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Microvascular Outcomes in Patients with Diabetes after Bariatric Surgery versus Usual-Care: A Matched Cohort Study

Rebecca O'Brien, MD¹, Eric Johnson, MS², Sebastien Haneuse, PhD³, Karen J. Coleman, PhD⁴, Patrick J. O'Connor, MD, MA, MPH⁵, David P. Fisher, MD¹, Stephen Sidney, MD, MPH⁶, Andy Bogart, MS⁷, Mary Kay Theis, MA, MS², Jane Anau, BS², Emily B. Schroeder, MD, PhD⁸, David Arterburn, MD, MPH²

¹The Permanente Medical Group, Kaiser Permanente Northern California, Oakland, CA

²Kaiser Permanente Washington Health Research Institute, Seattle, WA

³Department of Biostatistics, Harvard T.H. Chan School of Public Health, Boston, MA

⁴Department of Research and Evaluation, Kaiser Permanente Southern California, Pasadena, CA

⁵HealthPartners Institute, HealthPartners, Minneapolis, Minnesota

⁶Division of Research, Kaiser Permanente Northern California, Oakland, CA

⁷RAND Corporation, Santa Monica, CA

⁸Institute for Health Research, Kaiser Permanente Colorado, Denver, CO

Abstract

Background: Bariatric surgery improves glycemic control in type 2 diabetes mellitus (T2DM), but less is known about microvascular outcomes.

Objective: To investigate the relationship between bariatric surgery and incident microvascular complications of T2DM.

Design: Retrospective, matched cohort study from 2005–2011, with follow-up through September 2015.

Setting: Four integrated health systems in the United States

Corresponding Author and for reprints: David Arterburn, Kaiser Permanente Washington Health Research Institute, 1730 Minor Ave, Suite 1600, Seattle, WA, 98101; arterburn.d@ghc.org.

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Conflicts of Interest: None of the authors have any conflicts of interest to declare.

IRB Approval

All study procedures were reviewed in advance and approved by the Institutional Review Board at Kaiser Permanente Washington (KPWA) in Washington state, HealthPartners (HP) in Minnesota, Kaiser Permanente Northern California (KPNC), and Kaiser Permanente Southern California (KPSC).

Participants: Patients aged 19–79 with T2DM who underwent bariatric surgery (N=4,024) were matched on age, sex, BMI, HbA1c, insulin use, diabetes duration, and intensity of health care utilization to up to three non-surgical subjects (N=11,059).

Interventions: Bariatric procedures (76% gastric bypass, 17% sleeve gastrectomy, and 7% adjustable gastric banding) compared to usual care

Measurements: Adjusted Cox regression analysis investigated time to incident microvascular disease, defined as first occurrence of diabetic retinopathy, neuropathy, and/or nephropathy.

Results: Median follow-up was 4.3 years for both surgical and non-surgical patients. Bariatric surgery was associated with significantly lower risk of incident microvascular disease at 5 years [16.9% for surgery vs. 34.7% for non-surgical; Adjusted Hazard Ratio (HR): 0.41; 95% confidence interval (CI): 0.34–0.48]. Bariatric surgery was associated with lower cumulative incidence of diabetic neuropathy at 5 years [7.2% among surgery vs. 21.4% for non-surgical; HR: 0.37; 95% CI: 0.30–0.47], nephropathy [4.9% for surgery vs. 10.0% for non-surgical; HR: 0.41; 95% CI: 0.29–0.58], and retinopathy [7.2% for surgery vs. 11.2% for non-surgical; HR: 0.55; 95% CI: 0.42–0.73].

Limitations: Use of electronic health record databases could misclassify microvascular disease status for some patients.

Conclusion: In this large, multicenter study of adults with T2DM, bariatric surgery was associated with lower overall incidence of microvascular disease, including a lower risk of neuropathy, nephropathy, and retinopathy, than usual care.

Introduction

The profound effects of bariatric surgery on glycemic control is well established in multiple studies, including several randomized trials that have compared surgery to intensive medical and lifestyle treatment of T2DM (1–7). Remission of T2DM is common after bariatric surgery, with Roux-en-Y gastric bypass (RYGB) outperforming the sleeve gastrectomy (SG) in most reports (4, 8, 9).

More important than improvements in glycemic control is whether these glycemic changes reduce the incidence of major complications, such as microvascular events. T2DM is the primary cause of nephropathy, end stage renal disease, adult blindness, and neuropathy in the United States, which together lead to significant downstream costs and decreased quality of life (10–12). Thus, a major goal of diabetes treatment is to mitigate the risk of these long-term sequelae (13).

