

Metabolic Surgery for the Treatment of Type 2 Diabetes in Pancreas After Kidney Transplant Candidates

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ABSTRACT

Metabolic surgery for the treatment of type 2 diabetes mellitus (T2DM) in patients not morbidly obese (BMI <35) has been widely studied. Taking into account that ~12% of pancreas transplants are performed in patients with T2DM, our goal was to evaluate the impact of metabolic surgery on the management of obese patients with T2DM on waiting lists for a pancreas transplant. We performed a Roux-en-Y gastrointestinal bypass in 5 patients with insulin-dependent T2DM who were candidates for pancreas after kidney transplant and with a BMI <35. Three patients became insulin independent by the end of the first year while the other 2 reduced their insulin requirements by 70%. Furthermore, all patients achieved improved control of lipid levels. We concluded that the surgery was effective in controlling blood glucose and lipid metabolism in these obese T2DM kidney transplant recipients. In this population, a pancreas transplant, along with its associated morbidity, may be avoided.

IN THE LAST few decades, we have witnessed the emergence of new therapies for the treatment of diabetes mellitus (DM), including surgical procedures [1–5]. Simultaneous pancreas and kidney transplantation (SPK) is currently the treatment of choice for patients with type 1 diabetes mellitus (T1DM) and end-stage chronic renal failure [6]. A considerable number of patients with insulin-dependent type 2 diabetes mellitus (T2DM) may also benefit from SPK [1,3]. More recently, the surgical experience in the treatment of morbid obesity by various techniques entailed the resolution of T2DM and lipid metabolism disorders in most cases reported [7,8]. The impact of these procedures in patients not morbidly obese (body mass index [BMI] <35) is still a matter of debate, and its application on a large scale has been defined [4,5,9–11].

According to the United Network for Organ Sharing, 12% of pancreas transplants performed worldwide in the last decade were in patients with T2DM, with results similar to those obtained in patients with T1DM [3]. Considering the significant number of T2DM patients who are candidates for pancreas transplantation [12], we sought to determine what would be the best treatment for this select

group of patients: SPK or kidney transplantation alone (KTA) associated with a metabolic procedure?

Results of pancreas transplantation have been well documented [1–3,6,12–17]. However, the performance of this procedure depends on the availability of pancreas for donation. The shortage of organs for transplant is public knowledge. Waiting lists for any form of organ transplantation grow more rapidly than the capacity of the transplant system to solve it. Thus, even when receiving a KTA from a living donor, the patient remains diabetic, and the underlying condition tends to progress [1,2,12,13]. In addition, pancreas transplantation carries a not negligible morbidity, 2 to 3 times greater than a KTA [1,2].

As an alternative, a metabolic procedure [13] seems to offer improvement in the underlying disease (T2DM) without a dependence on external factors. Enabling the

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comprehensive treatment of these patients, without the need for 2 simultaneous grafts, would facilitate the logistics of treatment and promote a reduction in waiting lists for pancreas transplantation. This could offer a real benefit to the whole transplant system. It is worth emphasizing that the mortality associated with the metabolic procedures [7] tends to be lower than renal transplantation [1,2] and, as a consequence, than pancreas transplantation as well [6], decreasing the surgical risks for candidate patients.

The goal of the present study was to evaluate the effects of a metabolic procedure (Roux-en-Y gastrointestinal bypass) in insulin-dependent T2DM kidney transplant patients.

PATIENTS AND METHODS

This uncontrolled experimental study was conducted in patients who met the following inclusion criteria: successful kidney transplantation (creatinine level <2.0 mg/dL) for at least 6 months; insulin-dependent T2DM; BMI <35; normal or high serum C peptide (>1 ng/mL); negative anti-glutamic acid decarboxylase antibodies; negative anti-islet antibodies; and negative anti-insulin antibodies.

All patients were informed of the experimental nature of the procedure and were only enrolled after signing an informed consent form.

