Bariatric Surgery and Prevention of Type 2 Diabetes in Swedish Obese Subjects

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ABSTRACT

BACKGROUND

Weight loss protects against type 2 diabetes but is hard to maintain with behavioral modification alone. In an analysis of data from a nonrandomized, prospective, controlled study, we examined the effects of bariatric surgery on the prevention of type 2 diabetes.

METHODS

In this analysis, we included 1658 patients who underwent bariatric surgery and 1771 obese matched controls (with matching performed on a group, rather than individual, level). None of the participants had diabetes at baseline. Patients in the bariatric-surgery cohort underwent banding (19%), vertical banded gastroplasty (69%), or gastric bypass (12%); nonrandomized, matched, prospective controls received usual care. Participants were 37 to 60 years of age, and the body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) was 34 or more in men and 38 or more in women. This analysis focused on the rate of incident type 2 diabetes, which was a prespecified secondary end point in the main study. At the time of this analysis (January 1, 2012), participants had been followed for up to 15 years. Despite matching, some baseline characteristics differed significantly between the groups; the baseline body weight was higher and risk factors were more pronounced in the bariatric-surgery group than in the control group. At 15 years, 36.2% of the original participants had dropped out of the study, and 30.9% had not yet reached the time for their 15-year follow-up examination.

RESULTS

During the follow-up period, type 2 diabetes developed in 392 participants in the control group and in 110 in the bariatric-surgery group, corresponding to incidence rates of 28.4 cases per 1000 person-years and 6.8 cases per 1000 person-years, respectively (adjusted hazard ratio with bariatric surgery, 0.17; 95% confidence interval, 0.13 to 0.21; $P<0.001$). The effect of bariatric surgery was influenced by the presence or absence of impaired fasting glucose ($P=0.002$ for the interaction) but not by BMI ($P=0.54$). Sensitivity analyses, including end-point imputations, did not change the overall conclusions. The postoperative mortality was 0.2%, and 2.8% of patients who underwent bariatric surgery required reoperation within 90 days owing to complications.

CONCLUSIONS

Bariatric surgery appears to be markedly more efficient than usual care in the prevention of type 2 diabetes in obese persons. (Funded by the Swedish Research Council and others; ClinicalTrials.gov number, NCT01479452.)

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MULTIPLE STUDIES HAVE SHOWN ASSOciations between obesity and type 2 diabetes[1-6] and between changes in body weight and incident type 2 diabetes.[7,8] It is also well established that the worldwide increase in obesity is associated with an increase in the prevalence of type 2 diabetes.[9] Currently, 285 million people have type 2 diabetes, and this number is predicted to increase to 439 million by 2030.[10]

Among persons in a prediabetic state, the incidence of type 2 diabetes is reduced by approximately 40 to 45% with effective lifestyle changes or drug treatment,[11-15] and the effects persist, in part, 3 to 15 years later.[16-18] Most trials of lifestyle changes and drugs for the prevention of type 2 diabetes have included moderately obese patients. However, patients with severe obesity have the highest risk of type 2 diabetes,[1,2,19,20] and in this group, bariatric surgery is currently the only treatment that typically results in large, sustained weight losses. Although many studies have examined the effect of bariatric surgery on the remission of diabetes, there appears to be a paucity of studies examining the effect of surgery on the prevention of diabetes, possibly because a long follow-up period and a control group are required. The Swedish Obese Subjects (SOS) study assessed whether surgery can prevent diabetes.

The SOS study is a nonrandomized, prospective, controlled intervention trial comparing the long-term effects of bariatric surgery with the effects of usual care. We have previously shown that bariatric surgery results in long-term weight loss and reduces the incidence of several hard end points.[21-24] In 2004, we reported positive effects of bariatric surgery with respect to the development of type 2 diabetes as part of our examination of changes in cardiovascular risk factors.[21] We now report a detailed analysis of the long-term effects of bariatric surgery on the prevention of type 2 diabetes.

