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Original Research

Shifting Pancreas Transplantation Rates and Demographics are the Culmination of Many Strategic Policy Changes

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Abstract

The 2014 Pancreas Allocation System established national qualifying criteria for simultaneous kidney pancreas (SPK) transplantation. The 2019 UNOS Pancreas Transplantation Committee Policy 11.3.B modified these guidelines to expand transplantation. Subsequent effects on recipient demographics have not been studied. We analyzed 81 SPK transplantations performed at our center from June 2014 to December 2020 to compare recipient

demographics and outcomes before and after the 11.3.B policy change. National data were also investigated. Significant increases in age (38.9 v 46.4 years; $p = 0.01$) and c-peptide levels (1.7 v 4.9 ng/ml; $p = 0.01$) occurred following the removal of BMI and c-peptide requirements. No differences in BMI, outcomes, or complication rates were found. National and center trends showed increasing numbers of recipients with high c-peptide levels and decreasing numbers of recipients with undetectable c-peptide levels. Policy 11.3.B expanded transplantation access while maintaining suitable outcomes, reflecting its intended goals.

Keywords
Pancreas; policy; demographics; access; c-peptide; allocation

1. Introduction

On October 30, 2014, the United Network for Organ Sharing (UNOS) created the Pancreas Allocation System (PAS)/Policy 11 that established the precedent for national allocation rules for SPK transplantation. The initiation of this policy sought to institute a standardized national system to govern pancreas allocation by increasing pancreas utilization and reducing geographic inequities related to deceased donor pancreas allocation, access to transplantation, and waitlist accrual time. Importantly, the PAS created appropriate qualifying criteria for candidates waiting for a SPK transplant based on the patient's perceived insulin resistance [1, 2].

Initially, this policy included guidelines that restricted pancreas transplantation to those patients that had either a c-peptide ≤2 ng/mL, or a c-peptide >2 ng/mL and maximal allowable body mass index (BMI) of 28 kg/m^2. Notably, six months after the establishment of the PAS, only 6% of active adult candidates with c-peptide >2 ng/mL qualified for an SPK. This led UNOS to respond by increasing the maximal allowable BMI to 30 kg/m^2 on July 15, 2015 [1]. Ultimately, these strategies were successful in expanding access to pancreas transplantation as highlighted by increased volumes. Recognition of this effective policy implementation led to further momentum to revamp the pancreas allocation policies. To the UNOS policy maker's credit, they have appeared to be forward thinking as opposed to strictly reactionary. As such, there has been a motivation to better understand the spectrum of disease in patients with diabetes and whom amongst this cohort may benefit from SPK transplantation.

Our experience provides an excellent opportunity to identify these patients and transplant patterns that have arisen over the years because of policy candidacy improvements. To this end, since the implementation of the PAS, we have noticed apparent demographic changes in the recipients. It seemed that after the initial inception of the PAS, pancreas transplantation recipients were more in line with our understanding of a classic type 1 diabetic patient. This is reasonable given the reliance on c-peptide as a surrogate marker to target patients with insulin deficiency. Patients with lower BMI were also favored as they phenotypically align with what is considered to be type 1 diabetic disease. As such, patients with severe insulinopenia were likely prioritized to benefit from pancreas transplantation.

Criticism arose because as a rule the medical community has heavily relied on c- peptide and BMI as substitutes to determine the degree of insulin resistance; however, it is unclear if the

interpretation of these metrics to guide pancreas transplantation are appropriate [3-5]. Many studies have demonstrated that the measurement of c-peptide in the setting of chronic kidney disease is inaccurately elevated [6-8]. Moreover, it is has been shown that in carefully selected patients with type 2 diabetes, including those with higher c-peptides and BMI, it is possible to achieve comparable SPK outcomes to classic type 1 diabetic recipients [9-17].

To date, the UNOS Pancreas Transplantation Committee updated their policy by removing the c-peptide and BMI cut-offs from the 11.3.B Kidney-Pancreas waitlist time criteria in June 2018 [3]. This change was not implemented nationally until July 11, 2019. Though the effect of this policy change on recipient demographics and outcomes is not yet known, this policy change reflects an evolution in the role of pancreas transplantation for diabetes.

