Long-term Outcomes for Living Pancreas Donors in the Modern Era

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Background. Living donor segmental pancreas transplants (LDSPTx) have been performed selectively to offer a preemptive transplant option for simultaneous pancreas-kidney recipients and to perform a single operation decreasing the cost of pancreas after kidney transplant. For solitary pancreas transplants, this option historically provided a better immunologic match. Although short-term donor outcomes have been documented, there are no long-term studies. **Methods.** We studied postdonation outcomes in 46 segmental pancreas living donors. Surgical complications, risk factors (RF) for development of diabetes mellitus (DM) and quality of life were studied. A risk stratification model (RSM) for DM was created using predonation and postdonation RFs. Recipient outcomes were analyzed. **Results.** Between January 1, 1994 and May 1, 2013, 46 LDSPTx were performed. Intraoperatively, 5 (11%) donors received transfusion. Overall, 9 (20%) donors underwent splenectomy. Postoperative complications included: 6 (13%) peripancreatic fluid collections and 2 (4%) pancreatitis episodes. Postdonation, DM requiring oral hypoglycemics was diagnosed in 7 (15%) donors and insulin-dependent DM in 5 (11%) donors. RSM with three predonation RFs (oral glucose tolerance test, basal insulin, fasting plasma glucose) and 1 postdonation RF, greater than 15% increase in body mass index from preoperative (Δ body mass index >15), predicted 12 (100%) donors that developed postdonation DM. Quality of life was not significantly affected by donation. Mean graft survival was 9.5 (±4.4) years from donors without and 9.6 (±5.4) years from donors with postdonation DM. **Conclusions.** LDSPTx can be performed with good recipient outcomes. The donation is associated with donor morbidity including impaired glucose control. Donor morbidity can be minimized by using RSM and predonation counseling on life style modifications postdonation.

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The first clinical pancreas transplant from deceased donor (DD) was performed at the University of Minnesota on December 16, 1966.[1] Almost 13 years later, on June 20, 1979, the world's first LDSPTx was performed at the same institution.[2] Rational for living donor (LD) pancreas transplant was: to decrease the risk of rejection given the historically high rate of early rejection and immunologic loss of DD allografts; to offer a preemptive transplant option for simultaneous pancreas-kidney (SPK) recipients thus avoiding morbidity and mortality of dialysis; and to avoid a second operation pancreas after kidney (PAK), by offering SPK transplant.

Short-term and long-term outcomes of LDSPTx recipients have been well documented, and for 3 decades, have been comparable or better to the outcomes of DD transplants.[3-7] However, over the last decade with the improvement of brain-dead donor management, organ preservation, surgical technique, and especially immunosuppression, DD pancreas transplant outcomes have significantly improved.[8]

The short-term and intermediate-term outcomes for the living pancreas donors have been reported; however, there are limited data on long-term outcomes.[5,9] In this article, we present modern era perioperative, long-term metabolic, and quality of life outcomes in living pancreas donors. Our goal was to create, based on the available data, risk stratification model (RSM) that can be used for future evaluation of potential donors and donor risk reduction postoperatively.

METHODS

During modern era (January 1, 1994 to May 1, 2013), a total of 46 living-donor segmental pancreas transplants

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including 40 SPK, 2 PAK, and 4 PA were performed at the University of Minnesota. For all 40 LD SPK transplants, live donor segmental pancreas and kidney were procured simultaneously from the same donor. Of 46 LD, 12 cases were performed using laparoscopic hand-assisted technique, and 34 were open.

All donor and recipient information was kept in an institutional review board–approved database. For all donors, we entered basic demographics, preoperative and postoperative basic laboratory as well as metabolic testing. National social security database was used for ascertainment of mortality status. For all recipients, basic demographics, date, and causes of graft loss (GL) were documented.

Perioperative outcomes, risk factors (RFs) for development of postdonation diabetes mellitus (DM) and quality of life (QOL) were studied among the donors. Z test and χ^2 test were used for statistical analysis of RFs. Risk stratification model for development of postdonation DM was created using preoperative donor factors and postoperative modifiable donor factor. Quality of life survey was administered over the phone by trained research associate at the last follow-up in April 2015. Donors who had no follow-up for 4 years and recipients who had no follow-up for 2 years, without documentation of death, were considered to be "lost to follow-up."