METHODS

STUDY DESIGN

Between September 1, 1987, and January 31, 2001, a total of 4047 obese persons were enrolled in the SOS intervention trial, which is still ongoing. In brief, 6905 persons participated in a matching examination that was designed to enroll a control group that had mean characteristics that were similar to those of a surgery group, and 5335 were eligible for inclusion in the study (Fig. S1 in the Supplementary Appendix, available with the full text of this article at NEJM.org). Among these, 2010 participants who had chosen to undergo surgery formed the bariatric-surgery group, and a nonrandomized control group, comprising 2037 participants, was formed that was contemporaneously matched with the bariatric-surgery group on the basis of 18 matching variables (for details see the Supplementary Appendix).[21] The matching was performed in the entire SOS cohort; as reported previously,[21-24] the matching process unexpectedly resulted in the bariatric-surgery group having a higher mean body weight and more severe risk factors than the control group. Weight changes that occurred after matching made the study groups even more divergent with respect to these factors at baseline.[21-24] The current analysis includes 1658 patients who underwent bariatric surgery and 1771 controls, all of whom did not have diabetes at baseline. The requirement for this analysis that none of the patients have diabetes at baseline further reduced the similarity between the two groups. The cutoff date for the analysis was January 1, 2012. The rate of incident type 2 diabetes was a prespecified secondary end point of the SOS intervention trial and was analyzed according to the SOS protocol.

The study groups had identical inclusion and exclusion criteria. The inclusion criteria were an age of 37 to 60 years and a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) of 34 or more in men and 38 or more in women before or at the time of the matching examination. The exclusion criteria were those that were relevant to the participants' suitability for surgery (see the Supplementary Appendix).

All the patients in the surgery and control groups entered this study with the intention of losing weight. In the bariatric-surgery group, 311 participants underwent banding, 1140 vertical banded gastroplasty, and 207 a gastric bypass procedure. Patients in the control group received the customary treatment for obesity at their primary health care centers. The standard treatment for obesity in Sweden ranges from advanced lifestyle modification (including recommendations regarding eating behavior, food selection, energy intake, and physical activity) to no treatment. According to questionnaires administered at 6 months, 1 year, and 2 years, 54%

of the control group had tried to lose weight with professional guidance, and 46% had not received professional guidance.

Physical examinations were performed at the matching and baseline examinations and after 6 months and 1, 2, 3, 4, 6, 8, 10, and 15 years. Biochemical assays were performed at the matching visit, at baseline, and after 2, 10, and 15 years. From 1987 through 2009, glucose concentrations were measured in venous whole blood at the Central Laboratory, Sahlgrenska University Hospital, which is accredited according to International Organization for Standardization/International Electrotechnical Commission (ISO/IEC) 15 189 standards. After 2009, venous plasma glucose was measured, and the measurements were converted to those for blood glucose (for details see the Supplementary Appendix).

Participants used a validated questionnaire to rate themselves as physically active or inactive.[21,25-27] Energy intake was measured with the use of the validated SOS Food Questionnaire.[21,28]

STUDY OVERSIGHT

The study was approved by all the relevant ethics review boards in Sweden, and written or oral informed consent was obtained from all participants. The protocol, including the statistical analysis plan, is available at NEJM.org. The authors vouch for the completeness and accuracy of the data and analyses and for the fidelity of the study to the protocol. All the authors had access to the raw data. None of the study sponsors had any role in the interpretation of the data or the writing of the manuscript.

DIABETES

We considered a participant to have type 2 diabetes if he or she reported the use of diabetes medication or if there was documentation of a fasting blood glucose level of 110 mg per deciliter (6.1 mmol per liter) or higher. If fasting plasma glucose was measured, the cutoff value for a diagnosis of diabetes was 126 mg per deciliter (7.0 mmol per liter) or higher.[29,30] Fasting glucose concentrations were measured at the time of matching, at baseline, and at 2, 10, and 15 years. The study was initiated before repeated measurements were routinely used for the diagnosis of type 2 diabetes; therefore, single fasting glucose determinations were used. Impaired fasting glucose was defined as a fasting blood glucose level that was at least 90 mg per deciliter (5.0 mmol per liter) and less than 110 mg per deciliter or a fasting plasma glucose level that was at least 100 mg per deciliter (5.6 mmol per liter) and less than 126 mg per deciliter.[29,30]

STATISTICAL ANALYSIS

Mean values, with standard deviations, and percents were used to describe the baseline characteristics. Differences between treatment groups were evaluated with the use of t-tests for continuous variables and with the use of a logistic-regression model for dichotomous variables. Participants were followed until the diagnosis of type 2 diabetes or until their last examination. Data from participants in whom type 2 diabetes did not develop during the follow-up period were therefore censored at the last follow-up examination.

