Bariatric Surgery or Medical Therapy for Obesity

TO THE EDITOR: Mingrone et al. and Schauer et al. (April 26 issue)\textsuperscript{1,2} report the results of rigorous randomized, controlled trials comparing various types of bariatric surgery with medical therapy for obesity-associated type 2 diabetes. However, we would like to raise the important issue of micronutrient assessment and management in patients undergoing bariatric surgery. The risk of deficiency (of thiamine; vitamins B\textsubscript{6}, B\textsubscript{12}, and D; calcium; iron; or copper, zinc, or both) is increasingly recognized after malabsorptive bariatric surgery, but these deficiencies may be inadequately diagnosed.\textsuperscript{3} For example, we recently described the incidence and prevalence of copper deficiency after Roux-en-Y gastric bypass surgery as 18.8\% and 9.6\%, respectively.\textsuperscript{4}

Consensus guidelines recommend that patients should be comprehensively monitored for micronutrient deficiencies after bariatric surgery.\textsuperscript{5} Unfortunately, the articles by Mingrone et al. and Schauer et al. do not describe such monitoring. Given the high prevalence of preoperative and postoperative deficiencies of specific nutrients,\textsuperscript{3} it is important for clinicians to be aware of these potential complications and to appropriately monitor and treat patients for deficiencies of vitamins, minerals, and trace elements after these increasingly common surgical procedures for obesity.

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TO THE EDITOR: Schauer et al. and Mingrone et al. report that bariatric surgery led to major improvements in metabolic control and remission of type 2 diabetes. According to the accompanying editorial by Zimmet and Alberti,\textsuperscript{1} these two studies “are likely to have a major effect on future diabetes treatment.” However, the beneficial role of a huge negative energy balance per se may have been neglected. In patients with type 2 diabetes, a very-low-calorie diet results in fast (within a few days), dramatic amelioration of metabolic control, with eventual reversal of the diabetic state.\textsuperscript{2}

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state. Similar striking results have also been observed in very obese patients with type 2 diabetes after only 1 week of a very-low-calorie diet.

In expert hands, a very-low-calorie diet is a very effective, reasonably safe, and reversible treatment for patients with type 2 diabetes. “The inclusion of bariatric surgery in future algorithms for the treatment of type 2 diabetes,” as stated by Zimmet and Alberti, should require controlled trials in which the benchmark medical therapy to which bariatric surgery is compared includes treatment with a very-low-calorie diet.

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TO THE EDITOR: Schauer et al. report “in obese patients with uncontrolled type 2 diabetes, 12 months of medical therapy plus bariatric surgery achieved glycemic control in significantly more patients than medical therapy alone.” We would like to call attention to a contradiction between what is stated in the title — obese patients — and the eligibility criteria, a body-mass index (BMI, the weight in kilograms divided by the square of the height in meters) of 27 to 43. According to the Centers for Disease Control and Prevention, the definition of obesity should be restricted to persons with a BMI of 30 or higher. This definition must be clarified, since bariatric surgery for nonobese patients with type 2 diabetes is still controversial. In addition, the authors reported that 51 of 150 patients had a BMI of less than 35 before treatment assignment. Can the authors present outcome data regarding the subgroup of patients with a BMI of less than 30 who underwent surgery?

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DR. SCHAUER AND COLLEAGUES REPLY: Gletsu-Miller and Ziegler rightly emphasize the importance of perioperative monitoring for micronutrient and macronutrient deficiencies related to bariatric surgery. We did reference our nutrition assessment protocol, and our study protocol (available with the full text of our article at NEJM.org) is compatible with accepted guidelines.1,2 We add that clinicians should continuously counsel patients on the importance of compliance with vitamin and nutrient regimens that may avert such nutritional deficiencies.

Frontoni and colleagues suggest that a “huge negative energy balance” such as that which occurs with a very-low-calorie diet may be a primary mechanism that explains the rapid improvement in glycemic control after bariatric surgery. Further, they suggest that a very-low-calorie diet may be a therapeutic method for treating type 2 diabetes. We concur that a negative energy balance is probably one mechanism of surgical improvement and remission of type 2 diabetes; however, evidence suggests that bariatric surgery does have important weight-loss–independent effects that exceed the benefits of a very-low-calorie diet.

