Pancreas transplantation is associated with improved quality of life among patients with diabetes mellitus by eliminating the need for exogenous insulin injection, frequent blood draws, and diet restriction. Pancreas transplantation also attenuates the acute complications experienced by patients with diabetes, including hypoglycemia and severe hyperglycemia. Euglycemia after successful pancreas transplantation has been shown to stabilize or even improve common complications of diabetes, including nephropathy, neuropathy, retinopathy, and macrovascular disease. Historically, pancreas transplantation has been limited due to early graft failure secondary to surgical complications. In the 1980s, 25% of all pancreas grafts were lost due to technical failures; however, surgical advances have led to improved pancreas graft survival. Between 2004 and 2008, the technique failure rate of pancreas transplants in the US decreased to 7–9%. Therefore, pancreas transplantation alone is a viable management strategy for nonuremic patients with diabetes mellitus.

Patient weight pretransplant and posttransplant is of growing concern as obesity is an emerging problem in the transplant population. Leonard et al noted that the prevalence of obese liver transplant candidates rose from 15% in 1990 to 25% in 2003. Likewise, Kim et al reported that 34.4% of liver transplant candidates were obese in 2011. A similar trend has been shown in kidney, heart, and lung transplant recipients. In addition, the literature has demonstrated that transplant recipients gain excessive weight within the first year posttransplant after liver, kidney, and heart transplantation.
Immunosuppressive medications used after solid organ transplantation have been linked to weight gain. However, pancreas transplant alone (PTA) recipients are a unique subset of solid organ transplant recipients who are also susceptible to weight loss after transplantation due to independence from exogenous insulin, decreased frequent carbohydrate intake previously utilized to avoid hypoglycemia unawareness, and presence of gastrointestinal symptoms limiting intake, such as gastroparesis. The incidence of significant weight changes among PTA recipients and the effect on pancreas graft survival is unknown. We hypothesized that significant weight changes (weight gain or loss) would have detrimental effects on graft survival.

**MATERIALS AND METHODS**

**Study Population and Design**

This was a single-center cohort study among PTA recipients transplanted between January 1, 2005, and July 31, 2017, at the University of Wisconsin Hospital. Patients were included in the study if they (1) had at least 1 year of pancreas graft survival and (2) had follow-up at the University of Wisconsin Transplant Clinic with documented weight changes. To look for the effects of weight changes exclusively among PTA, patients were excluded if the pancreas transplant was in the form of combined (in the past) or simultaneous transplantation with other organs, including the kidney. However, previous PTA recipients were included if they met the above selection criteria. Patients were divided into 3 groups based on weight change from transplant to the 1-year posttransplant interval: (1) no significant weight change, (2) significant weight gain, and (3) significant weight loss. We defined significant weight gain as ≥7% of weight gain from the baseline at 1 year. The definition of significant weight gain is not consistent in the literature, weight gain of 3% and 5% have also been used, but we chose the most commonly used conservative measure of 7% weight gain as significant. Significant weight loss was defined as an unintentional weight loss of ≥5% from the baseline at 1 year, which is a commonly used definition in the literature. This study was approved by the University of Wisconsin School of Medicine and Public Health Institutional Review Board.

**Variables and Definitions**

Clinical information on transplant recipients included age at the time of transplant, gender and race, type of transplant, induction immunosuppressive medication, body mass index, and weight at various time periods. We also looked for the acute rejection of the pancreas treated in the first year of transplant along with the hospital admissions due to gastroparesis symptoms within 1-year posttransplant. We chose rejection as one of the variables as most, if not all, rejections were treated with steroid pulse, which may contribute to weight gain. We also looked for admission due to gastroparesis as one of the variables, as the incidence of gastroparesis would be significantly higher in this population and may get exacerbated by some of the medications mainly steroids and mycophenolate mofetil and contribute for a weight loss. Pancreas graft failure (uncensored and death-censored) was the outcome of interest. Pancreas graft failure was based on the current United Network for Organ Sharing criteria for pancreas graft failure, which include removal of the pancreas graft, reregistration for a pancreas transplant, registration for an islet transplant after receiving pancreas, and requirement for insulin that is ≥0.5 units/kg/d for 90 consecutive days or recipient death. The patient’s last follow up was censored at death or graft failure for those who experienced it, or at last blood test among those with a functioning graft.

**Surgical Technique**

The surgical technique was consistent throughout the study period. All procured pancreases were preserved with University of Wisconsin solution. There was enteric drainage of exocrine secretions and systemic venous drainage of endocrine secretions. No Roux-en-Y limbs were performed. The final orientation of the graft was behind the right colon with head up and tail toward the pelvis.

