Insulin Cessation and Diabetes Remission After Bariatric Surgery in Adults With Insulin-Treated Type 2 Diabetes

Diabetes Care 2015;38:659–664 | DOI: 10.2337/dc14-1751

Ali Ardestani,[1] David Rhoads,[2] and Ali Tavakkoli[1,3]

OBJECTIVE

The impact of bariatric surgeries on insulin-treated type 2 diabetes (I-T2D) in the general population is largely undocumented. We assessed changes in insulin treatment after bariatric surgery in a large cohort of I-T2D patients, comparing Roux-en-Y gastric bypass surgery (RYGB) with laparoscopic adjustable gastric banding (LAGB), controlling for differences in weight loss between procedures.

RESEARCH DESIGN AND METHODS

Of 113,638 adult surgical patients in the Bariatric Outcomes Longitudinal Database (BOLD), 10% had I-T2D. Analysis was restricted to 5,225 patients with I-T2D and at least 1 year of postoperative follow-up. Regression models were used to identify factors that predict cessation of insulin therapy. To control for differences in weight loss patterns between RYGB and LAGB, a case-matched analysis was also performed.

RESULTS

Of I-T2D patients who underwent RYGB (n = 3,318), 62% were off insulin at 12 months compared with 34% (n = 1,907) after LAGB (P < 0.001). Regression analysis indicated that RYGB strongly predicted insulin cessation at both 1 and 12 months postoperatively. In the case-matched analysis at 3 months, the proportion of insulin cessation was significantly higher in the RYGB group than in the LAGB group (P = 0.03), and the diabetes remission rate was higher at all time points after this surgery. RYGB was a weight-independent predictor of insulin therapy cessation early after surgery, whereas insulin cessation after LAGB was linked to weight loss.

CONCLUSIONS

I-T2D patients have a greater probability of stopping insulin after RYGB than after LAGB (62% vs. 34%, respectively, at 1 year), with weight-independent effects in the early months after surgery. These findings support RYGB as the procedure of choice for reversing I-T2D.

Obesity and associated type 2 diabetes have reached epidemic proportions, becoming a major health concern in the U.S. and worldwide. The International Diabetes Federation reported that 366 million people had diabetes in 2011 worldwide and estimated that 552 million people will be affected by 2030 (1).

Various interventions have been shown to control or improve type 2 diabetes (2–4). However, bariatric surgery is one of the very few modalities known to bring type

[1]Department of Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA
[2]Pediatric Endocrine Unit, Massachusetts General Hospital, Harvard Medical School, Boston, MA
[3]Center for Weight Management and Metabolic Surgery, Brigham and Women's Hospital, Harvard Medical School, Boston, MA

Corresponding author: Ali Tavakkoli, atavakkoli@partners.org.

Received 21 July 2014 and accepted 26 November 2014.

A slide set summarizing this article is available online.

PATHOPHYSIOLOGY/COMPLICATIONS

2 diabetes into remission and even to prevent the development of diabetes in obese patients (3–6). As a result, weight loss operations such as Roux-en-Y gastric bypass (RYGB) and laparoscopic adjustable gastric banding (LAGB) have been incorporated in the treatment guidelines of diabetes societies, including the American Diabetes Association and the International Diabetes Federation (7).

Although bariatric surgeries lead to significant improvement in glucose homeostasis, most patients included in studies are only on oral hypoglycemic agents. Our knowledge of outcomes in insulin-treated patients is based on studies with small numbers of subjects limited to trial settings (8,9), but it is unclear whether these outcomes can be extrapolated to the general population. Insulin requirement is in fact associated with a lower diabetes remission rate. With >25% of type 2 diabetic patients being treated with insulin, a more detailed understanding of diabetes improvement following surgery in this patient cohort is required.

To fill this knowledge gap, we reviewed the Bariatric Outcomes Longitudinal Database (BOLD), a nationwide database of >100,000 bariatric patients from >100 bariatric centers, to identify and analyze a large cohort of insulin-treated patients who had undergone bariatric surgery. In particular, we were interested in examining the role of surgical procedure versus weight loss in the postsurgical cessation of patients' insulin therapy.