Laferrière et al. found that patients who underwent gastric bypass had superior glycemic control at 1 month after surgery as compared with patients who had equivalent weight loss induced by a very-low-calorie diet alone.3 Furthermore, they found that an incretin effect not seen after a very-low-calorie diet possibly explained the differential benefit of surgery. We likewise found that gastric bypass, due to an incretin effect possibly driven by gut hormones such as glucagon-like peptide 1, gastrointestinal peptide, and peptide YY3-36, induced superior glycemic improvement as compared with operations such as banding and sleeve gastrectomy, which appear to elicit weight loss but no or only a modest incretin ef-
Dr. Mingrone and Colleagues Reply: Frontoni and colleagues suggest that a low-calorie diet is a better treatment for obese patients with type 2 diabetes than surgery. The beneficial effects of starvation on diabetes were the basis for the “Allen diet,” which was described by Frederick Madison Allen as a diabetes therapy in 1920. More recent investigations have shown that a 7-day period of a very-low-calorie diet can reduce hepatic glucose output and improve insulin sensitivity and secretion. Hence, reduced caloric intake may contribute to early improvement of diabetes after bariatric surgery.

However, our patients generally consume a semiliquid diet of 1000 to 1200 kcal per day after bariatric surgery, a caloric intake that is almost twice as high as the 400 to 800 kcal per day in very-low-calorie diets. When comparing patients with similar caloric intake, a significant improvement of insulin resistance by the homeostasis model assessment of insulin resistance (HOMA-IR) is seen as early as 7 days after Roux-en-Y gastric bypass, but not after gastric banding or calorie restriction. Furthermore, as early as 1 week after biliopancreatic diversion, insulin sensitivity measured with the use of the euglycemic–hyperinsulinemic clamp is almost doubled. There is also evidence that bariatric surgery and dietary weight loss result in substantially different changes in gastrointestinal hormones involved in glucose homeostasis. All together, these data support the view that mechanisms beyond pure energy restriction play a role, at least after gastrointestinal bypass procedures (such as Roux-en-Y gastric bypass and biliopancreatic diversion).

Finally, although in clinical investigations the effects of a very-low-calorie diet on glucose disposal in type 2 diabetes are clear and sound, the application of a very-low-calorie diet as a long-term treatment of diabetes in real clinical practice is very difficult, if not impossible. In fact, as Yki-Järvinen observed in a recent editorial in Diabetes, “remission in a week may not be a cure for life.”

Gletsu-Miller and Ziegler appropriately note that either restrictive or malabsorptive bariatric surgery can be associated with deficiency of vitamins and trace elements. In fact, the supplementation of both is part of the standard treatment in patients after bariatric surgery. In our series, we reported four cases of typical microcytic anemia in patients with low serum iron levels and a high iron-binding capacity, and these patients presented with a marked reticulocyte...
response and increase in the hemoglobin level after the intravenous administration of iron.

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Since publication of their article, the authors report no further potential conflict of interest.

Comparative Effectiveness of Revascularization Strategies

TO THE EDITOR: Although Weintraub et al. (April 19 issue) should be recognized for their attempts to assess the possible effects of unmeasured confounding in their analysis of revascularization strategies, a critical, previously identified, and in fact quantified confounder in these databases was not considered. A recent analysis explicitly identified factors not captured in the National Cardiovascular Data Registry that contributed to ineligibility for surgery in more than 50% of patients undergoing percutaneous coronary intervention (PCI) for left main coronary artery disease; ineligibility was independently associated with a mortality hazard that was five times as great as that associated with eligibility.

On the basis of the sensitivity analyses presented by the authors, the presence of a covariate such as surgical ineligibility with a hazard ratio of 5 would have to be present in only 10 to 15% of patients undergoing PCI in order to negate observed differences in ASCERT (a partnership of the American College of Cardiology Foundation [ACCF] and the Society of Thoracic Surgeons [STS] titled the ACCF and STS Database Collaboration on the Comparative Effectiveness of Revascularization Strategies). As such, the use of these data to examine the comparative outcomes of two nonrandomized therapies (the selection of which is often based on unmeasured clinical factors, particularly in elderly patients, many of whom may be frail and therefore ineligible for surgery) has a high probability of generating erroneous conclusions, and should therefore be avoided.


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TO THE EDITOR: According to a meta-analysis of 23 studies comparing the effects of coronary-artery bypass grafting (CABG) and PCI, and according to data from the SYNTAX trial, stroke is significantly more likely to occur with CABG. In the ASCERT study, the unadjusted data show that the CABG group had a higher prevalence of cerebrovascular disease at baseline. However, it would be interesting to know whether the authors performed any analysis in which the stroke rates after CABG and PCI were compared.

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