Original Investigation

Association of Bariatric Surgery With Long-term Remission of Type 2 Diabetes and With Microvascular and Macrovascular Complications

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IMPORTANCE Short-term studies show that bariatric surgery causes remission of diabetes. The long-term outcomes for remission and diabetes-related complications are not known.

OBJECTIVES To determine the long-term diabetes remission rates and the cumulative incidence of microvascular and macrovascular diabetes complications after bariatric surgery.

DESIGN, SETTING, AND PARTICIPANTS The Swedish Obese Subjects (SOS) is a prospective matched cohort study conducted at 25 surgical departments and 480 primary health care centers in Sweden. Of patients recruited between September 1, 1987, and January 31, 2001, 260 of 2037 control patients and 343 of 2010 surgery patients had type 2 diabetes at baseline. For the current analysis, diabetes status was determined at SOS health examinations until May 22, 2013. Information on diabetes complications was obtained from national health registers until December 31, 2012. Participation rates at the 2-, 10-, and 15-year examinations were 81%, 58%, and 41% in the control group and 90%, 76%, and 47% in the surgery group. For diabetes assessment, the median follow-up time was 10 years (interquartile range [IQR], 2-15) and 10 years (IQR, 10-15) in the control and surgery groups, respectively. For diabetes complications, the median follow-up time was 17.6 years (IQR, 14.2-19.8) and 18.1 years (IQR, 15.2-21.1) in the control and surgery groups, respectively.

INTERVENTIONS Adjustable or nonadjustable banding (n = 61), vertical banded gastroplasty (n = 227), or gastric bypass (n = 55) procedures were performed in the surgery group, and usual obesity and diabetes care was provided to the control group.

MAIN OUTCOMES AND MEASURES Diabetes remission, relapse, and diabetes complications. Remission was defined as blood glucose <110 mg/dL and no diabetes medication.

RESULTS The diabetes remission rate 2 years after surgery was 16.4% (95% CI, 11.7%-22.2%; 34/207) for control patients and 72.3% (95% CI, 66.9%-77.2%; 219/303) for bariatric surgery patients (odds ratio [OR], 13.3; 95% CI, 8.5-20.7; *P* < .001). At 15 years, the diabetes remission rates decreased to 6.5% (4/62) for control patients and to 30.4% (35/115) for bariatric surgery patients (OR, 6.3; 95% CI, 2.1-18.9; *P* < .001). With long-term follow-up, the cumulative incidence of microvascular complications was 41.8 per 1000 person-years (95% CI, 35.3-49.5) for control patients and 20.6 per 1000 person-years (95% CI, 17.0-24.9) in the surgery group (hazard ratio [HR], 0.44; 95% CI, 0.34-0.56; *P* < .001). Macrovascular complications were observed in 44.2 per 1000 person-years (95% CI, 37.5-52.1) in control patients and 31.7 per 1000 person-years (95% CI, 27.0-37.2) for the surgical group (HR, 0.68; 95% CI, 0.54-0.85; *P* = .001).

CONCLUSIONS AND RELEVANCE In this very long-term follow-up observational study of obese patients with type 2 diabetes, bariatric surgery was associated with more frequent diabetes remission and fewer complications than usual care. These findings require confirmation in randomized trials.

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Obesity and diabetes have reached epidemic proportions[1,2] and constitute major health and economic burdens. Worldwide, 347 million adults are estimated to live with diabetes and half of them are undiagnosed.[2]

Studies show that type 2 diabetes is preventable. The incidence of diabetes can be reduced by as much as 50% by lifestyle and pharmacological interventions.[3,4] Bariatric surgery reduced the long-term incidence of diabetes by about 80% (adjusted hazard ratio [HR], 0.17; 95% CI, 0.13-0.21) in the Swedish Obese Subjects (SOS) study.[5,6]

Remission from established diabetes is much less common following lifestyle interventions,[7] exercise alone,[8] weight loss medication,[9] and antidiabetic drug treatment.[10] Lifestyle interventions and pharmacotherapy do not reduce the incidence of cardiovascular events in obese individuals with diabetes[11] or in other high-risk groups with increased body weight.[12,13] In contrast, short-term diabetes remission occurs after bariatric surgery in 60% to 90% of patients.[5,14-20] These short-term remission rates cannot be extrapolated to long-term outcomes. The principal aim of the current report was to determine diabetes remission rates after bariatric surgery as compared with usual care after a median follow-up of 10 years. Another aim of this study was to examine the association of bariatric surgery with microvascular and macrovascular diabetes complications after a median follow-up of 18 years.

