Bariatric Surgery for Severe Obesity in Two Adolescents With Type 1 Diabetes

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KEY WORDS

bariatric surgery, diabetes mellitus, type 1, adolescents

ABBREVIATIONS

CVD—cardiovascular disease

DKA—diabetic ketoacidosis

HbA1c—hemoglobin A1c

OSA—obstructive sleep apnea

QoL—quality of life

RYGB—Roux-en-Y gastric bypass

T1DM—type 1 diabetes mellitus

T2DM—type 2 diabetes mellitus

VSG—vertical sleeve gastrectomy

Dr Chuang conceptualized the case series and drafted the initial manuscript; Dr Zeller interpreted the quality of life measurements used in the case series, wrote the interpretations for the manuscript, and reviewed and revised the manuscript; Dr Inge helped obtain data used in the case series and critically reviewed and revised the manuscript; Dr Crimmins help conceptualize and design the outline for the case series and critically reviewed and revised the manuscript; and all authors approved the final manuscript as submitted.

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abstract

Bariatric surgery has been effective in treating type 2 diabetes mellitus (T2DM); it has not been used frequently in obese patients with type 1 diabetes mellitus (T1DM). This is the first case series reporting on the effect of bariatric surgery on diabetes control in adolescents with T1DM. Patient A is a 19-year-old obese man with T1DM who underwent vertical sleeve gastrectomy. At 12 months after surgery he demonstrated 28% reduction in BMI. His daily total insulin requirement had decreased; however, hemoglobin A1c remained primarily unchanged at 8.8%. Patient B is a 13-year-old obese girl with an initial clinical diagnosis of T2DM controlled on only metformin. She underwent Roux-en-Y gastric bypass; at 1 month after surgery she presented in diabetic ketoacidosis and was found to have positive islet cell antibodies, which were also present before surgery. Her diagnosis was revised to T1DM, and she was started on insulin. By 28 months after surgery her BMI had decreased by 42%. Since initiation of insulin, her daily total insulin requirement had decreased, but hemoglobin A1c had significantly worsened from 6.3% to 10%. We found that despite significant weight loss, improvements in cardiovascular risk factors (dyslipidemia and obstructive sleep apnea), and quality of life in our patients, bariatric surgery does not necessarily lead to improved glycemic control of T1DM. Patients with T1DM have ongoing dependency on exogenous insulin, and optimal glycemic control still depends on patient compliance with diabetes care. *Pediatrics* 2013;132:e1031–e1034

Obesity is common in youths with Type 1 diabetes mellitus (T1DM), with an estimated prevalence of 12.6%.¹ Those with T1DM on intensive insulin therapy have an elevated risk for overweight and obesity because of the anabolic effects of insulin and the use of simple sugars for hypoglycemic treatments.² T1DM is a significant risk factor for cardiovascular disease (CVD); therefore, additional obesity-related risk factors for CVD, which include dyslipidemia, hypertension, and obstructive sleep apnea (OSA), must be treated in this population. Bariatric surgery has not been used frequently in patients with T1DM but could be a reasonable option to treat their severe obesity and related comorbidities. Roux-en-Y gastric bypass (RYGB) and vertical sleeve gastrectomy (VSG) both result in significant weight loss and type 2 diabetes (T2DM) reversal, with glycemic changes occurring before any significant weight loss.^{3–12} Surgical alteration of the gut leads to rapid changes in the secreted incretins and metabolic milieu, which may explain improved insulin resistance and secretion.^{13–17}

The metabolic effects of bariatric surgical procedures in severely obese patients with T1DM are not well understood. As the number of pediatric patients with severe obesity and T1DM increases, it will be important to define how bariatric surgery affects these patients.

