



Conversion from Prediabetes to Diabetes in Individuals with Obesity, 5-Years Post-Band, Sleeve, and Gastric Bypass Surgeries

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Abstract

Background Identifying risk factors for conversion to diabetes among individuals with obesity and prediabetes is important for preventing diabetes.

Purpose We assessed conversion rates to diabetes 5 years after three types of metabolic surgery and examined predictors of diabetes development.

Methods We accessed data of individuals with prediabetes, defined as fasting glucose (FG) 100–125 mg/dL (5.6–6.9 mmol/L) or HbA1c 5.7–6.4% at baseline (preoperatively), who underwent metabolic surgeries in Clalit Health Services during 2002–2011.

Results Of 1,756 individuals with prediabetes, 819 underwent gastric banding (GB), 845 sleeve gastrectomy (SG), and 92 Roux-en-Y gastric bypass (RYGB). Mean age was 41.6 years and 73.5% were women. Five years post-surgery, 177 (10.1%) had developed diabetes. Conversion rates by type of surgery were 14.4%, 6.3%, and 6.5% for GB, SG, and RYGB, respectively ($p < 0.001$). Conversion was more rapid following GB than SG or RYGB ($\chi^2(2) = 29.67, p < 0.005$). In a multiple-logistic-regression model, predictors of diabetes development 5 years postoperatively were (1) weight loss during the first postoperative year and (2) preoperative levels of both FG and HbA1c within the prediabetes range. Baseline weight, age, and sex, were not associated with conversion to diabetes. Conversion rates were lower (4.7%) five years postoperatively for patients who lost > 25% of their baseline weight, compared to those who lost less than 15% of their weight during the first postoperative year: (14.0% < 0.001).

Conclusions Our findings emphasize the importance of preoperative glycemic control and weight loss during the first year postoperatively, for the long-term prevention of diabetes in patients with prediabetes undergoing metabolic surgery.

Keywords Metabolic surgery · Pre-diabetes · Diabetes · Obesity

Introduction

Obesity and elevated levels of fasting glucose (FG) and HbA1c, in the prediabetes or even in normal ranges, are well-established risk factors for conversion to type 2 diabetes

[1–3]. Among persons with obesity and diabetes, metabolic surgery has demonstrated greater efficacy in normalizing glucose control than conventional medical therapy [4–15]. In a study of obese patients with impaired FG, the incidence of diabetes was lower in those who underwent gastric banding

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than in those with lower BMI who did not undergo a surgical procedure [8]. Fifteen-year follow-up of the Swedish Obese Subjects (SOS) study showed that metabolic surgery reduced the risk of type 2 diabetes by 78% among individuals with obesity and by 87% among individuals with obesity and impaired FG [9]. However, only 18% of the participants of that study had impaired FG at baseline and comparisons between surgical procedures were not possible. In another Swedish national study [4], researchers concluded that RYGB protected from new onset of pharmacological treatment for type 2 diabetes, as well as induced remission of pharmacological treatment. Thus, a remaining gap of knowledge is whether different types of metabolic procedures are differentially effective in the long-term prevention of diabetes among persons with obesity and prediabetes.

We previously reported 5-year outcomes of gastric banding (GB), sleeve gastrectomy (SG), and Roux en-Y gastric bypass (RYGB) performed in individuals with obesity and diabetes in a nationwide healthcare organization [10]. Here, we aimed to assess whether a comparable benefit was reflected among persons with prediabetes, and to determine rates of conversion to diabetes at 5 years after three common surgeries for obesity and metabolic disorders. We also examined possible predictors of diabetes development in addition to the surgical intervention.

Research Design and Methods

Electronic data on patients who underwent surgery for obesity and metabolic disorders during 2002–2011 in Clalit Health Services (CHS), the largest healthcare organization in Israel, were accessed until December 2015. Study eligibility criteria were prediabetes, defined by FG 100–125 mg/dL ((5.6–6.9 mmol/L) or HbA1c 5.7–6.4% (39–46 mmol/mol) in the year preceding surgery, the absence of a diagnosis of diabetes, and complete follow-up data regarding diabetes status 5-year post-surgery. Metformin was not prescribed for diabetes prevention in Israel during the study period. All individuals had BMI > 40 kg/m² at baseline, or BMI > 35 kg/m² with at least one obesity-related risk factor, as required for eligibility to undergo metabolic surgery in CHS. Baseline, 1, and 5-year follow-up values were accessed for body weight, height, calculated BMI, FG, HbA1c, systolic and diastolic blood pressure, total cholesterol, LDL-cholesterol, HDL-cholesterol, and triglycerides. Baseline information was accessed regarding smoking status and the presence of cardiovascular disease. The main outcome was conversion to diabetes, defined as FG ≥ 126 mg/dL (7.0 mmol/L) or HbA1c ≥ 6.5% (48 mmol/mol), during the 5 years following three types of surgery for obesity and metabolic disorders. The study was approved by the Rabin Medical Center Ethics Committee.