Methods

The SOS study has previously been described.[5] In brief, 2010 individuals chose to undergo surgery, and a contemporaneously matched obese control group of 2037 participants was created using 18 variables from a matching examination and a group matching procedure (eAppendix in the Supplement). The surgery and control groups had identical inclusion and exclusion criteria. The inclusion criteria were an age of 37 to 60 years and a body mass index (BMI) of 34 or more in men and 38 or more in women before or at the time of the matching examination (calculated as weight in kilograms divided by height in meters squared). The exclusion criteria (eAppendix in the Supplement) were established to exclude patients with unacceptable surgical risks. Baseline examinations were undertaken 4 weeks before the start of the intervention.

The current analyses include all patients with type 2 diabetes at baseline. Diabetes remission and diabetes complications were prespecified secondary end points of the SOS study. The primary outcomes of this report were diabetes remission, relapse, and incidence of diabetes complications.

Patients in the control group received the customary lifestyle and pharmacological treatment for obesity and diabetes at their primary health care centers. Both study groups had identical follow-up with physical examinations and questionnaires at baseline and after 0.5, 1, 2, 3, 4, 6, 8, 10, and 15 years. Centralized biochemistry (**Table**) was performed at baseline and after 2, 10, and 15 years. All samples were taken after an overnight fast and analyzed at the Central Laboratory, Sahlgrenska University Hospital, Gothenburg, Sweden, accredited according to International Organization for Standardization/International Electrochemical Commission 15189:2007 standards.

Diabetes-Related Definitions

Self-reported information about diabetes medication and diabetes duration was obtained and glucose concentrations were measured during a baseline examination and at follow-up visits at 2, 10, and 15 years after study entry. From 1987 through 2009, fasting glucose concentrations were measured in venous whole blood. After 2009, venous fasting plasma glucose was measured, and the concentrations were converted to those for blood glucose.[6] The study was initiated before repeated measurements were routinely used for the diagnosis of type 2 diabetes; therefore, single fasting glucose determinations were used.

Type 2 diabetes was defined as fasting blood glucose of 110 mg/dL or higher, corresponding to a fasting plasma glucose that was 126 mg/dL or higher,[21,22] or diabetes medication use (insulin, oral antidiabetic drugs, or both). (To convert glucose to mmol/L, multiply by 0.0555.)

Diabetes remission was defined as blood glucose levels lower than 110 mg/dL and no diabetes medication. Patients in diabetes remission could either have impaired fasting glucose (90-110 mg/dL) or normal fasting blood glucose (<90 mg/dL).[21,22]

For patients with diabetes with onset before age 35 years, type 1 diabetes and latent autoimmune diabetes of adults were ruled out by excluding patients positive for glutamate decarboxylase antibodies or islet cell antibodies or with C-peptide values lower than 1.11 ng/mL at baseline. In total, 4 patients (2 in the control and 2 in the surgery group) were excluded.

Diabetes Complications

Microvascular and macrovascular diabetes complications requiring hospital or specialist outpatient treatment or that were associated with death during follow-up were traced by searching the Swedish Cause of Death Register and the Swedish National Patient Register.

The inpatient components of the National Patient Register and the Cause of Death Register have 99% coverage.[23] For specialist outpatient care, the National Patient Register coverage for somatic diseases has been assessed as 78%.[24] Validation studies demonstrated that 80% to 90% of the diagnoses in the National Patient Register are accurate.[25,26] There is no nationwide primary health care register in Sweden. However, patients with the diabetes complications defined by the *International Classification of Diseases* and intervention codes in eTable 1 of the Supplement are rarely treated exclusively in primary care in Sweden.

Cumulative incidence calculations use the composite end points microvascular complications (eyes, kidneys, and peripheral nerves, whichever came first) and macrovascular complications (legs, heart, and brain, whichever came first).

