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Simultaneous pancreas-kidney transplantation reduces excess mortality in type 1 diabetic patients with end-stage renal disease

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Simultaneous pancreas-kidney transplantation reduces excess mortality in type 1 diabetic patients with end-stage renal disease.

Background. Diabetic renal disease continues to be the most significant cause of end-stage renal disease (ESRD) in the United States. Renal transplantation improves diabetic ESRD patient survival; however, the diabetic state remains associated with poor patient survival. Simultaneous pancreas-kidney (SPK) transplantation can restore normoglycemia and thus may improve outcomes.

Methods. We assessed the impact of SPK on age-range–matched type 1 diabetic patients who underwent renal transplantation at a single center. The observed/expected life span and annual mortality rates (AMRs) were used as measures of survival. A Cox proportional hazards analysis was used to analyze the impact of potential variables on mortality in SPK recipients.

Results. SPK transplantation ($N = 335$) increased the observed/expected life span compared with diabetic cadaveric (DM-Cad, $N = 147$) and live-donor (DM-Live, $N = 160$) transplant recipients ($P = 0.004$) and significantly reduced the AMRs (SPK, 1.5%; DM-Cad, 6.27%; DM-Live, 3.65%, $P = 0.008$, SPK vs. other DM). Moreover, the SPK observed/expected life span and AMR were not significantly different from that of age-range–matched nondiabetic transplant recipients ($N = 492$). The only variable that was significantly associated with patient survival was discharge serum creatinine (relative risk 1.16, $P \leq 0.0154$).

Conclusion. These data demonstrate that SPK improves the ability for type 1 diabetic patients to live more of their expected life span. This suggests that glycemic control, even as a late intervention in a diabetic patient's lifetime, may beneficially affect survival.

Diabetic renal disease is the most significant cause of end-stage renal disease (ESRD) in the United States, and diabetic ESRD patients manifest the highest mortality rates of any group of ESRD patients. While renal transplantation may improve diabetic ESRD patient survival, the diabetic state remains associated with poor patient and graft outcomes. United Network for Organ Sharing (UNOS) data support this conclusion. Nondiabetic patients who receive a cadaveric renal transplant have a greater than 80% five-year survival, and a nearly 90% five-year survival is documented for recipients of living-donor transplants [1]. However, patients with type 1 diabetes who receive a cadaveric renal allograft have a 73.4% five-year survival rate, and those receiving a living-donor renal allograft have an 84% five-year survival rate. To enhance these results, physicians and surgeons have focused on improving immunosuppression, pretransplant medical evaluation, prophylactic medical strategies, and simultaneously, honing the techniques of simultaneous pancreas-kidney (SPK) transplantation.

Simultaneous pancreas-kidney transplantation improves certain sequelae of diabetes, including retinopathy [2] and neuropathy [3]. This occurs concomitant with the demonstrable effects of SPK transplantation, restoration of renal function, and normoglycemia. Early studies emphasized concerns regarding the morbidity and mortality associated with SPK transplantation [4–6]. They also raised a critical point: If SPK transplantation is to be effective as therapy for type 1 diabetes, then it must improve the ability for patients to approximate a normal life expectancy more than kidney transplantation alone. As such, a simple measure of the effectiveness of SPK transplantation is to evaluate the SPK recipient survival as a ratio of the length of patient survival following the transplant event compared with the average life span of an age-matched healthy individual from the same population [7].

We used this outcome measure (observed/expected life span) to address this question: How effective is SPK

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transplantation at our center in restoring normal life expectancy in diabetic ESRD patients?

METHODS

The study cohort consisted of all type 1 diabetic patients who developed ESRD between the ages of 21 and 40 and received an initial kidney or SPK transplantation at the University of Wisconsin between 1966 through December 31, 1995. Data on each individual were obtained from a pretransplant clinical file, and prospectively compiled post-transplant and institution-specific dialysis databases. Study entry was defined as the date of admission to the center's dialysis program or date of transplantation. Follow-up was terminated on December 31, 1998, or at time of death or at last follow-up clinic visit.