Because diabetes status was evaluated at discrete follow-up times, at years 2, 10, and 15, we consider the data on underlying continuous time to diabetes to be interval-censored data. Therefore, we used a discrete-time survival approach, with a complementary log–log regression model[31] to evaluate the cumulative incidence of type 2 diabetes and the treatment effect of bariatric surgery. This approach corresponds to the Cox proportional-hazards regression model when continuous time to event is observed in intervals,[31] and it provides relative-risk estimates as hazard ratios.

The treatment effect in the bariatric-surgery group as compared with the control group, expressed as hazard ratios with 95% confidence intervals, was evaluated in an unadjusted analysis with a single covariate for treatment group (surgery or control) and in an analysis that was adjusted for preselected baseline traditional risk factors for type 2 diabetes. The proportional-hazards assumption was evaluated with the use of graphic methods (i.e., the log–log plot) and by testing the interaction between time and treatment. In secondary subgroup analyses, the cumulative incidence of type 2 diabetes was calculated separately in various subgroups defined according to baseline factors. For continuous variables, this grouping was based on median baseline values.

The association between risk factors and the effect of bariatric surgery on the development of diabetes was tested by including the corresponding interaction term (i.e., the product of the type of treatment [surgery or control] and the corresponding variable) in the complementary log–log proportional-hazards model. Dichotomous vari-

ables could have one of two values (e.g., male or female sex). For other variables, the interaction tests used the original continuous variables. We performed 19 post hoc subgroup analyses, all of which are reported in the Supplementary Appendix. P values for interaction have been corrected for 19 multiple tests with the use of the false-discovery-rate method of Benjamini and Hochberg.[32] The numbers needed to treat to prevent one diabetes event over the course of 10 years was calculated as the reciprocal of the absolute difference in risk between the bariatric-surgery group and the control group.

Since the rates of loss to follow-up were considerable at longer follow-up times, sensitivity analyses that were based on multiple imputation of missing outcome data were also performed (see the Supplementary Appendix). In addition, we compared the baseline characteristics and the 10-year characteristics of participants who had dropped out at 15 years with those of participants who had not dropped out at 15 years.

All P values are two-sided, and P values of less than 0.05 were considered to indicate statistical significance. The intention-to-treat principle was applied for all the calculations. The Stata statistical package, version 12.1, was used.

RESULTS

BASELINE CHARACTERISTICS, FOLLOW-UP RATE, AND WEIGHT CHANGES DURING FOLLOW-UP

The differences between the surgery group and the control group increased between the time of the matching examination (Table S1 in the Supplementary Appendix) and the time of the baseline examination (Table 1). At baseline, patients in the bariatric-surgery group weighed, on average, 6 kg more, and most of the risk factors we analyzed were more pronounced than were those in the controls (Table 1).

The median follow-up time was 10 years (range, 0 to 15). The rates of loss to follow-up were 12.9% at 2 years and 31.2% at 10 years (see Table S2 in the Supplementary Appendix, which also provides the rates in each study group).

At 15 years, the rate of loss to follow-up had increased to 36.2%; in addition, 30.9% of the participants had not yet been followed for 15 years and were therefore not eligible for the 15-year analysis (Table S2 in the Supplementary Appendix). This resulted in an unadjusted 15-year par-

ticipation rate of only 32.9%. After adjustment for follow-up of less than 15 years and for death, the 15-year participation rate was 53.5%. Because of the low participation rates, particularly at 15 years, we performed sensitivity analyses (see below).

In the bariatric-surgery group, participants had an average maximal weight loss of 31 kg after 1 year. Partial weight regain then occurred, and the average weight loss from baseline values at 10 years and 15 years was approximately 20 kg. The mean weight changes in the control group never exceeded 3 kg in weight gain or weight loss (Fig. S2 in the Supplementary Appendix). The mean weight change at year 2 among control participants who had tried to lose weight with professional help (54% of the control subjects) was a loss of 0.6 kg (95% confidence interval [CI], −1.3 to 0.0), as compared with a gain of 1.4 kg (95% CI, 0.7 to 2.0) among participants who had not received help (P<0.001). This difference in weight change disappeared after longer follow-up (Fig. S3 in the Supplementary Appendix). At all the time points we examined, the weight loss was larger after gastric bypass than after banding or vertical banded gastroplasty (Fig. S3 in the Supplementary Appendix).