We have previously shown that, in patients with T2DM who undergo bariatric surgery, the risk of incident microvascular disease is reduced for every year that they are in remission from T2DM – even if the patient eventually relapses back to T2DM (indicating a legacy effect) (14). However, a detailed 2016 review of long-term microvascular diabetes outcomes concluded there was inadequate data to support a superior effect of bariatric surgery compared to medical therapy (15).

Two recently published studies help inform this question (4, 16). The STAMPEDE trial randomized 150 patients with obesity and T2DM to RYGB, SG, or intensive medical and lifestyle intervention (4). At 5-years follow-up, there was a decrease in urinary albumin-to-creatinine ratio in the SG group only. There was no change in retinopathy in any group, and neuropathy was not examined. The STAMPEDE trial is limited by a relatively small sample size, which means it is underpowered for rare outcomes.

The prospective Swedish Obesity Subjects (SOS) matched cohort study followed 2,010 bariatric patients (RYGB 13%, gastric banding 19%, vertical-banded gastropasty 68%) and 2,037 matched patients who received usual care (16). The incidence of microvascular disease at 15 years follow-up was significantly lower in the surgery group than the control group (HR 0.56, 95% CI: 0.48–0.66), including among subgroups with prediabetes (0.18, 95% CI 0.11–0.30), established diabetes (HR: 0.54, 95% CI: 0.40–0.72), and normoglycemia (0.63, 0.48–0.81) at baseline. A limitation of the SOS study was the small number of RYGB procedures and lack of SG procedures, which are now the two most common bariatric procedures worldwide (17).

To address these gaps in the literature, we conducted a matched cohort study to determine whether bariatric surgery was associated with a lower incidence of microvascular disease than usual care for severe obesity and T2DM. We hypothesized that patients undergoing bariatric surgery would have a lower risk of any incident microvascular disease (composite of the first occurrence of retinopathy, neuropathy, or nephropathy). We further hypothesized that bariatric surgery patients would have a lower risk of incident retinopathy, nephropathy, and neuropathy compared to non-surgical patients.

Methods

Settings

We conducted a retrospective observational cohort study of adults with T2DM who underwent bariatric surgery between 2005–2011 while enrolled in one of four US integrated health care systems from the Health Care Systems Research Network: Kaiser Permanente Washington (KPW) in Washington state, HealthPartners (HP) in Minnesota, Kaiser Permanente Northern California (KPNC), and Kaiser Permanente Southern California (KPSC). All study procedures were reviewed and approved by the Institutional Review Board at each site and permitted to conduct the research without explicit consent from the participants.

Data Sources

At each study site, standardized electronic medical records, insurance claims, and other data systems (18) were used to extract data, including enrollment and insurance coverage, demographics, blood pressure, height, weight, laboratory values, medications dispensed, deaths, outpatient, inpatient, and emergency department use, and inpatient and outpatient diagnosis and procedure codes of all enrollees.

Surgical Participants

The bariatric population included adults (19–79 years old) with severe obesity (BMI ≥ 35 kg/m²) and T2DM who had a primary (first observed) bariatric surgical procedure between 1/1/2005 – 12/31/2011. Following an approach adopted in prior studies (14, 19, 20), we used a combination of bariatric registries, chart reviews, International Classification of Diseases (ICD-9) codes (43.89, 44.31, 44.38, 44.39, 44.68, 44.69, 44.95), and Current Procedure Terminology (CPT) procedure codes (43633, 43644, 43645, 43659, 43770, 43775, 43842, 43843, 43844, 43845, 43846, 43847) to identify bariatric procedures. Patients were classified as having T2DM if they met one of two criteria at the time of the procedure: (i) T2DM, defined as a HbA1c $\geq 6.5\%$ /48 mmol/mol or fasting plasma glucose ≥ 126 mg/dL at the most recent measurement within two years prior to surgery, or (ii) medication-treated T2DM, defined as a current prescription for any diabetes medication at the time of bariatric surgery.