Living donor segmental pancreas transplants recipient outcomes were studied and compared with the DD pancreas outcomes of our center. Graft survival (GS) rates were calculated using Kaplan-Meier analysis. Graft loss was defined as return to exogenous insulin use after insulin independence, graft explant, recipient reregistered for transplant or recipient's demise.

Donors

All potential donors were evaluated by multidisciplinary team including endocrinologists, nephrologists, cardiologists, social workers, psychiatrists, and transplant surgeons. The donation criteria and postdonation follow-up testing at our institution have evolved over time; Table 1 shows most current donation criteria that were used in the modern era. Specific metabolic testing oral glucose tolerance test (OGTT), intravenous glucose tolerance test, acute insulin response to arginine (AIRa)/acute insulin response to glucose (AIRg) have been described previously in detail.[9-11]

All pancreas donors received pneumococcal, *Haemophilus influenzae* type B and meningococcal vaccines before surgery to decrease the risk of gram positive sepsis in cases when splenectomy was performed. Surgical predonation evaluation included aortogram, computed tomography angiogram or magnetic resonance angiogram, which was the modality of choice in the later years, due to being noninvasive and providing details of the parenchyma and venous anatomy.[9,12,13] Open and laparoscopic procurement operations have been previously described by the University of Minnesota as well as other groups.[5,9,13-17] Postoperative management was standard for patients undergoing a major abdominal operation; it varied based on open versus laparoscopic technique. Routine monitoring included vital signs, urine output, serial hemoglobins, amylase, and plasma glucose levels. If suspected postoperatively, splenic radionucleotide scan and abdominal computer tomography scan have been used to evaluate splenic viability and peripancreatic fluid collections. Additional annual postdonation follow-up studies included OGTT and glycosylated hemoglobin A1C (HgbA1C); however, not all donors have been routinely screened.

TABLE 1.

Criteria for living segmental pancreas donation

Exclusion criteria
Subjects were excluded from consideration if any of the following criteria apply: (1) DM II in any first degree relative or gestational diabetes in donor (2) First degree relative with DM I (other than recipient) (3) BMI>27 kg/m^2 if >45 years old or BMI>30 kg/m^2 if ≤45 years old (4) >59 years old (5) Age of donor <10 years greater than age of diagnosis of DM I in recipient
Additional criteria
Beginning December 1, 1996, subjects were excluded from donation if any of the following were detected: (1) Impaired glucose tolerance or diabetes by National Diabetes Data Group Criteria (2) HgbA1C >6% (3) Glucose disposal rate<1% during IVGTT (4) Elevated titer of islet cell autoantibodies (CIA)
Relative exclusion criteria
The following characteristics were evaluated by endocrine staff and considered for possible exclusion: (1) Glucose value >150 mg/dL during 75 g OGTT (2) Basal, fasting insulin >20 μU/mL (marker of insulin resistance) (3) Acute insulin response to glucose or arginine <300% basal insulin (4) Clinical evidence of insulin resistance (eg, polycystic ovarian syndrome) (5) Evidence for >1 autoimmune endocrine disorder (thyroid, adrenal, pituitary, gonads)

IVGTT, intravenous glucose tolerance test.

Recipients

Recipient management including the surgical procedure, immunosuppression, and postoperative care has been previously described in detail.[9] In brief, recipient surgery involved a midline abdominal incision. Preferentially, pancreas graft was implanted on the right with donor splenic artery anastomosed to the common iliac, external iliac, or hypogastric artery. Branches of the internal iliac vein were ligated, and the venous anastomosis was performed between donor splenic vein and recipient common/external iliac vein, optimizing the lay and minimizing the tension on the graft. Exocrine secretions were primarily managed by bladder drainage with an exception of 6 organs where duct was injected with 2.5 mL of silicone and 2 organs that were enterically drained. In case of SPK, kidney graft was placed on the left with anastomosis to the external iliac artery and vein and ureteral implantation using a modified Lich technique. For induction therapy, antithymocyte globulin (10 mg/kg intravenous) for 5 to 10 days was used for all recipients; calcineurin based therapy with prednisone taper plus azathioprine or mycophenolate mofetil were used for maintenance therapy.[18] Due to higher thrombosis rate of segmental pancreas grafts, the anticoagulation management evolved over time eventually consisting of postoperative heparin drip with transition to warfarin for 6 months followed by antiplatelet agent.