Statistical Analysis

Mean values, standard deviations, and percentages were used to describe the baseline characteristics. Differences between

Table. Baseline Characteristics and Weight Changes in Swedish Obese Subjects Control and Surgery Patients With Type 2 Diabetes at Baseline

Baseline Information	Control Group (n = 260)	Surgery Group (n = 343)[a]	t Test	P Value
Men, No. (%)	104 (40)	141 (41)		.72
Age, mean (SD), y	50.4 (6.3)	48.7 (5.9)	3.5	.001
Weight, mean (SD), kg	116 (17)	123 (19)	−4.6	<.001
Body mass index, mean (SD)[b]	40.0 (4.6)	42.1 (4.7)	−5.5	<.001
Waist/hip ratio	1.01 (0.07)	1.02 (0.08)	−1.6	.11
Smokers, No. (%)	53 (21)	85 (25)		.24
Previous CV event, No. (%)	15 (5.8)	21 (6.1)		.86
Diabetes duration, mean (SD), y	3.3 (4.5)	2.9 (4.7)	1.2	.22
Median (IQR), y	2 (0-5)	1 (0-4)		
Fasting blood glucose, mg/dL	156 (48)	156 (48)	−0.1	.89
Fasting serum insulin, mU/L	25.6 (17.9)	28.7 (19.5)	−2.0	.04
Insulin range, mU/L	3.6-125.3	5.7-261.0		
HOMA-IR, mean (SD)	9.7 (7.6)	11.0 (8.1)	−2.0	.04
Systolic BP, mean (SD), mm Hg	144 (19)	150 (19)	−4.3	<.001
Diastolic BP, mean (SD), mm Hg	87 (11)	92 (11)	−4.9	<.001
Total cholesterol, mean (SD), mg/dL	221 (45)	228 (48)	−2.0	.05
HDL cholesterol, mean (SD), mg/dL	48 (11)	48 (12)	−0.4	.67
Triglycerides, mean (SD), mg/dL	255 (211)	256 (193)	−0.1	.91
Oral diabetes medication, No. (%)	102 (39.2)	121 (35.3)		.35
Insulin treatment, No. (%)	34 (13.1)	42 (12.2)		.81
2-y weight change, mean (SD), kg	−3.0 (8.0)	−26.3 (14.5)	21.1	<.001
No. of patients at 2 y	207	304		
10-y weight change, mean (SD), kg	−4.4 (12.4)	−22.5 (15.4)	11.6	<.001
No. of patients at 10 y	134	239		

Abbreviations: BP, blood pressure; CV, cardiovascular; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment of insulin resistance; IQR, interquartile range.

SI conversion factors: To convert glucose to mmol/L, multiply by 0.0555; total and HDL cholesterol to mmol/L, multiply by 0.0259; triglycerides to mmol/L, multiply by 0.0113.

[a] Sixty-one patients underwent banding; 227 patients underwent vertical banded gastroplasty, and 55 patients underwent gastric bypass.

[b] Calculated as weight in kilograms divided by height in meters squared.

treatment groups were evaluated with *t* tests for continuous variables and logistic regression models for dichotomous variables.

Remission of diabetes was calculated as the proportions of surgery and control patients not fulfilling diabetes criteria at 2, 10, and 15 years of follow-up, respectively. Relapse from remission was defined as the proportion of patients who fulfilled diabetes criteria at the 10-year follow-up among those who were in remission at year 2. Multivariable logistic regression models were used to identify predictors for both remission and relapse. Because information on diabetes remission was obtained from personal health examinations, the effects of dropout during follow-up were evaluated with multiple imputation analyses and characteristics of participants and nonparticipants were compared. With a chained equations approach, a sequence of univariate imputation models based on logistic regression was used to generate imputed remission and relapse data for missing outcome values. A total of 30 imputed data sets were generated based on age, sex, treatment group (surgery/control), BMI at baseline, and prior blood glucose measurements for the outcome variables. Data were imputed and analyzed using the Stata multiple imputations procedure (version 12.1; StataCorp).