CASE REPORTS

We report on 2 adolescents with T1DM who underwent RYGB and VSG. We describe the effect of their procedures on weight, metabolic indices, glycemic control, and diabetes management. In addition, we describe changes in patient quality of life (QoL) with regard to their general health and weight-related day-to-day functioning, using age-salient psychometrically sound self-report measures (SF-36 and IWQOL-Kids).^{18,19}

Patient A is a 19-year-old white man who was diagnosed with T1DM at age 9 after

presenting with diabetic ketoacidosis (DKA). Elevated autoantibodies to glutamic acid decarboxylase and insulin were documented. He developed obesity 10 years before undergoing VSG. At the time of his surgery his BMI was 42.3 kg/m². Diabetes control was suboptimal on a basal bolus insulin regimen and metformin (Table 1). He had persistent dyslipidemia despite treatment with simvastatin (Table 1). He also had severe OSA that was managed with continuous positive airway pressure. QoL^{18,20} was markedly impaired, with noted deficits in the areas of physical functioning and discomfort caused by his excess weight. At his last follow-up (12 months after surgery), BMI was 30.2 kg/m² (28% reduction). Postoperative changes in weight, hemoglobin A1c (HbA1c), average daily insulin use, and lipids are documented in Table 1. He now takes insulin boluses postprandially due to gastrointestinal symptoms that may prematurely halt meal intake. Mild hypoglycemic episodes occur 2 to 5 times per week, but he has had no severe hypoglycemic events. Since surgery, he has had one emergency department visit for hyperglycemia, ketonuria, and vomiting. He is now off statin therapy; his symptoms of OSA have also dramatically improved, and he no longer uses continuous positive airway pressure. Follow-up responses on self-report QoL assessments indicate clinically meaningful improvements in weight-related day-to-day functioning.¹⁹

Patient B is a 13-year-old white girl who was clinically diagnosed with T2DM at age 12. At the time of diabetes diagnosis her BMI was 60 kg/m². An oral glucose tolerance test was diagnostic, with fasting glucose of 127 mg/dL; fasting insulin was 50 IU/mL, and HbA1c was 6.3%. On examination she had severe acanthosis nigricans; she did not report polyuria or polydipsia. She was diagnosed with T2DM because of the clinical and biochemical evidence of significant insulin resistance. After she started taking metformin 2000 mg/day, her diabetes control remained adequate until the time of her gastric bypass (Table 1). She also had polycystic ovarian syndrome, characterized by elevated androgen levels and oligomenorrhea that was being managed with oral contraceptive pills. Her self-reported QoL^{18,20} was markedly impaired, with deficits in her perceptions of her general health status, physical functioning, and weight-related physical discomfort and body esteem. At the time of surgery, BMI was 58.9 kg/m².

Shortly after she underwent RYGB, her metformin was discontinued because blood glucose values improved to a range of 80 to 125 mg/dL. One month after surgery she was admitted with DKA; HbA1c at that time was 7.5%. At that time her clinical picture was consistent with insulinopenia and T1DM; analysis of serum for autoantibodies demonstrated elevated glucagon autoantibodies and islet cell antibodies. To determine

TABLE 1 Changes in Weight, Insulin Use, and Metabolic Indices After Bariatric Surgery

Variables	Patient A		Patient B	
	Before Surgery	12 mo After Surgery	Before Surgery	28 mo After Surgery
Weight (kg)	125	91	159	93
HbA1c (%)	8.6	8.8	6.3	10
Average insulin use				
IU/day	115	90	100 ^a	60
IU/kg/day	0.9	1.0	0.6 ^a	0.6
Low-density lipoprotein (mg/dL)	180	81	109	73
High-density lipoprotein (mg/dL)	32	45	41	59
Triglycerides (mg/dL)	198	188	86	58

^a Since initiation of insulin, which occurred after gastric bypass.

whether the autoimmune process was present before the RYGB, an islet cell antibody screen was also sent from stored serum obtained before surgery. This analysis identified elevation of the same autoantibodies. With the revised diagnosis of T1DM, a basal bolus insulin regimen was initiated.

