rejection, 2 due to insulin resistance, 1 due to bleeding, and 2 from an unknown cause). Four had death with a functional graft, ranging from 4.3 months to 7.6 years post pancreas retransplant. And none of these deaths were related to immediate postsurgical complications. Of these 15 patients with repeat pancreas graft failure, 9 also developed kidney graft failure at last follow-up (5 due to death, 3 due to rejection, and 1 due to BK nephropathy). The

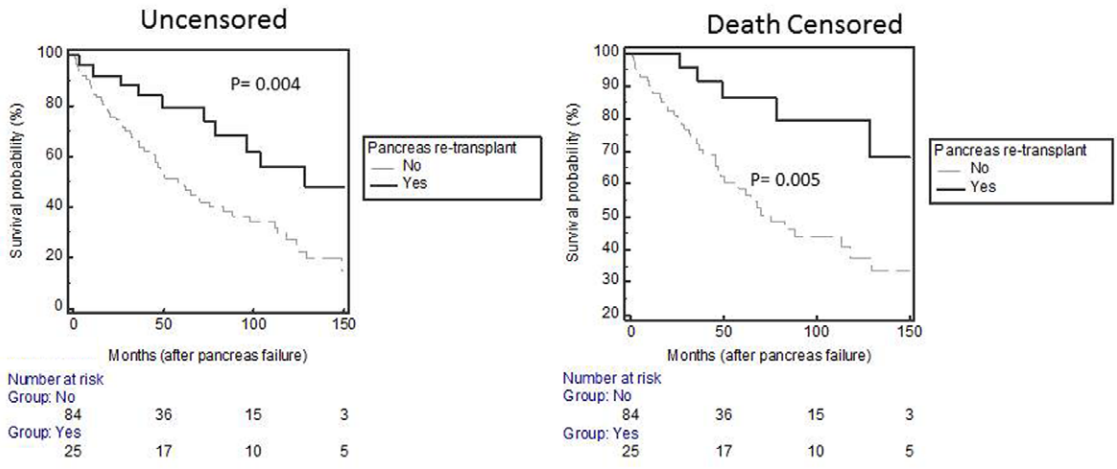

FIGURE 2. Kidney graft survival after pancreas graft failure in SPK recipients stratified by whether the patient underwent pancreas retransplantation (uncensored or death censored). SPK, simultaneous pancreas-kidney.

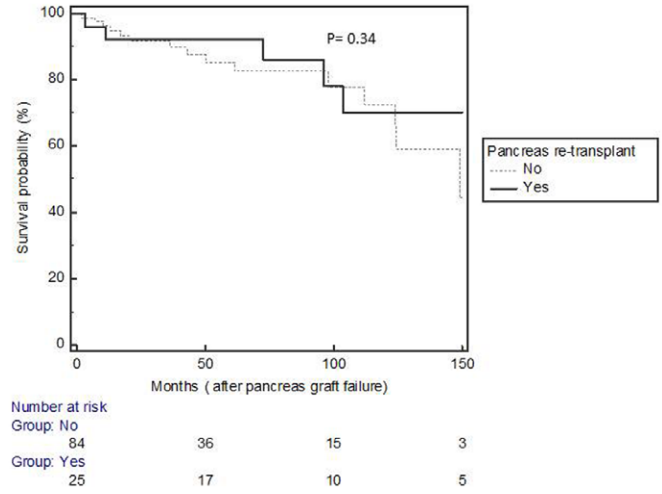

FIGURE 3. Patient survival after pancreas graft failure comparing pancreas retransplantation to no pancreas retransplantation.

remaining 10 patients with functional pancreas repeat grafts had a mean follow-up of 7.8 ± 4.5 years ranging from 1.9 to 13.2 years.

As the majority of patients did not undergo pancreas retransplant, we reviewed their medical records to look for the specific reason for that. Unfortunately, 49 (58%) of 84 patients did not have an evaluation or documentation of why the patient was not considered for a pancreas retransplant. The others failed prescreens or were turned down during evaluation for pancreas retransplant, mainly due to cardiovascular disease (9), death during the evaluation process (4), obesity (3), incomplete evaluations (3), financial/social issues (3), high surgical risk due to wound infections (2), severe orthostatic hypotension (1), or other (including severe infections, malignancy, severe insulin resistance and patient choice) (9).