While the definition of type 1 and 2 diabetes represents an established paradigm for characterizing this disorder, there is increasing recognition that diabetes reflects a spectrum of disease. Specifically, there is a group of patients with a heterogenous manifestation of poor glycemic control with elements of both insulin insufficiency and insulin resistance. These patients with so-called type 1.5 diabetes tend to present at ages 30-49 and have a slightly elevated weight pattern with highly variable levels of β-cell destruction as reflected by c-peptide [18-20]. As such, this more inclusive pancreas allocation policy may provide an avenue of definitive glucose regulation and renal replacement for these types of patients. Here, we provide a detailed analysis of pancreas transplant trends since 2014. We assess the shifting demographics in our SPK recipients through the varying pancreas policy changes and look closely at our center's experience from the beginning of the PAS. More specifically, SPK transplantation is evaluated before and after the implementation of the 11.3.B pancreas policy change.

2. Materials and Methods

2.1 Study Population

This was a retrospective study of 81 adult patients who received a SPK transplantation at Montefiore Medical Center from June 2014 to December 2020. C-peptide yearly trends for new listings and SPK were assessed. SPK transplantations performed before July 11, 2019 were classified as "pre-11.3.B policy change" and those performed after were classified as "post-11.3.B policy change". National SPK data was also obtained from the UNOS STAR (Standard Transplant Analysis and Research) files to evaluate for yearly trends in c-peptide for new listings and SPK transplants as well as changes in recipient age, BMI, and c-peptide levels following the 11.3.B policy change. All patients underwent the same surgical approach with transplantation of the pancreas on the right with systemic venous drainage, Y-graft arterial reconstruction, and enteric drainage. All kidneys were transplanted in the left iliac fossa. Rabbit anti-thymocyte globulin was used for induction therapy and intravenous immunoglobulin was added if the patient had donor-specific antibody. Immediate release tacrolimus or extended-release tacrolimus (Envarsus XR), mycophenolate mofetil or mycophenolic acid, and steroids were used for maintenance immunosuppression.

2.2 Data Analysis

Recipient information was collected from patients' electronic medical records and included variables such as, age, sex, pre-transplantation BMI, and c-peptide levels, presence of donor-specific

antibodies, presence of panel reactive antibodies (PRA), time on the waitlist, and history of hypertension (HTN) and/or hyperlipidemia (HLD). Donor characteristics including age, BMI, Kidney Donor Profile Index (KDPI), and Public Health Service (PHS) high risk status were obtained from patient charts or UNOS DonorNet®. Cold and warm ischemia times were also recorded for both kidney and pancreas grafts.

Kidney graft function was evaluated by delayed graft function, post-operative creatinine, post-operative estimated glomerular filtration rate (eGFR), and graft failure requiring dialysis. Pancreas graft function was evaluated by post-operative hemoglobin A1c (HbA1c), need for resumption of anti-diabetic medication, and graft loss. Pancreatic loss was defined as insulin utilization >1 unit/kg or pancreatectomy. Complications were classified according to the Clavien-Dindo classification: Grade II – complication requiring pharmacologic intervention; Grade IIIA – complication requiring invasive intervention without general anesthesia; Grade IIIB – complication requiring invasive intervention with general anesthesia; Grade IV – end organ failure or graft loss; and Grade V – death. Estimated GFR was calculated using the Modification of Diet in Renal Disease (MDRD) formula.

Statistical analyses were performed in SPSS version 27.0. Groups were compared using two-tailed t-tests for continuous variables and Fischer's exact test for categorical variables. Survival analyses were performed via the log-rank (Mantel-Cox) test. A p-value of <0.05 was considered statistically significant. Figures were made in Prism GraphPad version 8.

This study was approved by the Albert Einstein College of Medicine Institutional Review Board.

3. Results

3.1 Recipient Demographics

There was a total of 81 SPK transplants performed at Montefiore Medical Center from June 2014 to December 2020. Overall, year to year, there are notable recipient demographic changes (Figure 1). A total of 51 SPK transplants were performed before the 11.3.B policy change on July 11, 2019; and 30 transplants were performed following this policy change.