At her last follow-up (28 months after surgery), BMI was 34.9 kg/m² (42% reduction). Postoperative changes in weight, HbA1c, average daily insulin use, and lipids are documented in Table 1. She is taking her insulin boluses postprandially. Hypoglycemic episodes occur 2 to 5 times per week. Since her initial DKA admission, she has had 2 visits to the emergency department for uncontrolled hyperglycemia and 1 admission for vomiting and dehydration. She is no longer on oral contraceptive pills and has regular menses. Her self-reported QoL across the first two postoperative years reflected net improvements in weight-related QoL and physical health that were clinically meaningful.^{18,19} However, her QoL scores temporarily decreased at 12 months, coinciding with interpersonal problems, concerns with excess skin, and reported stress related to diabetes management.

DISCUSSION

This case series is the first we know of that reports on the effects of RYGB and VSG on glycemic control in adolescents with T1DM. Both patients demonstrated a continued decrease in total daily insulin dosage during the first 3 to 12 months after surgery. The reduction in absolute insulin use probably resulted from an improvement in insulin resistance that occurred with weight loss. However, the insulin dosage per kilogram remained largely unchanged (Table 1).

There are only 2 published case series reporting outcomes of adults with T1DM after RYGB, and the data appear conflicting. Czupryniak et al reported on 3 patients who experienced significant

reductions in insulin use and HbA1c after RYGB.²¹ Another case series by Mendez et al reported on 3 patients; postoperatively all had suboptimal glucose control, and only 1 had a reduction in insulin use.²² The clinical course of our adolescents is consistent with the latter case series and suggests that unlike in patients with T2DM, glycemic control does not necessarily improve in patients with T1DM. Because of progressive islet cell destruction and consequent insulinopenia, patients with T1DM have ongoing dependency on exogenous insulin despite interventions aimed at improving insulin sensitivity.

An important consequence of RYGB that affects diabetes management is the change in glucose absorption kinetics. Others have documented higher and earlier postprandial glucose peaks after RYGB, presumably caused by rapid delivery of carbohydrate to the jejunum.^{23,24} The altered glucose kinetics may complicate matching of insulin administration with glucose excursions, which can lead to increased hyperglycemia or hypoglycemia. Patients may also choose to take insulin postprandially because of the risk of food intolerance and gastrointestinal symptoms. Taking insulin boluses postprandially has been associated with increased glucose variability and suboptimal postprandial glucose profiles in patients with T1DM.^{25,26}

Bariatric surgery does improve obesity-related comorbidities. RYGB- and VSG-induced weight loss significantly improves the lipid profile of previously obese patients within 1 year.^{27,28} Both our patients had a decrease in low-density lipoprotein and an increase in high-density lipoprotein levels after surgery (Table 1). Patient A also demonstrated dramatic improvement in his symptoms of OSA, which has been shown to be independently associated with CVD.^{29–31} Given that diabetes is a major cardiovascular risk factor, with dyslipidemia and OSA conferring additional risk,^{32–34}

bariatric surgery may help prevent development of future vascular complications. Finally, existing literature strongly indicates that adolescents who undergo RYGB show notable improvements in QoL.³⁵ Both our patients reported critical and positive changes in their day-to-day functioning in parallel with their improved health and weight status.

It is also of particular importance that in the setting of the current obesity epidemic it may become increasingly difficult to correctly diagnose T1DM. Before surgery, the diabetes type should be confirmed with islet cell autoantibodies to determine optimal management. It is an interesting observation that patient B had a higher risk for developing T1DM before surgery (positive autoantibodies) but clearly had a clinical phenotype of insulin resistance and met criteria for T2DM. She did not develop severe insulin deficiency until shortly after surgery. This is not uncommon, because patients with T1DM have islet cell antibody positivity before the development of diabetes symptoms. The stress from a major surgery may have triggered additional pancreatic decompensation.

CONCLUSIONS

Although RYGB and VSG lead to improvement of T2DM, the impact on T1DM is unclear. Despite significant weight loss, improvements in cardiovascular risk factors, and QoL, the surgeries do not necessarily lead to improved glycemic control. Optimal glycemic control still depends on patient compliance with diabetes care. Larger prospective studies are needed to better define the effect of bariatric surgery on a growing population of severely obese adolescents with T1DM.

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