The SPK and age-range–matched diabetic renal transplant recipient cohort was analyzed to evaluate the impact of certain variables on patient and renal allograft survival. Recipient parameters examined that were handled as categorical variables included race (Caucasian vs. other races given the proportion of Caucasian patients who receive transplants in our program), history of pretransplant dialysis (yes or no), and use of mycophenolate mofetil (yes or no). Other variables that were examined included age at transplant, duration of diabetes prior to transplant, pretransplant serum creatinine (S_{Cr}), S_{Cr} at discharge from transplant hospitalization, patient height, weight, body mass index (BMI), human lymphocyte antigen (HLA)-A, -B, and -DR matching. Donor variables that were examined included cytomegalovirus (CMV) status, race, age, and weight. A Cox proportional hazards model was used to assess the main effects of potential risk factors and their interactions with patient groups on patient survival and renal graft loss. Rejection rates, readmission rates, CMV infection rates, and cardiac death rates were estimated using Kaplan–Meier methodology and were compared using the log-rank test.

An additional cohort of patients, age-range–matched patients who received either a cadaveric or living-donor renal transplant for nondiabetic, nonhypertensive renal failure, were included in the observed/expected life span analysis. These patients had chronic glomerulonephritis, interstitial nephritis, congenital renal disease, polycystic kidney disease, or genitourinary abnormalities as the cause of their renal failure and were designated as the primary renal disease cohort (1° renal).

Graft survival time was calculated as the time interval from transplantation to the date of graft failure or date of last follow-up [8]. Patient survival was calculated as the time from initial therapy for ESRD to death date or, if death was not reported, date of the last follow-up. Survival curves were generated according to the Kaplan–Meier method. The equality of the survivor function across the different treatment or category groups was tested using the log-rank test. For additional analyses, the annual mortality rate (AMR) was also calculated. The expected life span was calculated using state-specific life tables [7]. A ratio of observed/expected survival was calculated for each patient [7]. The median or 0.5 observed/expected survival for a population, defined as the percentage of patients who reached 0.5 observed/expected life span, was analyzed by Kaplan–Meier methodology.

Data are reported as mean ± SD. Differences in proportions and means were tested using the chi-square and *t*-test, respectively. A P value < 0.05 was considered significant. Statistical analyses of the data set were performed using SAS statistical software (SAS Institute, Inc., Cary, NC, USA).

RESULTS

Observed/expected life span was calculated for 335 SPK, 147 cadaveric (DM-Cad), and 160 living-donor (DM-Live) transplant recipients. Demographic characteristics for these individuals are shown in Table 1. The average follow-up for these patients was 13 ± 5.9 years. There were no significant differences in age at the time of transplant or duration of diabetes prior to transplantation. The vast majority of patients, greater than 80%, were Caucasian, and male patients slightly outnumbered female transplant recipients.

There were 96 deaths in the DM-Cad cohort, 68 deaths in the DM-Live patient groups, and 35 deaths in the SPK cohort during the study time period. The initial analysis focused on the impact of SPK transplantation on patient survival. The absolute patient survival is shown in Figure 1. In addition to the diabetic patients, this analysis included 492 age-range–matched 1° renal allograft recipients. These patients had higher rates of survival following transplantation compared with patients in the other transplant groups (1° renal vs. all others, $P = 0.0029$). SPK transplant recipients had a significantly greater percentage survival compared with age-range–matched DM-Live and DM-Cad recipients (SPK vs. DM-Live and DM-Cad, $P = 0.004$).

Annual mortality rates for each patient cohort were also calculated (Table 1). Not surprisingly, 1° renal patients had an AMR (1.7%) that was significantly less than DM-Cad (6.27%) and DM-Live (1° renal vs. DM-Live and DM-Cad, 3.65%, $P = 0.008$). However, the SPK recipients' AMRs (1.5%) were not significantly different from that of 1° renal patients.

To further evaluate the survival benefit of SPK transplantation, we compared the ratio of observed/expected life span among the selected patient groups. Seventy-six percent of SPK patients reached their median or 0.5 observed/expected life span. This was not significantly different from the percentage of 1° renal patients who

Table 1. Patient demographics for transplant patients between ages 21 and 40

Characteristic	1° Renal	DM-Cad	DM-Live	SPK
N	492	147	160	335
Gender *M/F*	290/202	81/66	97/63	204/131
%	59/41	55/45	60/40	61/39
Age *years*	30.2 ± 6.8	32.3 ± 6.4	31.3 ± 6.3	34 ± 5.9
Race %				
Caucasian	389[a] (79)	120[a] (82)	112[a] (70)	328[a] (98)
African American	74 (15)	7 (5)	2 (2)	3 (1)
Other	29 (6)	3 (2)	1 (1)	
Not defined		17 (11)	45 (28)	3 (1)
Duration of diabetes *years*	N.A.	17 ± 7	18 ± 5.8	16 ± 8
Pretransplant dialysis (Yes/No)	352/140 (72/28)	108/39 (73/27)	110/50 (69/31)	206/129 (62/38)
Annual mortality rate (AMR) %	1.7%	6.27%	3.65%	1.5%[b]

