The benefit of weight loss on glycemic control in type 2 diabetes is well known; weight management is foundational to good diabetes care. Intensive lifestyle intervention, which produces modest (5–10%) weight loss can produce durable (demonstrated up to 4 years) improvement in HbA1c and some cardiovascular risk factors (1,2). As for bariatric surgery, a recent systematic review and meta-analysis (3) of 621 bariatric surgery studies (>135,000 patients) reported that diabetes “improved or resolved” in 84%. Thus, there is a growing appreciation for the role of bariatric surgery as a tool in diabetes management.

The appreciation that bariatric surgery might yield remission of diabetes stimulated the American Diabetes Association (ADA) to convene a consensus committee to define the terms “partial remission,” “complete remission,” and “durable remission” (4). This is an important step because slight variation in definition can yield significant differences in remission rates (5). If we are to be able to develop evidence to support recommendations for this procedure in diabetes, we must be able to compare results across studies.

Surgery for obesity has typically been reserved for patients with more severe obesity, and current guidelines (6) for the diagnosis and management of obesity indicate bariatric surgical procedures for patients with BMI ≥ 40 kg/m² or for patients with a serious comorbidity (such as type 2 diabetes) and BMI ≥ 35 kg/m². These BMI cut points are drawn from observations of large populations that show that as BMI increases, the risk for morbidity and mortality increases. The BMI is an excellent tool for assessing risk for diabetes and other obesity-associated diseases on a population basis, but physicians treat patients not populations, and the BMI is not an exact instrument for detecting risk for diabetes in individuals.

Lacking sophisticated risk algorithms that incorporate BMI to help tailor treatment recommendations, physicians must rely on medical judgment when they stray from the strict interpretation of the guidelines. Such a concept was presented in the Diabetes Care Symposium held last month at the Scientific Sessions of the ADA and is featured in this issue of Diabetes Care. Specifically, in an article in this issue, the team of investigators (7) did stray from that strict interpretation in studying a bariatric surgical procedure for obese patients with BMI 30–35 kg/m² who had long-standing, poorly controlled type 2 diabetes.

Cohen et al. (7) report on a series of 66 consecutive patients with poorly controlled diabetes and BMI 30–35 kg/m² who underwent laparoscopic Roux-en-Y gastric bypass at a single site in Brazil. The improvements in glyceremia and cardiovascular risk factors demonstrated by these patients were remarkable. Mean HbA1c fell from 9.7 ± 1.5 to 5.9 ± 0.1%, and 88% of patients achieved the criteria the authors use to define diabetes remission (HbA1c < 6.5% without diabetes medications) and sustained remission during up to 6 years of follow-up. Among the 66 surgical patients, there was a 15% rate of minor surgical complications (eight port-site hematomas, one anastomotic ulcer, and one urinary tract infection), but there were no major surgical complications.

The study is of good quality. Although it was not a randomized clinical trial, the patients were consecutively enrolled, and there were no dropouts over a mean follow-up of 5 years, which lessens the likelihood that the results are biased by patient selection or missing data. However, the definition of remission does not follow exactly that recommended by the ADA (normal HbA1c and fasting glucose while off diabetes medications for at least 1 year), and there may be significant differences in remission rates when the HbA1c cut point is set at 6.5% rather than 6.0% (5). A recent report by Schauer et al. (8) showed remission rates of 42% in 50 diabetic patients who underwent Roux-en-Y bypass when the HbA1c cut point was 6.0% off medications for 1 year.

Furthermore, several factors affect the generalizability of the article’s (7) results. The surgeries were performed at a single site by a highly skilled surgical team, and, importantly, the patients were preselected for having β-cell function. The team evaluated anti-GAD or islet cell antibodies and C-peptide levels (overnight fasting and following a mixed meal) to exclude patients with undetectable β-cell function. Thus, one must be careful not to generalize the results of the study into a community care setting, in which surgical teams may not be as experienced and the selection of patients for surgery not so precise.

What are the messages that practitioners should take home from this article? First, it reinforces the importance of weight management in diabetes care. Granted, the improvements in diabetes were not entirely mediated by weight loss—the Roux-en-Y bypass has been shown to affect gastrointestinal incretin hormones (9,10). Still, weight management is something that all diabetologists need to emphasize in their care routine because of the impact it can have on glycemia and risk factors (1,2).