RESULTS

Donor and Recipient Characteristics and Predonation Profile

Of 46 LDs, 40 (87%) were alive at the time of the last follow-up; 6 (13%) were lost to follow-up (>4 years). There were no known deaths reported according to national social security database. Of 40 donors, 36 (90%) responded to the quality of life phone survey that was conducted in April 2015. The median donor follow-up was 12 years (range, 2-21 years).

Donor demographics are shown in Table 2. The majority of LDs donated simultaneously segmental pancreas and kidney 40 (88%); there were 2 (4%) PAK and 4 (8%) pancreas alone donors. Eighty percent of donor/recipient pairs were related, 59% were women, 87% were white. Mean age at donation was 42 (±10) years with median 45 years and range of 20 to 58 years.

Of 46 recipients, 7 (15%) were lost to follow-up (>2 years). Mean recipient age at transplant was 37 (±9) years, with median 35 years and range of 14 to 58 years. Recipient group consisted of 63% women, 96% white.

Table 3 represents donor predonation profile. Mean body mass index (BMI) was 25 (±3.7) kg/m^2 but ranged from 18.2 to 35.3 kg/m^2. Body mass index exceptions were made for 4 donors where other predonation parameters were within the established donation criteria. Additional predonation screening parameters that would be indicative of metabolic syndrome were as follows: mean systolic blood pressure 119 (±13) mm Hg, cholesterol 197 (±35) mg/dL, HgbA1C 5.3 (±0.3)%, OGTT 2 h 98 (±17) mg/dL. Mean creatinine at donation was 0.9 (±0.2) mg/dL. Mean fasting plasma glucose (FPG) at the time of donation was 89 (±9) mg/dL with range from 75 to 118 mg/dL. Although at the time, FPG of 100 mg/dL or greater could still be considered normal; due to the changes in American Diabetes Association guidelines, FPG greater than 99 mg/dL is currently considered abnormal. The results of basal insulin testing that would indicate the potential for insulin resistance were as follows mean 7.4 (±4.9) μU/mL with a range of 2 to 20 μU/mL. One recipient had borderline basal insulin value with corresponding low AIRa 2.2 (fold increase from basal insulin) but was within the established criteria otherwise. Three measures of AIR were used, with mean values of 8 (±5) for AIRa, 9.4 (±4) for AIRg, and 7.6 (±4.6) for AIR900. Two donors had AIRa less than 3-fold increase from the basal insulin, which was one of the relative exclusion criteria; however, with further evaluation by the multidisciplinary team, donors were found to be within the absolute donation criteria and were approved.

TABLE 2.

Donor demographics (n = 46)

Type of transplant		Ethnicity	
SPK	88%	Caucasian	87%
PAK	4%	African-American	4%
PTA	8%	Other	9%
Donor source		**Age**	
LR	80%	Mean (years)	42 ± 10
LUR	20%	Median/Range (years)	45 (20-58)
Sex		**Surgical approach**	
Female	59%	Open	34
Male	41%	Laparoscopic	12

PTA, pancreas alone

TABLE 3.

Predonation donor profile

	Mean	Range
BMI	25 ± 3.7 kg/m^2	(18.2-35.3[a] kg/m^2)
SBP	119 ± 13 mm Hg	(92-144 mm Hg)
Cholesterol	197 ± 35 mg/dL	(129-271 mg/dL)
Cr	0.9 ± 0.2 mg/dL	(0.6-1.3 mg/dL)
Hgb A1C	5.3 ± 0.3%	(4.5-5.9%)
FPG	89 ± 9 mg/dL	(75-118[a] mg/dL)
OGTT 2 h	98 ±17 mg/dL	(67-132 mg/dL)
Basal insulin	7.4 ± 4.9 μU/mL	(2-20[a] μU/mL)
AIR	(Fold increase from basal insulin)	
AIRa	8 ± 5	(1.7[a]-22.3)
AIRg	9.4 ± 4	(3.3-14.4)
AIR900	7.6 ± 4.6	(3.6-19.7)

[a] Values that were given exception and were outside of the standard donation criteria at the time of the donation or the values that would be considered outside of the criteria at present due to changes in guidelines of ADA.
SBP, systolic blood pressure

Perioperative Outcomes

Intraoperatively, 5 (11%) donors required blood transfusion. Cumulative incidence of splenectomy was 20%; 5 (11%) donors underwent splenectomy at the time of donation and 4 (9%) required splenectomy during the reexploration for splenic infarct. Postoperatively, 6 (13%) donors developed symptomatic pseudocyst/peripancreatic fluid collections, all of which were managed by the interventional radiology; 2 (4%) donors were diagnosed with pancreatitis. Other complications included 3 (7%) incisional hernia, 5 (11%) nausea/vomiting, and 1 (2%) wound infection (Table 4). There was no statistical significance in perioperative complications based on open versus laparoscopic approach.

