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The Effects of Bariatric Surgery on Obese Patients with Type 2 Diabetes

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INTRODUCTION

Obesity is defined as a body mass index (BMI) of 30 kg/m^2 or greater. Its prevalence as a potential risk factor for diabetes continues to rise in the United States and is recognized globally as one of the most challenging contemporary threats to public health.[1] The reported percentage of obese US adults with type 2 diabetes mellitus (T2DM) is estimated between 25-30%. The worldwide prevalence of the disease in the adult population is projected to rise from 8.3% in 2010 to an estimated 10% by 2030. On the other hand, obesity is estimated to rise from 33% in 2005 to about 58% by 2030.[1]

Patients with T2DM have been shown to have a poor quality of life and poor health-related outcomes compared to the general population. When this disease is compounded with obesity, its complications have resulted in even poorer outcomes.[2] The increased risk of developing diabetes-related microvascular and macrovascular complications, including major cardiovascular events, neuropathy, and nephropathy, makes achieving glycemic and weight control crucial for halting disease progression and improving overall health and wellbeing.

Current treatments for type 2 diabetes are limited to glucose-lowering medications and lifestyle modifications. Over the years, several improvements have been made in pharmacotherapy for type 2 diabetes with various classes of oral medications including biguanides and glitazones which reduce insulin resistance, sulfonylureas and incretin mimetics which improve insulin secretions, and insulin and noninsulin injectables. Even with these medications, less than half of patients attain the American Diabetes Association (ADA) recommended HbA1c levels of less than 7%.[1,3] Lifestyle modifications are important, but

realistically, control of weight by diet and exercise alone is difficult to achieve as patients tend to regain the weight within a short period. Therefore, the use of bariatric surgery would improve obesity associated T2DM. The indications for bariatric surgery according to the current guideline from the National Institute of Health include BMI ≥ 40 kg/m^2, or BMI between 35 and 40 kg/m^2 with at least two obesity-related comorbidities of which diabetes is considered a key risk factor.[4]

Bariatric surgery including Roux-en-Y gastric bypass, sleeve gastrectomy, and adjustable gastric band may play a role in glycemic control by improving insulin secretion and sensitivity, specifically through improvement in the main incretin hormones known as glucagon-like peptide-1 (GLP-1) and gastric inhibitory peptide (GIP).[5] These surgical interventions have been shown to provide effective long-term treatment for patients by providing durable weight loss, improving obesity-related comorbidities and fostering better health outcomes.[2]

Achieving glycosylated hemoglobin levels below 7% can be very challenging in obese diabetic patients. Therefore, the effect of bariatric surgery compared to standard medical therapy alone in attaining this goal and thus improving health-related outcomes in these patients needs examination. To explore this treatment approach, medical literature on bariatric surgery, obesity and type 2 diabetes mellitus, including the impact of these surgical interventions on patients' overall health, were reviewed.

DISCUSSION

The idea of quality of life encompasses a broad multi-dimensional concept which consists of both positive and negative aspects of life of which health is without a doubt one of

the most important qualifiers.[1] Health-related outcomes for the context of this paper focuses on objective findings including weight loss, glucose homeostasis, control of blood pressure, and LDL cholesterol levels, improved physical fitness, and reduction in other risk factors for diabetes complications.

In a randomized, parallel-group, pragmatic clinical trial conducted by Halperin and colleagues, results showed that after 1 year, 58% of patients randomized to Roux-en-Y gastric bypass group (RYGB) achieved hemoglobin A1c levels below 6.5% compared to 16% of patients in the intensive medical and weight management program.[2] Though both treatments were shown to improve general quality of life measures, RYGB provided an even greater improvement in weight, fat mass, waist circumference, blood pressure, and triglyceride levels.[2] However, one limitation of the study was the small number of participants available for 1 year follow-up and the relatively low number of participants with diabetes-related comorbidities which limits its applicability to patients with more disease-related complications.