INCIDENCE OF DIABETES

During the follow-up period, type 2 diabetes developed in 392 patients in the control group and 110 in the bariatric-surgery group (Fig. 1A), corresponding to incidence rates of 28.4 cases (95% CI, 25.7 to 31.3) per 1000 person-years and 6.8 (95% CI, 5.7 to 8.3) per 1000 person-years, respectively (P<0.001), on the basis of observed 15-year data. The unadjusted hazard ratio with surgery was 0.22 (95% CI, 0.18 to 0.27; P<0.001) (Fig. 1A). After multivariable adjustments, the hazard ratio was 0.17 (95% CI, 0.13 to 0.21; P<0.001) (Table 2). In addition to treatment group (surgery or control), the strongest univariable predictors of diabetes outcome were baseline blood glucose concentration and the presence or absence of impaired fasting glucose (Table S3 in the Supplementary Appendix).

SENSITIVITY ANALYSES

The characteristics at baseline and at 10 years within each study group were similar among participants who remained in the study for 15 years and those who dropped out before the 15-year assessment (Tables S4 and S5 in the Supplementary Appendix). Given the low participation rate and the

Table 1. Baseline Characteristics of Study Participants.*

Characteristic	Control Group (N=1771)	Bariatric-Surgery Group (N=1658)	T or z Value†	P Value
Male sex (%)	27.4	27.0	0.28	0.78
Age (yr)	48.4±6.2	46.9±5.9	7.5	<0.001
Weight (kg)	114.5±16.5	120.5±16.1	−10.8	<0.001
Body-mass index‡	40.2±4.7	42.4±4.5	−14.3	<0.001
Waist circumference (cm)	119.8±11.4	125.1±10.7	−14.0	<0.001
Hip circumference (cm)	123.4±9.9	127.1±9.8	−11.1	<0.001
Waist-to-hip ratio	0.973±0.074	0.987±0.076	−5.4	<0.001
Blood glucose (mg/dl)	79.0±11.0	80.3±10.8	−3.3	0.001
Impaired fasting glucose (%)§	16.4	18.2	−1.4	0.17
Serum insulin (mU/liter)	16.9±9.6	20.1±11.7	−8.6	<0.001
HOMA-IR¶	3.4±2.2	4.1±2.6	−8.0	<0.001
Blood pressure (mm Hg)				
Systolic	137.1±17.7	143.9±18.5	−11.0	<0.001
Diastolic	84.9±10.5	89.5±11.1	−12.4	<0.001
Lipid levels (mg/dl)				
Total cholesterol	216.1±40.1	226.0±42.4	−7.0	<0.001
HDL cholesterol	52.7±12.8	52.9±12.3	−0.5	0.61
Triglycerides	167.1±101.9	187.6±118.4	−5.4	<0.001
Median urinary albumin excretion (μg/min)	7.1	8.1		0.001
Smoking (%)	20.8	26.0	−3.6	<0.001
Prior myocardial infarction or stroke (%)	1.9	1.5	0.8	0.42
Physically active (%)				
During leisure time	66.4	53.7	7.5	<0.001
At work	59.2	61.2	−1.2	0.23
Total daily caloric intake (kcal)	2596±1050	2913±1208	−8.2	<0.001

* Plus–minus values are means ±SD. To convert the values for glucose to millimoles per liter, multiply by 0.05551. To convert the values for insulin to picomoles per liter, multiply by 6.945. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586. To convert the values for triglycerides to millimoles per liter, multiply by 0.01129. HDL denotes high-density lipoprotein.
† The T or z value is the test statistic for the comparison between the control group and the surgery group. The T-value test is a test of equal means for continuous variables, and the z-statistic is a test of equal proportions (%) for dichotomous variables.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.
§ Impaired fasting glucose was defined as a blood glucose level of at least 90 mg per deciliter and less than 110 mg per deciliter.
¶ The homeostasis model assessment of insulin resistance (HOMA-IR) was calculated as fasting glucose level (in milligrams per deciliter) × fasting insulin level (in microunits per milliliter) ÷ 405.