**Immunosuppression and Rejection Treatment**

Patients undergoing pancreas transplant received induction immunosuppression with a depleting agent (anti-thymocyte globulin or alemtuzumab) or nondepleting agent (basiliximab) based on immunological risk factors as previously described. Patients with pretransplant donor-specific antibodies, previous pancreas graft failure due to rejection, and planned early steroid withdrawal were more likely to receive lymphocyte-depleting induction therapy. Patients were typically maintained on a triple immunosuppressive regimen with a calcineurin inhibitor (tacrolimus), antiproliferative agent (mycophenolate mofetil or mycophenolic acid), and corticosteroids (prednisone). Rarely, PTA recipients underwent early steroid withdrawal. Doses and drug levels were individually adjusted based on the patient’s clinical condition, including infection, malignancy, and rejection. Most PTA recipients were maintained on tacrolimus with a trough goal of 9–12 ng/mL for the entire posttransplant period unless complicated by infection or malignancy or rise in serum creatinine. The initial mycophenolate sodium dose was 720 mg by mouth 3 times daily for 1 month, then twice daily. Prednisone was tapered to 10 mg daily by 8 weeks posttransplant, with further taper determined by the managing provider.

Treatment of pancreas rejection was based on the type and severity of rejection and graded by Banff criteria scoring of pancreas allograft biopsies as explained before. Briefly, all patients received intravenous steroid pulse as the first line of treatment. Anti-thymocyte globulin or intravenous immunoglobulin or plasmapheresis were added based on the severity and types of rejection.

**Patient Evaluation**

Nonuremic type I patients with diabetes were PTA candidates. The majority of patients underwent extensive cardiac workup including cardiac catheterization. Contraindications for transplantation parallel other solid organ transplant criteria (cardiovascular disease, active infection, cancer, noncompliance, and poor social support).

**Statistical Analysis**

Continuous data were presented as median with interquartile range, when appropriate and analyzed using the Kruskal-Wallis test. Categorical data were presented as an absolute number with a percentage and analyzed using Fisher’s exact test or the chi-square test, when appropriate. Uncensored and death-censored graft failures were analyzed using
Kaplan-Meier analyses. P values < 0.05 were considered statistically significant. Risk factors associated with death-censored pancreas graft failure were studied using univariate and multivariate stepwise Cox regression analyses. All variables in Table 1, along with weight gain, weight loss, rejection treated with steroid pulse within the first year of transplant, and hospital admission for gastroparesis were analyzed in univariate analysis. Only significant variables (if any) in univariate were analyzed in multivariate. We also looked for the total and death censored graft failure dividing into 3 tertile categories based on the weight change at the first year posttransplant period by the Kaplan-Meier analyses.

RESULTS

A total of 105 PTA recipients fulfilled our selection criteria. Twenty-eight recipients had significant weight gain at the 1-year posttransplant interval, 27 had significant weight loss, and 50 patients did not have significant weight change. Comparing the groups (Table 1), patients in the weight gain group were predominantly female and had a shorter wait time for pancreas transplantation. All other baseline characteristics were similar between groups.

There was no significant difference in years of posttransplant follow up between the groups (Table 2). There was a significant median weight change difference (% weight change) between the groups starting from 3 months posttransplant to the last follow up (Figure 1). The weight gain group gained a median of >10% of their body weight at 5 years and at last follow up, weight loss group lost around 5%–8%, while no weight change group gained <2.5%. The weight loss group had a significantly lower incidence of acute rejection (4%) within the first year of transplant compared to the weight gain (29%) or no weight change group (30%) (P = 0.02). Eleven percent of the weight gain group, 15% of the weight loss group, and 6% of the no weight change group were admitted to the hospital within the first year of a transplant due to gastroparesis symptoms. Twenty-five percent of pancreas grafts failed at last follow up in weight gain group compared to 7% in weight loss group and 22% failure in the no weight change group. Death censored graft failure or death censored graft failure with detectable c-peptide of >1 ng/mL was similar between the groups. Also, HgbA1c at last follow up among the groups were not significantly different at last follow up.

In the univariate analysis (Table 3) where we sought to examine possible factors associated with the death censored graft failure, only acute rejection within the first year of transplant (hazard ratio 2.66; 95% confidence interval, 1.02–6.94, P = 0.04) was associated with death censored graft failure. None of the other variables from the baseline characteristics were significantly associated with death censored graft failure. Neither significant weight gain or weight loss was associated with graft failure. Due to this reason, multivariate analysis was not performed. This was further supported by the Kaplan-Meier survival analysis (Figure 2).

We also looked for the effects of weight changes by dividing the cohort into tertile categories. The first tertile included weight change between −19% and −3.89%; second tertile with −3.54% to +4.35%; and third tertile of 4.42% and 23.48%. By Kaplan-Meier survival analysis, there were still no significant differences in graft failure among the groups (Figure 3).