After population selection, the following exclusion criteria were applied based on information in the two years before surgery: (a) less than one full year of continuous enrollment, (b) a history of gastrointestinal surgery for cancer, (c) pregnancy in the year before surgery (d) gestational diabetes when it was the sole diabetes diagnosis, (e) metformin as the sole indicator of possible T2DM (i.e. no other T2DM, labs, or diagnoses), (f) pre-existing neuropathy, retinopathy, or nephropathy (defined below), and (g) maximum pre-operative BMI <35 kg/m², leaving us with 4,972 patients. We further excluded 850 patients who were missing pre-operative BMI, HbA1c, and/or serum creatinine measures in the 2 years before surgery. Surgical patients who were missing BMI, HbA1c, or creatinine differed from those who had complete data (Appendix Table 1); specifically, they were more likely to be non-Hispanic white; from the HealthPartners site; had their procedure in the first year of our study (2005); and have a shorter observed duration T2DM at the time of surgery. Of the remaining 4,122 patients, 4,024 could be matched to at least one non-surgical patient (Figure 1).

Matched Non-Surgical Participants

For each bariatric patient, we identified up to three matched non-surgical controls via a two-step process. First, among all patients with diabetes and at least one BMI ≥ 35 kg/m² who did not undergo bariatric surgery during the study period (N=320,345), we identified a pool of potential controls who were enrolled at the time of the surgery, satisfied the study inclusion/exclusion criteria, and matched the bariatric patient on the basis of study site, gender, age (± 10 years), BMI (± 5 points), HbA1c level ($\pm$ absolute 1.5%) and insulin use. Second, for each control in the pool we calculated their Mahalanobis distance from the bariatric patient on the basis of age, BMI, HbA1c, diabetes duration, and the number of days of health care utilization in the 7–24 months prior to the date of surgery.(21) Finally, up to three controls were selected based on the shortest Mahalanobis distance. Throughout, non-surgical patients could only be used as a control for one surgical patient (matching without replacement). Additional details on the process we used to establish the matched cohort are provided in the Statistical Appendix.

Outcome and censoring definitions

The primary outcome measure was time to incident microvascular disease (composite indicator of the first occurrence of retinopathy, neuropathy, or nephropathy). Retinopathy was defined by the first appearance of either 1) ICD-9 diagnosis code 362.0x (diabetic retinopathy) 2) a retinal surgical procedure code or other retinopathic code (See Appendix Table 2) plus ICD-9 diagnosis code 250.5x (diabetes with ophthalmic manifestations). Neuropathy was identified based on first occurrence of ICD-9 diagnosis codes (250.6 [diabetes with neurological manifestations] or 357.2 [polyneuropathy in diabetes]). Finally, nephropathy was identified based on a patient having at least two eGFR measures <60 mL/min/1.73 m² separated by at least 90 days without any intervening values ≥ 60 mL/min/1.73 m². We estimated the eGFR using serum creatinine values and the CKD-EPI equation (22). We chose not to use urine protein measures to define incident nephropathy because nearly 25% of our cohort had no baseline urine protein measurements. Patients were censored at the first incidence of cancer (excluding non-melanoma skin cancer), disenrollment, death, study end (9/31/2015), or a period of 13 months with no measurement of weight or blood pressure (see Appendix Table 3). In secondary analyses, we considered each of the three component microvascular outcomes separately.

Statistical analysis

Cox hazards regression models were used to investigate the association between bariatric surgery vs. usual care (non-surgical controls) and incident microvascular disease. Patients were followed from the index date (the date of bariatric surgery or, for non-surgical patients, the date of surgery for the patient to whom they had been matched) until the first occurrence of either incident microvascular disease or a censoring event. Based on preliminary analyses, proportional hazards was assessed to not hold for bariatric surgery vs. usual care ($p < 0.001$ for an interaction with log-time in the Cox model). We therefore fit a flexible time-varying hazard ratio association as a function of time since surgery, using restricted cubic splines with knots at the 5th, 35th, 65th and 95th percentiles of the observed follow-up time scale.(23)

A priori we identified potential confounders of the association between bariatric surgery and microvascular disease. Our two-part matching strategy was designed to ensure balance between the bariatric cases and the non-surgical controls for many of these factors (see above), with exact balance achieved for select matching covariates (e.g. gender and insulin use). We also fit the Cox models for the primary and secondary outcomes adjusting for all of the following covariates: age, race/ethnicity (Hispanic, non-Hispanic white, non-Hispanic black, non-Hispanic other), surgical year, BMI, smoking status (current, former, never), duration of observed diabetes before surgery (defined as first observed diagnosis, laboratory value, or prescription indicating T2DM), insulin use, oral diabetes medication use, uncontrolled blood pressure (defined as either systolic ≥ 140 or diastolic ≥ 90 at two consecutive measures on different days), use of ACE-inhibitor, angiotensin receptor blocker (ARB) medications, use of any other antihypertensive medication, insurance type (commercial, Medicare, Medicaid, other), triglycerides ≥ 250 mg/dL, use of cholesterol lowering medication (statin or other), use of aspirin or other platelet inhibitor, and history of cardiac or cerebrovascular event before surgery (defined based on ICD-9 codes). Because of potential variation in care between health systems, study site (HP, KPSC, KPNC, and

KPWA) was adjusted for via stratification of the baseline hazard function. Note, by including variables used in the matching and/or Mahalanobis distance calculation in the Cox models, our analyses provide two (parallel) adjustments for their potential confounding effects.