The metabolic surgery defined as the standard procedure was the Roux-en-Y gastroplasty with jejunoileal bypass. The technique consists of creating a new gastric chamber with volumetric capacity of ~100 cm³, excluding the remaining stomach from the normal intestinal transit and redirecting the bolus through a Roux-en-Y reconstruction. The section of the biliopancreatic limb was held at 75 cm from the angle of Treitz. The anastomosis of the alimentary limb with biliopancreatic limb was performed at 150 cm from the previous sectioned area of the small intestine. In the excluded stomach, we chose to perform routine gastrostomy for administration of immunosuppressive drugs and for feeding (in case of surgical complication with the new gastric chamber).

The variables analyzed before and after the procedure were daily insulin dose, BMI, fasting blood glucose, glycosylated hemoglobin, serum cholesterol, triglycerides, creatinine, patient survival at 1 year, and surgical, clinical, and/or immunologic complications.

This study was approved by the Research Ethics Committee of the Pontificia Universidade Católica do Rio Grande do Sul-PUCRS in January 2011 (CEP 10/05309).

Statistical Analysis

Continuous data were described by using mean values \pm SDs or median and range (depending on its distribution). Categorical data were expressed by using counts. To evaluate the effect of intervention over time on selected variables, we used a linear mixed model for repeated measurements (growth model) allowing for a random intercept. In addition, to express variation over time, we calculated the percent change from baseline to 12 months. Patient data were presented by using individual profile plots. Significance level was set at $\alpha = 0.05$. Data were analyzed by using SPSS version 18.0 (IBM SPSS Statistics, IBM Corporation, Armonk, NY, United States).

RESULTS

In the period between January 2011 and December 2012, a total of 10 T2DM kidney transplant patients were referred

Table 1. Demographic Data (N = 5)

Characteristic	Mean \pm SD	Range
Age, y	53 \pm 6	42–65
Body mass index	33 \pm 1	30–34
Time of T2DM, y	15 \pm 5	5–27
Time on insulin, y	5 \pm 2	4–10
Time of kidney transplant, y	5.6 \pm 2	4–10

Abbreviation: T2DM, type 2 diabetes mellitus.

to the transplant team as candidates for pancreas after kidney transplant. Five patients (3 women/2 men) were selected for the procedure. Their demographic data are presented in Table 1.

Metabolic improvement was observed for every included patient, after the metabolic surgery. Daily insulin dose (Fig 1A), BMI (Fig 1B), fasting blood glucose (Fig 1C), glycosylated hemoglobin (Fig 1D), serum cholesterol (Fig 1E), and serum triglycerides (Fig 1F) all decreased markedly from the time of the procedure.

In terms of insulin requirements, 3 patients became insulin-free (end of the second postoperative month, end of the third postoperative month, and end of the first year postprocedure, respectively). The remaining 2 patients had an average reduction in the daily requirement at ~70% of the preprocedure dose (Fig 1A).

Table 2 presents the estimated means for selected variables obtained in a linear mixed model over time and its statistical significance. With respect to BMI, an average 23% reduction was observed for the 4 patients who completed a 6-month period of monitoring. All the patients fell into the “normal” or “overweight” range (Fig 1B).

One patient died in the fourth postoperative month of infectious complications. In addition, another patient presented with wound infection, treated properly with local drainage only. Two patients had difficulty with the introduction of solid foods. Those were treated successfully with nutritional counseling and dietary supplements.

Finally, all the changes occurred in the context of stable renal function, as depicted in Fig 1G. Only 1 patient presented with deterioration of renal function, as she deteriorated clinically after developing septic shock. This patient died 4 months after surgery, as previously mentioned.

DISCUSSION

Indication of metabolic surgery for the treatment of T2DM is fairly recent, and the experience with this form of treatment is limited to a few publications [5,9–11]. When the transplant variable is added to this scenario, the data are even scarcer. The treatment of T2DM with bariatric surgery in patients morbidly obese with kidney transplant has been reported in a few studies [18,19]. There are no reports to date, to the best of our knowledge, of metabolic surgery in renal transplanted patients with a BMI <35.

In this case series, we observed a significant improvement in the metabolic (glycemic and lipids) control. Levels of

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