DISCUSSION

In this series of 105 PTA recipients transplanted over >12 years, we found an incidence of significant weight changes at 1 year posttransplant period of around 50%, with 25% gaining and 25% losing significant weight. Interestingly, these weight changes occurred in both weight gain and weight loss groups when measured at 3 months posttransplant and were durable to last follow up. Despite the majority of patients utilizing steroid maintenance immunosuppression, only 25% gained significant weight and 25% even had weight loss. Clinically

### TABLE 1.

| Variables                              | Significant weight gain (n = 28) | Significant weight loss (n = 27) | No significant weight change (n = 50) | P     |
|----------------------------------------|---------------------------------|---------------------------------|--------------------------------------|-------|
| Female                                 | 21 (75%)                        | 15 (56%)                        | 20 (40%)                             | 0.01  |
| Age at time of transplant (y)          | 42.3 (12.7)                     | 46.6 (11.8)                     | 44.3 (16.3)                          | 0.22  |
| Caucasian                              | 28 (100%)                       | 27 (100%)                       | 50 (100%)                            | NS    |
| Waiting time on list (d)               | 40.5 (45)                       | 66 (84)                         | 50.5 (105.6)                         | 0.29  |
| Types of transplant                    |                                 |                                 |                                      |       |
| DBD                                    | 27 (96%)                        | 25 (93%)                        | 47 (94%)                             | 0.82  |
| DCD                                    | 1 (4%)                          | 2 (7%)                          | 3 (6%)                               | 0.43  |
| Previous pancreas transplant recipients| 1 (4%)                          | 2 (7%)                          | 6 (12%)                              |       |
| Types of diabetes                      |                                 |                                 |                                      |       |
| Type I                                 | 25 (89%)                        | 27 (100%)                       | 47 (94%)                             | 0.44  |
| Type II                                | 0                               | 0                               | 0                                    |       |
| Other                                  | 3 (11%)                         | 0                               | 3 (6%)                               |       |
| Induction immunosuppression            |                                 |                                 |                                      |       |
| Basiliximab                            | 9 (32%)                         | 3 (11%)                         | 15 (30%)                             | 0.10  |
| Alemtuzumab                            | 10 (36%)                        | 6 (22%)                         | 14 (28%)                             |       |
| Anti-thymocyte globulin                | 9 (32%)                         | 18 (67%)                        | 21 (42%)                             |       |
| Early steroids withdrawal              | 1 (4%)                          | 0 (0%)                          | 0 (0%)                               | 0.18  |
| Weight at time of transplant (kg)      | 66 (21.7)                       | 79.4 (24.6)                     | 76.5 (14.7)                          | 0.06  |
| BMI at transplant (kg/m²)              | 25.0 (5.7)                      | 27.3 (5.1)                      | 25.8 (5.0)                           | 0.40  |

Continuous variables are presented as median with (interquartile range). P value < 0.05.

BMI, body mass index; DBD, donation after brain death; DCD, donation after circulatory death.
significant weight change was not associated with decreased pancreas allograft survival. However, although not statistically significant, a significant weight loss group had better uncensored and death censored graft survival.

Obesity is a major public health concern with its incidence rising worldwide among all age groups. According to the Center for Disease Control and Prevention, in the prevalence of obesity in 2015–2016 was 39.8%, affecting >93 million US adults. Obesity, ranging from overweight to severely obese, is associated with multiple chronic diseases, including cardiovascular disease, diabetes, kidney disease, malignancies, and musculoskeletal ailments namely. Posttransplant weight gain is a common problem in solid organ transplant recipients. In 1 study describing 203 kidney transplant recipients, patients gained 9% of their body weight in 3 years posttransplant. Various studies have found that patients gain an average of 5–10 kg of weight after kidney transplantation, which has been linked with inferior patient and graft survival.