RESEARCH DESIGN AND METHODS

The American Society for Metabolic and Bariatric Surgery Centers of Excellence developed BOLD to prospectively collect information on patients undergoing bariatric surgery, and it has been used in previously published works (10–12). Several important measures taken to ensure quality and accuracy of the data include ongoing staff training, business and validation rules to reject data entry errors, automated data quality reports, and site inspections for data verification (10–12). All patients provide written informed consent to secondary use of their data for research. BOLD is also available to researchers in the form of a deidentified national data repository. The use of BOLD was mandatory for participants in the Bariatric Center of Excellence program, and its funding was included in the program fees.

After obtaining approvals from our Institutional Review Board and the BOLD Data Dissemination Committee, we were provided with a data subset on patients who had undergone bariatric surgery between 2007 and 2010. Patient follow-up information was formatted in 1-month, 3-month, and subsequent biannual entries. Inclusion criteria for the present study were *1*) RYGB or LAGB surgical procedure, *2*) age ≥18 years, *3*) presence of insulin-treated diabetes regardless of duration, *4*) BMI ≥35 kg/m^2, and *5*) availability of 12 months of postoperative follow-up data. Patients who had hand-assisted or robotic-assisted approaches were excluded because of their limited number (<10) and the experimental feature of these procedures. Patients were placed into the RYGB group or the LAGB group according to the surgical procedure.

Comorbidities in BOLD, including type 2 diabetes, were each assigned a disease severity level using the following 6-point Likert scale to facilitate tracking comorbidity changes after the surgery (13): 0 = no symptoms or evidence of diabetes; 1 = elevated fasting glucose; 2 = diabetes, controlled with oral medication; 3 = diabetes, controlled with insulin; 4 = diabetes, controlled with insulin and oral medication; and 5 = diabetes, with severe complications (retinopathy, neuropathy, renal failure, blindness). Patients with type 2 diabetes severity level ≥3 were included and considered to be in type 2 diabetes clinical remission if they reached level 1 or 0 postoperatively, as defined by DeMaria et al. (11). Patients who were reclassified postoperatively as severity level ≤2 were counted as having ceased insulin therapy (11).

Weight loss in the present study is reported as percent excess body weight loss (%EBWL), the weight-loss parameter captured in BOLD as originally recommended by the American Society for Metabolic and Bariatric Surgery Standards Committee (14). Although several authorities have recommended using change in BMI or total weight to monitor weight loss after surgery (15), we opted to retain %EBWL for consistency with other reports from this database (10–12). Metropolitan Life Insurance Tables (1999) were used to calculate %EBWL (16).

To minimize the impact of outliers, the nonparametric Wilcoxon rank sum test was used to compare continuous variables. The χ^2 test was used to compare categorical variables. In addition to comparative statistics, two separate regression models were developed for the overall cohort to evaluate the impact of various factors on insulin therapy cessation at two postoperative time points: 1 month and 12 months. Data are presented as mean and SD unless stated otherwise.

To highlight the impact of procedure on insulin therapy and control for other factors, including weight loss, a case-matched analysis was performed. We used the Coarsened Exact Matching (CEM) procedure within Stata software (StataCorp, College Station, TX) to match the RYGB and LAGB patients (17). With this statistical approach, causal inferences can be drawn from an observational study by choosing well-matched samples from the two experimental groups, essentially simulating a randomized controlled trial (18). The preoperative characteristics used for matching, including age, BMI, and sex, have all been shown to have a significant impact on glucose homeostasis after bariatric procedures (19–21). Furthermore, to minimize the impact of weight loss in the comparison, the groups were also matched for %EBWL at 1, 3, 6, and 12 months (19–22). In exact matching, all patients were first arranged into strata, each of which had identical values for all the coarsened preoperative covariates, and then all patients within any stratum who did not have at least one observation for each unique value of the grouping variable were removed. One-to-one exact matching was used to eliminate the requirement of adding weights in a parametric model to carry out comparisons and control for variations across the groups. Patients who could not be matched were removed from the case-matched analysis.

RESULTS

Within the study period, we identified 11,419 adult patients who had insulin-treated type 2 diabetes, comprising ~10% of the 113,638 patients who had undergone bariatric surgery. Of the 5,225 patients who met all inclusion criteria, 3,318 had undergone RYGB (63.5%) and 1,907 had undergone LAGB (36.5%). Baseline characteristics of these two groups were similar in terms of sex and race, but RYGB patients were on average 1.8 years younger and had a 2.1 kg/m^2 higher preoperative BMI (Table 1). Additionally, compared with the LAGB group, preoperative RYGB patients had a slightly higher proportion on oral diabetic medications plus insulin (severity level 4) and a slightly lower proportion on insulin alone (severity level 3).