strong treatment effect at 15 years, we also examined the effects of surgery at other follow-up times (Table S6 in the Supplementary Appendix). The treatment effects on the incidence of type 2 diabetes were at least as strong after 2 years and 10 years of follow-up as after 15 years. Finally, analyses of the treatment effects calculated from observed-plus-imputed outcome data at 10 years and at 15 years yielded relative effects of diabetes treatment (hazard ratio with bariatric surgery, 0.16 and 0.21, respectively) that were similar to those calculated on the basis of observed data only (hazard ratio, 0.16 and 0.22, respectively) (Table S6 in the Supplementary Appendix).
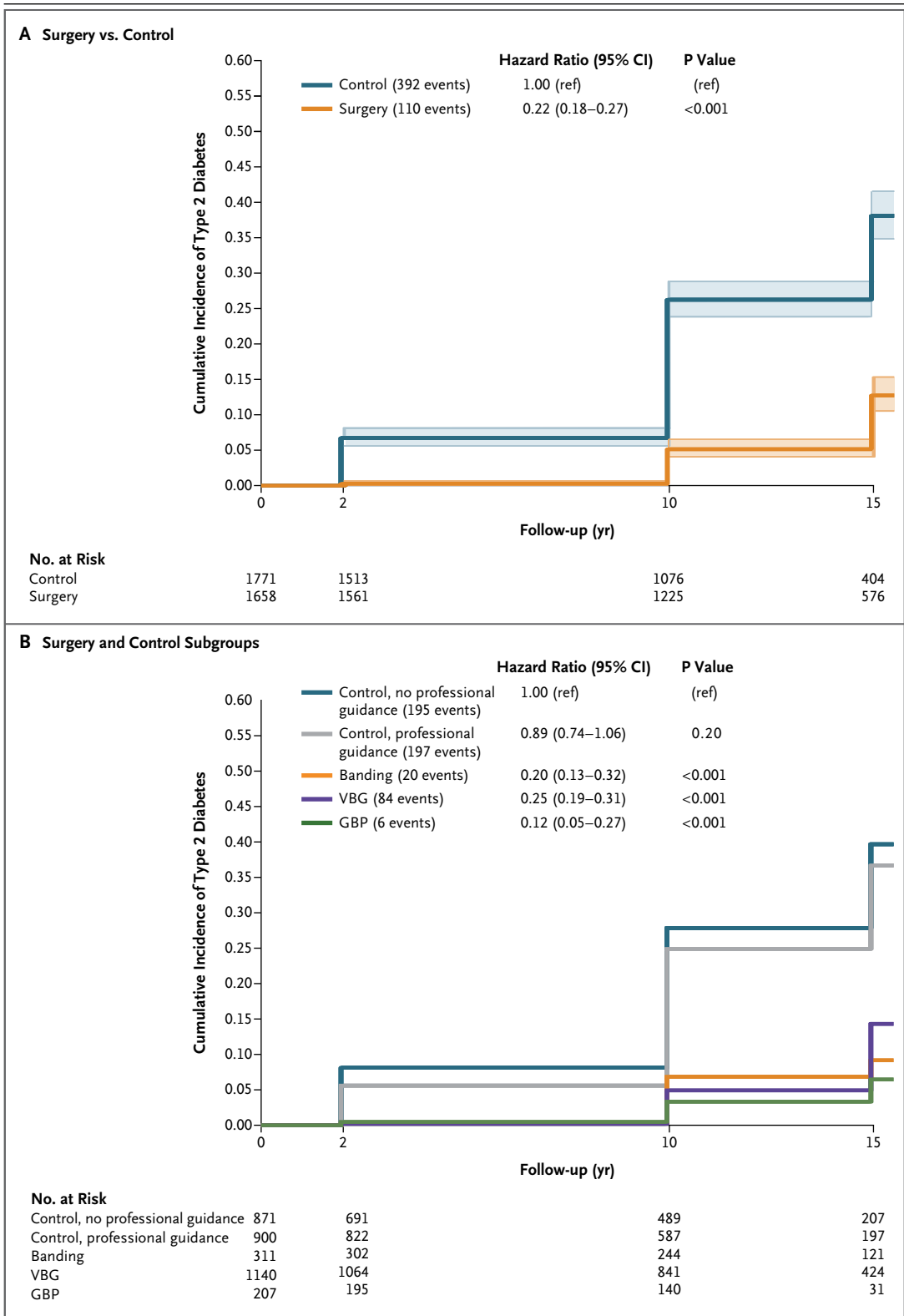
A **Surgery vs. Control**