Missing data were encountered at baseline for race/ethnicity, smoking status, blood pressure, and triglyceride levels. We performed multiple imputation via chained equations, with unordered categorical variables and multinomial logistic regression for imputation of race/ethnicity and smoking status, and logistic regression for elevated blood pressure and triglyceride levels.(24) Ten imputed datasets were generated, with the results combined using Rubin's rules. Additional detail is provided in the Appendix.

We conducted three sensitivity analyses to examine the impact of: (i) not adjusting for potential confounders that were not included in the matching process (vs. adjusting for those confounders in our main analysis), (ii) using 1-to-1 and 10-to-1 matching, and (iii) an assessment of robustness of the 5-year results to unmeasured confounding using the E-value methodology of VanderWeele and Ding.(25) Throughout, we used SAS version 9.4 (SAS Institute, Cary NC) for data manipulation, Stata 15.1 for multiple imputation and analysis, and R for visualization.

Role of funding source.

The funders, National Institutes of Diabetes and Digestive and Kidney Diseases, did not have any role in the design, conduct, or reporting of results.

Results

Participants

The final analytic sample consisted of 4,024 surgical patients and 11,059 non-surgical matches (Table 1). Median follow-up was 4.3 years for both surgical and non-surgical patients, and one, three, and five-year retention rates were similar for non-surgical (90%, 67%, and 56%) and surgical (90%, 69%, and 56%) patients. From Table 1, surgical patients were primarily middle aged, female, had commercial insurance, and more than 40% were racial/ethnic minorities. Seventy six percent of bariatric patients had RYGB in years 2005–2011, with 17% having SG and 7% AGB. At the index date, half of patients had a BMI of 40–49.9 kg/m², the mean HbA1c was 7.1%, and 38% had T2DM for five years or more before baseline. More non-surgical patients had been current smokers in the two years before surgery (13.7% vs. 9.7%). More non-surgical patients had been using medications to control hypertension.

Effect of Bariatric Surgery vs. Usual Care on Risk of Incident Microvascular Disease

Figure 2 panels A-D and Table 3 provide estimates of the cumulative probability of incident microvascular disease over time after bariatric surgery and non-surgical care (for matched controls), as well as the cumulative probability of each of the indicators of microvascular disease (nephropathy, neuropathy, and retinopathy). The 1, 3, 5, and 7-year rates of incident microvascular disease were 6.0%, 11.8%, 16.9%, and 22.5% after bariatric surgery, and

11.2%, 24.3%, 34.7%, and, 44.2% for the matched controls. The differential rate of incident microvascular disease was primarily driven by the incidence of neuropathy, which occurred at a lower rate post-surgery compared to non-surgical controls. Rates of retinopathy were also lower in surgical patients vs. non-surgical patients. The cumulative incidence rates of nephropathy were similar among surgical patients and non-surgical patients (2.7% vs. 2.8%) in the first year after surgery; however, the rates of nephropathy were lower among surgical patients at all time points after 1 year.

Figure 2 panels E-H show the change in adjusted hazard ratio over time for each of our outcomes. The hazard ratio for all microvascular events declined after the index date favoring surgery and remained relatively stable after 1 year. Bariatric surgery was associated with a stable decrease in the risk of neuropathy over time. The risk of nephropathy was initially higher among surgical patients but declined rapidly and remained lower among surgical patients at years 1 through 7. The hazard ratio for retinopathy followed a trajectory similar to the composite index of all microvascular events, aside from a slight strengthening of the association after four years post-surgery.

Table 2 shows the key results from the multivariable adjusted Cox models investigating the association between bariatric surgery vs. usual care and incident microvascular disease at 1, 3, and 5 years after the index date. At 5 years, bariatric surgery was associated with a significantly lower risk of incident microvascular disease compared to matched non-surgical patients who had not received surgery (HR: 0.41; 95% CI: 0.34, 0.48). Bariatric surgery was associated with a lower 5-year risk of diabetic neuropathy (HR: 0.37; 95% CI: 0.30–0.47), nephropathy (HR: 0.41; 95% CI: 0.29–0.58) and retinopathy (HR: 0.55; 95% CI: 0.42–0.73) compared to non-surgical patients. Appendix Table 4 shows the full Cox models.