[a] $P \leq 0.001$ vs. other races
[b] $P = 0.008$ vs. DM-Cad, DM-Live; N.S. vs. 1° renal

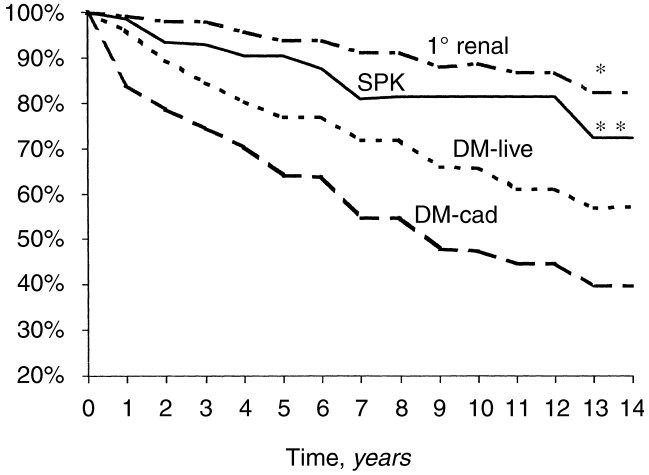

Fig. 1. Kaplan-Meier estimates of simultaneous pancreas-kidney (SPK), diabetic cadaveric (DM-Cad), live-donor (DM-Live), and the primary renal disease cohort (1° renal; defined in the Methods section) transplant patient survival. *$P = 0.0029$ 1° renal vs. all others; **$P = 0.004$ SPK vs. DM-Cad, DM-Live.

reached their median observed/expected life span (77%). In an attempt to account for population variability, the same analysis was undertaken by matching the populations for race. In this analysis, 1° renal patients manifested a trend toward a higher percentage of patients achieving their median or 0.5 observed/expected life span (81%, $P = 0.078$). In contrast, only 70% of DM-Live patients ($P = 0.002$ vs. SPK) and 39% of DM-Cad patients ($P = 0.003$ vs. SPK) achieved their median or 0.5 observed/expected life span. To gauge better the potential impact of transplant survival in the contemporary era of immunosuppression, observed/expected life spans for SPK and other DM transplant patients, transplanted after 1985 (Fig. 2A), were also evaluated. The median observed/expected life span for SPK patients was significantly greater than age-range–matched diabetic transplant recipients ($P = 0.0021$). This advantage remained even when analyzing SPK patients who had been on dialysis prior to transplantation (Fig. 2B).

To avoid the potential bias introduced by the increasing number of SPK transplants that occurred at our institution since the introduction of mycophenolate mofetil, a separate analysis also was performed, analyzing SPK ($N = 215$) versus DM-Live ($N = 111$) patient survival and observed/expected life span for these patient groups who received their transplants between 1985 and 1993. SPK patients manifested a significantly greater survival ($P = 0.03$; Fig. 3). Furthermore, a greater percentage of SPK recipients were estimated to reach their median observed/expected life span (78%) than DM-Live patients (68%, $P = 0.001$).

Since SPK median observed/expected life span approximated that of the 1° renal cohort, we were interested in determining variables that might have salutary effects on SPK recipient survival in comparison to the DM-Cad and DM-Live patients. A number of characteristics were examined that might distinguish SPK recipients from DM-Cad and DM-Live patients in terms of patient survival (Table 2). Race, duration of diabetes, pretransplant creatinine, BMI, HLA matching, donor age, weight, race, and CMV status had no significant impact on the overall DM transplant patient mortality. Indeed, the only variable associated with an increased overall mortality risk was a higher discharge S_{Cr} value following the incident transplant hospitalization (RR 1.16 for each 0.1 mg/dL, $P \leq 0.0154$). When SPK patients were compared with DM-Cad patients, a number of variables lowered the relative mortality risk for SPK patients, including a shorter duration of diabetes ($P = 0.001$), no pretransplant dialysis ($P = 0.001$), use of mycophenolate mofetil ($P = 0.001$), and younger donor age ($P = 0.001$). However, these characteristics did not reduce mortality risk when comparing SPK with DM-Live transplant recipients ($P =$ NS for each).