After surgery, the number of patients who ceased insulin therapy increased with time in both groups, but the proportion in the RYGB group was approximately twice that in the LAGB group at all four postoperative time points. One month after surgery, 30.7% of RYGB patients were off insulin vs. 14.5% of LAGB patients ($P < 0.001$). In the RYGB group at 3, 6, and 12 months, 44.6%, 55.4%, and 62.5% were off insulin, respectively. Corresponding proportions for the LAGB group (22.2%, 29.5%, and 33.9%, respectively) were all significantly lower ($P < 0.001$) (Fig. 1). Clinical remission of type 2 diabetes (severity level 0 or 1) was reported in 22.5%, 34.4%, 43.2%, and 50.3% of patients in the RYGB group vs. 7.0%, 11.3%, 16.0%, and 19.3% of patients in the LAGB group at 1, 3, 6, and 12 months, respectively.

RYGB patients achieved significantly greater weight loss (%EBWL 19.7%, 36.8%, 53.2%, and 62.8% at 1, 3, 6, and 12 months, respectively). In contrast, patients in the LAGB group achieved significantly lower weight loss at the corresponding time points (%EBWL 14.5%, 21.9%, 29.4%, and 32.3%, respectively; $P < 0.001$).

Multiple regression analyses for the overall study cohort revealed that surgical choice of RYGB was a strong predictor of postoperative cessation of insulin therapy both early (1 month) and late (12 months), controlling for age, sex, preoperative BMI, and %EBWL. At the early stage, younger age and greater weight loss were also weaker predictors of insulin therapy cessation. Age, sex, and preoperative BMI were similarly weak predictors of insulin therapy cessation at the later stage (Table 2). Overall, the data reveal that the choice of surgical intervention is the strongest predictor of insulin therapy cessation at both early and late time points, with minimal contributions from other factors.

The second analysis focused on a matched cohort comprising 198 patients from each group using the CEM method. The resulting groups exhibited no significant differences in characteristics (~72% female, 84% Caucasian, average age 56 years, BMI 46.4 kg/m^2). Severity of diabetes did not differ significantly between groups, with ~60% of patients categorized as severity level 4 (insulin and oral medication) in each. Despite the matched postoperative %EBWL for the two groups, a greater percentage of the RYGB group was able to cease insulin treatment compared with the LAGB group; the difference at 3 months was statistically significant (RYGB 37.1%, LAGB 26.3%, $P = 0.03$) (Fig. 2). RYGB patients in the matched cohort reported 14.4%, 28.0%, 30.7%, and 35.7% clinical remission of type 2 diabetes at 1, 3, 6, and 12 months, respectively, whereas LAGB patients reported 7.0%, 12.9%, 19.3%, and 24.4% clinical remission at corresponding time points (P values 0.02, <0.001, 0.01, and 0.01 for 1, 3, 6, and 12 months, respectively).

CONCLUSIONS

The role of bariatric surgery in bringing type 2 diabetes into remission is well recognized (5,6,8,11). Although a high diabetes remission rate has been reported with metabolic procedures, lower remission rates are observed in patients on insulin therapy (22). Because ~30% of U.S. patients with diabetes are on insulin therapy, providing their health-care providers with data on the likely outcomes of metabolic interventions could be of great value (23). Apart from the ideal outcome of diabetes remission, insulin cessation itself would dramatically benefit the patient in terms of cost, complexity of dosing, administration, and risks associated with insulin therapy (e.g., weight gain, hypoglycemia). Insulin therapy cost ~$6 billion in the U.S. in 2012, and an estimated 100,000 emergency room visits and 30,000 hospitalizations annually are attributed to hypoglycemia (24). Despite the importance of understanding the impact of bariatric procedures on insulin-treated patients, few studies have specifically focused on this patient cohort.