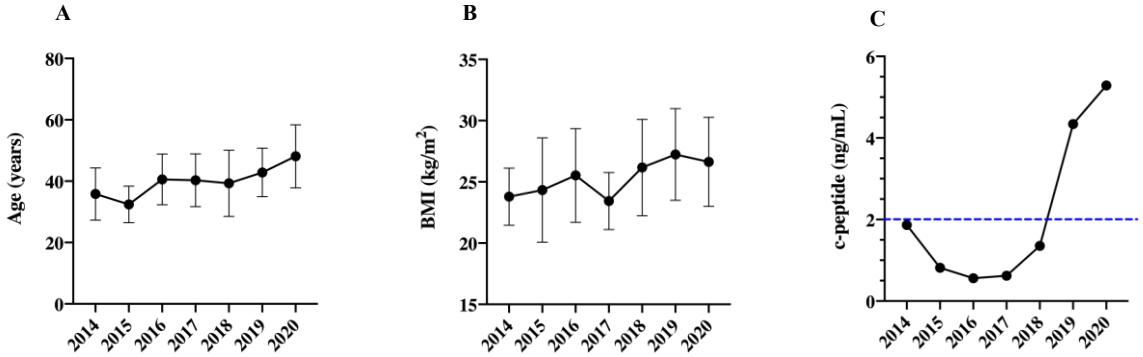

Figure 1 A: Mean center cohort recipient age by year. B: Mean center cohort recipient BMI (kg/m^2) by year. C: Mean center cohort c-peptide levels (ng/mL) by year.

The mean age of SPK recipients increased after the 11.3.B policy change was implemented (38.9 ± 9 v 46.4 ± 10 years; $p = 0.01$, Table 1). Recipient BMI was not significantly higher in the pre-11.3.B policy change group compared to the post-11.3.B policy change group (25.4 ± 3.8 v 26.8 ± 3.7 kg/m^2; $p = 0.11$, Table 1). We present yearly raw data of c-peptide ≤2 and c-peptide >2 for SPK transplants at our center and at the national level that demonstrates increasing numbers of recipients with c-peptide >2 ng/mL at the time of transplant (Figure 2). This trend was also reflected in our newly listed patients. Clearly there is an overall yearly rise in mean c-peptide when comparing newly listed and transplanted patients (Figure 2).

Table 1 Characteristics of simultaneous pancreas-kidney recipients and donors before and after the removal of c-peptide and BMI requirements from the OPTN/UNOS 11.3.B Kidney-Pancreas waitlist time criteria on July 11, 2019.

	Overall cohort	**Pre-11.3.B policy change**	**Post-11.3.B policy change**	***p*-value**
	n = 81	n = 51	n = 30	
Recipients				
Age (y)	41.7 ± 10	38.9 ± 9	46.4 ± 10	0.01
Sex				
Female (%)	33 (40.7)	21 (41.2)	12 (40.0)	0.92
BMI (kg/m^2)	25.8 ± 3.7	25.4 ± 3.8	26.8 ± 3.7	0.11
c-peptide (ng/mL)	2.9 ± 3.3	1.7 ± 2.7	4.9 ± 3.4	0.01
c-peptide >2	37 (45.7)	14 (27.5)	23 (76.7)	0.01
Outside criteria*	4 (4.9)	0 (0.0)	4 (4.9)	0.02
ABO				0.18
A	18 (22.2)	15 (29.4)	3 (10.0)	
AB	4 (4.9)	3 (5.9)	1 (3.3)	
B	15 (18.5)	9 (17.6)	6 (20.0)	
O	44 (54.3)	24 (47.1)	20 (66.7)	
Hypertension	77 (95.1)	47 (92.2)	30 (100.0)	0.29
Hyperlipidemia	39 (48.1)	25 (49.0)	14 (46.7)	0.82
PRA I (%)	16 ± 29	13 ± 26	21 ± 32	0.26
PRA II (%)	14 ± 26	15 ± 26	12 ± 25	0.57
DSA (n)	14 (17.3)	10 (19.6)	4 (13.3)	0.55
Induction				
Anti-thymocyte globulin	64 (79.0)	39 (76.5)	25 (83.3)	0.63
Anti-thymocyte globulin/IVIG	16 (20.0)	11 (21.6)	5 (16.7)	0.60
UNOS wait time (days)	777 ± 670	729 ± 608	859 ± 768	0.40
Center wait time (days)	488 ± 467	459 ± 483	536 ± 441	0.48
Donors				
Age (y)	24.0 ± 7	23.3 ± 7	25.4 ± 7	0.18
BMI (kg/m^2)	24.0 ± 3.9	24.0 ± 3.7	24.1 ± 4.4	0.91