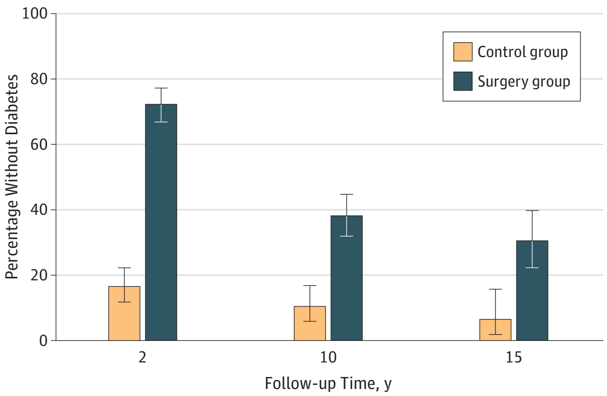
For cumulative incidence of microvascular and macrovascular complications, the time interval was calculated between the start of the intervention and death or first hospitalization due to diagnoses or treatments in eTable 1 of the Supplement. Those who died for reasons other than microvascular or macrovascular complications, emigrated, or were alive without microvascular or macrovascular complications on December 31, 2012, were treated as censored observations. Log-rank test was used to test for differences between surgery and control groups. In addition, Cox proportional hazards regression models were used to analyze time to event. The differences between the bariatric surgery group and the control group, expressed as HRs with 95% confidence intervals, were evaluated in unadjusted analyses with a single covariate for treatment group (surgery or control) and in analyses adjusting for preselected baseline risk factors (sex, age, fasting glucose, BMI, diabetes duration) for diabetes complications.

To mimic an intent-to-treat analysis, we assessed patients according to the original treatment primarily applied. Sensitivity analyses were conducted by excluding control group patients who received bariatric surgery during follow-up and surgery group patients who underwent additional bariatric surgery procedures (conversion from banding or vertical banded gastroplasty to gastric bypass or a reversal of banding). All *P* values are 2-sided, and *P* values of less than .05 were considered statistically significant. Stata version 12.1 was used for the analyses.

Results

In the ongoing prospective SOS intervention study, 4047 obese individuals were enrolled between September 1, 1987, and

Figure 1. Prevalence of Diabetes Remission in the Bariatric Surgery and Control Groups



	2	10	15
Total participants			
Control	207	135	62
Surgery	303	236	115
Odds ratio (95% CI)	13.3 (8.5-20.7)	5.3 (2.9-9.8)	6.3 (2.1-18.9)

Diabetes remission was defined as fasting blood glucose levels lower than 110 mg/dL and no diabetes medication. Odds ratios (ORs) are unadjusted and calculated using logistic regression analysis. The control group was the reference group. *P* < .001 for the 2- and 10-year follow-up; *P* = .001 for the 15-year follow-up. Error bars indicate 95% CIs.

January 31, 2001. The current analyses include all control (n = 260) and surgery (n = 343) patients with type 2 diabetes at baseline (Table). In the surgery group, 61 patients underwent nonadjustable or adjustable banding, 227 underwent vertical banded gastroplasty, and 55 had gastric bypass. Diabetes status was determined at SOS health examinations until May 22, 2013. Information on diabetes complications was obtained from national health registers until December 31, 2012. For diabetes assessment, the median follow-up periods were 10 years (interquartile range [IQR], 2-15) and 10 years (IQR, 10-15) for the control and surgery groups, respectively. The mean (SD) follow-up periods were 7.0 (5.8) and 9.1 (5.5) years, and the numbers of person-years per group were 1820 and 3121, respectively. For diabetes complications, the median follow-up was 17.6 years (IQR, 14.2-19.8) and 18.1 years (IQR, 15.2-21.1) in the control and surgery groups and the numbers of person-years, 2733 and 4429, respectively.

Fasting blood glucose was elevated to a similar extent in the control (156 mg/dL) and surgery patients (156 mg/dL), and the diabetes duration (3.3 and 2.9 years, respectively) was not significantly different between groups. The control group had lower body weight (116 vs 123 kg), while the waist-to-hip ratio was similar (1.01 vs 1.02) in the 2 groups. There were no differences in the proportions of surgery and control patients receiving insulin or oral diabetes medication (Table).

