

Evaluating the Benefits of Treating Type 2 Diabetes with Bariatric Surgery

An Endocrine Society Statement to Providers on Study Findings Related To Medical versus Surgical Treatment of Obese Patients with Type 2 Diabetes

This week's (March 26, 2012) issue of the *New England Journal of Medicine* includes two randomized controlled trials reporting superior weight loss and diabetes remission for surgical compared to medical treatment of obese patients with type 2 diabetes.

Observational studies have suggested that weight loss surgery can rapidly improve glycemic control and even produce remission of diabetes in severely obese patients with type 2 diabetes. This improvement and/or remission of diabetes is noted before meaningful weight loss occurs, and is thought to be due to a weight-loss independent change in the incretin hormone milieu as a result of the alteration in intestinal anatomy. Complete remission is defined as a fasting glucose level below 101 mg per deciliter and a glycated hemoglobin level of less than 6.0% for at least 1 year without active pharmacologic therapy. Until now, however, there has been a paucity of randomized controlled trials showing greater efficacy for surgical versus medical therapy, and for the variety of weight loss procedures available.

The two studies published this week are each single center, randomized, non-blinded, controlled trials evaluating surgery versus medical treatment in obese patients with type 2 diabetes whose glycated hemoglobin level was >7.0%. Mingrone et al. randomized 60 patients with BMI ≥ 35 kg/m² or more and at least 5 years of diabetes to medical therapy or either gastric bypass or the more malabsorptive biliopancreatic diversion, with 2 year follow-up. They found complete remission of diabetes at 2 years had occurred in none of the medically treated group versus 75% in the gastric bypass group and 95% in the biliopancreatic diversion group. Schauer et al. randomized 150 patients with BMI of 27-43 kg/m² to medical therapy alone or medical therapy plus Roux-en-Y gastric bypass or sleeve gastrectomy. After one year, complete remission of diabetes was seen in 12% of the medically treated group versus 42% in the gastric bypass group and 37% in the sleeve gastrectomy group.

In interpreting these findings, The Endocrine Society notes the differences between the two studies which likely contribute to the difference in magnitude of the results:

- The BMI of the patients in the Schauer study started at a BMI of as low as 27 and was restricted to up to 43, whereas the Mingrone study accepted patients with BMI over 35 kg/m². This may have affected remission rates of diabetes even though the studies report that preoperative BMI did not predict control of diabetes after surgery. While this is certainly the case,

severity of diabetes is influenced by BMI and thus the relationship between BMI and remission is complex.

- The Schauer study reports an average diabetes duration of 8 years and an average preoperative glycated hemoglobin level of 8.9 to 9.5%, with 44% of patients using insulin and using an average of nearly three diabetes agents. The Mingrone study accepted patients with at least 5 years of diabetes and an average diabetes duration of approximately 6 years with over half on three or more diabetes medications. There is evidence to suggest that the longer a patient has diabetes the less likely that remission will occur after weight loss surgery. The differences in remission rates between the two studies reflect several factors including the duration of diabetes.
- The procedures themselves, being malabsorptive (biliopancreatic diversion) or primarily restrictive (sleeve gastrectomy) or both (gastric bypass) are known to differ in diabetes remission rates. Notably, the more malabsorptive procedures seem to produce a higher rate of diabetes remission. This also impacts the difference in remission rates between the two studies.

Importantly, these studies are relatively short-term. Future randomized controlled trials that follow patients for over 2 years will be required to understand the differences in long term remission of diabetes.

Despite these reservations, the findings strongly favor surgical over medical intervention for both weight loss and remission of diabetes in severely obese patients. However, what these studies do not highlight is the risks of surgery, specifically the short and long term surgical, nutritional and metabolic complications. These include but are not limited to anastomotic leak, ulcer, stricture and fistula and internal hernia in addition to iron deficiency and anemia, vitamins B12 and thiamine deficiencies, copper deficiency and metabolic bone disease.

In interpreting these two studies, it should be noted that the numbers of patients in each study was relatively small, and the subjects were highly selected. . Moreover, both studies were conducted in bariatric surgical centers where the surgeons and medical personnel are experienced in the care of patients with severe obesity and consequently peri- and post-operative adverse events are low (where reported). In both studies the medical treatment approach was quite successful as practiced under study conditions and in the hands of experts, resulting in substantial average reduction in glycated hemoglobin and weight loss despite the continued use of hypoglycemic agents that usually cause weight gain.

Sustained long-term benefits will require maintenance of the metabolic changes achieved. Bariatric surgery is not a guarantee of successful weight loss and maintenance. In view of the progressive nature of beta-cell failure in the natural history of type 2 diabetes, only long-term studies can establish the ability of surgery to impact quality of life and mortality in type 2 diabetes. Future research should address the effectiveness of intensive postoperative nutritional and endocrine care in reducing morbidity and mortality from obesity-associated chronic diseases. Medical treatment has shown evidence that tight control of diabetes reduces the progression to secondary manifestations of diabetes such as retinopathy, neuropathy, and nephropathy. Therefore it is likely that remission of diabetes even if temporary will still lead to a reduction in the progression to secondary complications of diabetes, which would be an important outcome of weight loss surgery.

The Endocrine Society recommends that practitioners consider several factors in recommending surgery for their obese patients with type 2 diabetes. These include the patient's BMI and age, the number of years of diabetes, and an assessment of the ability to comply with the long-term lifestyle changes that are required to maximize success of surgery and minimize complications. Importantly, shared decision-making is critical in making a decision about bariatric surgery. The success of weight loss surgery in patients with obesity and diabetes ultimately depends on the partnership of patient, endocrinologist, surgeon, and a support team in the continuum of the long-term care of the patient.

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