### TABLE 2. Outcomes

| Variables                                      | Significant weight gain (n = 28) | Significant weight loss (n = 27) | No significant weight change (n = 50) | P  |
|------------------------------------------------|---------------------------------|---------------------------------|--------------------------------------|----|
| Posttransplant follow up (y)                   | 5.1 (3.7)                       | 4.7 (4.1)                       | 3.5 (4.1)                            | 0.08|
| Delta weight change at 3 mo from transplant (%) | 1.7 (6.1)                       | −6.4 (6.8)                      | −1.8 (6.7)                           | <0.001|
| Delta weight change at 6 mo from transplant (%) | 6.4 (6.8)                       | −6.0 (9.4)                      | −0.1 (6.4)                           | <0.001|
| Delta weight change at 12 mo from transplant (%) | 10.8 (5.1)                      | −9.3 (5.6)                      | 0.0 (4.9)                            |    |
| Delta weight change at 24 mo from transplant (%) | 9.8 (10.1)                      | −9.9 (7.8)                      | 1.4 (9.3)                            | <0.001|
| Delta weight change at 60 mo from transplant (%) | 8.0 (25.6) (n = 16)             | −5.8 (12.9) (n = 11)            | 0.4 (7.9) (n = 18)                   | 0.02|
| Delta weight change at last follow up from transplant (%) | 10.9 (10.1)                     | −8.5 (12.8)                     | 2.1 (9.4)                            | <0.001|
| Acute rejection within first y and treated with steroid pulse (%) | 8 (29%)                        | 1 (4%)                          | 15 (30%)                             | 0.02|
| No. of patients admitted with gastroparesis symptoms in first y posttransplant (%) | 3 (11%)                        | 4 (15%)                         | 3 (6%)                               | 0.44|
| Total pancreas graft failure at last follow up | 7 (25%)                         | 2 (7%)                          | 11 (22%)                             | 0.19|
| Death censored pancreas graft failure at last follow up | 6 (21%)                        | 2 (7%)                          | 9 (18%)                              | 0.33|
| Death censored graft failure with normal c-peptide (>1 ng/mL) | 3 (11%)                        | 0                               | 6 (12%)                              | 0.18|
| HgbA1c at last follow up (%)                   | 5.4 (0.8) (n = 21)              | 5.6 (0.6) (n = 25)              | 5.4 (0.8) (n = 39)                   | 0.95|

Continuous variables are presented as median with (interquartile range).

### FIGURE 1. Significant weight gain group, continues to gain weight from the beginning and the weight loss group continues to lose weight.
of follow up. Among >92,000 first time kidney only transplant recipients in a prior study, weight loss of >5% during first posttransplant period was independently associated with the risk of graft failure. To the best of our knowledge, there is no data about the effect of weight loss among pancreas transplant recipients.

In this study, we observed novel differences in weight change posttransplant among PTA recipients at our center compared to other solid organ transplant recipients. It is a common belief that the preponderance of solid organ transplant recipients gains significant weight, but this was not seen in PTA recipients at our center. Approximately half of our patients did not have any significant weight change, while surprisingly 25% lost weight and only 25% gained significant weight. Rates of acute rejection requiring steroid pulse were similar between the weight gain and no weight change groups; however, the rejection rate was significantly lower in the weight loss group, which indicates steroid alone may not be a factor associated with weight gain in this population. This finding may reassure

TABLE 3.
Variables associated with death censored graft failure

| Variables                        | HR   | P     | 95% CI of HR |
|----------------------------------|------|-------|--------------|
| Age at time of transplant        | 0.98 | 0.47  | 0.94-1.03    |
| Male                             | 0.82 | 0.70  | 0.30-2.23    |
| Depleting induction immunosuppressive | 0.67 | 0.42  | 0.25-1.77    |
| Wait time on the list            | 0.99 | 0.91  | 0.99-1.0     |
| Previous pancreas transplant     | 1.03 | 0.98  | 0.14-7.81    |
| Weight at time of transplant     | 1.02 | 0.21  | 0.98-1.05    |
| BMI at time of transplant        | 1.11 | 0.11  | 0.97-1.28    |
| Significant weight gain          | 1.23 | 0.68  | 0.45-3.34    |
| Significant weight loss          | 0.33 | 0.14  | 0.07-1.45    |
| Rejection within first year of transplant | 2.66 | 0.04  | 1.02-6.94    |
| Hospital admission within the first year due to gastroparesis | 1.14 | 0.86  | 0.25-5.07    |

BMI, body mass index; CI, confidence interval HR, hazard ratio.

FIGURE 2. No significant difference in uncensored or death censored graft survival comparing weight changes.

FIGURE 3. No significant difference in uncensored or death censored graft survival after dividing into tertile categories of weight changes.
PTA recipients, who may be worried about steroid pulse and weight gain. Intriguingly, significant weight changes were not associated with graft and patient survival. Further analysis of possible variants thought to correlate with weight change did not demonstrate any significant association with graft loss.

Our observations have the limitations inherent in this type of study. As a single-center, observational, nonrandomized study, it may not be possible to generalize our results to other centers. Also, due to the small sample size, it was not possible to precisely identify what factors were associated with weight loss or weight gain. Due to the nature of this type of study, it was not possible to exactly clarify what type of weight changes patients had, that is, water weight or muscle or adipose tissue. However, to our best knowledge, this is the first reported series among PTA recipients reporting the incidence of significant weight gain and weight loss after transplantation and effect on graft survival. In summary, our study illustrates that PTA recipients may represent a unique subset of allograft recipients, where approximately half of them may experience significant weight gain or significant weight loss. Moreover, these weight changes were not associated with worse graft outcomes. Also, weight gain was not associated with a tendency to have high HgbA1c at last follow up. Further research is needed to further elucidate the role of weight changes post pancreas transplant on patient outcomes.

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