Treating Diabetes With Surgery

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That type 2 diabetes remission may be induced by bariatric surgery in patients with grade 2 (body mass index [BMI] ≥35) and grade 3 (BMI ≥40) obesity soon after operation and preceding weight loss has stimulated new ideas regarding diabetes treatment. Some investigators have proposed surgical intervention for patients with type 2 diabetes with grade 1 obesity (BMI ≥30), with some even proposing bariatric surgery as the primary treatment for patients with type 2 diabetes and BMI as low as 27. The term metabolic surgery is commonly used to describe this class of surgical procedures because they primarily modify a patient’s physiology for the better as opposed to simply correcting or removing an anatomic defect.

Extending surgical treatment to these categories of patients has substantial implications for the health care system. In 2012, data from the National Health and Nutrition Examination Survey (NHANES)3 indicated that 69.2% of the US population had a BMI of 25 or higher, 35.9% had a BMI of 30 or higher, 15.5% had a BMI of 35 or higher; and 6.3% had a BMI of 40 or higher. Approximately 20% of the US adult population has a BMI ranging from 30 to 35, and the prevalence of type 2 diabetes in this population is approximately 20%. Thus, approximately 4% of the US population has a BMI ranging from 30 to 35 and diabetes. Any proposal to treat this large number of patients surgically must be carefully evaluated.

In this issue of JAMA, 2 reports directly address this proposed intervention. Ikramuddin and colleagues1 conducted a multinational, multicenter randomized controlled trial of 120 patients with poorly controlled type 2 diabetes and BMIs ranging from 30 to 39.9. All of the patients of this trial underwent lifestyle modification and intensive medical management for their obesity, diabetes, hypertension, and dyslipidemia using the Look AHEAD (Action for Health in Diabetes trial) protocol. Standardized Roux-en-Y gastric bypass was added to patients randomized to the intervention group. The primary end point assessed at 1 year was the triple end point consisting of the number of medications required to achieve this end point and weight loss. At 12 months, the composite end point was achieved in 28 patients (49%) in the gastric bypass group (95% CI, 36%-63%) and in 11 patients (19%) in the lifestyle-medical management group (95% CI, 10%-32%). The largest effect was on diabetes with control of dyslipidemia and hypertension being similar between the 2 groups. Three fewer medications were required to achieve control of glycemia, dyslipidemia, and hypertension in the surgical group compared with the lifestyle-medical management group. In addition, weight loss was greater in the surgical group (26.1% of baseline body weight) than in the lifestyle-medical management group (loss of 7.9% of baseline body weight).

However, the favorable metabolic outcome following gastric bypass surgery was offset in part by a higher complication rate in the surgical group. One of the 60 surgical patients experienced multiple perioperative complications that led to anoxic brain injury, which presumably will be permanent. Other reported surgical complications during the 1-year follow-up included nutritional deficiencies, symptoms of hypoglycemia, anastomotic stricture, bleeding, bowel obstruction, and other complications. Although the induction of remission of type 2 diabetes is regarded as a positive event in the health of an individual patient or a population of patients, several issues remain unresolved.

First, the overall health benefit should be considered. The frequency and severity of complications reported by Ikramuddin et al1 is problematic. The devastating complication of anoxic brain injury in a single patient among a total of 60 patients’ operations performed by an experienced surgeon demonstrates that, although these events are rare in large series of bariatric operations, severe complications occur. For example, the Longitudinal Assessment of Bariatric Surgery (LABS) Consortium6 reported a combined end point of complications of 4.3% but a mortality rate of 0.2% among 4776 participants with a mean BMI of 46.5 following Roux-en-Y gastric bypass or laparoscopic gastric banding. The LABS trial did not investigate its effect on patients with BMIs lower than 35. A very large series will be required to determine the perioperative safety of gastric bypass in the population of patients with BMIs lower than 35.

