

Outcomes of Roux-en-Y gastric bypass surgery for severely obese patients with type 1 diabetes: a case series report

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Abstract: Roux-en-Y gastric bypass surgery (RYGB) reverses type 2 diabetes (DM2) in approximately 83% of patients with morbid or severe obesity. This procedure has been performed in small numbers of severely obese patients with type 1 diabetes (DM1), but the impact on glycemic control and insulin requirement in this population has not been widely described. We report three patients with DM1 and severe obesity that underwent RYGB. Weight, glyce-mic control, and insulin requirements before and one year after the procedure were compared. Significant weight loss was achieved by all three patients but insulin requirements decreased in only 2 patients. In contrast, glycemic control (A1C) remained suboptimal in all three patients up to one year after the surgery. These findings suggest that RYGB leads to important weight loss and positively affects insulin sensitivity. However, reaching optimal glycemic control in patients with DM1 diabetes remains challenging due to persisting insulin deficiency.

Keywords: gastric bypass, Roux-en-Y, obesity, diabetes, insulin

Introduction

Obesity is commonly found in patients with type 2 diabetes (DM2). This growing epidemic has also affected populations with type 1 diabetes (DM1). Recently, the prevalence of obesity in the United States among young patients (3–19 years old) with DM1 was found to be over 12%.¹ For patients with DM2 and morbid or severe obesity, defined as body mass index (BMI) over 40 kg/m², bariatric surgery has resulted in reversal of type 2 DM in approximately 83% of cases.² Of the available bariatric surgical techniques, diabetes reversal ranges from 66% after gastric banding to 95% with the biliopancreatic diversion with duodenal switch (BPD).³ There is increasing evidence that in addition to caloric restriction, significant changes in secretion of gut peptides or incretins occur with surgery leading to important enhancement of insulin production and utilization.⁴

In contradistinction to DM2, results of these procedures in severely obese patients with DM1 are limited. Czupryniak et al presented two cases of severely obese patients with DM1 who underwent Roux-en-Y gastric bypass surgery (RYGB). They reported remarkable improvement of glycemic control based on a decrease in glycosylated hemoglobin (A1C) of 9.5% to 5.7% in the first case and 10.4% to 7.3% in the second case. These authors suggested that RYGB led to improvement in insulin resistance, favorably affecting glycemic control. Nevertheless, insulin therapy was still required after 2 years in both cases although the insulin requirement decreased from 0.6 units/kg

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to 0.5 units/kg in the first case and from 0.95 units/kg to 0.78 units/kg in the second case.⁵

Case reports

We retrospectively gathered data on three female patients with the diagnosis of DM1 with severe obesity that electively underwent RYGB. The first patient (Patient A) was a 29-year-old female with a history of DM1 since age 21. Her diagnosis was confirmed by undetectable C-peptide (<0.1 ng/mL) and elevated glutamic acid decarboxylase autoantibodies (GAD-65) at 4.1 nmol/L. Since her last pregnancy at age 23, her weight significantly increased to maximum preoperative weight of 115 kg (BMI 40.6 kg/m²). She was unable to lose weight by lifestyle changes and was successfully screened for RYGB. Her average A1C the year before RYGB surgery reflected poor glycemic control (8.2%). Insulin was delivered through a continuous subcutaneous infusion system (CSII). Her total daily insulin dose before the surgery was 65.5 units, (0.57 units/kg). Within the first month after the RYGB surgery, her insulin requirements decreased to 0.37 units/kg without much prandial insulin on a very minimal diet. However, as her diet advanced, prandial insulin doses were reintroduced. One year after the procedure her weight had decreased to 75.5 kg corresponding to a 34.4% weight reduction. Her total insulin dose was 45 units (0.60 units/kg). Her average A1C for the year after the surgery decreased to 7.5%.

The second patient (Patient B) was a 62-year-old female who had been diagnosed with DM1 since age 9. Undetectable C-peptide (<0.05 ng/mL) was documented in her records confirming her diagnosis. Other comorbidities included depression, dyslipidemia, and history of stroke. She had a preoperative weight of 110.4 kg (BMI 43.9 kg/m²). Her insulin was delivered through a CSII system. Her total daily insulin dose prior to RYGB was 52.2 units (0.47 units/kg). Her average preoperative A1C was 7.6%. One year after the procedure her weight had decreased to 77.5 kg (29.8% weight reduction). Her total daily insulin dose had decreased to 35.6 units (0.46 units/kg). Her average A1C for the year after the surgery was 7.8%.