Sensitivity Analyses

Results of the sensitivity analyses are provided in Appendix Figures 1 and 2. A matched, unadjusted analysis of our primary outcome was not significantly different than the fully adjusted model (Appendix Figure 1). Our primary outcome results using 3-to-1 matching were qualitatively similar to using 1-to-1 and 10-to-1 matching (Appendix Figure 2). The E-values for the point estimate and upper confidence bounds for incident of microvascular disease at 5 years reported in Table 2 were 3.09 and 2.70; the corresponding E-values for incident retinopathy at 5 years were 3.04 and 2.08. We also found that there were no differences in the frequency of microvascular disease surveillance across surgical and non-surgical groups over 5 years follow-up (Appendix Table 5).

Conclusions

Prior studies have demonstrated that most patients who undergo bariatric procedures experience a remission of their T2DM (20, 26). However, less is known about whether bariatric surgery reduces the risk of incident microvascular disease (15). In the current study, bariatric surgery was associated with half the incidence of microvascular disease at 5 years compared to usual medical care. This finding was driven primarily by a lower rate of neuropathy, but we also observed a lower incidence of nephropathy and retinopathy through 5 years of follow-up.

Only three other studies of microvascular outcomes after bariatric surgery have included a non-surgical population as a comparator. These include: the STAMPEDE randomized trial (4), which reported on changes in microalbuminuria and retinopathy; the prospective SOS cohort study (16, 27, 28), which reported on neuropathy, nephropathy, and retinopathy incidence (using ICD-9-CM and ICD-10 codes, nationwide registries, and albuminuria measures); and a retrospective cohort study by Johnson and colleagues that included 2,580 bariatric patients and 13,371 matched controls and reported incident end stage microvascular events (29). We place our findings in the context of these and other relevant studies below.

Among the types of microvascular disease, renal outcomes have been the most frequently studied following bariatric surgery. Despite use of various definitions for renal outcomes, prior studies suggest that the outcomes of bariatric surgery are favorable for those with and without renal disease at baseline (28, 30–36). We observed a 59% lower incidence of nephropathy at 5 years among bariatric patients. The recently-published five-year data from the STAMPEDE trial showed a significantly better urinary albumin-to-creatinine ratio in the SG versus medical therapy group ($P<0.001$), but no between-group differences in creatinine-based measures of renal function (4). Johnson and associates previously reported a significant reduction in end-stage renal disease in bariatric surgery patients compared with matched non-surgical patients (29). In the most recent study of microvascular outcomes, bariatric patients with CKD stage III or higher had significant improvements in eGFR as compared to matched controls, with the greatest improvement in RYGB patients compared to SG patients (35).

In our surgical cohort, we observed a 63% lower hazard of neuropathy at 5 years, defined by ICD-9-CM codes, compared to the usual-care group. Few prior population-based studies report specifically on neuropathy independent of other microvascular outcomes (27, 29). Schauer et al found that there was a 50% reduction in questionnaire-based patient-reported neuropathy (4). Miras and associates failed to show any improvement in peripheral nerve conduction at 12-to-18 months in a small ($n = 70$) prospective case-control study (37).

We also report a 45% lower hazard of incident diabetic retinopathy at 5 years, defined using diagnosis and procedure codes, in surgical versus non-surgical patients. It is well established that strict glycemic control is an important factor in preventing progression of diabetic retinopathy (38–40) and that bariatric surgery is superior to medical treatment in achieving T2DM remission (1–7). Despite this, outcomes to date on the impact of bariatric surgery on diabetic retinopathy have been mixed with some studies showing improvement (41), while others reporting progression (42–45). Johnson *et al* showed fewer cases of blindness or retinal surgery in the surgical group vs. the non-surgical group (29). Five-year data from the STAMPEDE study showed no evidence of benefit of RYGB or SG compared to intensive lifestyle and medical treatment on retinopathy rates (4). The SOS study did not examine retinopathy independent of other microvascular outcomes (27).