TABLE 4.

Perioperative donor outcomes

Intraoperative	% (n)
Transfusion (1-5 units)	9% (4)
Transfusion (6-10 units)	2% (1)
Splenectomy	11% (5)
Postoperative	
Pseudocyst/peripancreatic fluid collection	13% (6)
Pancreatitis	4% (2)
Splenic infarct (requiring splenectomy)	9% (4)
Nausea/vomiting	11% (5)
Wound infection	2% (1)
Incisional hernia	7% (3)

TABLE 5A.

Incidence of diabetes postdonation

	% of affected donors (n)	Mean time of onset from donation, y
Oral hypoglycemics-dependent	15% (7)	9.2 ± 3.3 (range, 5-15.8)
Insulin-dependent	11% (5)	7 ± 5.4 (range, 0.5-12.8)

Postoperative Diagnosis of Diabetes

Postdonation DM requiring oral hypoglycemic management was diagnosed in 7 (15%) donors with mean time of onset postdonation of 9.2 (±3.3) years (range, 5-14.8 years). Insulin-dependent DM was diagnosed in 5 (11%) donors with mean time of onset postdonation 7 (±5.4) years (range, 0.5-12.8 years) (Table 5A). All donors in this group had at least 1 HgbA1C of 6.5 or greater at diagnosis.

Predonation profile was compared between 3 postdonation groups: nondiabetic donors, donors requiring oral hypoglycemics, and insulin-dependent donors. The following parameters were reviewed: relation to the recipient, BMI, systolic blood pressure, cholesterol, renal function (creatinine and glomerular filtration rate), Hgb A1C, FPG, OGTT 2 h, basal insulin, AIRa. Predonation, OGTT 2 h, and FPG were found to be higher in insulin-dependent donors as compared to nondiabetic: 125 ± 6 mg/dL OGTT and 100 ± 16 mg/dL FPG versus 94 ± 15 OGTT mg/dL and 87 ± 7 FPG, respectively ($P \leq 0.05$). Basal insulin was higher in both groups requiring oral hypoglycemics and insulin as compared with nondiabetic group: 12 ± 7.6 μU/mL and 12 ± 7.1 μU/mL versus 5.6 ± 2.6 μU/mL ($P \leq 0.05$) (Table 5B). Predonation, there was a trend toward higher BMI in diabetic groups versus nondiabetic, but that did not achieve statistical significance; in contrast, during postdonation follow-up, both oral hypoglycemics and insulin dependent groups had significantly higher BMI as compared with the nondiabetic group: 30 ± 7 kg/m^2 and 29.1 ± 5.5 kg/m^2 versus 24.8 ± 3.1 kg/^{2}, respectively ($P \leq 0.05$) (Table 5C). There was a trend toward lower AIRa in diabetic groups as compared with nondiabetic but it was not significant. Remainder of the abovementioned predonation parameters was not found to be different between the groups.

Although baseline BMI did not significantly impact postdonation DM development, ΔBMI greater than 15% (= [postdonation BMI - predonation BMI]/predonation BMI × 100) over the observation period was a significant RF for development of postdonation DM.

Relative risk for postdonation DM associated with predonation FPG of 100 mg/dL or greater, basal insulin of 9 μU/mL or greater, OGTT 2 h of 120 mg/dL or greater, and postdonation ΔBMI greater than 15%, ranged between 4.6 and 6 with high specificity (0.82-1), but low sensitivity. Using these RFs, RSM was created to assist in predicting the risk for development of postdonation DM among potential donors as well as for predonation counseling on postdonation risk modification (Table 6). Risk stratification model showed that presence of 2 or greater RFs associated with 100% rate of becoming diabetic postdonation; the same time, none of the donors with "0" RFs became diabetic.

TABLE 5B.

Predonation risk factors for diabetes in donors

	OGTT 2 h, mg/dL	Basal insulin, μU/mL	Fasting glucose, mg/dL
Nondiabetic	94 ± 15	5.6 ± 2.6	87 ±7
Oral hypoglycemics	96 ± 4	12 ± 7.6[a]	92 ± 10
Insulin-dependent	125 ± 6[a]	12 ± 7.1[a]	100 ± 16[a]

[a] $P \leq 0.05$ comparing to nondiabetic donors.