Mortality adjusted in-person participation rates at SOS-arranged health and laboratory examinations after 2, 10, and 15 years were 81%, 58%, and 41% in the control group and 90%, 76%, and 47% in the surgery group, respectively. There were no major differences in baseline characteristics between 15-year nonparticipants and participants (eTable 2 of the Supplement). Of the controls, 8.5% had obtained bariatric surgery during follow-up. In addition, 28% of the banding patients and 16% of the vertical banded gastroplasty patients were converted to gastric bypass or had the band removed during follow-up.

eFigure 1 of the Supplement shows weight changes for control and surgery patients. At 2 years, the mean (SD) weight loss was 3.0 (8.0) kg (2.4%) in the control group and 26.3 (14.5) kg (21.2%) in the surgery group (*P* < .001). The corresponding mean (SD) weight losses from baseline to 10 years were 4.4 (12.4) kg (3.6%) and 22.5 (15.4) kg (18.0%), respectively (*P* < .001).

Bariatric Surgery and Diabetes Remission

Figure 1 shows the prevalence of diabetes remission after 2, 10, and 15 years. The proportion in remission after 2 years was 72.3% (219/303) in the surgery group and 16.4% (34/207) in the control group (unadjusted OR, 13.3; 95% CI, 8.5-20.7; *P* < .001). The difference in the proportion of patients in remission between surgery and control groups at 2 years remained significant after multivariable adjustments (OR, 40.5; 95% CI, 21.0-78.2; *P* < .001) (eTable 3 in the Supplement). The proportion of surgery patients in remission decreased to 38.1% (90/236) and 30.4% (35/115) after 10 and 15 years, respectively, but remained higher than in the controls (10 years: OR, 5.3; 95% CI, 2.9-9.8, and 15 years: OR, 6.3; 95% CI, 2.1-18.9) (Figure 1). Sensitivity analyses using multiple imputations of missing end points for remission did not change the main results (eTable 3 and eTable 4 in the Supplement). The remission results shown in Figure 1 remained unchanged when analyses were restricted to patients who had continued the original treatment during follow-up (ORs, 14.4 [95% CI, 9.1-22.9], 5.9 [95% CI, 3.1-11.3], and 12.3 [95% CI, 2.8-53.3] for 2, 10, and 15 years, respectively).

All types of bariatric surgery were associated with higher remission rates compared with usual care (eFigure 2 in the Supplement). There were no significant subgroup-treatment interactions regarding diabetes remission.

Diabetes Remission and Relapse in the Surgery Group

Figure 2 shows that short diabetes duration at baseline was associated with higher diabetes remission rates in surgery patients after 2, 10, and 15 years of follow-up. The unadjusted findings of Figure 2 were confirmed by multivariable logistic regression analyses in which short diabetes duration was associated both with high remission rate at 2 years (*P* < .001) and with low relapse rate between 2 and 10 years of follow-up (*P* = .03). Baseline BMI was not associated with diabetes remission or relapse, while the weight change between baseline and 2 years was associated with relapse between 2 and 10 years (eTable 5 in the Supplement).

Bariatric Surgery and Diabetes Complications

Bariatric surgery was associated with decreased incidence of microvascular complications (incidence rate, 41.8 [95% CI, 35.3-49.5] and 20.6 [95% CI, 17.0-24.9] per 1000 person-years in the control and surgery groups, respectively; HR, 0.44; 95% CI, 0.34-0.56; *P* < .001) and macrovascular complications (incidence rate, 44.2 [95% CI, 37.5-52.1] and 31.7 [95% CI, 27.0-37.2] per 1000 person-years, respectively; HR, 0.68; 95% CI, 0.54-0.85; *P* = .001) (**Figure 3**). Exclusion of 22 controls who obtained surgery during follow-up yielded similar results (HR, 0.44; 95% CI, 0.34-0.58, and HR, 0.65; 95% CI, 0.52-0.82, for microvascular and macrovascular complications, respectively).

After multivariable adjustments, the HRs remained significant for microvascular and macrovascular diabetes complications (HR, 0.43; 95% CI, 0.33-0.58; *P* < .001, and HR, 0.74; 95% CI, 0.58-0.94; *P* = .01, respectively). These calculations also showed that longer diabetes duration at baseline was significantly associated with increased incidence of microvascular (*P* < .001) and macrovascular (*P* < .001) diabetes complications (eTable 6 in the Supplement).