The present study revealed that 62% and 34% of the RYGB and LAGB groups, respectively, were able to stop insulin therapy 1 year after surgery. Moreover, clinical remission of diabetes was observed in 50.3% and 19.3% of the RYGB and LAGB groups, respectively. These data lead to several important conclusions: *1*) advanced type 2 diabetes, as defined by insulin therapy, is amenable to remission by bariatric surgery; *2*) many of those who do not achieve remission no longer require insulin postoperatively; *3*) RYGB appears superior to LAGB for its ability to improve metabolic parameters in this patient subset, especially at the earlier time point of 3 months; and *4*) the weight loss–independent improvement in glucose control following RYGB is observed even in a cohort with insulin-treated type 2 diabetes.

The findings are useful for patients and physicians when discussing modalities for diabetes management. Of note, these findings were obtained from a large national cohort (rather than a selected group of patients in a trial setting) and, therefore, are more applicable to the average diabetic patient on insulin.

The present study provides a context for smaller studies on diabetes improvement in insulin-treated patients. Schauer et al. (25) found that 79% of 52 insulin-treated diabetic patients were off insulin

Table 1—Comparison of preoperative patient characteristics between the LAGB and RYGB groups in the overall BOLD cohort

	LAGB (n = 1,907)	RYGB (n = 3,318)
Female sex	66.4	66.9
Race (% Caucasian)	81.4	81.8
Age (years)	54.9 (10.7)	53.1 (9.8)‡
Preoperative BMI (kg/m^2)	45.8 (7.2)	47.9 (8.4)‡
Diabetes severity		
Insulin	30.9	26.3‡
Insulin and oral medication	61.5	65.3‡
Severe complications†	7.6	8.4

Data are presented as % or mean (SD). ‡$P < 0.01$. †Retinopathy, neuropathy, renal failure, or blindness.

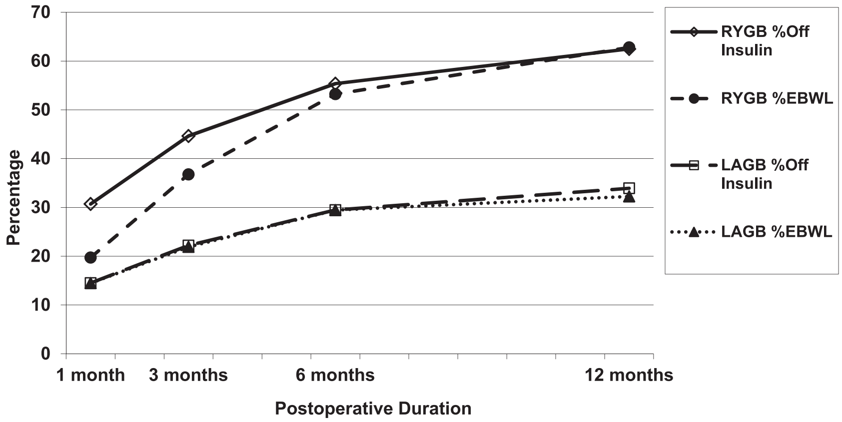

Figure 1—Comparison of %EBWL and percentage of patients off insulin following bariatric procedures in the overall BOLD cohort. $P < 0.001$ for all comparisons between RYGB and LAGB.

at an average of 20 months' follow-up, consistent with our observed 62% insulin cessation at 12 months. Our observed 34% insulin cessation 1 year after LAGB is similar to the 39% reported by Singhal et al. (26) in a cohort of 69 insulin-treated patients who had undergone LAGB.

The greater likelihood of insulin cessation and diabetes remission in the present insulin-treated cohort after RYGB could be due to the greater degree of weight loss after this procedure. In fact, Busetto et al. (27) ascertained from the meta-analysis by Buchwald et al. (28) that ~95% of the variability in diabetes remission can be explained by the difference in weight loss after these procedures. The importance of degree of weight loss was assessed in RYGB patients by Casella et al. (22), who showed that weight loss alongside duration of diabetes was an important independent factor in predicting diabetes improvement in patients after surgery. Similarly, in a study of 71 insulin-treated patients who had undergone RYGB, Kadera et al. (29) observed that percent excess weight loss and insulin dosing, but not diabetes duration, were significant predictors of diabetes remission in this population. The present study also demonstrates that the degree of weight loss as well as age, sex, and preoperative BMI contributes to insulin therapy cessation after surgery but that these factors are weak predictors after accounting for the choice of surgical procedure. For insulin-treated type 2 diabetic patients considering weight loss surgery, these results highlight the important consideration that the type of surgical intervention can be a major determinant in the resolution of diabetes.