Statistical Analysis

Means and standard deviations (SDs) were calculated, and one-way analysis of variance (ANOVA) and chi-square tests were used to compare patient characteristics by surgical procedure (GB, SG, and RYGB). Pairwise comparisons were performed using Gabriel's post hoc test to assess differences in conversion to diabetes between pairs of surgical procedures, and also according to 1-year postoperative weight-loss, categorized as more than 25%, 15–25%, and less than 15%.

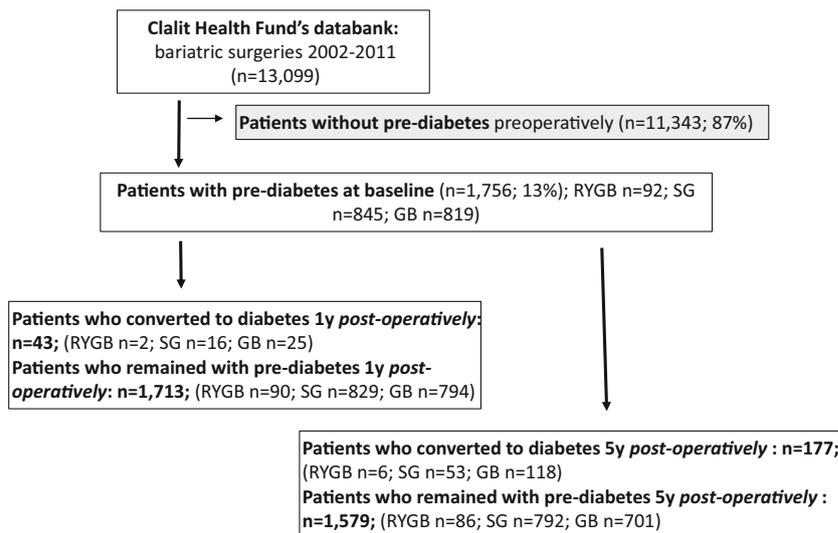
We used multivariate logistic regression models, adjusted for age, sex, and baseline weight to examine predictors of diabetes development during the 5-year post-surgery. Finally, we assessed conversion to diabetes following each surgical procedure using Kaplan-Meier survival analysis. A log rank test was used to compare conversion to diabetes for the different types of surgical procedures. The statistical significance level was set at 0.05 and the power analysis was set at 90%. All analyses were conducted using the SPSS (Chicago, IL) for Windows Software, version 20.0.

Results

Of 13,099 procedures for obesity and metabolic disorders performed in CHS during the years 2002–2011, 1,756 (13.4%) were performed in patients with FG or HbA1c values defining prediabetes: 819 underwent GB, 845 SG, and 92 RYGB (Fig. 1). The mean age was 41.6 ± 11.7 years and 73.5% were women. Table 1 presents demographic and baseline clinical characteristics of the study population by the types of procedures performed. Mean BMI (43.5 kg/m²) and mean HbA1c (5.9%, 41 mmol/mol) were similar in all groups. FG, total cholesterol, and triglycerides were lower for those who underwent RYGB than for those who underwent SG and GB ($p < 0.05$) (Table 1).

At 1-year post-surgery, 20.4% (358) patients had lost >25% of their baseline body weight, 20.0% (352) had lost 15–25%, and 300 (17.1%) had lost 15% or less. At 5-year post-surgery, 10.1% of the patients (177/1756) had developed diabetes. For patients who lost >25% of their body weight during the first postoperative year, the conversion rate to diabetes was lower at 1 and 5 years postoperatively compared to patients who lost less than 15% of their initial weight: 1.4 vs. 4.0%, $p = 0.11$ and 4.7 vs. 14.0%, $p < 0.001$, respectively (Fig. 2). In a multiple logistic regression model, weight loss during the first year postoperative was a predictor for diabetes development 5 years postoperatively. Patients who lost 15% of their initial weight during the first-year post-surgery had a 2.5-fold increased risk (95% CI 1.32–4.68, $p = 0.005$) to convert from prediabetes to diabetes, compared to those who lost >25% of their initial weight during the first year after surgery.