It is evident that there are factors at play that may mitigate the potential beneficial impact of improved glycemic control with bariatric surgery on the incidence of retinopathy. These include (1) an overly-rapid decrease in HbA1c (which was found to be associated with early worsening of diabetic retinopathy in the Diabetes Control and Complications Trial) (46), (2)

post-bariatric surgery hypoglycemia (47), (3) discontinuation of fenofibrate and ARBs after bariatric surgery (use of these medications can reduce the risk of retinopathy, but may be discontinued after bariatric surgery in patients who have remission of their diabetes) (48, 49), (4) pregnancy (weight loss can reduce infertility, increasing the chance of pregnancy, which may worsen retinopathy) (50), and (5) vitamin deficiencies, particularly vitamin A, D, B12, copper, and folate deficiencies (51–55). Despite these potential negative effects of bariatric surgery on retinal outcomes, we observed a strong association with lower retinopathy risk over time.

Several factors limit the interpretation of our results. First, the observational study design precludes causal inference and residual unmeasured confounding by indication might be present. Second, we adjusted for health system in our models, but we could not adjust at the level of clinic or provider, which is a potential source of unmeasured confounding due to differences in care quality. However, our sensitivity analyses indicate that the E-value for the upper bound of the confidence intervals at 5 years follow-up for each outcome (reported in Table 2) was >2 ; following VanderWeele and Ding.(25), this suggests that the results could only be explained by an unmeasured confounder that was associated with both receipt of bariatric surgery and risk of microvascular disease by a risk ratio of >2 , beyond the measured confounders. For our study, we believe it is implausible that this degree of confounding remains unmeasured, and, as such, do not believe that our conclusions would change. Third, data used to define incident microvascular disease (retinopathy, nephropathy, and neuropathy) were collected as part of routine clinical care across four large, integrated health care systems, so that missing data (eye exams, blood tests, and neuropathy assessment) may have resulted in misclassification of microvascular complication status for some patients. Fourth, since neuropathy was not identified using an objective endpoint, it may be misclassified, as neuropathy symptoms such as paresthesias are common.

Not all patients will be interested in bariatric surgery as a treatment for their T2DM, but providers should engage all patients with T2DM and a BMI ≥ 35 kg/m² in a shared decision making conversation that discusses the benefits and risks of bariatric procedures (56). Our study results add to a growing body of evidence suggesting that bariatric surgery not only improves glucose, blood pressure, and lipid control, but is likely to reduce macrovascular complications, microvascular complications, as well as improve survival in patients with severe obesity and T2DM (57). The findings from this study should help patients and providers to better understand the potential trade-offs of bariatric surgery as treatment for T2DM and help them to make more informed decisions about their care.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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None of the authors have any conflicts of interest to disclose. All authors contributed to the plan of the study, including data abstraction and preparation for analyses, interpretation of analyses, and writing of the manuscript. RO and DEA were responsible for the oversight of the manuscript and its writing. SH, EJ, AB, and MKT were responsible for data abstraction, preparation, and analyses as well as the summary and writing of methods and

results including the appendices. DA was responsible for overseeing the conduct of the study in general and guiding the hypothesis formation and testing. RO and DEA take full responsibility for the contents of the manuscript.

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Figure 1.

Flow diagram for identification of eligible patients who underwent bariatric surgery and had type 2 diabetes without history of microvascular disease

Figure 2.A. Cumulative Incidence of Microvascular Disease Among Surgical and Matched Non-Surgical Patients

Figure 2.B. Cumulative Incidence of Incident Neuropathy Among Surgical and Matched Non-Surgical Patients

Figure 2.C. Cumulative Incidence of Nephropathy (eGFR <60) Among Surgical and Matched Non-Surgical Patients

Figure 2.D. Cumulative Incidence of Incident Retinopathy Among Surgical and Matched Non-Surgical Patients

Figure 2.E. Time-varying Hazard Ratio for All Microvascular Disease Events Comparing Surgical and Matched Non-Surgical Patients

*Shaded area represents the 95% confidence interval

Figure 2.F. Time-varying Hazard Ratio for Neuropathy Events Comparing Surgical and Matched Non-Surgical Patients

Figure 2.G. Time-varying Hazard Ratio for Nephropathy (eGFR <60) Events Comparing Surgical and Matched Non-Surgical Patients

Figure 2.H. Time-varying Hazard Ratio for Retinopathy Events Comparing Surgical and Matched Non-Surgical Patients

Figure 2.

A-H. Kaplan-Meier-derived estimates of the cumulative incidence of microvascular disease (A-D) and time-varying hazard ratio comparing the risk of incident microvascular disease (E-H). Separate estimates for neuropathy (B, F), nephropathy (C, G), and retinopathy (D, H) are shown, as well as a composite estimate for incident microvascular disease due to any of the three (A, E).