B **Surgery and Control Subgroups**

SUBGROUP ANALYSES

In the control group, there was no difference in the incidence of type 2 diabetes between participants who had tried to lose weight with professional guidance and those who had not received professional guidance (hazard ratio with professional guidance, 0.89; P=0.20) (Fig. 1B). All types of bariatric surgery were associated with a reduced incidence of type 2 diabetes (Fig. 1B). The hazard ratio with gastric bypass was 0.12 (95% CI, 0.05 to 0.27; P<0.001), but the analysis was based on only six cases of diabetes among the 207 subjects. The hazard ratios with banding (0.20; 95% CI, 0.13 to 0.32; P<0.001) and vertical banded gastroplasty (0.25; 95% CI, 0.19 to 0.31; P<0.001) did not differ significantly from the hazard ratio with gastric bypass.

Interactions between risk factors and treatment are shown in Table S7 in the Supplementary Appendix. The effect of bariatric surgery on the incidence of type 2 diabetes was highly significant in all subgroups, but the interaction between risk factors at baseline and treatment was significant only in the subgroups defined according to presence or absence of impaired fasting glucose (P=0.002 for the interaction), fasting blood glucose level (P=0.007), fasting serum insulin concentration (P=0.007), and value for the homeostasis model assessment of insulin resistance (P=0.001). The interaction between treatment and BMI with respect to the incidence of diabetes was not significant (P=0.55). The risk of type 2 diabetes and the relative preventive effect of bariatric surgery increased with increasing baseline glucose and insulin levels (Fig. 2A and 2B), whereas baseline BMI was not related to

Table 2. Adjusted Hazard Ratios for the Incidence of Diabetes.*

Variable	Adjusted Hazard Ratio (95% CI)	z Value	P Value
Surgery vs. no surgery	0.17 (0.13–0.21)	−15.3	<0.001
Male sex	1.19 (0.92–1.53)	1.3	0.18
Age, per 6.1 yr	1.23 (1.12–1.36)	4.2	<0.001
Blood glucose, per 10.7 mg/dl	2.18 (1.99–2.39)	16.9	<0.001
Serum insulin, per 10.8 mU/liter	1.03 (0.94–1.13)	0.7	0.51
Body-mass index, per 4.7 units	1.00 (0.90–1.11)	0.0	0.99
Waist-to-hip ratio, per 0.08 units	1.18 (1.06–1.32)	3.0	0.003
HDL cholesterol, per 12.5 mg/dl	0.87 (0.78–0.98)	−2.4	0.02
Triglycerides, per 105.2 mg/dl	0.98 (0.89–1.07)	−0.5	0.59
Urinary albumin excretion, per third†	1.24 (1.10–1.39)	3.5	<0.001
Leisure-time physical activity vs. no leisure-time physical activity	1.16 (0.95–1.41)	1.5	0.14

* The adjusted hazard ratios were calculated with the use of a multivariable complementary log–log regression model. The hazard ratios for continuous variables (except those for urinary albumin excretion) are expressed per 1 SD difference at baseline in the study population.
† The lower third of urinary albumin excretion values was less than 5.8 μg per minute; the middle third, 5.8 to less than 12.5 μg per minute; and the upper third, 12.5 μg or more per minute.

the incidence of type 2 diabetes or the preventive effect of surgery (Fig. 2C).

The number needed to treat to prevent one diabetes event was low in all the subgroups, reflecting the strong treatment effect of bariatric surgery. In the subgroup defined according to the presence or absence of impaired fasting glucose, the number needed to treat was 1.3 (Table S7 in the Supplementary Appendix).

ADVERSE EVENTS

Postoperative mortality and other complications of bariatric surgery over the first 90 days are reported in Table 3. A total of 3 patients (0.2%) died within 90 days after surgery, and at least one complication was reported in 245 patients (14.8%). In 46 patients (2.8%), the complications were serious enough to require a reoperation. A total of 89.0% of the operations were undertaken with open surgery.