Does this mean that the guidelines are incorrect and that the criterion should be lowered to a BMI of 30 for a surgical indication in patients with diabetes? We can’t make such a sweeping change based on this one study. We need the collective weight of multiple studies to demonstrate which bariatric surgical procedures should be implemented for which subgroup of patients and at what stage of a stepped-care approach to diabetes management. It is not that the guidelines are incorrect; it is that they provide guidance for a population. This article is an important step in gathering the data to help us tailor treatment approaches, ultimately to lead to better approaches to diabetes care.

There is much to be done to develop the evidence base to guide recommendations for surgical approaches to diabetes. The article (7) in this issue of Diabetes Care takes a good step in defining patients with residual β-cell function. We need agreement on the definition of remission, and even the ADA recommendation is not explicit about the exact HbA1c to define remission. Some seem to interpret this as <6.0% and others as <6.5%. Studies must compare types of surgery as well as less invasive interventions with attention to equipoise across groups. Because different procedures have been shown to vary in risk (11) and different approaches (medical vs. surgical) might vary in cost, those factors must be considered in studies. Studies must be conducted in multiple sites, and there should be an attempt to mimic medical
practice settings. Durability of remission is paramount. In the Swedish Obese Subjects study (12), which had less average weight loss than the current study and which demonstrated weight regain over time, diabetes recurred in nearly half of the patients in whom it had remitted. Observation should be for at least 5 years. With studies following these parameters, there would be an excellent evidence base to inform guidelines, and we might develop recommendations that are better tailored to office practices where individuals, not populations, are treated.

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References
1. Wing RR; Look AHEAD Research Group. Long-term effects of a lifestyle intervention on weight and cardiovascular risk factors in individuals with type 2 diabetes mellitus: four-year results of the Look AHEAD trial. Arch Intern Med 2010;170:1566–1575
2. Pi-Sunyer X, Blackburn G, Brancati FL, et al.; Look AHEAD Research Group. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the Look AHEAD trial. Diabetes Care 2007; 30:1374–1383
3. Buchwald H, Estok R, Fahrbach K, et al. Weight and type 2 diabetes after bariatric surgery: systematic review and meta-analysis. Am J Med 2009;122:248–256, e5
4. Buse JB, Caprio S, Cefalu WT, et al. How do we define cure of diabetes? Diabetes Care 2009;32:2133–2135
5. Pournaras DJ, Aasheim ET, Søvik TT, et al. Effect of the definition of type II diabetes remission in the evaluation of bariatric surgery for metabolic disorders. Br J Surg 2012;99:100–103
6. National Institutes of Health. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults: the evidence report. Obes Res 1998;6(Suppl. 2):S1–S209S
7. Cohen RV, Pinheiro JC, Sichavon CA, Salles JE, Wajchemberg B, Cummings DE. Effects of gastric bypass surgery in patients with type 2 diabetes and only mild obesity. Diabetes Care 2012;35:1420–1428
8. Schauer PR, Kashyap SR, Wolski K, et al. Bariatric surgery versus intensive medical therapy in obese patients with diabetes. N Engl J Med 2012;366:1567–1576
9. Cummings DE, Overduin J, Shannon MH, Foster-Schubert KE, 2004 ABS Consensus Conference. Hormonal mechanisms of weight loss and diabetes resolution after bariatric surgery. Surg Obes Relat Dis 2005;1:358–368
10. Korner J, Bessler M, Inabnet W, Taveras C, Holst JJ. Exaggerated glucagon-like peptide-1 and blunted glucose-dependent insulinotropic peptide secretion are associated with Roux-en-Y gastric bypass but not adjustable gastric banding. Surg Obes Relat Dis 2007;3:597–601
11. Flum DR, Belle SH, King WC, et al.; Longitudinal Assessment of Bariatric Surgery (LABS) Consortium. Perioperative safety in the longitudinal assessment of bariatric surgery. N Engl J Med 2009;361:445–454
12. Sjöström L, Lindroos AK, Peltonen M, et al.; Swedish Obese Subjects Study Scientific Group. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. N Engl J Med 2004;351:2683–2693