Type 2 diabetes mellitus is characterized by the development of insulin resistance and poor insulin sensitivity which results in progressive hyperglycemia and in some cases, subsequent microvascular and macrovascular complications.[5] Most patients with the disease are overweight or obese. Although lifestyle modification and oral medications improve glycemic levels, the disease progresses in majority of patients leading to the need for insulin therapy.[5] The Diabetes surgery study conducted on participants with poorly controlled diabetes showed weight loss in patients who underwent gastric bypass was 26.1% at 1-year post-op compared with 7.8% at 1 year for patients randomized to the lifestyle-medical management group.[6] In a metabolic sub study of the STAMPEDE trial, results showed that insulin sensitivity in noninsulin-

using participants increased at 24 months after bariatric surgery compared with no observed changes in participants in the intensive medical treatment group.[5] β-cell function also changed significantly within the same time period that changes in the percentages of truncal fat and body weight occurred.[5]

The metabolic effects from chronic glucose toxicity can be debilitating to normal organ function. Patients with type 2 diabetes have shown significantly higher levels of CA 19-9, a screening tool used to diagnose pancreatic cancer and a marker for pancreatic tissue damage caused by diabetes.[7] A 12 week follow up study by Tu and colleagues showed that CA 19-9 could be an effective indicator of insulin resistance and glucose metabolism in patients with obesity and type 2 diabetes.[7] The study showed clinical evidence that rapid metabolic control and improved glycemic control were attained after RYGB; improvements that might be linked to regulation of CA 19-9 levels in these patients. However, the study was limited by the small sample size and short follow up period. It was also unclear whether serum levels of CA 19-9 changed significantly in response to rapid improvements in glucose levels.[7]

An important determinant of health is physical fitness as good fitness is associated with reduced mortality and improved cardiometabolic health.[8] In a randomized parallel group trial, researchers used a six-minute walk test to evaluate fitness, self-reported physical activity, and cardiometabolic risk factor records in 38 patients with type 2 diabetes. At 18-24 months after randomization to RYGB or a medical therapy program, results showed improved physical activity after surgery compared to the medical group in which improvement in exercise levels was not fully sustained for a long period of time.[8] In contrast, the Short Form Health Survey SF-36 showed self-reported quality of life and physical function were similar between the two

groups over the follow-up period even though objective measures showed greater improvement in the RYGB group.[8]

Cardiovascular disease remains one of the primary causes of morbidity and mortality in patients with obesity and diabetes[9] due to plaque buildup leading to myocardial infarction and stroke. The Swedish Obese Subjects (SOS) study investigated the effect of bariatric surgery on cardiovascular events. The nonrandomized controlled trial involving 607 subjects concluded that bariatric surgery led to reduced incidence of fatal and nonfatal cardiovascular events.[9] The study found that in diabetic patients, the benefits of bariatric surgery with respect to myocardial infarctions were related to patients' baseline levels of serum total cholesterol and triglycerides with significantly greater benefit occurring in patients with higher lipid levels.[9]

In a retrospective observational matched cohort study of patients with severe obesity and diabetes who received usual care in 1 of 4 integrated healthcare systems, Fisher and colleagues tested the hypothesis that patients who underwent bariatric surgery would experience a lower incidence of coronary artery diseases and cerebrovascular events[10] when compared with their matched cohorts who received a combination of intensive lifestyle and medical treatment. The study found at years 1, 3, 5 and 7, incidences of macrovascular disease were 0.5%, 1.1%, 2.1% and 3.2% respectively after bariatric surgery while the incidence rates for the matched cohorts were 1.1%, 2.6%, 4.3% and 6.2%. These results were significant and showed improvements in cardiovascular risk scores as measured through validated tools such as the Framingham risk equation.[10]