KDPI (%)	23 ± 15	23 ± 16	22 ± 12	0.85
Terminal creatinine (mg/dL)	2.4 ± 2.3	2.5 ± 2.4	2.2 ± 2.0	0.61
PHS high risk	31 (38.3)	17 (33.3)	14 (46.7)	0.25
Organ procurement organization				
Local	26 (32.1)	21 (41.2)	5 (16.7)	0.02
Import	55 (67.9)	30 (58.8)	25 (83.3)	0.02
Kidney CIT (min)	718 ± 245	706 ± 257	738 ± 226	0.57
Kidney WIT (min)	40 ± 8	38 ± 8	43 ± 8	0.01
Pancreas CIT (min)	705 ± 224	655 ± 235	789 ± 178	0.01
Pancreas WIT (min)	35 ± 10	32 ± 8	41 ± 10	0.01

Note: Values reported as mean ± SD or n (%).

Abbreviations: BMI, body mass index; CIT, cold ischemia time; KDPI, Kidney Donor Profile Index; OPTN, Organ Procurement and Transplantation Network; PHS, Public Health Service; min, minutes; UNOS, United Network for Organ Sharing; WIT, warm ischemia time.

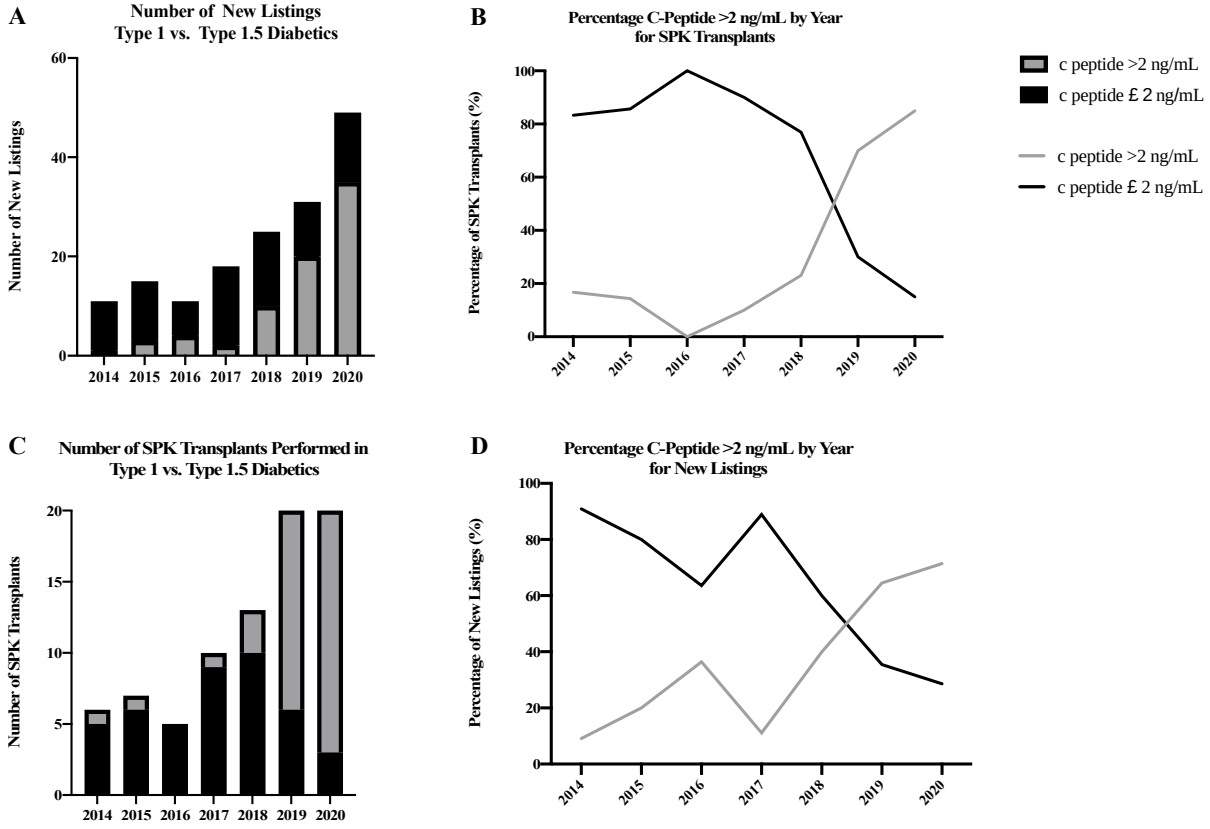

Figure 2 A: Number of SPK transplantations performed at our center in Type 1 (c peptide ≤2 ng/mL) and Type 1.5 (c peptide >2 ng/mL) diabetics per year. B: Percentage of center SPK transplantations performed in patients with c peptide ≤2 ng/mL or c peptide >2 ng/mL over time. C: Number of Type 1 (c peptide ≤2 ng/mL) and Type 1.5 (c peptide >2 ng/mL) added to SPK waitlist at our center per year. D: Percentage of new listings in patients with c peptide ≤2 ng/mL or c peptide >2 ng/mL over time.

C-peptide levels increased significantly after the 2019 policy change (1.7 ± 2.7 v 4.9 ± 3.4 ng/mL; p = 0.01, Table 1). The proportion of patients with a pre-transplant c-peptide of >2 ng/ml almost tripled after the policy change (27.5% v 76.7%; p = 0.01). Additionally, there was a 13% increase in beneficiaries who otherwise would not have been transplanted under the prior policy (Figure 3).

