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# Bariatric Surgery for Type 2 Diabetes Getting Closer to the Long-term Goal

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## JAMA SURGERY

### Three-Year Outcomes of Bariatric Surgery vs Lifestyle Intervention for Type 2 Diabetes Mellitus Treatment: A Randomized Clinical Trial

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**IMPORTANCE** Questions remain about the role and durability of bariatric surgery for type 2 diabetes mellitus (T2DM).

**OBJECTIVE** To compare the remission of T2DM following surgical and nonsurgical treatments.

**DESIGN, SETTING, AND PARTICIPANTS** In this 3-arm randomized clinical trial conducted at the University of Pittsburgh Medical Center from October 1, 2009, to June 26, 2014, in Pittsburgh, Pennsylvania, outcomes were assessed 3 years after treating 61 obese participants aged 25 to 55 years with T2DM. Analysis was conducted with an intent-to-treat population.

**INTERVENTIONS** Participants were randomized to either an intensive lifestyle weight loss intervention for 1 year followed by a low-level lifestyle intervention for 2 years or surgical treatments (Roux-en-Y gastric bypass [RYGB] or laparoscopic adjustable gastric banding [LAGB]) followed by low-level lifestyle intervention in years 2 and 3.

**MAIN OUTCOMES AND MEASURES** Primary end points were partial and complete T2DM remission and secondary end points included diabetes medications and weight change.

**RESULTS** Body mass index (calculated as weight in kilograms divided by height in meters squared) was less than 35 for 26 participants (43%), 50 (82%) were women, and 13 (21%) were African American. Mean (SD) values were 100.5 (13.7) kg for weight, 47.3 (6.6) years for age, 7.8% (1.9%) for hemoglobin A<sub>1c</sub> level, and 171.3 (72.5) mg/dL for fasting plasma glucose level. Partial or complete T2DM remission was achieved by 40% (n = 8) of RYGB, 29% (n = 6) of LAGB, and no intensive lifestyle weight loss intervention participants (P = .004). The use of diabetes medications was reduced more in the surgical groups than the lifestyle intervention-alone group, with 65% of RYGB, 33% of LAGB, and none of the intensive lifestyle weight loss intervention participants going from using insulin or oral medication at baseline to no medication at year 3 (P < .001). Mean (SE) reductions in percentage of body weight at 3 years were the greatest after RYGB at 25.0% (2.0%), followed by LAGB at 15.0% (2.0%) and lifestyle treatment at 5.7% (2.4%) (P < .01).

**CONCLUSIONS AND RELEVANCE** Among obese participants with T2DM, bariatric surgery with 2 years of an adjunctive low-level lifestyle intervention resulted in more disease remission than did lifestyle intervention alone.

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**Bariatric surgery is more effective** than intensive medical or lifestyle interventions for inducing weight loss and remission of type 2 diabetes as demonstrated in randomized clinical trials for patients with obesity—even for those with relatively lower body mass



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index (BMI), ranging from 30.0 to 34.9 (calculated as weight in kilograms divided by height in meters squared).<sup>1</sup> Bariatric procedures may be associated with better survival and fewer cardiovascular events compared with nonsurgical management of patients with diabetes as shown in long-term observational studies; but even the best observational studies may not be definitive because of concerns about unmeasured confounding variables and selection bias. Thus, longer-term randomized clinical trials are also needed to provide definitive evidence of the durability and superiority of bariatric procedures compared with the best available medical and lifestyle treatment of type 2 diabetes.

In a recent study published in *JAMA Surgery*, Courcoulas and colleagues<sup>2</sup> randomized 61 adults with a BMI between 30 and 40 and type 2 diabetes to receive Roux-en-Y gastric bypass (RYGB), laparoscopic adjustable gastric band (LAGB) procedure, or an intensive lifestyle intervention for 1 year, followed by a low-level lifestyle intervention delivered to all 3 treatment groups in years 2 and 3. The primary outcome, partial or complete diabetes remission—defined as a hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) level less than 5.7% without taking any medications for diabetes—was achieved by 8 patients (40%) in the RYGB group, 6 (29%) in the LAGB group, and no patients in the intensive lifestyle group (P = .004). Improvements in diabetes control were particularly impressive for RYGB given that this group had the highest baseline HbA<sub>1c</sub> level (8.5% RYGB, 7.8% for LAGB, and 7.0% for lifestyle). At year 3, patients in the RYGB group also had greater weight loss, compared with the LAGB and lifestyle groups (−25% RYGB, −15% LAGB, and −5.7% for lifestyle; P < .01). The higher HbA<sub>1c</sub> levels in the RYGB group at baseline almost certainly means that those patients

had less endogenous insulin production than in the other 2 groups and were further along in the progressive beta-cell decline that accompanies diabetes, which likely explains the more rapid relapse of diabetes observed in the RYGB patients. Yet another important aspect of this study was that 26 patients (43%) had a BMI less than 35, which further supports bariatric surgery as an effective treatment for diabetes in patients with mild to moderate obesity.

These findings are similar to the results of the STAMPEDE trial, in which 150 adults at a single medical center with a BMI between 27 and 43 and uncontrolled diabetes were randomized to receive intensive medical therapy alone or to receive intensive medical therapy plus RYGB or sleeve gastrectomy.<sup>3</sup> Patients randomized to undergo bariatric surgery had significantly greater improvements in weight, diabetes control, and quality of life at 3 years. Patients randomized to receive RYGB lost more weight and improved their diabetes more than those randomized to receive sleeve gastrectomy.