Figure 4 illustrates that the association between bariatric surgery and reduction of diabetes complications was gradually decreasing with increasing diabetes duration at baseline (*P* = .03 for interaction). In contrast, baseline BMI did not influence the association between bariatric surgery and diabetes complications (*P* = .67 for interaction).

Postoperative Mortality

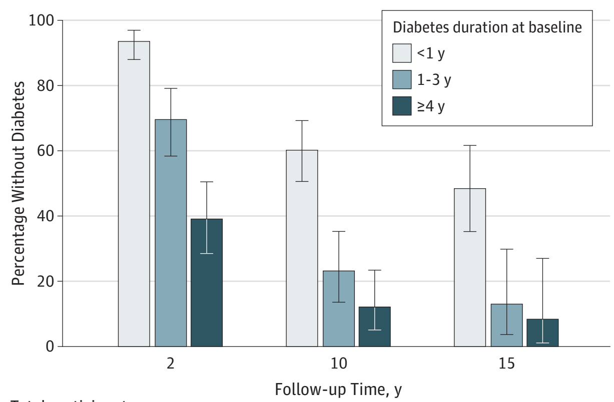
Within 90 days from the start of the study, 2 of 343 patients in the surgery group (0.58%) and 1 of 260 patients in the control group (0.38%) had died.

Discussion

Type 2 diabetes has traditionally been considered a chronic disease and typically less than 15% of treated patients achieve remission with nonsurgical methods.[7-10,27] In this report, 72% of surgically treated patients were in remission at the 2-year examination while 16% had remitted in the control group. Our 2-year results are in agreement with a large number of retrospective studies[14,15,28,29] and with 6 prospective controlled studies.[16-20,30]

The excellent 2-year remission rates in the SOS surgery group were followed by frequent relapses. Although the rates were significantly more favorable than those for the control group, only 38% and 30% of the surgery patients were still in remission after 10 and 15 years, respectively. While this is in agreement with our preliminary report from

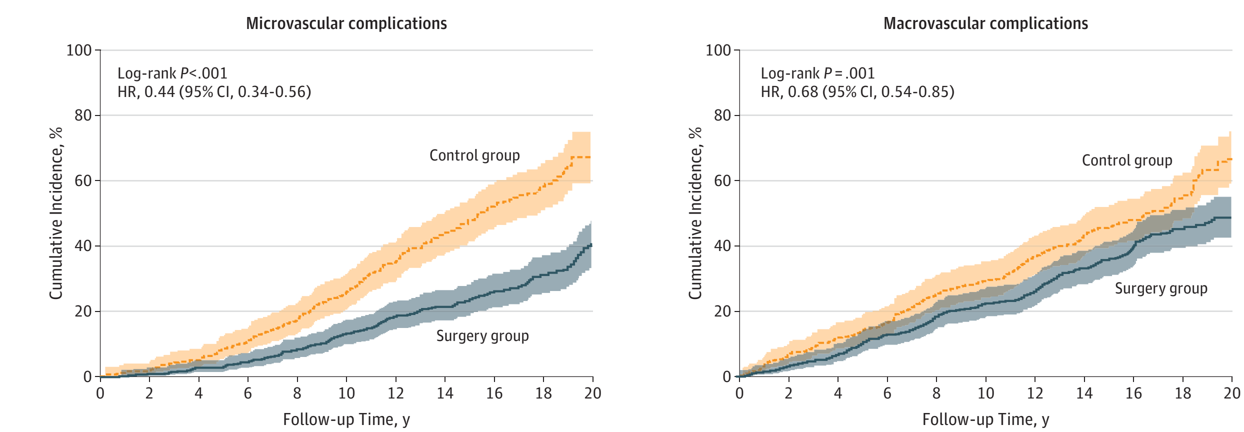
Figure 2. Diabetes Remission by Diabetes Duration in the Surgery Group



Total participants	2	10	15
<1 y	139	113	60
1-3 y	82	65	31
≥4 y	82	58	24

Diabetes remission was defined as fasting blood glucose levels lower than 110 mg/dL and no diabetes medication. Error bars indicate 95% CIs.

