Can Bariatric Surgery Help Obese Patients Avoid Incident Diabetes?

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Study Overview

Objective. To determine whether undergoing bariatric surgery decreases the risk of developing incident diabetes in a group of severely obese patients.

Design. Nonrandomized, prospective controlled trial.

Setting and participants. This study is one of several that have been conducted using data from the Swedish Obese Subjects (SOS) trial. SOS is one of the largest and longest running studies of bariatric surgery, having begun in 1987. Patients were enrolled through January of 2001 and follow-up is still ongoing at this time. At enrollment, patients were required to be aged 37 to 60 years, have a BMI of ≥ 34 for men and ≥ 38 for women, and to meet other suitability criteria for undergoing the surgery.

This particular study focused on patients in the SOS trial who were not diabetic at baseline, and included 1658 bariatric surgery patients and 1771 controls. Among the surgical patients, 1140 underwent vertical banded gastroplasty (VBG or stomach-stapling, a now obsolete procedure), 311 underwent gastric banding, and 207 gastric bypass. The control group of patients also entered the trial with a goal of losing weight but did not desire surgery, and they received usual medical care for obesity, the specifics of which varied from person to person. In, fact only 54% of the control group later reported seeking professional guidance to aid in their weight loss. Both groups were followed with physical examinations, blood work, and questionnaires at the same intervals for up to 15 years after trial enrollment.

Main outcome measures. The primary outcome of interest was the development of incident diabetes mellitus. Diabetes was considered to be present if a patient either reported taking a medication for diabetes or had a documented fasting glucose of ≥ 110 mg/dL (126 mg/dL if sample was from plasma glucose). Only 1 such value was required for a diabetes diagnosis and samples were taken at 2, 10, and 15 years post-surgery to be compared with samples from trial baseline. The investigators also reviewed the amount of weight lost in each group.

Differences in incident diabetes rates between the 2 groups were analyzed using survival methods that accounted for the discrete nature of follow-up (ie, done just at time points 2 y, 5 y, and 15 y, as opposed to continuous observation over that same period). Namely, they used a log-log regression model rather than a Cox proportional hazards model. Both crude and multivariable models, including interaction terms, were built for the "treatment-incident diabetes" relationship, with adjustment for variables that are known to independently increase one's diabetes risk. Subgroup analyses were also performed to determine whether the surgical treatment effect was greater in some patients than in others. Given the large number of statistical tests that were run as a result of these analyses, corrected *P* values for multiple tests were used.

Results. At baseline, there were already some significant differences between the surgical and control groups. This was due to the fact that matching was performed for the overall trial population rather than for the nondiabetic patients included in this analysis.

Gender breakdown was similar between groups, with 27% of the patients in each arm being male. Otherwise, the bariatric group was slightly younger (46.9 y vs 48.4 y) and heavier (120.5 kg vs 114.5 kg), with higher fasting blood glucose (80.3 mg/dL vs 79.0 mg/dL) and serum insulin levels (20.1 μU/L vs 16.9 μU/L). Furthermore, the surgical patients had slightly higher blood pressure (SBP 143.9 mm Hg vs 137.1 mm Hg, DBP 89.5 mm Hg vs 84.9 mm Hg) and cholesterol levels (total cholesterol 226 mg/dL vs 216.1 mg/dL) than the controls. They were also more likely to be smokers (26% vs 20.8%) and had higher daily caloric intake (2913 kcal vs 2596 kcal).

Patients were followed for a median of 10 years after baseline, but there was a large amount of loss to follow-up at each time point (12.9% at 2 years, 31.2% at 10 years, and 36.2% at 15 years), and, due to a rolling enrollment period, not all patients in this analysis had reached 15 years of participation at the time of this study (this represented an additional 30.9% of patients with no 15-year time-point data).

Weight loss was significantly greater among the bariatric surgical patients versus controls, although it was not entirely sustained over the follow-up period. At 1 year, the average mean weight loss in those who had surgery was 31 kg, with a subsequent regain to a mean of 20 kg below baseline weight at the 10- and 15-year time points. The control group's mean weight, on the other hand, stayed within ± 3 kg of their baseline weight at all time points.

Incident diabetes, the main outcome measure, differed significantly between the 2 groups, with an incident rate of 28.4 cases (95% CI 25.7–31.3) per 1000 person-years in the control group versus 6.8 cases (95% CI 5.7–8.3) per 1000 person-years in surgical patients. This translated to a crude hazard ratio of 0.22 for incident diabetes in surgical patients compared with controls, which was further reduced to a HR of 0.17 in multivariable models.

Because of the high rates of loss to follow-up at the 10- and 15-year checks, the investigators compared those who were lost with those who remained in the trial at 15 years, both with respect to baseline covariates and with respect to values obtained at the 10-year check. Patients who were lost to follow-up had similar baseline characteristics to those who remained in the study at 15 years. Additionally, patients who had 10 but not 15 years of data were similar to those who completed the 15-year follow-up when the 10-year check-in data were compared. There was no comparison available for the status of patients who dropped out between 2 and 10 years with respect to their health and weight at time of dropout versus the 15-year cohort.