Given the apparent importance of renal function at discharge following the transplant hospitalization, fac-

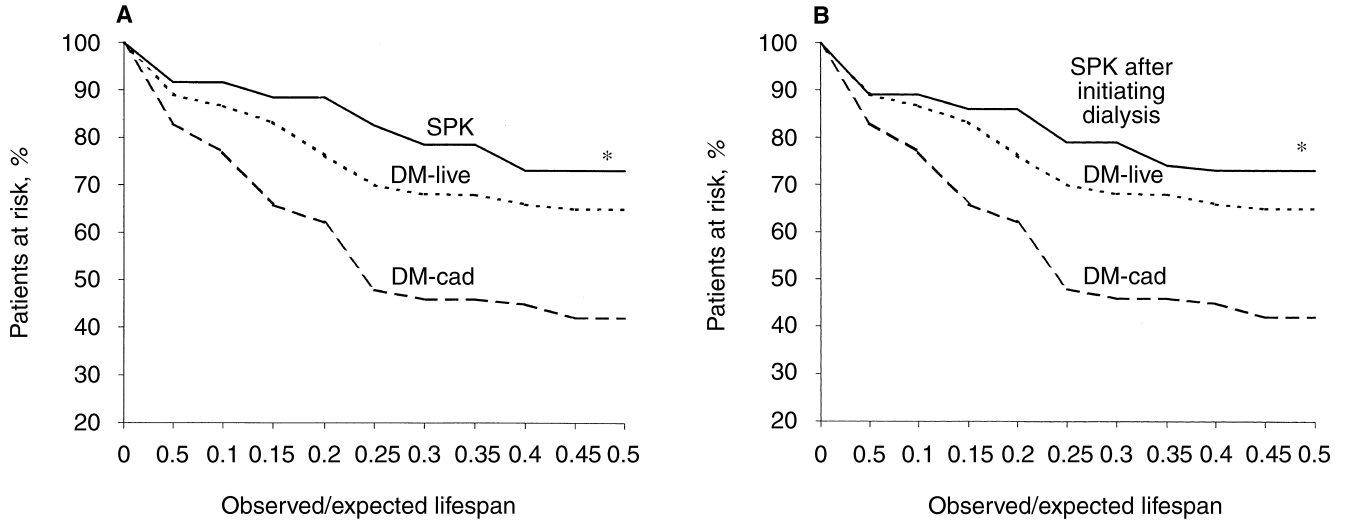

Fig. 2. (*A*) Observed/expected life span for SPK ($N = 335$), diabetic cadaveric (DM-Cad, $N = 102$), live-donor (DM-Live, $N = 126$), *$P = 0.0021$ SPK vs. DM-Cad and DM-Live. (*B*) Observed/expected life span for SPK patients who were on dialysis at the time of transplant ($N = 206$) compared with diabetic cadaveric (DM-Cad) ($N = 102$) and live-donor (DM-Live, $N = 126$) renal transplant recipients. *$P = 0.01$ SPK vs. DM-Cad and DM-Live.

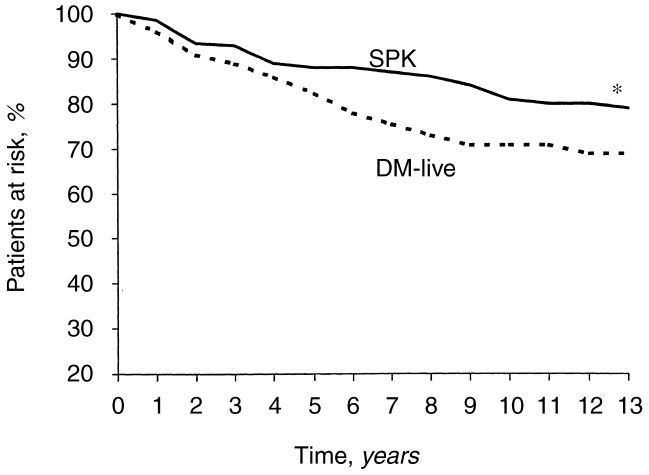

Fig. 3. Kaplan–Meier estimates of SPK ($N = 215$) vs. live-donor (DM-Live, $N = 111$) transplant recipient patient survival in patients transplanted between 1985 and 1993 (pre-mycophenolate mofetil, *$P = 0.03$).

tors affecting renal graft survival were also evaluated. Renal graft survival in the SPK population was equivalent to that observed in DM-Live patients (Fig. 4). In both cases, renal graft survival was significantly greater compared with DM-Cad patients ($P = 0.002$). A higher discharge S_{Cr} also was associated with a reduction in renal allograft survival in each cohort (RR 1.18 for each 0.1 mg/dL increase, $P = 0.0001$). The only other characteristic that was significantly associated with a preferential effect on SPK renal graft outcome was older donor age (RR 1.027 for each year, $P = 0.015$). Interestingly, a longer duration of diabetes conferred an increased risk for earlier renal graft loss in SPK recipients (RR 1.061 for each year of diabetes, $P = 0.01$).