TABLE 5C.

Predonation and postdonation donor BMI

	BMI, kg/m^2	
	Pre	Post
Nondiabetic	24.9 ± 3.2	24.8 ± 3.1
Oral hypoglycemics	26.4 ± 4.8	30 ± 7[a]
Insulin Dependent	27.3 ± 5.3	29.1 ± 5.5[a]

[a] P ≤0.05 comparing to non-diabetic donors.

Postdonation Quality of Life Survey

Of 40 donors who stayed in contact with the center, 36 (90%) responded to the quality of life survey. All previously diagnosed diabetic donors (n = 12) have responded. All former donors answered that they were happy with their choice to donate (Figure 1A). On the question "would they do it again?", 92% of non-DM donors and 67% of DM donors responded "definitely"; 1 DM donor responded "probably not" (Figure 1B). Comparing their quality of life before and after the donation, both 67% of non-DM and DM donors felt that it was the same; 13% of non-DM donors and 25% of DM donors thought that it was "somewhat worse" (Figure 1C). Although, there were

TABLE 6.

RSM for prediction of postdonation diabetes

Risk factors	Diabetics	Nondiabetics
FPG ≥100 mg/dL (n = 4)	100%[a]	0[a]
FPG <100 mg/dL (n = 36)	22%	78%
Basal insulin ≥9 μU/mL (n = 5)	80%[a]	20%[a]
Basal insulin <9 μU/mL (n = 19)	16%	84%
OGTT 2 h ≥120 mg/dL (n = 5)	100%[a]	0[a]
OGTT 2 h <120 mg/dL (n = 30)	17%	83%
ΔBMI >15% (n = 7)	86%[a]	14%[a]
ΔBMI ≤15% (n = 32)	19%	81%

Risk factors	RR	95% CI	*P*
FPG ≥100 mg/dL	5.6	(2.4-8.3)	<0.001
Basal insulin ≥9 μU/mL	5.1	(1.6-15.6)	0.005
OGTT 2 h ≥120 mg/dL	6	(2.6-13.4)	<0.001
Δ BMI >15%	4.6	(2.1-10.0)	<0.001

No. risk factors	Diabetics	Nondiabetics
0 (n = 21)	0	100%
1 (n = 8)	75%	25%
≥2 (n = 6)	100%	0

[a] $P \leq 0.05$ comparing within the diabetic and nondiabetic groups.
RR, relative risk; 95% CI, 95% confidence interval.