Subgroup analysis showed that when control patients who entered professional weight loss programs were compared with those who did not, there was no difference in incident diabetes (HR with guidance, 0.89, $P = 0.2$). The investigators also looked at interaction between surgical treatment and the baseline covariates. They found that higher baseline glucose and insulin levels predicted greater diabetes preventive effects of surgery, but that baseline BMI did not modify the effect of surgery with respect to incident diabetes ($P = 0.55$).

Conclusion. Based on this nonrandomized trial, the authors conclude that performing bariatric surgery in obese patients can reduce their risk of incident type 2 diabetes by 78% relative to those who remain in usual care.

Commentary

Obesity and diabetes have increased considerably in prevalence over the past few decades, and much research has been dedicated to helping patients achieve and maintain both weight loss and the diabetes remission that often accompanies it. For patients with severe obesity, bariatric surgery has proven to be the most effective mechanism of weight loss, and there are now recommendations to support the role of surgery in diabetes resolution [1,2]. However, providers are also interested in helping at-risk patients avoid developing diabetes in the first place. A number of trials have shown that prediabetic or overweight patients who adhere closely to lifestyle changes, such as improved diet and getting more physical activity, can substantially reduce their risk of developing diabetes [3]. In this study, the investigators tackled the idea that bariatric surgery could be viewed as another form of diabetes prevention, rather than just a curative intervention.

This study is the first to look at a large group of bariatric surgical patients and evaluate diabetes prevention as the primary outcome. In addition to the fact that it addresses a novel research question, the impressive scope of the overall trial should be emphasized. Compared to most other studies of bariatric surgery, the SOS trial is one of the largest and longest-running in the world and has yielded very important information on weight loss, overall mortality, cancer risk, and risk of heart disease after surgery [4–6]. Additional strengths of this study include the numerous biological and sociodemographic measures used to quantify baseline risk for developing diabetes, rather than relying on 1 measure alone.

The study was limited by the fact that at baseline, the 2 groups were not similar with respect to a number of characteristics. Importantly, the surgical group appeared to have a higher risk of diabetes. Although the SOS trial as a whole relied on matching to try to equalize the 2 groups at baseline, this analysis selected just for non-diabetics, thus explaining the lost effectiveness of the matching process. Furthermore, due to the fact that the trial was not randomized—patients self-selected into the 2 groups—there are probably unmeasured factors that differ between the groups (eg, motivational level and other personal characteristics) that may have also impacted the outcomes. The definition of the outcome itself may have resulted in over- or under-diagnosis of diabetes: the investigators used a 1-time fasting blood measure (rather than sequential measures, an oral GTT or HbA1c) to define incident diabetes.

Although the trial is ambitious in its long follow-up period, there was a substantial group of patients who were either lost to follow up before the 15-year time point or who had not yet been enrolled for 15 years at the time of the analysis. This raises the important question of whether or not the results of those who remained present are similar to what would have been seen in the people who dropped out. The investigators make an attempt to compare these 2 populations in a supplementary online appendix and do successfully show that those who stay in are similar to those who are lost, at least at baseline and at the 10-year mark. What is unclear, unfortunately, is what was happening to patients who dropped out between the 2- and 10-year mark. Perhaps these were people who were regaining weight more quickly and got discouraged?

Another potential issue with this analysis is that most of the patients in the surgical group underwent a now obsolete procedure, VBG. Had the number of lap bands been higher, perhaps the diabetes preventive effect would have been attenuated. On the other hand, gastric bypass has a very high success rate for diabetes remission, and perhaps had more patients in the study undergone bypass, the preventive effect would have been larger.

Finally, for clinicians who care for diverse patient populations, the uniformity of patient race (Caucasian) and gender (mostly women) in this study might limit its generalizability. The relationship between weight and diabetes risk varies between patients according to racial and ethnic background [7], and it could be that in a mostly Asian or Hispanic population, for example, this intervention would have a different impact than it did here. Also, although the authors did find that baseline BMI did not interact with surgery to predict the risk of incident diabetes, the mean BMI in this group was above 40, corresponding to a diagnosis of morbid obesity. Given the growing tendency to perform bariatric surgery in lower weight groups, it would be important to know if this intervention is as powerful for diabetes prevention in people with lesser degrees of obesity.

Applications for Clinical Practice

This novel analysis of bariatric surgery for diabetes prevention showed that, compared with usual care for obese patients, surgery substantially reduced the rates of incident type 2 diabetes. While promising, this finding should not yet translate into regular clinical practice, and must be weighed against the health risks and costs associated with the use of bariatric surgery. Furthermore, weight loss and diabetes prevention efforts should be tailored to individual patient characteristics, including one's ability to conform to lifestyle modification, which can also be a potent preventive measure.

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