We also examined rates of hypertension, poor glycemic control, and rejection episodes, as each could influence renal graft survival. Glycosylated hemoglobin values > 6.5 mg/dL in SPK patients were associated with an increased rate of renal graft failure ($P = 0.0002$), as was a mean systolic blood pressure greater than 140 mm Hg ($P = 0.0083$). Interestingly, SPK recipients also had significantly higher rates of renal allograft rejection ($P = 0.0003$) compared with DM-Cad and DM-Live patients (Table 3).

Finally, any history of diabetes and renal failure can predispose to multiple vascular and infectious complications. Kalker et al demonstrated that pancreas transplantation did not significantly affect amputation rates in diabetic transplant recipients in a retrospective study that encompassed a large percentage of patients evaluated in this analysis [9]. Therefore, we chose to focus on other possible outcome measures: rates of hospitalization, CMV infection, and cardiac death. SPK patients incurred significantly higher rates hospital readmission in the first year following transplantation ($P = 0.0003$) and a trend toward a greater number of CMV infections ($P = 0.07$; Table 3). Interestingly, there were no significant differences in cardiac death rates between patient groups when assessed in their entirety. However, age stratifying the patient cohorts unmasked significant differences in cardiac death rates in transplant patients between ages 30 and 39. SPK recipients ($N = 202$) had significantly fewer cardiac deaths than DM-Live ($N = 59$, $P = 0.005$ vs. SPK) and DM-Cad ($N = 57$, $P = 0.004$ vs. SPK) patients in this age category.

Table 2. Impact of variables on young diabetic kidney transplant recipient survival

Characteristic	Patient survival (all)	SPK vs. DM-Cad	SPK vs. DM-Live
Race	NS	$P = 0.0001$, RR = 0.44	
Duration of diabetes prior to transplant	NS	$P = 0.0001$, RR = 0.45	NS
Pre-Tx S_{Cr}	NS	$P = 0.0001$, RR = 0.41	NS
Discharge S_{Cr}	$P \leq 0.0154$; RR 1.16	$P = 0.0001$, RR = 0.41	NS, $P = 0.052$, RR = 0.632
Pre-Tx dialysis	NS	$P = 0.0001$, RR = 0.47	NS
BMI	NS	NS	NS
HLA-A match	NS	$P = 0.0001$, RR = 0.44	NS
HLA-B match	NS	$P = 0.0001$, RR = 0.44	NS; $P = 0.07$, RR = 0.6
HLA-DR match	NS	$P = 0.0001$, RR = 0.42	NS; $P = 0.057$, RR = 0.61
MMF use	NS	$P = 0.0001$, RR = 0.45	NS
Donor age	NS	$P = 0.0001$, RR = 0.44	NS
Donor weight	NS	$P = 0.0001$, RR = 0.33	NS
Donor race	NS	$P = 0.0001$, RR = 0.44	NS
Donor CMV status	NS	$P = 0.0004$; RR = 0.41	NS

Abbreviations are: RR, relative risk; Tx, transplant; S_{Cr}, serum creatinine; BMI, body mass index; MMF, mycophenolate mofetil; CMV, cytomegalovirus. The number of patients was: $N = 335$ for SPK, $N = 160$ for DM-Live, $N = 147$ for DM-Cad. The RR for pre-Tx S_{Cr} was handled as a continuous variable and the RR for discharge S_{Cr} was calculated for every 0.1 mg/dL > 1.0 mg/dL.