Fig. 1 Study flow chart. RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; GB, gastric banding



The elevated preoperative FG levels [2.1 CI (1.26, 3.57)] and the combination of elevated preoperative FG and HbA1c levels [3.0 CI (1.67–5.39)] were stronger predictors than HbA1c levels for diabetes conversion. Baseline weight, age, sex, and the number of visits to a dietitian post-surgery were not associated with conversion to diabetes.

Five years postoperatively, mean BMI values remained considerably below baseline levels (GB 35.2 ± 6.6, SG. 34.9 ± 6.6, RYGB 33.3 ± 6.5), as did mean FG: 101.2, 89.4, and 89.3 mg/dL, respectively (Table 2). No changes in mean

HbA1c were observed between baseline and 5-year follow-up in any of the surgery groups.

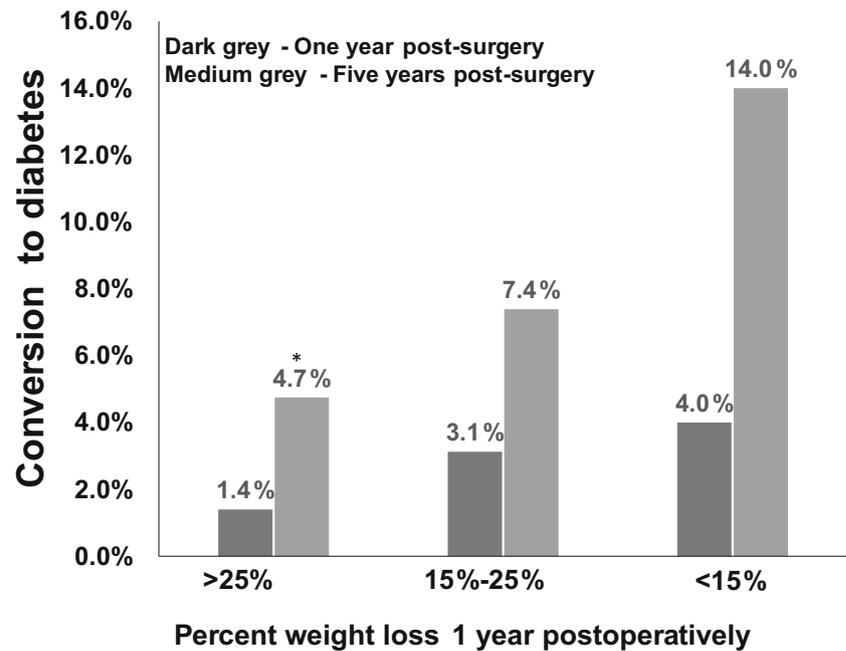
The proportions of individuals who developed diabetes 5 years postoperatively differed between surgical procedures: 14.4%, 6.3%, and 6.5%, for GB, SG, and RYGB, respectively ($p < 0.001$) (Table 2). In addition, as shown by the Kaplan-Meier survival analysis (Fig. 3), conversion from prediabetes to diabetes was more rapid among those who underwent GB than those who underwent SG or RYGB. The survival distributions for the three types of surgeries were statistically different ($\chi^2(2) = 29.67, p < 0.005$).

Table 1 Baseline characteristics of the study population by bariatric procedure

Characteristics	All	Gastric banding	Sleeve gastrectomy	Roux en-Y gastric bypass	<i>p</i> value
<i>N</i>	1756	819	845	92	–
Age, years	41.6 ± 11.7	42.3 ± 11.7	40.9 ± 11.7	41.1 ± 11.7	.04
Sex, % female	73.5	74.2	72.4	76.1	.60
Weight, kg	119.2 ± 19.8	117.9 ± 19.1	119.9 ± 19.9	121.7 ± 23.8	.08
BMI, kg/m ²	43.5 ± 5.6	43.4 ± 5.5	43.5 ± 5.6	43.7 ± 6.2	.88
Blood pressure, mmHg					
Systolic	127.9 ± 14.8	128.5 ± 15.8	127.8 ± 14.0	125.3 ± 13.9	.25
Diastolic	78.7 ± 9.5	78.8 ± 9.6	78.7 ± 9.6	78.0 ± 8.0	.81
Fasting glucose, mg/dL	106.8 ± 15.3	108.3 ± 16.3 ^{a,b}	105.4 ± 14.0 ^c	101.3 ± 12.3	.001
HbA1c, %	5.9 ± 0.32	5.9 ± 0.34	5.9 ± 0.31	5.9 ± 0.23	.32
Lipid biomarkers, mg/dl					
Total cholesterol	193.2 ± 37	194.3 ± 37 ^b	193.2 ± 38	183.5 ± 29	.04
Triglycerides	166.1 ± 91.3	172.7 ± 86.9 ^b	163.7 ± 96.8 ^c	134.2 ± 62.9	.001
LDL-cholesterol	115.8 ± 31.7	116 ± 32.7	116.1 ± 31.4	110.4 ± 25.3	.27
HDL-cholesterol	44.9 ± 10.7	44.9 ± 10.8	44.7 ± 10.6	46.2 ± 10.2	.44