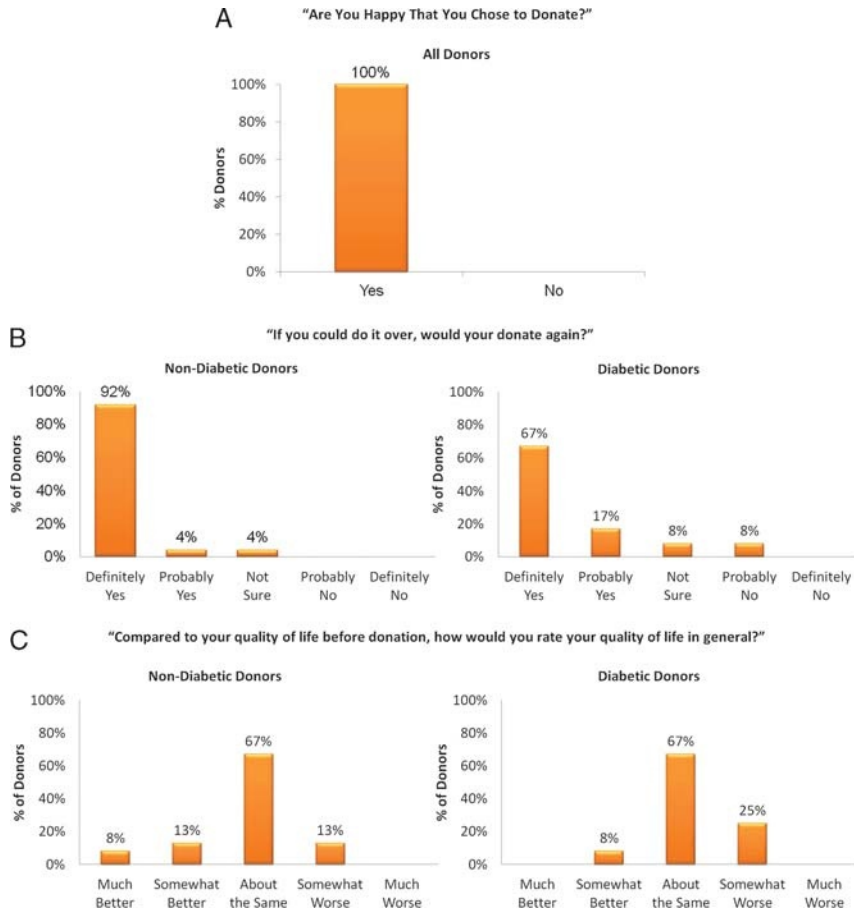

FIGURE 1. A, LD responses (n = 36) to the QOL survey question 'Are you happy that you chose to donate?'. *X*-axis indicates type of response, *Y*-axis indicates % of LDs. B, Responses from nondiabetic LDs (n = 24) and diabetic LDs (n = 12) to the QOL survey question 'If you could do it over, would you donate again?'. *X*-axis indicates type of response, *Y*-axis indicates % of LDs. C, Responses from nondiabetic LDs (n = 24) and diabetic LDs (n=12) to the QOL survey question 'Compared with your quality of life before donation, how would you rate your quality of life in general?' *X*-axis indicates type of response, *Y*-axis indicates % of LDs.

fewer negative responses from the non-DM as compared with the DM donors, statistically there was no difference. The donors with negative responses to the prior 2 question attributed their feelings to the following factors: the overall process of aging, untreated depression, postdonation DM, and pancreatitis management.

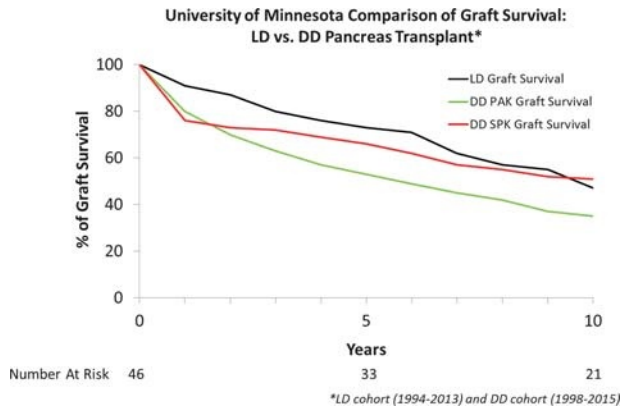

FIGURE 2. Comparison of pancreas graft survival for LDSPTx versus DD PAK and DD SPK at the University of Minnesota. X-axis indicates years posttransplant. Y-axis indicates % of graft survival. For LD pancreas grafts, number at risk is included at the bottom. LD cohort represents transplants performed between 1994 and 2013; DD cohort represents transplants performed between 1998 and 2015.

Recipient Outcomes

Mean GS for LDSPTx was 9.6 (±5) years. Comparing to the DD GS outcomes for our center, LDSPTx GS was at 91% versus 80% DD PAK and 76% DD SPK at 1 year, 73% versus 53% DD PAK and 66% DD SPK at 5 years, and 47% versus 35% DD PAK and 51% DD SPK at 10 years (Figure 2).

For grafts from non-DM donors, mean GS was 9.6 (±5.4) years (range, 0-18 years); from DM donors, mean GS was 9.5 (±4.4) years (range, 1-15 years). Graft failure rate was higher for DM donor grafts, 75% (9) versus 39% (11) for non-DM donors ($P \leq 0.05$) (Table 7A).

Chronic rejection was the most common cause of GL for recipients of organs from non-DM donors, 55% (6) versus 34% (3) from DM donors. Chronic GL of unknown etiology was the most common cause of GL for recipients from DM

TABLE 7A.

Pancreas graft loss in living donor recipients

	Non-DM donors	DM donors
Absolute number	11/28	9/12
Percent lost	39%	75%[a]

[a] $P \leq 0.05$ comparing to the nondiabetic donors.

donors, 44% (4) versus 18% (2) from non-DM. Due to the small numbers, these results were not significant. Other causes of GL included vascular thrombosis (n = 2), acute rejection (n = 1), pancreatitis (n = 1) and extrapancreatic malignancy (n = 1) (Table 7B).