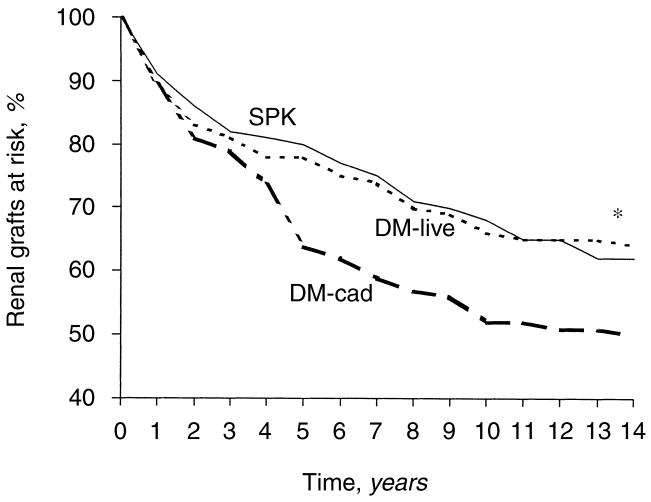

Fig. 4. Kaplan-Meier estimates of SPK ($N = 335$), diabetic cadaveric (DM-Cad, $N = 147$), and live-donor (DM-Live, $N = 160$) renal graft survival. *$P = 0.002$ SPK vs. DM-Cad and DM-Live vs. DM-Cad; $P =$ NS SPK vs. DM-Live.

DISCUSSION

Restoring life span and quality of life are two of the most important goals of medical therapy. For patients with a chronic illness, years gained as the result of an intervention can be assessed in many ways [10]. We chose to analyze that incremental increase in life span by comparing it to an individual's "normal" life span in that population [7]. In so doing, this single-center retrospective study highlighted the differences in life expectancy achieved by SPK transplantation in comparison to kidney transplantation alone in type 1 diabetic patients with ESRD.

Simultaneous pancreas-kidney recipient survival was greater than that of DM-Cad and DM-Live patients, similar to the report of Douzdjian et al [11]. More importantly, SPK patients achieved observed/expected life spans that were not significantly different from 1° renal patients. Why did SPK patients fare so well? Pre-emptive transplantation is one possibility. Residual renal function may significantly potentiate survival following transplantation [8, 12]. Indeed, more than 35% of the SPK recipients in this study were not yet on dialysis, compared with less than 25% of the DM-Cad and DM-Live recipients.

The fact that SPK patients experienced complications at rates greater than DM-Cad and DM-Live patients is not surprising. Other studies have demonstrated similar findings [13, 14]. However, it is possible that the care associated with such complications enhanced an encounter bias whereby SPK patients were followed up more often and had earlier and more frequent medical interventions compared with DM-Cad and DM-Live patients.

Interestingly, SPK recipients had rates of cardiac death that were equivalent to or better than DM-Cad or DM-Live recipients. Low cardiac risk patients are accepted for SPK transplantation at our center [8]. This may account for some of the disparity between our results and those reported by Manske, Wang, and Thomas [6], who noted that a history of congestive heart failure significantly increased mortality risk for SPK patients. However, Gaber et al have suggested that SPK transplantation may actually improve short-term cardiovascular risk [15]. Their echocardiographic study demonstrated improvements in left ventricular hypertrophy in SPK patients compared with other diabetic transplant recipients.

One mechanism for the improvements in cardiovascular risk associated with SPK transplantation could be the restoration of normoglycemia. Several large epidemiologic studies have demonstrated that hyperglycemia is a risk factor for progression of atherosclerosis and coronary heart disease [16–20]. It is possible that restoration of normoglycemia affects the myocardial vascular bed differently, especially with the aforementioned salutary

Table 3. Patients free of complication at one year

Complication	DM-Cad	DM-Live	SPK	*P* value
Renal graft rejection	57.2%	57.1%	34.6%	$P = 0.0003$ SPK vs. DM-Cad, DM-Live
CMV infection	93%	92%	86%	$P = 0.07$ SPK vs. DM-Cad, DM-Live
Readmission	49%	51%	22%	$P = 0.0003$ SPK vs. DM-Cad, DM-Live

effects in reducing left ventricular mass, such that SPK recipients have improvements in long-term cardiac survival. Long-term analyses in the diabetic transplant population are necessary to answer this question definitively.

Restoring normoglycemia may have even more profound effects on SPK patient survival aside from these theoretical benefits. The Diabetes Complications and Control Trial demonstrated that intensive insulin therapy slowed the progression of retinopathy and neuropathy and reduced the occurrence of microalbuminuria in type 1 diabetic patients [21]. SPK, by restoring normoglycemia, appears to have the same effects [22] to prevent or stabilize diabetic complications including retinopathy [2], neuropathy [3], and the development of recurrent diabetic nephropathy in simultaneously transplanted kidneys [23]. Tyden et al recently suggested that restoring normoglycemia with SPK transplantation, even after a long history of diabetes, may be the most significant factor positively affecting survival in SPK recipients [22]. In our population, long-term pancreas graft function nearly mirrors survival [24] and supports the premise that restoration of normoglycemia has marked effects on patient survival, even as a late intervention in a diabetic patient's lifetime.