DISCUSSION

The results of this analysis show that bariatric surgery, as compared with usual care, reduces the long-term incidence of type 2 diabetes by 78% in
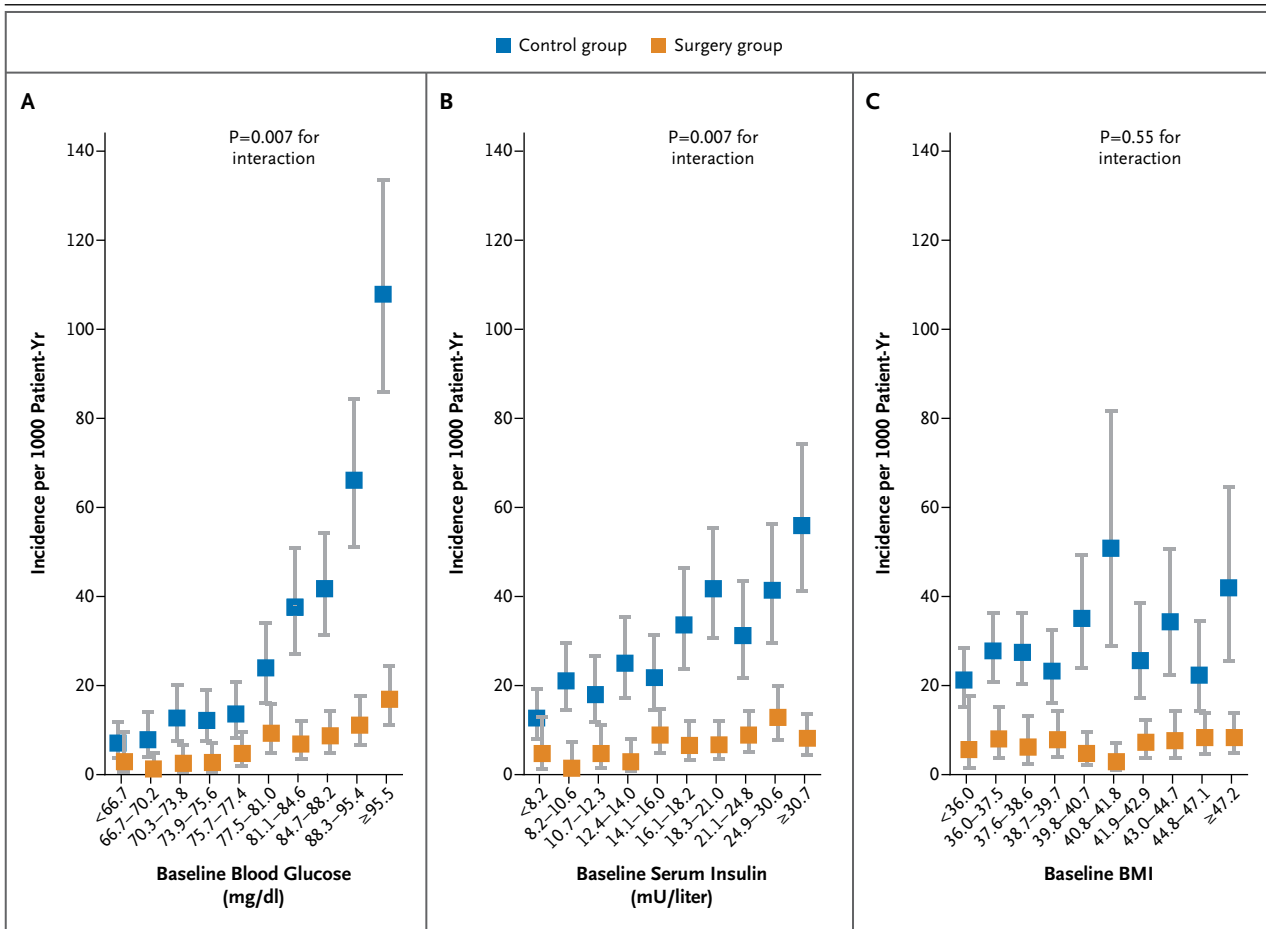
Figure 2. Interaction between Selected Risk Factors and Treatment.