p values represent comparisons between the three surgery groups. Superscript letters designate statistically significant differences between group pairs. ^a Difference between GB and SG ^b Difference between GB and RYGB. ^c Difference between SG and RYGB. Values are means ± standard deviations or percentages

Fig. 2 Percent conversion to diabetes, at 1- and 5-year post-bariatric surgery, according to weight loss groups. Dark grey—1-year post-surgery; Medium—5-year post-surgery. * $p < 0.001$ between $>25\%$ weight-loss group and $<15\%$ weight-loss group



Discussion

In this large cohort of obese individuals with prediabetes, elevated preoperative glucose levels, less weight loss during the first year postoperatively, and GB compared to SG and RYGB surgery were predictors of greater conversion from prediabetes to diabetes 5-year post-surgery.

A lack of association of baseline weight with conversion to diabetes, as observed in the current study, was also reported by the SOS study [11]. However, data from the Scandinavian Obesity Registry [12] showed an association of preoperative weight-loss with improved postoperative weight-loss. Our finding that greater weight loss 1 year postoperatively predicts

lower conversion to diabetes concurs with both the STAMPEDE study [13], which comprised patients who underwent RYGB and SG, and the Longitudinal Assessment of Bariatric Surgery Study [14]. These studies described distinct trajectories of weight change during the initial 1–3 years following surgery, and the association of these trajectories with increased remission of comorbidities at 3–7 years postoperatively. These findings emphasize the importance of monitoring patients, specifically during the initial years post-surgery to optimize postoperative weight loss and to ensure better long-term success of the metabolic surgery.

Elevated preoperative levels of FG and of the combination of FG and HbA1c were predictors of conversion to diabetes

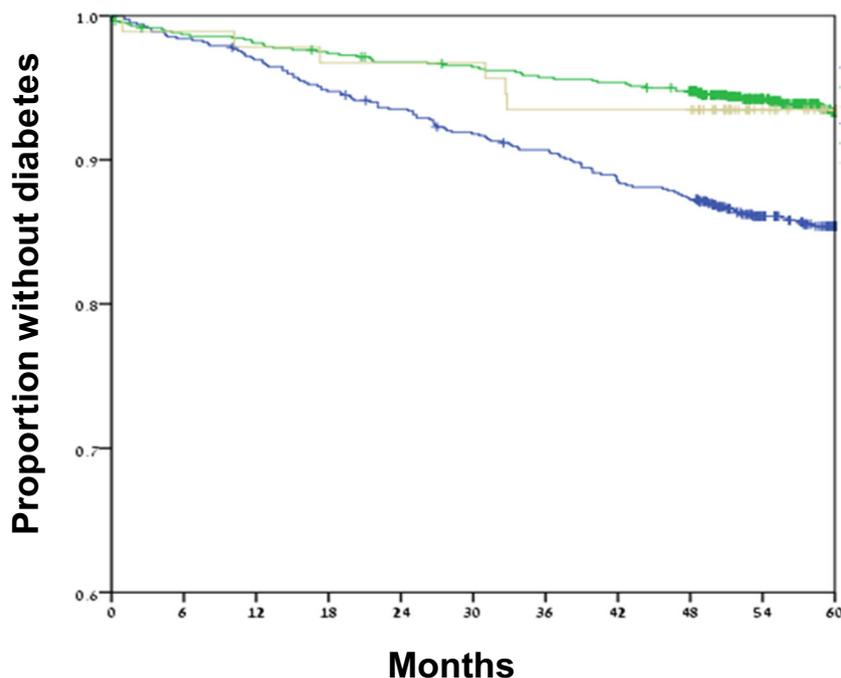
Table 2 Metabolic parameters and conversion rates to diabetes 1 and 5-year post-bariatric surgery