Not all graft thromboses in the ReTX$^-$ group were due to acute thrombosis. Only 6 of 12 patients had graft thrombosis within the first month of transplant. The mean interval from transplant to the graft failure among these 12 patients was 23.0 ± 44.9 months, ranging from 0 to 143 months. These patients were not retransplanted due to various reasons, including never evaluated (5), died during evaluation (2), not interested or did not complete evaluation (2), cardiovascular disease (1), developed gancyclovir resistant CMV (1), and severe orthostatic hypotension (1).

A total of 37 patients underwent resection of the previous pancreas transplant, 16 (64%) in the ReTx$^+$ group (prior to the repeat transplant) and 21 (25%) in the ReTx$^-$ group. The causes of graft failure in the ReTx$^+$ patients requiring graft resection were thrombosis (9), anastomotic enzyme leak (4),

TABLE 3.

Baseline characteristics after matching for the interval of pancreas graft failure

Variables	Pancreas ReTx$^+$ (n = 25)	Pancreas ReTx$^-$ (n = 25)	*P*
Males	19 (76%)	15 (60%)	0.23
Mean age at the time of transplant, y	39.8 ± 8.3		0.92
Caucasian	23 (92%)	22 (88%)	0.64
Types of transplant			1.0
DBD	20 (80%)	20 (80%)	
DCD	5 (20%)	5 (20%)	
Induction immunosuppression			0.15
IL-2 receptor antibodies (basiliximab or daclizumab)	12 (48%)	16 (64%)	
Alemtuzumab	9 (36%)	9 (36%)	
Anti-thymocyte globulin	4 (16%)	0 (0%)	
Mean KDPI (%)	30 ± 23	32 ± 22	0.82
Mean cold ischemia time (pancreas), h	15.3 ± 4.1	13.6 ± 4.6	0.16
Mean cold ischemia time (kidney), h	16.5 ± 4.4	14.0 ± 4.4	0.04
Mean HLA mismatch (out of 6)	4.6 ± 1.0	4.4 ± 1.1	0.53
Graft thrombosis as a cause of pancreas graft failure	11 (44%)	8 (32%)	0.38
Rejection as a cause of pancreas graft failure	3 (12%)	3 (12%)	1.0
Pancreas graft failure within 90 days of SPK	16 (64%)	16 (64%)	1.0
Mean interval from pancreas failure to pancreas retransplant, mo	15.4 ± 12.5		
Serum creatinine at time of pancreas failure, mg/dL	2.4 ± 2.1	2.2 ± 1.8	0.70
eGFR at time of pancreas failure	44.5 ± 28.0	48.1 ± 29.3	0.66

DBD, donation after brain death; DCD, donation after circulatory death; eGFR, estimated glomerular filtration rate; HLA, human leukocyte antigen; KDPI, kidney donor profile index; ReTx$^+$, underwent pancreas retransplant; ReTx$^-$, did not undergo pancreas retransplant; SPK, simultaneous pancreas-kidney.

