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An obesity remedy for diabetes

For obese patients with type 2 diabetes, surgery may be the best bet.

PRACTICE CHANGER

Consider bariatric surgery for patients with diabetes who are obese; surgery is associated with higher remission rates than medical therapy, regardless of the amount of weight lost.[1]

STRENGTH OF RECOMMENDATION

B: Based on a single nonblinded randomized controlled trial (RCT).

Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. *N Engl J Med.* 2012;366:1577-1585.

ILLUSTRATIVE CASE

A 43-year-old woman with a body mass index (BMI) of 38 kg/m^2 and a 5-year history of diabetes has a glycated hemoglobin (HbA1c) of 8.5% despite the use of oral hypoglycemic agents. Should you talk to her about gastric bypass surgery to treat her diabetes?

Diet and exercise are the first steps in addressing diabetes, but these interventions are often unsuccessful. The International Diabetes Federation (IDF) recommends consideration of bariatric surgery for patients who have a BMI >35 kg/m^2 and diabetes that lifestyle modification and pharmacotherapy have failed to control.[2]

Surgery for diabetes: Is there ample evidence?

Until recently, the IDF's recommendation was based on observational data and a single RCT that found increased resolution of diabetes following various bariatric procedures.[3-5] In the study detailed in this PURL, Mingrone et al took another look.

STUDY SUMMARY

Surgery led to higher remission rates

This single-center, nonblinded RCT compared 2 malabsorptive procedures—Roux-en-Y gastric bypass and biliopancreatic diversion, a more complicated procedure not commonly performed—with medical therapy.[1] The primary outcome was the rate of diabetes remission at 2 years, defined as a fasting glucose level <100 mg/dL and an HbA1c <6.5%. Changes in BMI and cholesterol levels were among the secondary endpoints.

To be eligible, patients had to be between the ages of 30 and 60 years and have a BMI ≥35 kg/m^2, a history of type 2 diabetes ≥5 years, and an HbA1c ≥7.0%. Exclusion criteria included a history of type 1 diabetes, diabetes caused by an underlying disease or steroid treatment, previous bariatric surgery, pregnancy, diabetic complications, other severe medical conditions, and acute hospitalization. Both the gastric bypass and biliopancreatic diversion procedures were performed by independent surgical teams.

Participants (N=60) were evaluated at baseline and at 1, 3, 6, 9, 12, and 24 months after the intervention by a team that included a dietician, a nurse, and a physician. All received a diet plan with daily exercise designed by their team. Those in the medical therapy group had their medications titrated to reach a goal HbA1c <7%. Pharmacotherapy was stopped based on normalization of blood sugars or HbA1c <6.5%.

Within 15 days postsurgery, patients in both surgical arms had their diabetes medications stopped based on their blood glucose levels.

At 2 years, 75% of the patients in the gastric bypass arm and 95% of the patients in the biliopancreatic diversion arm (number needed to treat=1.3 and 1, respectively) were considered to be in diabetes remission, defined as a fasting blood sugar of <100 mg/dL and an HbA1c <6.5% after one year without pharmacotherapy. (Notably, this differs from that of the American Diabetes Association, which requires an HbA1c <6.0% for classification as complete remission.) None of the patients in the medical therapy arm was in remission at the 2-year mark.

On average, blood sugars normalized for gastric bypass patients by 10±2 months, vs 4±1 months for biliopancreatic diversion patients (P=.01). The average HbA1c at the end of 2 years was significantly different among all 3 groups (6.35%±1.42 for those undergoing gastric bypass, 4.95%±0.49 for the biliopancreatic diversion group, and 7.69%±0.57 for the medical therapy group), as was the change in HbA1c from baseline (**TABLE**). Changes in BMI and the number of patients who achieved normalization of total cholesterol were similar for both surgical groups. Interestingly, neither baseline BMI nor amount of weight lost or pre-enrollment duration of diabetes were predictors of diabetes remission or normalization of fasting glucose levels.

There were no deaths associated with this study. There were 2 adverse events requiring reoperation: an incisional hernia in a patient in the biliopancreatic diversion group and an intestinal obstruction in a patient in the gastric bypass group. Six patients in the biliopancreatic diversion arm developed metabolic abnormalities, including iron deficiency anemia, hypoalbuminemia, osteopenia, and osteoporosis. In the gastric bypass arm, 2 patients developed iron deficiency anemia.