Figure 3. Cumulative Incidence of Microvascular and Macrovascular Diabetes Complications in the Surgery and Control Groups



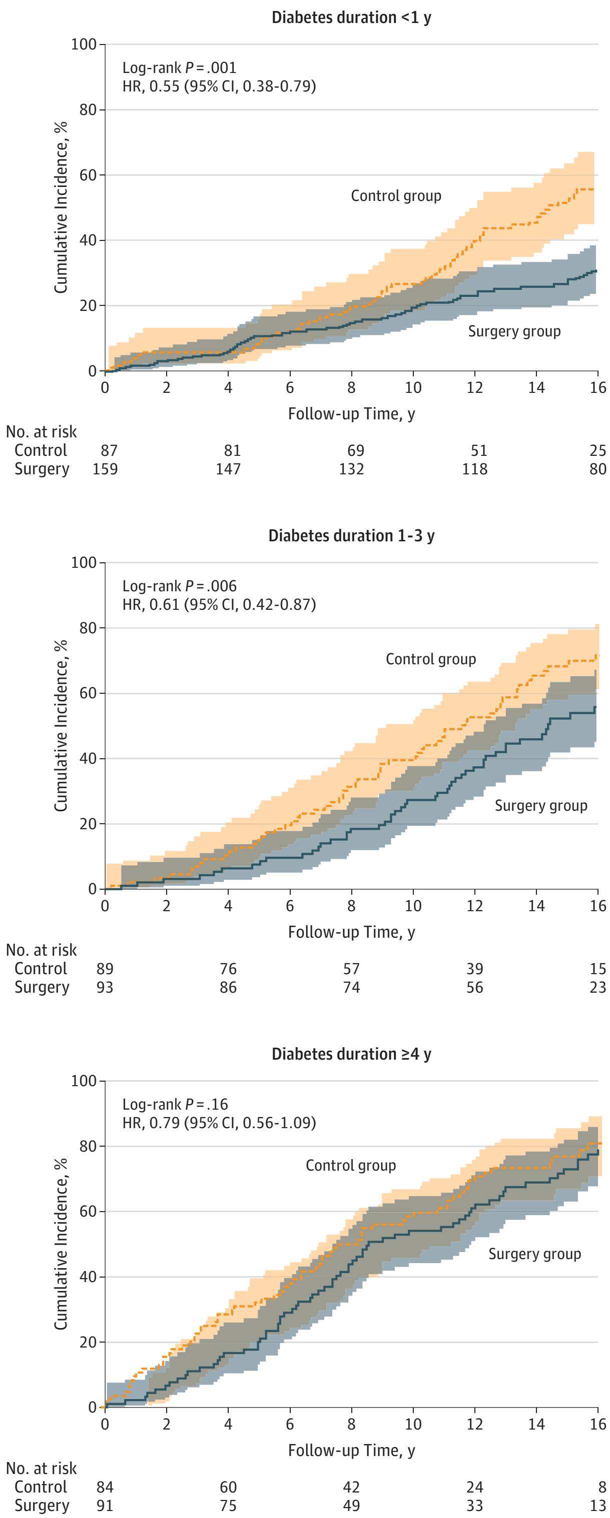
No. at risk

Microvascular	0	2	4	6	8	10	12	14	16	18	20
Control	260	251	239	222	201	177	146	104	68	46	19
Surgery	343	336	326	318	301	280	257	207	160	112	63

Macrovascular	0	2	4	6	8	10	12	14	16	18	20
Control	260	240	225	214	191	178	155	116	80	53	20
Surgery	343	330	315	294	270	254	238	186	142	92	54

For microvascular complications, there were 134 events in the control group and 106 events in the surgery group; for macrovascular complications, 142 events in the control group and 151 events in the surgery group. Diabetes complications requiring hospital treatment or specialist care or diabetes complications that were associated with death during follow-up were traced by cross-checking against the Swedish National Patient Register and the Cause of Death Registry until December 31, 2012. (eTable 1 of the Supplement lists the *International Classification of Diseases* codes and surgery procedures used for cross-checking.) The x-axes are truncated at 20 years, but all observations after 20 years were included in the statistical analyses. Shaded areas indicate 95% CIs. The incidence rates of microvascular complications per 1000 person-years were 41.8 (95% CI, 35.3-49.5) in the control group and 20.6 (95% CI, 17.0-24.9) in the surgery group. Incidence rates of macrovascular complications were 44.2 (95% CI, 37.5-52.1) and 31.7 (95% CI, 27.0-37.2), respectively.