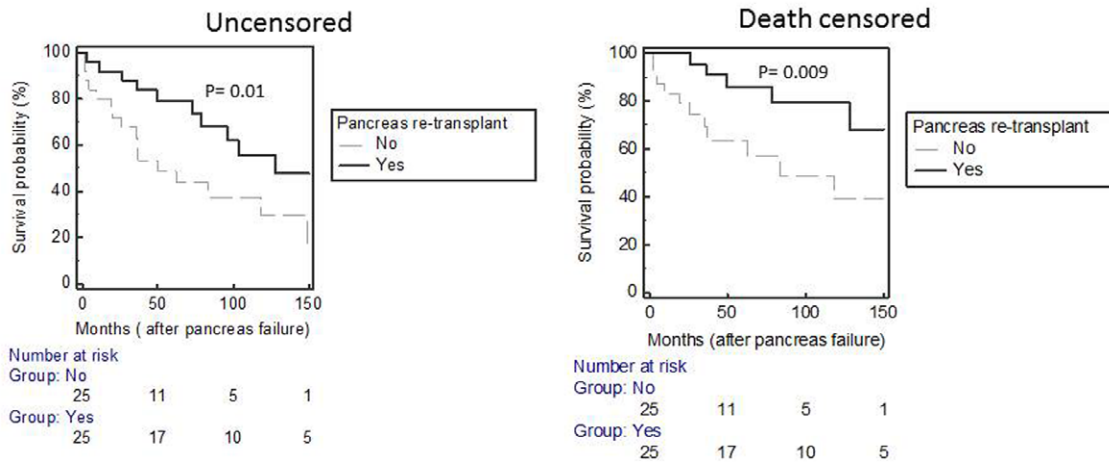

FIGURE 4. Kidney graft survival after pancreas graft failure in SPK recipients 1:1 matched for the interval between SPK transplant and graft failure stratified by presence or absence of pancreas retransplantation (uncensored or death censored). SPK, simultaneous pancreas-kidney.

TABLE 4.

Variables associated with kidney death-censored graft failure after pancreas failure

	Univariate analyses			Multivariate analyses		
Variables	**HR**	***P***	**95% CI of HR**	**HR**	***P***	**95% CI of HR**
Males	1.11	0.75	0.59-2.09			
Age	0.97	0.13	0.93-1.0			
White	1.05	0.94	0.32-3.39			
DBD	1.06	0.91	0.42-2.68			
IL-2 receptor antibodies for induction	1.22	0.51	0.67-2.19			
KDPI	1.24	0.71	0.38-4.07			
Pancreas cold ischemia time	0.97	0.37	0.91-1.04			
Kidney cold ischemia time	0.97	0.39	0.90-1.03			
HLA mismatch	0.90	0.37	0.71-1.40			
Graft thrombosis as a cause of pancreas failure	0.75	0.46	0.35-1.61			
Rejection as a cause of pancreas failure	2.42	0.005	1.31-4.48	2.17	0.02	1.12-4.19
Pancreas failure within 90 days	0.47	0.03	0.24-0.92	0.72	0.39	0.35-1.51
Interval from SPK to pancreas graft failure	1.0	0.08	0.99-1.01			
Interval from pancreas failure to repeat transplant	1.01	0.81	0.95-1.07			
eGFR at time of pancreas failure	0.99	0.08	0.98-1.01			
Pancreas retransplant	0.31	0.007	0.13-0.73	0.34	0.02	0.13-0.81

CI, confidence intervals; DBD, donation after brain death; eGFR, estimated glomerular filtration rate; HLA, human leukocyte antigen; HR, hazard ratio; KDPI, kidney donor profile index; SPK, simultaneous pancreas-kidney.

rejection (2), and pancreatitis (1). The causes of graft failure in the ReTx$^-$ patients requiring graft resection were thrombosis (10), infection (4), bleeding (3), anastomotic enzyme leak (2), and pancreatitis (2). The previous pancreas transplant was present at the time of retransplant in 9 of 25 patients in the ReTx$^+$ group. Of those 9 patients, 5 had the atretic pancreas allograft left in and the new graft was placed above it, and 4 had their old pancreas grafts removed to make room for the new pancreas allograft. In those 4 patients with pancreas removed at the time of repeat transplant, the previous duodenojejunostomy was staple divided then was closed in a hand sewn end to end fashion. The new duojejunostomy was placed distal to the previous anastomosis. For the initial transplant, the portal vein was placed on the inferior vena cava and arterial inflow on the right common iliac artery. For the retransplant, the venous drainage and arterial inflow were placed inferior to the previous anastomoses in most cases. In 1 case, the stump of the previous Y graft was used as arterial inflow.

DISCUSSION

In this series of 109 SPK recipients with isolated pancreas graft failure, we found that pancreas retransplant was associated with better kidney graft survival. Even though pancreas retransplant patients take the risks associated with repeat pancreas surgery, in an unadjusted or adjusted Cox regression analysis, and by Kaplan-Meier survival analysis, pancreas retransplant was associated with better uncensored and death-censored kidney graft survival in previous SPK recipients with isolated pancreas graft failure.