WHAT'S NEW?

Evidence of efficacy has grown

This is the first RCT to evaluate biliopancreatic diversion and only the second to evaluate gastric bypass as strategies for controlling diabetes. Similar findings were demonstrated at 12 months in an RCT of 150 obese patients with diabetes in which intensive medical therapy was compared with either gastric bypass or sleeve gastrectomy,[6] published concurrently with the Mingrone study. Like the Mingrone study, this study found that for select patients with diabetes, surgery may lead to better outcomes than medical management alone.

CAVEATS

Long-term effect is still uncertain

The long-term efficacy of surgery as a way to manage diabetes remains uncertain. Patients in this study were followed for just 2 years and the outcomes were metabolic measures rather than morbidity and mortality. A recent prospective observational study following patients for 6 years after gastric bypass found that the rate of remission for diabetes was 75% (95% confidence interval (CI), 63%-87%) at 2 years but dropped to 62% (95% CI, 49%-75%) at 6 years[7]

A larger study (N=4047) of longer duration—the Swedish Obese Subjects (SOS) cohort study —found a considerably larger drop: The diabetes remission rate for those who had surgery went from 72% at 2 years to 36% at 10-year follow-up, but that was still higher than the 10-year remission rate (13%) for the matched controls.[4] It is still not clear exactly how long diabetic remission lasts after bariatric surgery or what effect a 10-year respite from the disease will have on the long-term morbidity and mortality of patients with diabetes.

Surgical risks. In small studies such as the one by Mingrone et al,[1] it can be difficult to see the full extent of surgical complications. The much larger SOS study found low mortality rates (0.25%). But 13% of those who underwent bariatric surgery had postoperative complications (number needed to harm = 8), with 2.2% of patients requiring reoperation.[4] Additionally, women who become pregnant after bariatric surgery are at increased risk for internal hernias or bowel obstruction during pregnancy.[8]

Furthermore, malabsorptive-type surgeries are known to cause nutritional deficiencies, leading to disorders including anemia and osteoporosis.[6] Importantly, while women of childbearing-age who un-

TABLE

Surgery vs medical therapy for diabetes: Gastric bypass and biliopancreatic diversion are more effective

	Gastric bypass (n=20)	Biliopancreatic diversion (n=20)	Medical therapy (n=20)
HbA1c at 2 years (%)	6.35±1.42* (n=19)	4.95±0.49 (n=19)	7.69±0.57 (n=18)
HbA1c change from baseline* (%)	–25.18±20.89	–43.01±9.64	–8.39±9.93
BMI change from baseline* (%)	-33.31±7.88	-33.82±10.17*	-4.73±6.37
Total cholesterol normalization† (%)	100*	100*	27.3

BMI, body mass index.

*P<0.01 for post hoc analysis comparing surgical arm to medical therapy.

†Normalization of cholesterol was defined as a total cholesterol <201 mg/dL and HDL >40 mg/dL in men and >50 mg/dL in women (personal communication from author).

dergo bariatric surgery decrease their risk of developing gestational hypertension and gestational diabetes, they are more likely to have nutritional deficiencies during pregnancy and to have children with these deficiencies.[8]

CHALLENGES TO IMPLEMENTATION

The ideal candidate remains unclear

It is still not clear from this study which patients should be referred for bariatric surgery. Historically, BMI has been used as the main indication for bariatric surgery, but this and other, studies have found that remission of diabetes is independent of BMI and the amount of weight lost.[9] A predictive 10-point Diabetes Surgery Score has recently been developed: It uses age, BMI, duration of diabetes, and C-peptide levels to predict the likelihood of diabetes remission after surgery.[10] This scoring system has yet to be validated in non-Asian patients, and a threshold for recommending surgery has been not established. However, this tool indicates that younger patients with a shorter duration of diabetes (which was not a factor in the outcome of the Mingrone study) and no baseline use of insulin are most likely to benefit from surgery. Thus, these patients may be the ones we need to consider referring first.

Cost of surgery. Several studies have shown that bariatric surgery is cost-effective for the treatment of diabetes, and saves money after approximately 5 years.[11,12] However, patients with diabetes and obesity may be uninsured or underinsured, and have high out-of-pocket costs. One challenge will be to ensure that surgery is a viable option for patients with financial constraints. JFP

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