Table 1.

Baseline characteristics of patients with type 2 diabetes who underwent bariatric surgery and matched non-surgical patients, 2005–2011 *.

	Bariatric Patients	Matched Non-Surgical Patients
Number	4,024	11,059
Age (years), mean (SD)	47.6 (9.7)	48.7 (9.7)
Age Categories, N (%)		
18–29 y	124 (3.1%)	306 (2.8%)
30–44 y	1393 (34.6%)	3319 (30%)
45–54 y	1457 (36.2%)	4135 (37.4%)
55–64 y	940 (23.4%)	2894 (26.2%)
65–79 y	110 (2.7%)	405 (3.7%)
Female, N (%)	3052 (75.8%)	8266 (74.7%)
Race/Ethnicity		
Hispanic	748 (18.6%)	2008 (18.2%)
Non-Hispanic black	608 (15.1%)	1853 (16.8%)
Non-Hispanic white	1843 (45.8%)	4515 (40.8%)
Other	305 (7.6%)	709 (6.4%)
Unknown/Missing	520 (12.9%)	1974 (17.8%)
Health care site		
HealthPartners (HP)	161 (4%)	461 (4.2%)
Kaiser Permanente Northern California (KPNC)	1049 (26.1%)	3035 (27.4%)
Kaiser Permanente Southern California (KPSC)	2555 (63.5%)	6800 (61.5%)
Kaiser Permanente Washington (KPWA)	259 (6.4%)	763 (6.9%)
Insurance type		
Commercial	3790 (94.2%)	9946 (89.9%)
Medicaid	94 (2.3%)	365 (3.3%)
Medicare	81 (2%)	542 (4.9%)
Other	59 (1.5%)	206 (1.9%)
Year of surgery/index date		
2005	155 (3.9%)	393 (3.6%)
2006	280 (7%)	809 (7.3%)
2007	395 (9.8%)	1132 (10.2%)
2008	547 (13.6%)	1525 (13.8%)
2009	618 (15.4%)	1634 (14.8%)
2010	876 (21.8%)	2352 (21.3%)
2011	1153 (28.7%)	3214 (29.1%)
Total number of days of health care use in 7–24 months pre-index date, mean (SD)	18.2 (11.7)	14.0 (8.8)
BMI, kg/m², mean (SD)	44.9 (6.9)	43.8 (6.7)

	Bariatric Patients	Matched Non-Surgical Patients
BMI Categories, kg/m²		
35.0–39.9	1073 (26.7%)	3746 (33.9%)
40.0–49.9	2109 (52.4%)	5487 (49.6%)
50.0+	842 (20.9%)	1826 (16.5%)
Serum Creatinine, mg/dL	0.79 (0.17)	0.81 (0.41)
eGFR, mL/min/1.73 m²	96.6 (17.9)	94.8 (19.8)
HbA1c %, mean (SD)	7.10 (1.20)	7.14 (1.20)
Observed duration of diabetes in years, mean (SD)	4.63 (3.65)	4.50 (3.36)
0–4 years	2458 (61.1%)	6938 (62.7%)
5+ years	1566 (38.9%)	4121 (37.3%)
Use of oral diabetes medication	2731 (67.9%)	7467 (67.5%)
Use of insulin	674 (16.7%)	1883 (17%)
Dyslipidemia		
Triglycerides ≥ 150 mg/dL	1909 (47.4%)	5042 (45.6%)
[Missing Triglycerides]	19 (0.5%)	442 (4%)
Dyslipidemia diagnosis *	3126 (77.7%)	8607 (77.8%)
Use of a statin	1998 (49.7%)	5703 (51.6%)
Use of other lipid-lowering medications	222 (5.5%)	651 (5.9%)
Hypertension		
Uncontrolled hypertension	286 (7.1%)	1061 (9.6%)
[Missing BP measures]	180 (4.5%)	91 (0.8%)
Hypertension diagnosis *	2923 (72.6%)	7248 (65.5%)
Use of ACE inhibitors or ARB	2118 (52.6%)	6273 (56.7%)
Use of other antihypertensive medications	1644 (40.9%)	5763 (52.1%)
Cardiovascular disease		
1 cardiac event *	60 (1.5%)	267 (2.4%)
1 cerebrovascular event *	40 (1%)	173 (1.6%)
Use of platelet inhibitor	43 (1.1%)	353 (3.2%)
Smoking status, self-reported		
Current	389 (9.7%)	1517 (13.7%)
Former	1208 (30%)	2652 (24%)
Never	2209 (54.9%)	6374 (57.6%)
Missing	218 (5.4%)	516 (4.7%)

Values represent characteristics at the time of bariatric surgery for surgical patients (or equivalent index date for non-surgical patients) or for the two-year period prior to surgery (as indicated by *). For categorical variables, counts and percentages are presented; for continuous variables, means ± standard deviations are presented.