The third patient (Patient C) was a 36-year-old female with a history of DM1 since age 22. Her diagnosis was supported by undetectable C-peptide (<0.05 ng/mL). She had history of obesity for at least 10 years before she was successfully scheduled for a RYGB. At the time of her procedure her weight was 166.7 kg (BMI 53.2 kg/m²). She used a multiple daily injection insulin regimen. Her total daily insulin dose was 180 units (1.08 units/kg). Her average A1C for the year before the surgery was 8.1%. At one-year post procedure, her weight decreased to 96.4 kg for a 42.1% weight reduction. Her insulin requirements

Table 1 Characteristics of patients before Roux-en-Y gastric bypass surgery

	Patient A	Patient B	Patient C
Preoperative weight (kg)	115.0	110.4	166.7
Preoperative BMI (kg/m ²)	40.6	43.9	53.28
Preoperative insulin requirements (units/kg)	0.57	0.47	1.08
C-peptide (ng/mL)	<0.1	<0.05	<0.05
Average preoperative A1C (%)	8.2	7.6	8.1

Abbreviations: A1C, glycosylated hemoglobin; BMI, body mass index.

had decreased to a total daily dose of approximately 48.2 units (0.5 units/kg). Her average A1C for the year after the procedure increased to 8.8% (Tables 1 and 2).

Discussion

The striking results of bariatric surgery on severely obese patients with DM2 have brought into question traditional theories on the pathogenesis and therapeutics of diabetes mellitus. Complete resolution of this chronic condition is now the norm rather than the exception in severely obese patients that undergo bariatric procedures. Extending these benefits to patients with DM1 has created significant interest in this field.

The mechanisms leading to resolution of DM2 after RYGB are not clearly understood. Growing research has offered several important facts and proposed theories to better understand this phenomenon. Different bariatric techniques achieve different rates of DM2 diabetes resolution, with the most impressive results obtained from the partial gastrectomy with distal Roux-en-Y reconstruction (RYGB) and the BPD. Common endpoints of these techniques that use bypass procedure are rapid delivery of gastric content to the distal ileum and exclusion of proximal small intestine from the food path. Rapid delivery of gastric content to the distal part of the small intestine has been associated with increased secretion of gut hormones also known as incretins. This concept also known as the hindgut theory proposes that incretins, especially glucagon-like peptide (GLP-1) and peptide YY (PYY), contribute in great part to the improved

Table 2 Characteristics of patients after Roux-en-Y gastric bypass surgery

	Patient A	Patient B	Patient C
Postoperative weight (kg)	75.5	77.5	96.4
Postoperative BMI (kg/m ²)	26.7	30.8	30.8
Postoperative insulin requirements (units/kg)	0.60	0.46	0.50
Average postoperative A1C (%)	7.5	7.8	8.8

Abbreviations: A1C, glycosylated hemoglobin; BMI, body mass index.

metabolic control seen in the postoperative period.⁴ These two substances produced by the L cells of the distal ileum are known to have important metabolic actions. Given the smaller plasma concentration of GLP-1 compared to PYY, GLP-1 is considered to be more potent. Several beneficial effects have been attributed to GLP-1. Induced satiety through slow gastric emptying and action on the central nervous system has been linked to significant weight loss. More importantly, GLP-1 has been associated with increased insulin secretion by acting directly over the beta cell membrane receptors. GLP-1 also increases glycogenesis in hepatic and skeletal muscle cells. It also accelerates lipogenesis in adipocytes, which may result in improved insulin sensitivity.⁶ In addition, it has been shown in animal models with DM2, that GLP-1 increased beta-cell mass through regulation of proliferation, neogenesis, and apoptosis.⁷ This last quality of GLP-1 would suggest a hopeful scenario for patients with DM1 of whom their residual beta cell mass is mostly minimal or absent.

A different theory originally proposed by Pories and later explored by Rubino et al known as the 'foregut bypass' hypothesis, suggests that the exclusion of the duodenum and proximal jejunum from the gastrointestinal tract seems to prevent the secretion of a deleterious hormone (decretin) that could be implicated in the pathogenesis of diabetes.^{8,9} As to our knowledge, in despite of extensive research in this area, no substance has been identified yet.

Insulin sensitivity has been shown to notoriously improve after RYGB. Bikman et al suggested that something other than the weight loss contributed in great part for the change in insulin utilization. They proposed that improved insulin sensitivity and greater glucose transport is related to reduced inhibition of κ B kinase β activity and enhanced insulin signaling in muscle.¹⁰

In this small series of patients with DM1 diabetes, the RYGB bariatric procedure did not appear to significantly improve glycemic control. One year after the procedure, A1C was still not at goal for any of the three patients. Insulin requirements did decrease for two patients suggesting improved insulin sensitivity, while it remained unchanged in one.

We hypothesize that the resolution of DM2 after RGYB requires significant functioning beta cells mass. In DM1 where

insulin secretion is minimal or often absent, RGYB is less likely to positively impact glycemic control. Dependence of exogenous insulin therapy to achieve euglycemia precludes easily achieving optimal glycemic control in this patient population.

Conclusion

The RYGB bariatric procedure seems not to directly improve glycemic control in DM1. Achieving glycemic control is challenging in these patients even after decreasing their excess body weight and improving insulin sensitivity. Larger randomized case control studies are needed to demonstrate more definitive results.

Disclosure

No conflicts of interest were declared in relation to this paper.

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