DISCUSSION

The number of pancreas transplants in the United States has declined over the last decade despite improved outcomes over the same period.[8] Even with this change, the waiting time for pancreas has not decreased. Centers have become more selective in using pancreata. As part of the drop in pancreas Donor Risk Index, cold preservation time had decreased reflecting low tolerance for cold ischemia in pancreas transplantation. Living donor pancreas transplants offer the advantage of minimal cold ischemia in addition to avoidance of brain death, healthier donor pool, elective procedure, single cost-saving operation in case of SPK transplant, and better recipient outcomes.

In our center, the rate of LDSPTx has significantly decreased over the last few years (on intent) as we saw the need for assessing our donor outcomes and safety prior to actively continuing the LD pancreas program. The risk of living pancreas donation has been long discussed especially as it relates to metabolic outcomes, specifically postdonation hyperglycemic risk.

In our series, there was no donor mortality. Risk of major perioperative complications requiring reoperation was 10%. The new onset of DM requiring oral hypoglycemics management was diagnosed in 7 (15%) donors and insulin-dependent DM in 5 (11%). Thus, previously used selection criteria (Table 1) were associated with a significant risk of postdonation DM. Review of our data showed that 3 predonation RFs and 1 postdonation modifiable RF had significant correlation with development of postdonation DM. Based on this information, we are proposing the following modifications to the exclusion criteria: basal insulin of 9 μU/mL or greater and OGTT 2 h ≥120 mg/dL. In addition, we recommend expanding autoantibody screening to include GAD65, IA-2 and ZnT8. The modifiable RF (ΔBMI >15) should be used for predonation and postdonation counseling on lifestyle modifications and follow-up. This should be part of the informed consent discussion prior to donation. Our new modified Minnesota criteria for living segmental pancreas donation are presented in Table 8.

Postdonation QOL survey did not show statistical differences in donation perception of non-DM versus DM donors; however, anecdotally, several donors with DM, pancreatitis, and depression diagnoses felt that the donation impaired their QOL.

The recipient outcomes in our series remained excellent with improved 1- and 5-year GS for LDSPTx as compared with DD GS after SPK and PAK transplant at our center. Graft failure rate was higher for the recipients whose donors went on to become diabetic; therefore, it is unlikely that the larger proportion of the donated gland was the cause of the subsequent DM in the donor. Alternatively, other molecular and immunologic parameters of those grafts could potentially contribute to the subsequent development of DM in the donor and the disease recurrence in the recipient.

Taking into account the advantages of LDSPTx as discussed earlier, LD pancreas transplantation (especially SPK) should be offered in carefully selected donor-recipient pairs if metabolic risks for the donor are minimized by careful predonation screening and meticulous postdonation follow-up with interventions to prevent significant weight gain. Although, LDSPTx could be performed in any suitable clinical situation, it would be especially applicable in highly sensitized recipients with negative crossmatch, well-informed and motivated donor population, and geographical areas with long waiting time for DD pancreas. In the future, new noninvasive technologies for β cell mass assessment could be incorporated into the preoperative pancreas donor evaluation. Detailed informed consent should always be included as part of the predonation counseling.

This strategy could enable living donation to continue as a viable option in pancreas and possibly islet transplantation. Notably, first LD segmental pancreatectomy was performed in 1977 for islet isolation, and more recently, there was a published report of insulin independence following

TABLE 7B.

Causes of pancreas graft failure, by donor postdonation diabetes status

	Non-DM donors (n = 11)	DM donors (n = 9)
Chronic rejection	55% (6)	34% (3)
Chronic graft loss (unknown)	18% (2)	44% (4)
Thrombosis	18% (2)	0
Acute rejection	0	11% (1)
Pancreatitis	0	11% (1)
Malignancy	9% (1)	0

TABLE 8.

Modified Minnesota criteria 2016 for living segmental pancreas donation

Exclusion criteria
(1) DM II in any first degree relative or gestational diabetes in donor
(2) First degree relative with DM I (other than recipient)
(3) BMI > 30 kg/m^2
(4) >59 years old
(5) Age of donor <10 years greater than age of diagnosis of DM I in recipient
(6) Impaired glucose tolerance or diabetes by ADA guidelines
(7) Clinical evidence of insulin resistance (eg, Polycystic ovarian syndrome)
(8) Evidence for >1 autoimmune endocrine disorder (thyroid, adrenal, pituitary, gonads)
(9) HgbA1C >6%
(10) Glucose disposal rate <1% during IVGTT
(11) Elevated titer of autoantibodies (ICA, GAD65, IA-2 and ZnT8)
(12) Glucose value ≥120 mg/dl during 75 g. OGTT
(13) Basal, fasting insulin ≥9 μU/mL (marker of insulin resistance)
(14) Acute insulin response to glucose or arginine <300% basal insulin
Additional requirements
(1) Counseling to comply with postdonation diet and exercise program to prevent weight gain
(2) Detailed informed consent

LD distal pancreatectomy and islet allotransplantation.[19,20] However, the immediate future of living pancreas donation will be predominantly applicable to solid organ pancreas transplantation.