The incidence of type 2 diabetes per 1000 person-years in the bariatric-surgery and control groups is shown according to deciles of base-line blood glucose levels (Panel A), serum insulin levels (Panel B), and body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) (Panel C). In Panel A, P=0.002 for the interaction of treatment with the presence or absence of impaired fasting glucose. All incidence rates are adjusted for age and sex. The P values for interaction are unadjusted. For complete information on all calculated P values for interaction, see Table S7 in the Supplementary Appendix. To convert the values for glucose to millimoles per liter, multiply by 0.5551. I bars indicate 95% confidence intervals.

obese patients. This risk reduction was achieved despite a less favorable risk profile in the surgery group at baseline. Among patients with impaired fasting glucose, bariatric surgery reduced the risk by 87%, and type 2 diabetes did not develop in approximately 10 of 13 obese patients who underwent bariatric surgery. This risk reduction is at least twice as large as that observed with lifestyle interventions in moderately obese, prediabetic persons.[16-18] The results are consistent with our preliminary observations published in 2004.[21] Guidelines from the International Diabetes Federation,[33] the American Diabetes Association,[29] and other organizations[34,35] recognize bariatric surgery as an option for obese patients who have

type 2 diabetes but have not suggested bariatric surgery for the prevention of type 2 diabetes.

The rate of remission of type 2 diabetes is higher after gastric bypass than after banding,[36] and this may be related to greater weight loss after gastric bypass or to effects that are independent of weight loss.[37] In our study, the rate of incident type 2 diabetes after gastric bypass was not significantly lower than the rate after banding or vertical banded gastroplasty. However, the SOS study was not powered to detect such differences.

Obese patients with impaired fasting glucose, as compared with obese persons with normal fasting glucose levels, have a higher risk of type 2 diabetes (incidence among patients receiving usual

Table 3. Adverse Events during the First 90 Days after Surgery among the 1658 Participants in the Bariatric-Surgery Group.*

Event	Incidence	
	no. of events	*% of participants*
Death	3	0.2
Pulmonary complication	79	4.8
Thromboembolism	16	1.0
Vomiting	53	3.2
Wound infection	35	2.1
Other infections	24	1.4
Hemorrhage	18	1.1
Anastomotic leak, peritonitis, or abscess	23	1.4
Ileus	8	0.5
Wound dehiscence	9	0.5
Other complications	16	1.0

* A total of 89% of the operations were performed by means of open surgery. There were 284 adverse events. A total of 245 participants in the bariatric-surgery group (14.8%) had at least one event; 46 participants (2.8%) required reoperation during the first 90 days after surgery.

care, 91 cases per 1000 person-years vs. 20 cases per 1000 person-years) and appear to have a greater benefit from bariatric surgery (P=0.002 for the interaction). In contrast, the incidence of type 2 diabetes and the preventive effect of bariatric surgery were similar among participants with a BMI at or below the median of 40.8 and those with a BMI above the median. We previously observed that baseline BMI does not predict a benefit from bariatric surgery with respect to death,[22] cancer,[23] myocardial infarction,[24] or stroke,[24] and the current results suggest that baseline BMI does not predict a benefit of bariatric surgery with respect to incident type 2 diabetes.

Type 2 diabetes is a progressive disease, and the ability to produce insulin declines with time.[38] Improvement of insulin sensitivity by means of weight loss may not be enough to induce the remission of diabetes if the destruction of beta cells is advanced, and the diabetes remission rate is inversely related to the duration of diabetes at the time of bariatric surgery.[39] This observation, together with the clear and long-term decrease in the rate of incident type 2 diabetes among participants with prediabetes, also suggests that disturbances of glucose metabolism might be treated early, even before type 2 diabetes is diagnosed.

The SOS study has certain limitations. First, it

was not a randomized study, owing to ethical reasons related to the high postoperative mortality associated with bariatric surgery in the 1980s. Second, the diagnosis of type 2 diabetes was based on fasting glucose levels and self-reported use of diabetes medication. Diagnosis of type 2 diabetes that was based on results of an oral glucose-tolerance test or on glycated hemoglobin levels might have given slightly different results if, for example, there were group differences in the use of diabetes medication for the prevention of diabetes. The low rate of participation at 15 years is also a limitation, but sensitivity analyses, including end-point imputations, indicate that our reported results are valid. Ideally, our post hoc findings should be confirmed by prospective, controlled trials that are designed to study treatment effects on hard end points in predefined subgroups.

Our data indicate that bariatric surgery has a preventive effect on incident type 2 diabetes, particularly in participants with impaired fasting glucose. In contrast, baseline BMI did not influence the preventive effect of bariatric surgery on type 2 diabetes, implying that anthropometric data are not useful in the selection of candidates for bariatric surgery, whereas data on impaired fasting glucose may be helpful.

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