Successful pancreas transplantation restores insulin-independence in patients with type 1 diabetes mellitus.[13,14] Several studies have shown improvement in diabetic nephropathy in nonuremic type 1 diabetics who undergo pancreas transplant alone.[15-17] In addition, there are several studies showing that the progressive deterioration of renal function in pancreas transplant alone recipients is mainly related to immunosuppressive medications.[18-21] Although SPK is a very favorable option for diabetic end-stage renal disease

patients, pancreas after kidney transplants are also an attractive option for type 1 diabetic patients who have previously undergone kidney transplantation.[1,22] Kidney graft survival is higher in pancreas after kidney transplant recipients compared with diabetic recipients of kidney transplants alone, as measured from the time of the kidney as well as the pancreas transplants.[22,23]

The major benefits of SPK transplantation are decreased mortality and improved quality of life. Survival for SPK transplant recipients is much better than that of waitlisted patients who remain on dialysis.[24,25] The improved quality of life is due to freedom from frequent blood sugar monitoring, the need for insulin injection, glucose variability, and the need for dialysis.[26-28] SPK transplant recipients experience additional improvements in their sense of well-being, autonomy, and independence compared with diabetic patients who received a kidney transplant alone.[29,30] In addition, other significant morbidities associated with diabetes, including lipid metabolism, neuropathy, retinopathy, and fracture risk, improve after pancreas transplantation and restoration of a euglycemic state.[31-34] Given all these benefits, there is no doubt that pancreas transplantation, especially in the form of SPK, is the best choice in a suitable patient. However, when a pancreas graft fails, patients must either go back to using insulin to maintain ideal blood sugars or must bear the risk of pancreas retransplantation.

In the past, pancreas retransplantation was considered to have a high risk of technical failure and rejection compared with kidney retransplantation, so was rarely performed.[35] However, pancreas retransplantation is now more common and positive outcomes with repeat transplantation have been reported.[11,36-40] In 1 large series of 415 pancreas retransplants between 1978 and 2012, Rudolph et al[41] showed that pancreas retransplant outcomes have improved significantly over time, but rejection remains an important risk factor for pancreas retransplant graft failure. In the same study, the risk of technical failure and patient death were similar between primary versus repeat transplant.[41] Given the previous studies, and based on our findings, we believe pancreas retransplantation in an appropriate patient is the best option for the preservation of kidney allograft function in SPK recipients with isolated pancreas graft failure. Most of the patients in this study were not offered the option of pancreas retransplantation, usually due to medical conditions, based on provider discretion. But those who did undergo pancreas retransplantation did well, and this approach also helped preserve their kidney graft function. Clearly, providers should be cautious in offering pancreas retransplant, considering factors such as the cause of previous pancreas graft failure and the overall medical condition of the patient.

Our observations have the limitations inherent to this type of study. As a single center, observational, non-randomized study, it may not be possible to generalize our results to other centers. Despite the use of regression analyses and 1:1 matching based on the posttransplant interval of pancreas graft failure, there could be selection bias in the utilization of the pancreas retransplantation option. Pancreas repeat transplant recipients are usually maintained on the higher immunosuppressive medication and also had receive repeat induction immunosuppressive medications, which could help prevent rejection of the kidney, thus leading to prolonged graft function. Also, it was not possible to establish precisely why ReTx$^-$ patients were not selected or decided not to get retransplantation and multiple factors, including patient preference and non-medical factors, may have contributed. However, to our best knowledge, this is the largest reported series comparing kidney graft outcome among SPK recipients with failed pancreas based on whether or not they underwent pancreas retransplantation. In summary, pancreas retransplant after pancreas graft failure in SPK recipients is associated with better kidney graft survival. With modern era improvements in surgical techniques, immunosuppression and graft monitoring have overall led to better outcomes. In a suitable patient and otherwise healthy patient, the provider should consider a pancreas retransplant option in SPK patients with preserved kidney allograft function.

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