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REFERENCES

1. Kelly WD, Lillehei RC, Merkel FK, et al. Allotransplantation of the pancreas and duodenum along with the kidney in diabetic nephropathy. *Surgery*. 1967;61:827–837.
2. Sutherland DE, Goetz FC, Najarian JS. Living-related donor segmental pancreatectomy for transplantation. *Transplant Proc*. 1980;12(4 Suppl 2):19–25.
3. Gruessner RW, Leone JP, Sutherland DE. Combined kidney and pancreas transplants from living donors. *Transplant Proc*. 1998;30:282.
4. Gruessner RW, Sutherland DE, Drangstveit MB, et al. Pancreas transplants from living donors: short- and long-term outcome. *Transplant Proc*. 2001;33:819–820.
5. Humar A, Gruessner RW, Sutherland DE. Living related donor pancreas and pancreas-kidney transplantation. *Br Med Bull*. 1997;53:879–891.
6. Sutherland DE, Najarian JS, Gruessner R. Living versus cadaver donor pancreas transplants. *Transplant Proc*. 1998;30:2264–2266.
7. Sutherland DE, Radosevich D, Gruessner R, et al. Pushing the envelope: living donor pancreas transplantation. *Curr Opin Organ Transplant*. 2012;17:106–115.
8. Kandaswamy R, Skeans MA, Gustafson SK, et al. Pancreas. *Am J Transplant*. 2016;16(Suppl 2):47–68.
9. Gruessner RW, Kendall DM, Drangstveit MB, et al. Simultaneous pancreas-kidney transplantation from live donors. *Ann Surg*. 1997;226:471–480 discussion 480–472.
10. Seaquist ER, Robertson RP. Effects of hemipancreatectomy on pancreatic alpha and beta cell function in healthy human donors. *J Clin Invest*. 1992;89:1761–1766.
11. Kendall DM, Sutherland DE, Najarian JS, et al. Effects of hemipancreatectomy on insulin secretion and glucose tolerance in healthy humans. *N Engl J Med*. 1990;322:898–903.
12. Kandaswamy R, Stillman AE, Granger DK, et al. MRI is superior to angiography for evaluation of living-related simultaneous pancreas and kidney donors. *Transplant Proc*. 1999;31:604–605.
13. Tan M, Kandaswamy R, Sutherland DE, et al. Laparoscopic donor distal pancreatectomy for living donor pancreas and pancreas-kidney transplantation. *Am J Transplant*. 2005;5:1966–1970.
14. Oberholzer J, Tzvetanov I, Mele A, et al. Laparoscopic and robotic donor pancreatectomy for living donor pancreas and pancreas-kidney transplantation. *J Hepatobiliary Pancreat Sci*. 2010;17:97–100.
15. Park KT, Jun H, Kim MG, et al. Simultaneous pancreas-kidney transplantation from living donor using hand-assisted laparoscopic donor surgery: single-center experience. *Transplant Proc*. 2015;47:1096–1098.
16. Maruyama M, Kenmochi T, Akutsu N, et al. Laparoscopic-assisted distal pancreatectomy and nephrectomy from a live donor. *J Hepatobiliary Pancreat Sci*. 2010;17:193–196.
17. Han DJ, Sutherland DE. Pancreas transplantation. *Gut Liver*. 2010;4:450–465.
18. Sutherland DE, Gruessner RW, Dunn DL, et al. Lessons learned from more than 1,000 pancreas transplants at a single institution. *Ann Surg*. 2001;233:463–501.
19. Najarian JS, Sutherland DE, Matas AJ, et al. Human islet transplantation: a preliminary report. *Transplant Proc*. 1977;9:233–236.
20. Matsumoto S, Okitsu T, Iwanaga Y, et al. Insulin independence after living-donor distal pancreatectomy and islet allotransplantation. *Lancet*. 2005;365:1642–1644.