Second, it will be important to establish the long-term safety and the prevalence and severity of long-term complications. Intensive medical management of type 2 diabetes is not without adverse effects and as recently reported7 may not be without harm. Hypoglycemia and nutritional deficiencies cannot be assumed to be limited to 1 year of follow-up after bariatric operations. Other potential complications include marginal ulcer, intestinal obstruction, kidney stones, and fractures. Such complications may prove to be more problematic over time and

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require surveillance, appropriate supplementation, and potential interventions.

Third, the goal for improving glucose and other risk factors in type 2 diabetes is to reduce the future risk for microvascular and macrovascular complications. Induction of remission of type 2 diabetes has been reported to occur from 42% to greater than 80% of patients following bariatric surgery. Recurrence of type 2 diabetes has been reported in as many as 50% of patients who initially experienced remission. The diabetes recurrence rate following specific procedures such as Roux-en-Y gastric bypass, as well as the long-term benefit to patients who experience a temporary remission of diabetes remain to be defined.

Fourth, the economic ramifications of bariatric surgery in this population also must be evaluated. Diabetes is a chronic disease with multiple secondary health problems. The estimated cost of diagnosed diabetes in 2012 is $176 billion in direct medical costs and $69 billion in reduced productivity. Identification of the short- and long-term cost effects of surgical intervention for type 2 diabetes is exceedingly difficult because of the complexities and challenges associated with identification of all health care services provided to a given patient or population of patients.

The report by Ikramuddin et al adds to the bariatric surgery literature in important ways. These investigators used a widely accepted protocol for intensive medical management and assessed an end point considered optimal by the American Diabetes Association. The study was multicenter and multisurgeon and assessed outcomes that were of a single operation, the Roux-en-Y gastric bypass. This study design overcomes the limitations of prior randomized trials of bariatric surgery that lacked these features and had outcomes less generalizable than those reported by Ikramuddin.

Another report in this issue of JAMA is a systematic review from Maggard-Gibbons and colleagues investigating surgical intervention for weight loss and diabetes control among patients with BMI of 30 to 35. The investigators could only find 3 randomized trials enrolling a total of 290 patients that approximated these criteria. Individual patient data were available in 1 of these trials in which 13 patient had diabetes and BMIs of 30 to 35. Thus, very limited evidence available addressing surgical outcomes for patients at this weight led these investigators to alter their planned search criteria. For example, even though Maggard-Gibbons and colleagues wanted to determine the outcomes for patients with BMIs of 30 to 35, they included trials involving patients with BMIs of 35 or higher, as were indirect sources of evidence for which the results of surgical and medical outcomes were reported in separate studies. This analysis suggested that among patients with BMIs of 30 to 35 and diabetes, surgical intervention in comparison with nonsurgical treatment may be associated with greater short-term weight loss and better glucose outcomes. Few data were available reporting outcomes including complications beyond 2 years. Maggard-Gibbons et al concluded that the evidence was insufficient to reach conclusions regarding the appropriate use of bariatric surgery in this population.

Despite a substantial effort to standardize the methodology for the performance of systematic reviews, modification of the search criteria to determine which studies should be used as evidence is necessary. The difficulties encountered by Maggard-Gibbons et al in trying to answer an important clinical question highlight the problems associated with systematic reviews. Too limited inclusion criteria result in no guidance for clinicians caring for certain patients and criteria that are too broad lead to recommendations that represent expert opinion. Expert opinion cannot be viewed as evidence or serve as the basis for practice guidelines.

Recent large-scale trials of intensive medical management for obesity and diabetes have been disappointing. Substantial resources are required to reach modest weight loss and diabetes control. Bariatric surgery does result in substantial weight loss with excellent diabetes control but is offset by initial high cost and risks of surgical complications. The optimal approach for treatment of obesity and diabetes remains unknown. The answer will only come from more well-designed, randomized trials such as that performed by Ikramuddin et al that provide definitive answers.

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REFERENCES