Variable	Years post-surgery	All	Gastric banding	Sleeve gastrectomy	Roux en-Y gastric bypass	<i>p</i> value
N		1,756	819	845	92	
BMI, kg/m ²	1	35.1 ± 5.9	37.0 ± 5.9 ^{a,b}	34.1 ± 5.7	32.6 ± 5.3	< 0.001
	5	35.0 ± 6.64	35.2 ± 6.6 ^b	34.9 ± 6.6	33.3 ± 6.5	0.06
Weight, kg	1	96.1 ± 18.3	100.2 ± 17.9 ^{a,b}	93.9 ± 17.9	91.0 ± 19.8	< 0.001
	5	96.6 ± 20.3	96.8 ± 19.6	96.8 ± 21.0	93.4 ± 20.5	0.40
FG, mg/dL	1	92.4 ± 12.4	96.3 ± 11.8 ^{a,b}	89.6 ± 11.9	85.5 ± 12.1	< 0.001
	5	95.4 ± 21.5	101.2 ± 27.2 ^{a,b}	89.4 ± 10.3	89.3 ± 11.6	< 0.001
HbA1c, %	1	5.9 ± 0.3	5.8 ± 0.5	5.7 ± 0.5	5.7 ± 0.5	0.13
	5	5.8 ± 0.7	5.9 ± 0.8 ^a	5.7 ± 0.6	5.8 ± 0.4	0.007
Conversion to diabetes, %	1	2.4	3.1	1.9	2.2	0.30
	5	10.1	14.4 ^{a,b}	6.3	6.5	< 0.001

Variables presented are mean ± SD if not stated otherwise. *FG* fasting glucose

p values represent comparison between the three bariatric procedures. Superscript letters designate statistically significant differences between group pairs. ^a Difference between gastric banding and sleeve gastrectomy, ^b Difference between gastric banding and Roux-en-Y gastric bypass

Fig. 3 Conversion from pre-diabetes to diabetes; Kaplan-Meier survival analysis. Blue—gastric banding; Green—sleeve gastrectomy; Yellow—Roux en-Y gastric bypass $\chi^2(2) = 29.67$, $p < 0.005$



5 years postoperatively. Debédát et al. recently showed that preoperative glycemic control and weight loss during the first year post RYGB resulted in less diabetes relapse 5 years post-surgery [15]. Taken together, that study and ours emphasize the importance of achieving glycemic control prior to surgery, to maximize long-term results.

In the current study, mean FG decreased considerably after surgery, while significant changes in HbA1c were not observed. In our former study of patients with diabetes from the same population of the CHS, both FG and HbA1c decreased following surgery [10]. Our current findings suggest the possibility of a greater effect of metabolic surgery, and particularly SG, on hepatic insulin resistance than on peripheral insulin resistance, among individuals with impaired glucose tolerance yet who are not classified as having diabetes. Other studies have shown improved hepatic insulin resistance following metabolic surgery, in populations both free of diabetes [16, 17] and with diabetes [18]. Thus, the current study highlights the importance of investigating the effects of metabolic surgery on metabolic parameters particularly in individuals with isolate FG and isolate impaired glucose intolerance, distinct from individuals with either normal glucose levels or with diabetes.

Higher rates of conversion from prediabetes to diabetes were observed following GB than following SG or RYGB. This finding may be related to gut hormonal effects of SG and RYGB, which result in a greater increase in glucagon-like peptide-1 (GLP-1) compared to post-GB [19]. Other studies have attributed a role to increased GLP-1 secretion in improving metabolic parameters following metabolic surgery [20], such as following RYGB in persons without diabetes [17],

and following SG in mice fed a high-fat diet [21]. In addition, in the SCALE study of persons with pre-diabetes [22], liraglutide 3.0 mg, a GLP-1 analogue, prevented conversion from prediabetes to diabetes by 80%.

Limitations of this study include our reliance on a single nationwide HMO cohort, and fewer patients who underwent RYGB, reflecting the common procedures performed in Israel. In addition, the lack of a non-surgical pre-diabetic group for comparison is a limitation. Finally, although the oral glucose challenge test assesses peripheral insulin resistance more accurately than HbA1c, baseline data of this test were not available for our population since it is not performed routinely and is not a preoperative requirement for metabolic surgery. Strengths of our study include the relatively large cohort of patients with prediabetes, with a highly-diverse cultural background, and the electronic medical records platform, which enabled tracking a large number of patients up to 5-year post-surgery.

In conclusion, preoperative glucose level control and weight loss during the first-year post-surgery contribute substantially to lower conversion rates to diabetes following metabolic surgery. SG and RYGB appear to confer a better metabolic prognosis than GB for individuals with prediabetes and obesity. Further investigation is needed to discern the effect of the various types of surgery, specifically on isolate FG and isolate impaired glucose intolerance for the distinct population of individuals with prediabetes.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflicts of interest.

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