Figure 3 Number of transplants performed in patients of following three subgroupings: c-peptide ≤2 ng/mL and BMI ≤30 kg/m^2, c-peptide >2 ng/mL and BMI ≤30 kg/m^2 and c-peptide >2 ng/mL and BMI >30 kg/m^2.

Time spent on waitlist, sex distribution, blood type, class I PRA, class II PRA, DSA, type of induction agent, rates of hypertension, and rates of hyperlipidemia were comparable between groups (Table 1). Follow up duration ranged from 71 to 2,432 days, with an average of 972 days. In 79% of the study cohort, at least one year of follow-up data was available, and in 89% of the cohort, at least six months of follow-up was available.

3.2 Donor Demographics

Donor characteristics, including mean age, BMI, KDPI, terminal creatinine, and PHS high risk status did not differ significantly before and after the policy change (Table 1). After July 2019, the proportion of grafts that were imported (58.8% v 83.3%; p = 0.02) increased, along with the mean pancreas cold ischemia times (CIT) (655 ± 235 v 789 ± 178 minutes; p = 0.01). Similarly, the same pattern held true for warm ischemia times (WIT) for both pancreas (32 ± 8 v 41 ± 10 minutes; p = 0.01) and kidney grafts (38 ± 8 v 43 ± 8 minutes; p = 0.01) (Table 1).

3.3 Outcomes

The mean eGFR did not differ after the policy change at any of the post-operative follow-ups (1, 3, 6, and 12 months) (Table 2). Average peak amylase, a surrogate for ischemia reperfusion injury, also did not change significantly (236 v 327 U/L; p = 0.20) following the policy change (Table 2). Similarly, HbA1c also did not differ significantly between these groups at any of the post-operative follow-ups (3, 6, and 12 months) (Table 2).

Table 2 Outcomes of simultaneous pancreas-kidney recipients before and after the removal of c-peptide and BMI requirements from the OPTN/UNOS 11.3.B Kidney-Pancreas waitlist time criteria on July 11, 2019.