The American Diabetes Association triple endpoint study for diabetes examined endpoints of A1c < 7.0%, low-density lipoprotein cholesterol less than 100 mg/dL, and systolic blood pressure less than 130 mmHg.[6] The Diabetes Surgery Study which involved participants from 4 sites in the United States and Taiwan, randomized participants to either RYGB or intensive lifestyle and medical management. The purpose was to analyze the durability of attaining the composite triple endpoint. In the first year after randomization, 50% in the RYGB group and 16% in the lifestyle-medical management group attained the composite triple end point. Results showed 29 of the 42 participants in the RYGB group who achieved A1c < 7% at 1 year maintained that level at the 5-year follow-up, whereas in the lifestyle-medical management group, only 7 of the 18 participants who achieved same A1c goal at 1 year maintained it at 5 years.[6] These endpoint improvements permitted reductions in lipid-lowering and antihypertensive medications. The randomized controlled follow-up study, larger group size, greater range of ethnic groups, and the inclusion of the full range of diabetic treatment goals makes the study generalizable.[6]

Reduction in diabetes medication and subsequent diabetes remission as a result of glycemic control have been attributed to lowered caloric intake after bariatric surgery. This improvement in dietary intake may lead to improved life expectancy in these patients who undergo surgical procedures. In one study by Schauer and colleagues, results showed that in addition to significant changes in body weight and glycemic levels that occurred after sleeve gastrectomy or gastric bypass compared to medical therapy alone, the use of diabetes and cardiovascular medications was reduced after bariatric procedures.[3] In a separate study, Schauer and colleagues developed the Markov transition model in order to compare bariatric

surgery versus no surgical treatment in severely obese patients with diabetes. Their findings showed that a hypothetical 45-year-old female with diabetes and BMI of 45 kg/m^2 with no other comorbidities would gain an additional 38.4 years in life expectancy with surgery versus 31.7 years without surgery.[11] A similar patient with diabetes and BMI of 45 kg/m^2 and history of HTN, CAD and CHF, would have a shorter life expectancy but still gain an additional 22.3 years with surgery versus 15.6 years without surgery. However, the results showed that this gain in life expectancy decreased as BMI increased at which point nonsurgical treatment was associated with a longer life expectancy at BMI above 62 kg/m^2.[11]

Studies have shown that after bariatric surgery, patients lose up to 25% of their body weight. For those with type 2 diabetes, about 87% can achieve better glucose control with HbA1c levels below 6.5% and fasting plasma glucose below 126 mg/dL at least 1-year post-op.[1] An observational follow-up study of a randomized clinical trial also found that at 5 years post-op, an estimated 42% in the gastric bypass group and 88% in the lifestyle-medical management group used noninsulin medication.[6] Partial remission indicated by HbA1c levels below 6.5% for 1 year without medications occurred in 35% of surgical participants and full remission indicated by levels below 6.0% without medications occurred in 16% of surgical patients by 2 years post-op.[6]

However, bariatric surgeries are not without risks. In a meta-analysis by Buchwald and colleagues which included 22,094 patients in 136 bariatric studies, the 30-day operative risks were 0.5% for RYGB and 0.1% for restrictive procedures such as sleeve gastrectomy and laparoscopic adjustable gastric band (LAGB).[4] Nutritional deficiencies, including vitamins A, D, E,

and B12, iron deficiency and protein-calorie malnutrition, occurred in about 30-70% of patients especially those who lost about 10% of their body weight in 1 month.[4]

CONCLUSION

In patients with Type 2 diabetes mellitus and BMIs 35 kg/m^2 or higher, evidence that bariatric surgeries provide good control of both obesity and T2DM is increasing.[4] Thus, bariatric surgery has become a viable option for diabetes management in obese patients. Nonetheless, these surgeries are not without serious adverse risks.

Larger randomized trials examining the effects of bariatric surgery in obese T2DM patients are needed in order to enhance prudent clinical decision making. Clinicians also need to educate themselves on the mechanisms by which various procedures improve T2DM control. Improved glycemic control is not due to weight loss alone but is also a result of glucose hormonal changes. Furthermore, the progressive nature of T2DM involves the gradual deterioration of pancreatic beta cells. Therefore, this deleterious process should be stopped by performing bariatric surgeries in obese type 2 diabetics early in the course of treatment in order to preserve their beta cell function[4], reduce complications, and promote quality of life outcomes.

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