

## EDITORIAL



## Surgery or Medical Therapy for Obese Patients with Type 2 Diabetes?

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Type 2 diabetes is one of the fastest growing epidemics in human history and is closely associated with obesity.<sup>1</sup> Furthermore, the disease has multiple manifestations and is associated with progressive beta-cell failure.<sup>2</sup> Although lifestyle measures, including weight loss and physical activity, should be first-line treatment, success is difficult to achieve, and pharmaceutical intervention is almost always required.

Because of the multiplicity of causal factors involved, it is unrealistic to expect that a patient will achieve excellent glycemic control with any single oral hypoglycemic agent or any combination of agents.<sup>3</sup> The progressive nature of type 2 diabetes requires ongoing assessment of metabolic control and usually leads to an intensification of therapy with increasing doses of hypoglycemic agents, including insulin.<sup>4</sup>

Existing algorithms, such as that from the American Diabetes Association,<sup>4</sup> may actually set up clinicians for therapeutic failure. Each algorithmic step occurs because the preceding recommendation has failed, with the path finally ending with the administration of insulin, often combined with one or more oral agents. A frequent outcome of such therapy is weight gain, which is counterintuitive for the treatment of patients with type 2 diabetes.

Who could predict years after the discovery of insulin that surgeons would be challenging the physician's territory for treating diabetes?<sup>5</sup> In two articles,<sup>6,7</sup> investigators now describe the results of standard or intensive medical care versus bariatric surgery in severely obese patients with type 2 diabetes. Until now, only one randomized, controlled trial has shown the superiority of surgery (gastric banding) over medical care.<sup>8</sup>

The two new randomized, controlled trials published here provide further evidence that surgery can be more efficient than either standard or intensive medical treatment alone.

In one of the studies, Mingrone et al.<sup>6</sup> assigned patients to undergo Roux-en-Y gastric bypass, biliopancreatic diversion, or standard medical therapy. After 2 years, patients who had undergone either of the two surgical procedures had better glycemic control than did those receiving medical therapy. Rates of complete remission of diabetes (as defined by Buse et al.<sup>9</sup>) were 75% for gastric bypass and 95% for biliopancreatic diversion, as compared with no remissions for medical therapy. In the other study, Schauer et al.<sup>7</sup> compared intensive medical therapy with gastric bypass or sleeve gastrectomy. After 1 year, the primary end point, a glycated hemoglobin level of 6% or less, was achieved in 12% of patients in the medical-therapy group versus 42% in the gastric-bypass group and 37% in the sleeve-gastrectomy group.

In both studies,<sup>6,7</sup> bariatric surgery induced remission and was associated with a significant improvement in metabolic control over and above medical therapy, both conventional and intensive. Although type 2 diabetes has been the domain of physicians, surgeons may now be able to claim greater success in achieving improved metabolic control.

Is surgery, then, the universal panacea for obese patients with type 2 diabetes? We would answer, not yet. All controlled surgical studies to date have been short-term and have involved a relatively small number of patients. Will the results of bariatric surgery be as good in routine practice? The long-term benefits have yet to be

proved, although there is suggestive evidence of cardiovascular benefit and prolonged improvement in glycemia on the basis of the Swedish Obese Subjects (SOS) study (ClinicalTrials.gov number, NCT01479452).<sup>10,11</sup>

Surgery also is not without hazards in the perioperative period, particularly in the case of biliopancreatic diversion, although in practiced hands morbidity is low.<sup>3</sup> There are also potential long-term problems from micronutrient deficiencies.<sup>3</sup> Some patients are also unable to cope psychologically.

There is also the problem of “remission” versus “cure.”<sup>9</sup> Type 2 diabetes is often progressive, and worsening of glycemic control over time is likely in many patients. However, some years of improved glycemia may well result in less microvascular disease.<sup>4</sup> The final question, which is as yet untested, is whether bariatric surgery is suitable for all obese patients with type 2 diabetes, even those with a lower body-mass index.<sup>3</sup> Despite these reservations, it is not surprising that bariatric surgery has had increasing prominence in diabetes management, particularly given its dramatic effect on glycemic control independent of weight loss.

In a position statement released in 2011,<sup>3</sup> the International Diabetes Federation recognized bariatric surgery as an appropriate treatment for obese patients with type 2 diabetes in whom recommended glycemic targets are not reached with available medical therapies, especially when the patient has major coexisting illnesses, such as hypertension and dyslipidemia. That statement also recommended the inclusion of bariatric surgery in future algorithms for the treatment of type 2 diabetes.

The studies by Mingrone et al. and Schauer et al. are likely to have a major effect on future diabetes treatment. Nevertheless, more studies are needed, particularly those that may provide bet-

ter prediction of success and the expected duration of remission and long-term complications.

Meanwhile, the success of various types of bariatric surgery suggests that they should not be seen as a last resort. Such procedures might well be considered earlier in the treatment of obese patients with type 2 diabetes.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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This article (10.1056/NEJMe1202443) was published on March 26, 2012, at NEJM.org.

1. Chen L, Magliano DJ, Zimmet P. The worldwide epidemiology of type 2 diabetes mellitus — present and future perspectives. *Nat Rev Endocrinol* 2011 November 8 (Epub ahead of print).
2. U.K. Prospective Diabetes Study Group. U.K. Prospective Diabetes Study 16: overview of 6 years' therapy of type II diabetes: a progressive disease. *Diabetes* 1995;44:1249-58. [Erratum, *Diabetes* 1996;45:1655.]
3. Dixon JB, Zimmet P, Alberti KG, Rubino F. Bariatric surgery: an IDF statement for obese Type 2 diabetes. *Diabet Med* 2011; 28:628-42.
4. Nathan DM, Buse JB, Davidson MB, et al. Medical management of hyperglycaemia in type 2 diabetes mellitus: a consensus algorithm for the initiation and adjustment of therapy: a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetologia* 2009;52:17-30.
5. Zimmet P, Alberti KG, Rubino F, Dixon JB. IDF's view of bariatric surgery in type 2 diabetes. *Lancet* 2011;378:108-10.
6. Mingrone G, Panunzi S, De Gaetano A, et al. Bariatric surgery versus conventional medical therapy for type 2 diabetes. *N Engl J Med* 2012;366:1577-85.
7. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. *N Engl J Med* 2012;366:1567-76.
8. Dixon JB, O'Brien PE, Playfair J, et al. Adjustable gastric banding and conventional therapy for type 2 diabetes: a randomized controlled trial. *JAMA* 2008;299:316-23.
9. Buse JB, Caprio S, Cefalu WT, et al. How do we define cure of diabetes? *Diabetes Care* 2009;32:2133-5.
10. Sjöström L, Lindroos AK, Peltonen M, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med* 2004;351:2683-93.
11. Sjöström L, Peltonen M, Jacobson P, et al. Bariatric surgery and long-term cardiovascular events. *JAMA* 2012;307:56-65.

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