In addition to providing solid evidence on the efficacy of surgery relative to intensive lifestyle treatment, these studies and others indicate that RYGB is superior to both LAGB and sleeve gastrectomy in the initial control of type 2 diabetes.<sup>4</sup> In particular, the experience of Courcoulas et al<sup>2</sup> with LAGB is likely to be the best-case scenario: their patients received intensive follow-up and lifestyle intervention in a clinical trial setting. Although LAGB is often characterized as less invasive and low risk, this characterization overlooks the longer-term risks of revisions and reoperations associated with the procedure. Two recently published studies of the 5- and 7-year experience of patients who had LAGB indicate that 15% to 16% will have their band removed or revised,<sup>5,6</sup> with 29% experiencing a complication during their reoperation (a 19-fold higher rate of complications than during the original procedure).<sup>6</sup> Perhaps LAGB still has a role for some patients who seek a reversible treatment for obesity and diabetes, but it is probably time to remove the "low-risk" label for this procedure.

As observed in the reports by Courcoulas et al<sup>2</sup> and Schauer et al,<sup>3</sup> some weight regain is expected with all bariatric procedures, but it is still unclear how much and how soon, particularly among patients who undergo sleeve gastrectomy, for whom there are few to no long-term data available owing to its rapid introduction into main-

stream bariatric practice. Furthermore, diabetes is also likely to worsen or recur in many patients who undergo bariatric procedures during long-term follow-up, and prior studies have shown that patients with less severe diabetes (ie, those with recent onset, lower HbA<sub>1c</sub> levels, and no insulin use) at the time of surgery are more likely to achieve remission or control of diabetes and avoid relapse.<sup>7</sup> What is needed now is long-term evidence that surgery can durably improve glycemic control and reduce the risk of microvascular and macrovascular events. Toward that goal, 4 research groups (Cleveland Clinic, Joslin Diabetes Center in Boston, the University of Pittsburgh, and the University of Washington) that have completed 1- to 3-year randomized trials of bariatric procedures compared with medical and lifestyle management of diabetes have now formed the Alliance of Randomized Trials of Medicine vs Metabolic Surgery in Type 2 Diabetes (ARMMS-T2D) Consortium with planned follow-up of about 300 randomized participants through 7 years. In the next few years, large observational studies involving health care databases will shed further light on questions related to durability of weight loss and glycemic control and help identify the specific patient subgroups that are most likely to benefit—or be harmed—from bariatric procedures.

The report by Courcoulas et al<sup>2</sup> raises the issue of how to optimally manage patients with diabetes after bariatric surgery. As the authors report, 4 patients who had undergone bariatric surgical procedures (11%) had relapse of diabetes by 3 years. Many prior articles have focused on "cure" or remission of diabetes after bariatric surgery, but given that one-third of patients will experience diabetes relapse by 5 years,<sup>7</sup> it is unclear whether physicians and patients should continue to focus on the discontinuation of all diabetes medications as a primary goal. Metformin should be stopped before surgery because of the risk of lactic acidosis, but because metformin is not associated with a risk for hypoglycemia or weight gain, this medication could be reintroduced in most patients with hyperglycemia after bariatric procedures, unless gastrointestinal adverse effects or contraindications such as renal failure are present.<sup>8</sup> Given what is currently known, the most important question is not whether bariatric surgery alone is superior to medical therapy alone. The question is: how can surgical and medical therapy be used together to keep this high-risk population of patients healthy longer?

#### ARTICLE INFORMATION

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#### REFERENCES

- Gloy VL, Briel M, Bhatt DL, et al. Bariatric surgery versus non-surgical treatment for obesity: a systematic review and meta-analysis of randomised controlled trials. *BMJ*. 2013;347:f5934.
- Courcoulas AP, Belle SH, Neiberg RH, et al. Three-year outcomes of bariatric surgery vs lifestyle intervention for type 2 diabetes mellitus treatment: a randomized clinical trial. *JAMA Surg*. 2015;150(10):931-940.
- Schauer PR, Bhatt DL, Kirwan JP, et al; STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy for diabetes: 3-year outcomes. *N Engl J Med*. 2014;370(21):2002-2013.
- Hutter MM, Schirmer BD, Jones DB, et al. First report from the American College of Surgeons Bariatric Surgery Center Network: laparoscopic sleeve gastrectomy has morbidity and effectiveness positioned between the band and the bypass. *Ann Surg*. 2011;254(3):410-420.
- Dixon JB, Eaton LL, Vincent V, Michaelson R. LAP-BAND for BMI 30-40: 5-year health outcomes from the multicenter pivotal study. *Int J Obes (Lond)*. 2016;40(2):291-298.
- Altieri MS, Yang J, Telem DA, et al. Lap band outcomes from 19,221 patients across centers and over a decade within the state of New York [published online July 23, 2015]. *Surg Endosc*. doi:10.1007/s00464-015-4402-8.
- Arterburn DE, Bogart A, Sherwood NE, et al. A multisite study of long-term remission and relapse of type 2 diabetes mellitus following gastric bypass. *Obes Surg*. 2013;23(1):93-102.
- Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient: 2013 update: cosponsored by American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery. *Obesity (Silver Spring)*. 2013;21(suppl 1):S1-S27.