A case-matched analysis between the RYGB and LAGB groups was performed to control for the aforementioned factors to ascertain the impact of procedure type on diabetes remission. Of note, this matching likely compares the good LAGB responders with the poor RYGB responders. Nevertheless, given the distinct characteristics of the two procedures, this matching method offers the best approach to compare weight loss–independent differences. Despite nearly identical preoperative characteristics and postoperative weight loss, RYGB led to significantly improved rates of diabetes remission and insulin therapy cessation. The diabetes remission and insulin cessation differences were significant at 3 months, highlighting the early and weight-independent benefits of RYGB in glucose homeostasis. Multiple mechanisms have been implicated as contributing to the metabolic benefits of RYGB, including changes in hormone secretion patterns, intestinal glucose absorptive capacity, bile salt circulation, and microbiome composition (30–32), but their relative contributions to diabetes remission are still a matter of debate (33). However, weight loss plays a major role in metabolic benefits of both RYGB and LAGB later after surgery, highlighting the need to sustain the optimal weight loss in diabetic patients.

One limitation of the present study is its retrospective nature, despite prospective data collection. More importantly, BOLD does not track duration of diabetes, fasting blood glucose, HbA_{1c}, or insulin dosing, so a categorical clinical evaluation scale is used to assess diabetes severity rather than these more quantitative measures. Although the absence of these parameters from the database somewhat limits our comparison, the differences between groups even with the categorical assessments are striking and valuable. Insulin therapy should be a sufficiently robust indicator of diabetes severity, and its impact on lifestyle and simple binary character increase its accurate capture. We acknowledge that there is variation in practice in insulin administration, but given the size of the cohort, these variations should be similar between the two groups. In 219 diabetic patients, Kim and Richards (21) observed the same rate of diabetes remission at 12 months and 24–48 months of follow-up, which suggests that the 12-month follow-up presented in the current study is an adequate monitoring point. No data are provided on sleeve gastrectomy because very few cases were captured in BOLD over the study period.

Although a randomized controlled trial would be the optimal design to determine the efficacy of the bariatric surgery in insulin-treated diabetic patients, it would be difficult to justify a clinical trial comparing two procedures with different safety profiles and outcomes. Thus, evaluation of a large national cohort to ascertain the impact of bariatric surgery is the next best approach with applicable results for the general population.

Table 2—Factors that affect the odds of insulin cessation after bariatric surgery, identified using regression analysis of the overall BOLD cohort

	Early (1 month)	Late (12 months)
Sex (% male)	1.02 (0.88–1.19)	**0.85** (0.75–0.96)‡
Race (% Caucasian)	0.94 (0.83–1.10)	0.95 (0.85–1.05)
Procedure (% RYGB)	**2.21** (1.88–2.61)‡	**1.57** (1.34–1.84)‡
Age (years)	**0.98** (0.98–1.00)‡	**0.98** (0.98–0.99)‡
Preoperative BMI (kg/m^2)	1.00 (0.99–1.01)	**1.01** (1.00–1.02)†
%EBWL	**1.03** (1.02–1.04)‡	**1.02** (1.02–1.03)‡

Data are presented as odds ratio (95% CI). Boldface indicates factors with statistically significant impact at each stage. ‡$P < 0.01$. †$P < 0.05$.

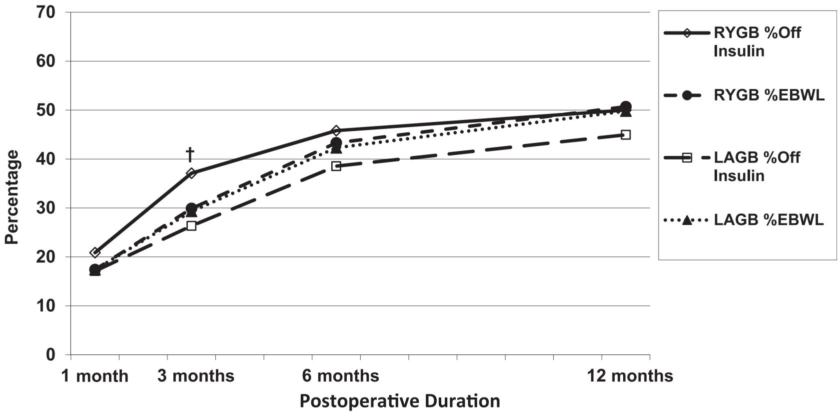

Figure 2—Comparison of %EBWL and percentage of patients off insulin following bariatric procedures in the matched cohort. †P = 0.03 for percentage off insulin at 3 months between RYGB and LAGB.