Certain caveats should be considered when interpreting this study. This is a single-center, retrospective study with all of the inherent limitations of such analyses. Many patients included in this analysis were referred to our center for transplantation, having received their pre-ESRD care and, in some cases, dialytic care elsewhere, complicating assessment of their pretransplant characteristics. Finally, while our center's standard criteria for patient selection have been published [24], this analysis cannot account for selection bias, especially the potential for cardiac-related preselection bias in choosing lower risk patients for the SPK transplant procedure [24]. The most stringent comparison population for SPK recipients may be age-matched DM-Live patients. However, patients in the post-1993 era of transplantation would represent this bias, as SPK has been increasingly offered to all eligible patients at our institution such that is the predominant transplant for type 1 diabetic patients. Recognizing that treatment modalities, in addition to selection criteria, have changed significantly during the time period covered by this study, we chose to focus on DM-Live and SPK recipients between 1985 and 1993. These time points were chosen as cyclosporine A became standard immunosuppressive therapy at our center after 1985, and there were no other marked changes in immunosuppression until 1993, with the use of mycophenolate mofetil. Limiting the analysis to age-range–matched individuals further reduced the likelihood for mismatched demographics influencing the results, especially in that era when the "experimental" nature of SPK transplantation steered many individuals to choose DM-Live rather than SPK transplantation. However, SPK recipients from that era still demonstrated significant improvements in absolute survival and median observed/expected life span compared with DM-Live patients.

In summary, this study highlights important considerations in evaluating life span for type 1 diabetic patients with ESRD. Renal transplant outcomes traditionally have been measured in short-term patient and graft survival. Improvements in immunosuppression and post-transplant care, however, have challenged the adequacy of these measures. We are now beginning to focus on long-term survival. SPK transplantation appears to confer better long-term survival for type 1 diabetic patients with ESRD than any previously defined therapy [22, 25]. By applying a different measure of survival (observed/expected life span), we clearly demonstrated the beneficial effect of SPK transplantation on survival in our population, the largest reported to date. SPK transplantation increased the ratio of observed/expected life span achieved by SPK recipients such that their survival was nearly indistinguishable from that of age-range–matched transplant recipients with nondiabetic renal disease.