Recipient outcomes	Overall cohort	Pre-11.3.B policy change	Post-11.3.B policy change	*p*-value
	n = 81	n = 51	n = 30	
Length of stay (days)	10.2 ± 7.6	10.3 ± 8.3	10.0 ± 6.3	0.89
DGF	19 (23.5)	10 (19.6)	9 (30.0)	0.42
Peak amylase (U/L)	270 ± 306	236 ± 230	327 ± 403	0.20
Post-operative eGFR (mL/min/1.73 m^2)				
3 months	68 ± 20	66 ± 19	71 ± 22	0.25
6 months	65 ± 18	64 ± 18	70 ± 20	0.30
12 months	63 ± 23	63 ± 21	62 ± 32	0.89
Post-operative HbA1c (%)				
3 months	5.3 ± 0.7	5.3 ± 0.7	5.3 ± 0.5	0.67
6 months	5.3 ± 0.6	5.3± 0.6	5.3 ± 0.6	0.88
12 months	5.6 ± 1.1	5.6 ± 1.2	5.3 ± 0.5	0.32
Return to anti-diabetic agent	12 (14.8)	11 (21.6)	1 (3.3)	0.03
Wound infections	14 (17.3)	6 (11.8)	8 (26.7)	0.13
Kidney graft loss	3 (3.7)	3 (5.9)	0 (0.0)	0.29
Pancreas graft loss	6 (7.4)	4 (7.8)	2 (6.7)	0.99
Deaths	4 (4.9)	2 (3.9)	2 (6.7)	0.62
‡ Clavien-Dindo classification				
Grade II	26 (32.1)	13 (25.5)	13 (43.3)	0.43
Grade IIIA	8 (9.9)	7 (13.7)	1 (3.3)	
Grade IIIB	9 (11.1)	6 (11.8)	3 (10.0)	
Grade IV	4 (4.9)	2 (3.9)	2 (6.7)	
Grade V	4 (4.9)	2 (3.9)	2 (6.7)	
1 year patient survival rate (%)	96.3	98.0	93.3	0.28
1 year graft survival rate (%)	97.5	100	93.3	0.06

Note: Values reported as mean ± SD or n (%).

‡ Clavien-Dindo classification of complications: Grade II – complication requiring pharmacologic intervention; Grade IIIA – complication requiring invasive intervention without general anesthesia; Grade IIIB – complication requiring invasive intervention with general anesthesia; Grade IV – end organ failure or graft loss; Grade V – death. Abbreviations: DGF, delayed graft function; eGFR, estimated glomerular filtration rate; HbA1C, hemoglobin A1C.

There was a significant difference (p = 0.03) between the pre-11.3.B policy change group requiring diabetic medications post-transplant compared to the post- 11.3.B policy change group. In the pre-11.3.B policy change group, 11 (21.6%) patients returned to using a diabetic medication post-transplant, while only one patient (3.3%) in the post-11.3.B policy change group returned to using a diabetic medication. There was no significant difference in delayed kidney graft function in the pre-11.3.B policy change group compared to the post-11.3.B policy change group (Table 2). There was also no significant difference in average hospital length of stay (LOS) (Table 2).

In terms of complications, Grade II complications (requiring pharmacologic treatment) included urinary tract infection, non-occlusive graft venous thrombosis, pneumonia, deep vein thrombosis, pulmonary embolus, atrial fibrillation with rapid ventricular response, and small bowel-obstruction. Grade IIIA complications (requiring invasive intervention without general anesthesia) included wound infection, peripancreatic abscess, gastrointestinal bleeding requiring endoscopy, and myocardial infarction. Grade IIIB complications (requiring invasive intervention with general anesthesia) included complications that required re-exploration such as bleeding, intraabdominal abscess, bowel ischemia, graft torsion, and pancreatic graft leak. There were no significant differences in complication rates across the grades (p = 0.43). The incidence of kidney graft loss (5.9% v 0%; p = 0.29), pancreas graft loss (7.8% v 6.7%; p = 0.99) and mortality (3.9% v 6.7%; p = 0.62) were also similar after the policy change. One year survival rates of grafts and patients did not differ between groups (Table 2).

Logistic regression showed that neither age, BMI, nor c-peptide were predictive of pancreas graft loss. There was also no correlation between these variables and complications graded III or more by Clavien-Dindo classification.

3.4 Beneficiaries of the 11.3.B Policy

To further understand the beneficiaries of the 11.3.B policy change we looked at three subgroups: c-peptide ≤2 ng/mL (group 1), c-peptide >2 ng/mL and BMI ≤30 kg/m^2 (group 2); which reflect the pre-policy environment and c-peptide >2 ng/mL and BMI >30 kg/m^2 (group 3); this last group reflecting the policy change. Before the policy change, 37 (73%) patients had c-peptide <2 ng/mL and 14 (27%) patients had c-peptide >2 ng/mL and BMI ≤30 kg/m^2. After the policy change only 7 (23%) patients had c-peptide ≤2 ng/mL, 19 (63%) patients had c-peptide >2 ng/mL and BMI ≤30 kg/m^2, and 4 (13%) patients had c-peptide >2 ng/mL and BMI >30 kg/m^2. The four patients who benefitted from the new 11.3.B policy included two pancreas graft losses, and one patient death. One patient had a superficial SSI and a deep SSI (Figure 3).