Moreover, the CEM method permitted us to simulate a randomized controlled trial with the BOLD observational data. Given the high incidence of diabetes and its impact on multiple organ systems, we advocate for collection of more quantitative data on diabetes in the national bariatric outcomes databases, including HbA_{1c} and disease duration.

In summary, RYGB appears to be a superior procedure for obese patients with diabetes who seek surgical treatment, especially those with more advanced disease being treated with insulin. Even patients with advanced disease have a 50% chance of diabetes remission and a >60% chance of stopping insulin therapy at 1 year, which could have a major positive impact on patient quality of life and lead to significant cost savings.

Duality of Interest. No potential conflicts of interest relevant to this article were reported.
Author Contributions. A.A. contributed to the study concept and design; data acquisition, analysis, and interpretation; and drafting of the manuscript. D.R. contributed to the data analysis and interpretation and critical revision of the manuscript. A.T. contributed to the study concept and design, data analysis and interpretation, and critical revision of the manuscript. A.A. is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Prior Presentation. This study was presented in abstract form at the 72nd Scientific Sessions of the American Diabetes Association, Philadelphia, PA, 8–12 June 2012.

References

1. Whiting DR, Guariguata L, Weil C, Shaw J. IDF diabetes atlas: global estimates of the prevalence of diabetes for 2011 and 2030. Diabetes Res Clin Pract 2011;94:311–321
2. Gregg EW, Chen H, Wagenknecht LE, et al.; Look AHEAD Research Group. Association of an intensive lifestyle intervention with remission of type 2 diabetes. JAMA 2012;308: 2489–2496
3. Pontiroli AE, Folli F, Paganelli M, et al. Laparoscopic gastric banding prevents type 2 diabetes and arterial hypertension and induces their remission in morbid obesity: a 4-year case-controlled study. Diabetes Care 2005;28:2703–2709
4. 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
5. Pories WJ, Swanson MS, MacDonald KG, et al. Who would have thought it? An operation proves to be the most effective therapy for adult-onset diabetes mellitus. Ann Surg 1995; 222:339–350; discussion 350–352
6. Carlsson LMS, Peltonen M, Ahlin S, et al. Bariatric surgery and prevention of type 2 diabetes in Swedish obese subjects. N Engl J Med 2012; 367:695–704
7. Dixon JB, Zimmet P, Alberti KG, Rubino F; International Diabetes Federation Taskforce on Epidemiology and Prevention. Bariatric surgery: an IDF statement for obese type 2 diabetes. Surg Obes Relat Dis 2011;7:433–447
8. Dorman RB, Serrot FJ, Miller CJ, et al. Case-matched outcomes in bariatric surgery for treatment of type 2 diabetes in the morbidly obese patient. Ann Surg 2012;255:287–293
9. Schauer PR, Bhatt DL, Kirwan JP, et al.; STAMPEDE Investigators. Bariatric surgery versus intensive medical therapy for diabetes—3-year outcomes. N Engl J Med 2014;370:2002–2013
10. DeMaria EJ, Pate V, Warthen M, Winegar DA. Baseline data from American Society for Metabolic and Bariatric Surgery-designated Bariatric Surgery Centers of Excellence using the Bariatric Outcomes Longitudinal Database. Surg Obes Relat Dis 2010;6:347–355
11. DeMaria EJ, Winegar DA, Pate VW, Hutcher NE, Ponce J, Pories WJ. Early postoperative outcomes of metabolic surgery to treat diabetes from sites participating in the ASMBS bariatric surgery center of excellence program as reported in the Bariatric Outcomes Longitudinal Database. Ann Surg 2010;252:559–566; discussion 566–567
12. Inabnet WB 3rd, Winegar DA, Sherif B, Sarr MG. Early outcomes of bariatric surgery in patients with metabolic syndrome: an analysis of the bariatric outcomes longitudinal database. J Am Coll Surg 2012;214:550–556; discussion 556–557