Table 2.

Results of matched, fully-adjusted Cox proportional hazards model comparing the risk of incident microvascular disease outcomes in surgical patients compared to matched* non-surgical patients

	Hazard Ratio (95% CI) at 1 Year after Index Date	Hazard Ratio (95% CI) at 3 Years after Index Date	Hazard Ratio (95% CI) at 5 Years after Index Date	Hazard Ratio (95% CI) at 7 Years after Index Date
Composite Index of Incident Microvascular Disease	0.38 (0.33, 0.44)	0.35 (0.30, 0.41)	0.41 (0.34, 0.48)	0.40 (0.30, 0.53)
Incident Diabetic Neuropathy	0.28 (0.23, 0.35)	0.30 (0.25, 0.37)	0.37 (0.3, 0.47)	0.48 (0.34, 0.67)
Incident Diabetic Nephropathy	0.29 (0.21, 0.42)	0.19 (0.14, 0.27)	0.41 (0.29, 0.58)	0.45 (0.29, 0.71)
Incident Diabetic Retinopathy	0.64 (0.52, 0.79)	0.68 (0.55, 0.84)	0.55 (0.42, 0.73)	0.37 (0.24, 0.58)

* The Composite Index of Incident Microvascular Disease = the first occurrence of neuropathy, nephropathy, or retinopathy; Matched on age, sex, BMI, site, insulin use, HbA1c, observed diabetes duration, and number of days of health care utilization in the 7–24 months prior to index date. Adjusted for all matching variables plus race/ethnicity, insurance type, diabetes duration, oral diabetes medication use, hypertension diagnosis, baseline blood pressure, angiotensin converting enzyme inhibitor and angiotensin receptor blocker use, other antihypertensive medication use, dyslipidemia diagnosis, statin use, other lipid lowering agent use, coronary heart disease, cerebrovascular disease, and smoking status.

Table 3.

Cumulative incidence rates and 95% confidence intervals for microvascular disease outcomes in surgical patients and matched non-surgical patients *

	1 year		3 years		5 years		7 years	
	Surgical Group	Non-surgical Group	Surgical Group	Non-surgical Group	Surgical Group	Non-surgical Group	Surgical Group	Non-surgical Group
Composite Index of Incident Microvascular Disease	6% (5.2%, 6.7%)	11.2% (10.6%, 11.8%)	11.8% (10.8%, 12.9%)	24.3% (23.4%, 25.2%)	16.9% (15.5%, 18.3%)	34.7% (33.6%, 35.8%)	22.5% (20.5%, 24.5%)	44.2% (42.7%, 45.7%)
Incident Diabetic Neuropathy	1.8% (1.4%, 2.3%)	6% (5.6%, 6.5%)	4.6% (3.9%, 5.3%)	14.1% (13.4%, 14.8%)	7.2% (6.3%, 8.2%)	21.4% (20.4%, 22.3%)	11.3% (9.7%, 12.8%)	27.6% (26.3%, 28.9%)
Incident Diabetic Nephropathy	2.7% (2.2%, 3.2%)	2.8% (2.5%, 3.2%)	3.6% (3%, 4.2%)	6.8% (6.2%, 7.3%)	4.9% (4.2%, 5.7%)	10% (9.3%, 10.7%)	6.4% (5.3%, 7.6%)	14% (13%, 15.1%)
Incident Diabetic Retinopathy	1.9% (1.5%, 2.4%)	3% (2.7%, 3.4%)	4.9% (4.2%, 5.6%)	7.3% (6.8%, 7.8%)	7.2% (6.3%, 8.2%)	11.2% (10.5%, 11.9%)	9.8% (8.4%, 11.2%)	15.9% (14.8%, 17%)

* The Composite Index of Incident Microvascular Disease = the first occurrence of neuropathy, nephropathy, or retinopathy; Matched on age, sex, BMI, site, insulin use, HbA1c, observed diabetes duration, and number of days of health care utilization in the 7–24 months prior to index date.