We assessed the trends in new listings compared to SPK transplants performed from January 2014 to December 2020. As the years progressed, we noticed an increase in the ratio of new listings to SPK transplants.

3.5 National Trends

There were 3,537 SPK transplantations performed nationally between January 2015 and September 2020, 859 of which were performed after the July 11, 2019 policy change. This national data did not demonstrate a significant change in mean age (42.0 ± 9 v 42.6 ± 9 years, p = 0.11) of SPK recipients after the policy change. While the BMI of SPK recipients after the policy change did not change significantly (25.6 ± 3.7 v 25.9 ± 4.0 kg/m^2, p = 0.06), there was a higher proportion of

patients with a BMI >30 kg/m^2 (8.4% v 12.1%, p = 0.01). In addition, the mean pre-transplant c-peptide increased significantly (1.2 ± 2.5 v 1.7 ± 2.9 ng/ml, p = 0.01).

4. Conclusions and Discussion

Pancreas allocation policies over the past seven years have evolved to equitably and appropriately increase access to transplantation. The creation of the PAS in 2014 was the first initiative to establish and standardize national pancreas allocation policies. In the early onset of the PAS, it set qualifying criteria for candidates on the SPK waitlist that reflected the patient's degree of insulin deficiency and resistance. Initially, this policy included guidelines that limited pancreas transplantation to those patients with specified c-peptide levels and/or a maximum allowable BMI. More recently this policy was amended to undue the constraints of these surrogate markers and is now only requiring an insulin regimen at the time of candidacy registration. Notably, this almost decade long process has resulted in expanded pancreas transplantation. However, with any policy implementation, nuances can arise that often beget deeper analysis. While we will highlight the changes that arose from the most dramatic policy shift in the latest iteration of the PAS, the entirety of this policy's overall impact and the cumulative modifications make an interesting study.

Curiously, we observed a decrease in transplanted patients with insulinopenia despite hard fought efforts that have resulted in an increase in pancreas transplantation. These patients primarily classified as having type 1 diabetes have contributed ever diminishingly to the transplant rate since 2019. For certain, the liberalization of the 11.3.B policy has increased the number of eligible patients, many of which have characteristics that would be nominally classified as type 1.5 diabetes. The emergence of this group and the suitability for transplant will be addressed further in the discussion, but this phenomenon may not represent the whole story when considering why there is a decrease in type 1 diabetic pancreatic transplants.

One theory is that there may be an exhaustion of eligible type 1 patients appropriate for transplant. In the U.S. there are 187,000 type 1 diabetic patients. The number of patients with uncontrolled type 1 diabetes, who would benefit from transplantation is an even smaller subset of patients; roughly one third of those patients [21]. We assessed the trends in c-peptide levels in waitlisted and transplanted patients as they varied over the years. We noticed a decreasing number of patients with undetectable c-peptide levels in SPK listings and transplants performed by our center from 2014 to 2020 (Figure 2). In contrast to the downtrend in the number of patients transplanted with negligible c-peptide levels, we observed a progressive increase in SPK recipients with c-peptide levels >2 ng/mL (Figure 2). This trend in our center was also reflected in the national data. As such, one may make the argument that the PAS changes were a stunning success, in that the problem was quickly identified and remedied. However, this phenomenon may have been coupled with a catalytic course of action that accelerated the observed recipient demographic changes.

As stated previously, the more inclusive version of policy 11.3.B proffered the opportunity for increased pancreatic transplantation and stands as perhaps the most dramatic change since the PAS inception. Here we assess the implications of this policy in our center. We observed an increase in our cohort's age (38.8 v 46.4 years; p = 0.01) and c-peptide (1.7 v 4.5 ng/mL; p = 0.01) following the enactment of this policy change. Mean c- peptide was 1.7 ng/mL pre-policy change and rose to 4.9 ng/mL post-11.3.B policy change (p = 0.01). This increasing trend of c-peptide levels did not

statistically affect patient morbidity, graft survival or patient survival (Table 2). The acceptance of c-peptide levels >2 ng/mL shows that there is potential for SPK to be a valuable treatment for not just classic type 1 diabetes and should be further substantiated in future studies. However, while the increase in the national mean c-peptide is statistically significant (1.2 ng/ml v 1.7 ng/ml; $p = 0.01$), it remains below 2.0 ng/ml.