13. Ali MR, Maguire MB, Wolfe BM. Assessment of obesity-related comorbidities: a novel scheme for evaluating bariatric surgical patients. J Am Coll Surg 2006;202:70–77
14. Oria HE, Carrasquilla C, Cunningham P, et al.; American Society for Bariatric Surgery Standards Committee, 2004–2005. Guidelines for weight calculations and follow-up in bariatric surgery. Surg Obes Relat Dis 2005;1:67–68
15. Belle SH, Berk PD, Courcoulas AP, et al.; LABS Consortium Weight Change Writing Group. Reporting weight change: standardized reporting accounting for baseline weight. Surg Obes Relat Dis 2013;9:782–789
16. Metropolitan Life Insurance Company. Metropolitan height and weight tables. Stat Bull Metropol Life Insur Co. 1983;64:2–9
17. Blackwell M, Iacus S, King G, Porro G. CEM: Coarsened Exact Matching in Stata. Stata J 2009; 9:524–546
18. Stuart EA. Matching methods for causal inference: a review and a look forward. Stat Sci 2010;25:1–21
19. Hamza N, Abbas MH, Darwish A, Shafeek Z, New J, Ammori BJ. Predictors of remission of type 2 diabetes mellitus after laparoscopic gastric banding and bypass. Surg Obes Relat Dis 2011;7:691–696
20. Sugerman HJ, Wolfe LG, Sica DA, Clore JN. Diabetes and hypertension in severe obesity and effects of gastric bypass-induced weight loss. Ann Surg 2003;237:751–756; discussion 757–758
21. Kim S, Richards WO. Long-term follow-up of the metabolic profiles in obese patients with type 2 diabetes mellitus after Roux-en-Y gastric bypass. Ann Surg 2010;251:1049–1055
22. Casella G, Abbatini F, Calì B, Capoccia D, Leonetti F, Basso N. Ten-year duration of type 2 diabetes as prognostic factor for remission after sleeve gastrectomy. Surg Obes Relat Dis 2011;7:697–702
23. Centers for Disease Control and Prevention. Age-adjusted percentage of adults with diabetes using diabetes medication, by type of medication, United States, 1997–2011 [article online], 2012. Available from http://www.cdc.gov/diabetes/statistics/meduse/fig2.htm. Accessed 24 November 2014
24. Geller AI, Shehab N, Lovegrove MC, et al. National estimates of insulin-related hypoglycemia and errors leading to emergency department visits and hospitalizations. JAMA Intern Med 2014;174:678–686
25. Schauer PR, Burguera B, Ikramuddin S, et al. Effect of laparoscopic Roux-en Y gastric bypass on type 2 diabetes mellitus. Ann Surg 2003;238: 467–484; discussion 84–85
26. Singhal R, Ahmed M, Krempic A, Kitchen M, Super P. Medium-term outcomes of patients with insulin-dependent diabetes after laparoscopic adjustable gastric banding. Surg Obes Relat Dis 2013;9:42–47
27. Busetto L, Sbraccia P, Frittitta L, Pontiroli AE. The growing role of bariatric surgery in the management of type 2 diabetes: evidences and open questions. Obes Surg 2011;21:1451–1457

28. 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
29. Kadera BE, Lum K, Grant J, Pryor AD, Portenier DD, DeMaria EJ. Remission of type 2 diabetes after Roux-en-Y gastric bypass is associated with greater weight loss. Surg Obes Relat Dis 2009;5:305–309
30. Rubino F, Gagner M, Gentileschi P, et al. The early effect of the Roux-en-Y gastric bypass on hormones involved in body weight regulation and glucose metabolism. Ann Surg 2004; 240:236–242
31. Pournaras DJ, Osborne A, Hawkins SC, et al. Remission of type 2 diabetes after gastric bypass and banding: mechanisms and 2 year outcomes. Ann Surg 2010;252:966–971
32. Stearns ATBATA, Balakrishnan A, Tavakkolizadeh A. Impact of Roux-en-Y gastric bypass surgery on rat intestinal glucose transport. Am J Physiol Gastrointest Liver Physiol 2009;297:G950–G957
33. Knop FK, Taylor R. Mechanism of metabolic advantages after bariatric surgery: it's all gastrointestinal factors versus it's all food restriction. Diabetes Care 2013;36(Suppl. 2):S287–S291