Figure 4. Cumulative Incidence of All (Microvascular and Macrovascular) Diabetes Complications by Diabetes Duration at Baseline



For a diabetes duration of <1 y, there were 51 events in the control group and 66 events in the surgery group; for 1-3 y, 66 events in control and 54 events in surgery patients; for ≥4 y, 69 events in control and 72 events in surgery patients. Interaction *P* value for diabetes duration and treatment was .03. The x-axes are truncated, but all observations after 16 y were included in statistical analyses.

2004, when less than half of the patients with diabetes had been followed up for 10 years,[5] other prospective long-term studies with non-surgically treated controls are not available for comparison.

Diabetes remission rates are typically higher after gastric bypass than after banding,[14,15] and a recent retrospective 5-year study showed 61% remission after gastric bypass but only 9% remission after banding.[31] However, at least 1 published study has failed to find differences in remission rate between surgical techniques.[32] In our study, weight losses were similar after gastric banding and gastric bypass at the 10-year follow-up, and there were no significant differences in diabetes remission. The disagreements between studies may be due to inadequate sample size or different definitions of diabetes remission (eg, fasting glucose, hemoglobin A_{1c}, or both).

Tight glycemic control by means of pharmacological treatment may reduce the incidence of microvascular disease (review[33]), but tight control is seldom achieved in obese patients with diabetes.[27] Lifestyle changes and pharmacotherapy have not typically reduced the incidence of diabetes-associated macrovascular disease.[11,34] In contrast, we recently demonstrated that bariatric surgery is associated with reduced 20-year incidence of myocardial infarction not only in obese patients in general[35] but also in obese patients with diabetes.[36] In addition, favorable 5-year effects of bariatric surgery on albuminuria have recently been reported by other researchers.[37]

The current report provides information about the long-term incidence of microvascular and macrovascular diabetes complications after bariatric surgery and usual care. In this study, bariatric surgery was associated with reduced long-term incidence of microvascular and macrovascular complications. The association between bariatric surgery and reduction of diabetes complications was not explained by unusually bad outcomes for the control group. On the contrary, the 16% remission rate at 2 years we observed in the control patients is in the higher range for lifestyle and pharmacological treatment reported in the literature.[7-10]

Short diabetes duration at baseline is associated with more favorable short-term diabetes remission rates after bariatric surgery.[29,32,38] Our current report confirms this and also extends the information by demonstrating that short diabetes duration at baseline is associated with higher remission rates at 10 and 15 years after surgery and with greater prevention of diabetes complications for up to 25 years.

The SOS study has certain limitations. First, a randomized design was not approved by the ethics review boards because of high postoperative mortality rates after bariatric surgery in the 1980s.[39] Second, the matching procedure created surgery and control groups that differed in some respects (patients in the surgery group were on average 1.7 years younger but had higher BMI, blood pressure, and fasting serum insulin compared with the controls), but the risk profile at baseline seemed to be less advantageous in the surgery group. Furthermore, the diagnosis of diabetes is based on fasting glucose levels and self-reported use of diabetes medication. The use of glucose tolerance tests or glycated hemoglobin levels might have changed the results to some extent. The low participation rate in physical and laboratory examinations at later time points was also a limitation. However, estimation based on multiple imputation procedures indicated that loss to follow-up only had minor effects on our remission estimates. In subgroup analyses according to surgery techniques, the low number of patients in each surgical treatment group is also a limitation. Our data on diabetes complications were based entirely on register linkage and not affected by loss to follow-up but were limited by the lack of information on primary outpatient care. Thus, we captured virtually all complications severe enough to be treated by a specialist, but we could have missed some mild complications treated in primary care.

Conclusions

In this very long-term follow-up observational study of obese patients with type 2 diabetes, bariatric surgery was associated with more frequent diabetes remission and fewer complications than usual care. These findings require confirmation in randomized trials.

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