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REFERENCES

1. U.S. Scientific Registry for Transplant Recipients and the Organ Procurement and Transplantation Network: 1997 An-

nual Report—Transplant Data: 1988–1996, UNOS. Division of Transplantation, Office of Special Programs, Health Resources and Services Administration, U.S. Department of Health and Human Services, Rockville, MD, 1997
2. Cheung ATW, Chen PCY, Leschinsky TV, Wiltse SL, Basadonna GP, Katznelson S, Perez RV: Improvement in conjunctival microangiopathy after simultaneous kidney-pancreas transplants. *Transplant Proc* 29:660–661, 1997
3. Nankivell BJ, Al-Harbi IS, Morris J, Clouston PD, O'Connell PJ, Chapman JR, Allen RDM: Recovery of diabetic neuropathy after pancreas transplantation. *Transplant Proc* 29:658–659, 1997
4. Rosen CB, Frohnert PP, Velosa JA, Engen DE, Sterioff S: Morbidity of pancreas transplantation during cadaveric renal transplantation. *Transplantation* 51:123–127, 1991
5. Corry RJ, Ngheim DD, Schulak JA, Beutel WD, Gonwa TA: Surgical treatment of diabetic nephropathy with simultaneous pancreatic duodenal and renal transplantation. *Surg Gynecol Obstet* 162:547–555, 1986
6. Manske CL, Wang Y, Thomas W: Mortality of cadaveric kidney transplantation versus combined kidney-pancreas transplantation in diabetic patients. *Lancet* 346:1658–1662, 1995
7. Becker BN, Becker YT, Pintar TJ, Collins BH, Pirsch JD, Friedman A, Sollinger HW, Brazy PC: Using renal transplantation to evaluate a simple approach for predicting the impact of end-stage renal disease therapies on patient survival: Observed/expected life span. *Am J Kidney Dis* (in press)
8. Lin H-M, Kauffman M, McBride MA, Davies DB, Rosendale JD, Smith CM, Edwards EB, Daily OP, Kirklin J, Shield CF, Hunsicker LG: Center-specific graft and patient survival rates 1997 United Network for Organ Sharing (UNOS) Report. *JAMA* 280:1153–1160, 1998
9. Kalker AJ, Pirsch JD, Heisey D, Sollinger HW, Belzer FO, Knechtle SJ, D'Alessandro AM: Foot problems in the diabetic transplant recipient. *Clin Transplant* 10:503–510, 1996
10. Wright JC, Weinstein MC: Gains in life expectancy from medical interventions: Standardizing data on outcomes. *N Engl J Med* 339:380–386, 1999
11. Douzdjian V, Rice JC, Gugliuzza KK, Fish JC, Carson RW: Renal allograft and patient outcome after transplantation: Pancreas-kidney versus kidney-alone transplants in type 1 diabetic patients versus kidney-alone transplants in nondiabetic patients. *Am J Kidney Dis* 27:106–116, 1996
12. Schnuelle P, Lorenz D, Trede M, Van Der Woude FJ: Impact of renal cadaveric transplantation on survival in end-stage renal failure: Evidence for reduced mortality risk compared with hemodialysis during long-term follow-up. *J Am Soc Nephrol* 9:2135–2141, 1998
13. Lee CM, Scandling JD, Krieger NR, Dafoe DC, Alfrey EJ: Outcomes in diabetic patients after simultaneous pancreas-kidney versus kidney alone transplantation. *Transplantation* 64:1288–1294, 1997
14. Anonymous: Simultaneous kidney-pancreas transplantation versus kidney transplantation alone: patient survival, kidney graft survival, and post-transplant hospitalization. *Am J Kidney Dis* 20:61–67, 1992
15. Gaber AO, El-Gebely S, Sugathan P, Elmer DS, Hathaway DK, McCully RB, Shokouh-Amiri MH, Burlew BS: Early improvement in cardiac function occurs for pancreas-kidney but not diabetic kidney-alone transplant recipients. *Transplantation* 59: 1105–1112, 1995
16. Balkau B, Shipley M, Jarrett RJ, Pyorola K, Pyorola M, Forhan A, Eschwege E: High blood glucose concentration is a risk factor for mortality in non-diabetic men: 20-Year follow-up in the Whitehall Study, Paris Prospective Study, and the Helsinki Policemen Study. *Diabetes Care* 21:360–367, 1998
17. Donahue RP, Abbott RD, Reed DM, Yano K: Postchallenge glucose concentration and coronary heart disease in men of Japanese ancestry: Honolulu Heart Program. *Diabetes* 36:689–692, 1987
18. Haffner SM: Epidemiological studies on the effects of hyperglycemia and improvement of glycemic control on macrovascular events in type 2 diabetes. *Diabetes Care* 22(Suppl 3):C54–C56, 1999
19. Cooper R, Liu K, Stamler J, Schoenberger JA, Shekelle RB, Collette P, Shekelle S: Prevalence of diabetes/hyperglycemia and associated cardiovascular risk factors in blacks and whites: Chicago Heart Association Detection Project in Industry. *Am Heart J* 108:827–833, 1984
20. Ostrander LD Jr, Lamphiear DE, Carman WJ, Williams GW: Blood glucose and risk of coronary heart disease. *Arteriosclerosis* 1:33–37, 1981
21. Diabetes Control and Complications Trial (DCCT) Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 329:976–986, 1993
22. Tyden G, Bolinder J, Solders G, Brattstrom C, Tibell A, Groth C-G: Improved survival in patients with insulin-dependent diabetes mellitus and end-stage diabetic nephropathy 10 years after combined pancreas and kidney transplantation. *Transplantation* 67: 645–648, 1999
23. Bohman SO, Tyden G, Wilczek H, Lundgren G, Jaremko G, Gunnarsson R, Ostman J, Groth CG: Prevention of kidney graft diabetic nephropathy by pancreas transplantation in man. *Diabetes* 34:306–308, 1985
24. Sollinger HW, Odorico JS, Knechtle SJ, D'Alessandro AM, Kalayoglu M, Pirsch JD: Experience with 500 simultaneous pancreas-kidney transplants. *Ann Surg* 228:284–296, 1998
25. Smets YFC, Westendorp RGJ, Van Der Pijl JW, De Charro FT, Ringers J, De Fijter JW, Lemkes HHPJ: Effect of simultaneous pancreas-kidney transplantation on mortality of patients with type-1 diabetes mellitus and end-stage renal failure. *Lancet* 353: 1915–1919, 1999