We also observed no significant increase in recipient BMI. The removal of the BMI requirement prompted concerns that there would be a drastic increase in mean recipient BMI. Notably, there was not a significant increase in our cohort recipients with a BMI >30 kg/m^2 (9.8% v 20.0%; $p = 0.35$) though the trend was for patients to be slightly larger. This was also reflected in the OPTN/UNOS national data that did not show a significant increase in mean BMI. Also, despite some unease of easing the candidacy criteria, only four beneficiaries of the 11.3.B policy change at our center had c-peptide levels >2 ng/mL and BMI >30 mg/m^2.

While there was no significant increase in the rate of complications, this study is likely underpowered to detect a difference due to the relatively low rate of severe complications. However, the data does note a slight increase in the warm ischemia time and peak post-operative amylase that could signify an increase in technical difficulty/complexity. Historically some older studies have found that high recipient BMI has been associated with an increase in the rate of technical failure, wound complications, dehiscence, ventral hernia, repeat laparotomy, pancreas graft failure, and death [22-27]. Follow up studies have since demonstrated otherwise [9-16], but our data suggests that increasing age may contribute to an increase in operative difficulty possibly due to redistributive central adiposity and age related iliac artery calcification. Certainly, arterial calcification can be an age-related gauge of disease progression. Moreover, studies have shown that the degree of iliac artery calcification is predictive of intraoperative vascular complications, graft loss, and death [28, 29]. Although we have not seen an increase in the rate of complications, it is conceivable that upward trends in age and a trending increase in BMI may prompt a recalibration of our operative approach as it relates to surgical experience.

We also took a closer look at the benefits of pancreas transplantation in clinical terms based on a comparison of our center's rates of return to antidiabetic medications in the pre-and post-11.3.B policy groups. In the pre-11.3.B policy change group 11 of 51 patients (22%) required a return to antidiabetic medications, with a median post-operative return on day 275.7, while the post-11.3.B policy change group included 1 out of 30 patients (3%) with a return to insulin on post-operative day 0 due to an explanted pancreas graft. As limited follow-up undoubtedly accounts for this difference, it is rash to draw conclusions from these trends.

There are several significant observations and potential consequences resulting from PAS policy changes. Of note, there seems to be a downtrend in patients with classic type 1 diabetes being transplanted and an uptrend in patients with moderate insulin resistance or a type 1.5 phenotype. More importantly, we demonstrated no significant changes in patient morbidity and survival for transplanting patients with moderate insulin resistance. These results seem to validate the changes to pancreas allocation policies that have become more inclusive of atypical diabetic patients with some insulin resistance. These recipients have largely led to a surge in center volume, which is driven by an increase in overall listed patients with a consistent ratio to waitlist patients (0.51; pre-11.3.B policy change as compared to 0.66; post-policy change).

Ultimately, the changes to pancreas policies reflects a culmination of policymakers to respond and anticipate the future of pancreas transplantation based on a careful understanding of trends.

Our conclusions represent a single center's experience and are drawn from a limited sample size. Larger multi-center studies with longer follow-up are warranted to determine the national impact of these policy changes. Lastly, post-operative renal parameter assessment was beyond the scope of this manuscript. Though pancreas implantation is protective against, diabetic nephrology, further studies may of be of interest to understand the impact of evolving allocation policy and renal functionality.

Author Contributions

AR – study conception and design, data acquisition, analysis and interpretation of data, drafting of manuscript, and critical revision; RT – study conception and design, data acquisition, analysis and interpretation of data, drafting of manuscript, and critical revision; AB – data acquisition, analysis and interpretation of data drafting of manuscript and critical revision; JPR – study conception and design, analysis and interpretation of data, and critical revision; NAM – data acquisition, and critical revision; JT – data acquisition, analysis and interpretation of data, and critical revision; MA – study conception and design; LLW – analysis and interpretation of data; YA – analysis and interpretation of data; CP – analysis and interpretation of data; PLC – analysis and interpretation of data; EA – analysis and interpretation of data; MEL – data acquisition, analysis and interpretation of data, and critical revision; MMK – study conception and design and critical revision; JAG – study conception and design, analysis and interpretation of data, drafting of manuscript, and critical revision.

Competing Interests

The authors of this manuscript have no conflicts of interest to disclose as described by OBM Transplantation.

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