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ORIGINAL CONTRIBUTIONS

The Comparative Effect of Roux-en-Y Gastric Bypass and Sleeve Gastrectomy on 10-Year and Lifetime Atherosclerotic Cardiovascular Disease Risk

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Abstract

Background Bariatric surgery reduces atherosclerotic cardiovascular disease (ASCVD) risk. However, the comparative effect of Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG) on 10-year and lifetime ASCVD risk, as defined by the American College of Cardiology/American Heart Association (ACC/AHA), remains unknown.

Methods Using the ACC/AHA ASCVD risk estimator, 10-year and lifetime ASCVD risks were calculated before and 1 year after bariatric surgery for patients aged 40–78 who underwent RYGB or SG at an academic medical center in California between 2003 and 2015. Change in risk was calculated by taking the difference between 1-year and baseline risk. Statistical analyses included the Wilcoxon signed rank test, Mann-Whitney *U* test, Quade's test, and multiple logistic regression.

Results There were 536 patients (mean age 52 ± 10 years, 20% male), of whom 438 underwent RYGB and 98 underwent SG. Patients undergoing RYGB were predominately female (82% vs 71%, $p = 0.021$) and had higher baseline BMIs (44.4 ± 8.4 vs 41.9 ± 8.0, $p < 0.001$) than patients undergoing SG. Compared with baseline, 10-year and lifetime ASCVD risks were significantly lower 1 year after surgery (aggregate of RYGB and SG, 4.2 ± 6.0% vs. 2.2 ± 3.5%, $p < 0.001$; 50 ± 11% vs. 39 ± 12%, $p < 0.001$, respectively). Patients who underwent RYGB had greater reductions in 10-year and lifetime ASCVD risks from baseline to 1 year after surgery than patients who underwent SG (1.7 ± 3.5% vs. 0.8 ± 2.4%, $p < 0.001$; 11 ± 23% vs. 0 ± 12%, $p < 0.001$, respectively).

Conclusions Although RYGB and SG significantly lower 10-year and lifetime cardiovascular disease risks by 1 year after surgery, patients who undergo RYGB may experience greater cardiovascular risk reduction relative to counterparts who undergo SG.

Keywords Cardiac · Risk · Bariatric surgery · Sleeve gastrectomy · Gastric bypass

Introduction

Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of morbidity and mortality in the USA. In 2013, the American Heart Association (AHA) and American College of Cardiology (ACC) released guidelines that aimed to reduce ASCVD risk through evidence-based recommendations [1, 2]. To achieve this goal, the Pooled Cohort Risk Assessment Equation was developed to risk stratify patients who could benefit from cholesterol-lowering therapies [3]. This equation incorporates known ASCVD risk factors to estimate 10-year and lifetime ASCVD risks, defined as coronary death, non-fatal myocardial infarction, or fatal/non-fatal stroke, and it is intended to inform patient-provider discussions

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around lifestyle modifications and statin initiation. This ASCVD risk estimator is widely used in clinical practice today and has been well-validated against observed ASCVD events in several studies [4, 5].

Obesity is a well-known independent risk factor for ASCVD and is closely related to other traditional ASCVD risk factors, including type 2 diabetes mellitus, hypertension, and dyslipidemia [6]. As its prevalence has risen substantially over the last few decades, obesity has become a target for intervention to reduce ASCVD risk. Bariatric surgery is an effective treatment for morbid obesity [7, 8], and the two most frequently performed procedures are Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG). In 2015, RYGB and SG accounted for 23.1% and 53.8% of all bariatric surgical procedures, respectively [9]. In previous studies, both RYGB and SG have been shown to reduce the prevalence of diabetes [10–12], hypertension [13], and dyslipidemia [14]. Although some studies have found that RYGB may have a greater effect on the reduction of these comorbidities [10, 11, 14] and on long-term weight loss [15], this is not a consistent finding [12, 13, 16, 17]. To better understand the impact of bariatric procedures on ASCVD risk, we compared the effect of laparoscopic RYGB and laparoscopic SG on the change in ACC/AHA 10-year and lifetime ASCVD risks from prior to surgery to 1 year after surgery at a single academic medical center.

Methods

Data for this study were obtained from a prospectively maintained database containing clinical information for patients who underwent RYGB or SG at Stanford University Hospital in California between 2003 and 2015. Inclusion criteria included successful completion of surgery with 1 year of data available. Patients were excluded from analysis if they required a re-operation after their initial surgery, had incomplete ASCVD risk data, or had unacceptable values for ASCVD risk calculation as defined in Fig. 1. Data were collected from patients who provided written informed consent, and approval for this study was provided by the Stanford University Institutional Review Board.

The RYGB technique involved the direct anastomosis of a small gastric pouch to the jejunum allowing food to bypass part of the small intestine and a jejuno-jejunal anastomosis for the flow of exocrine secretions [18]. In SG, a portion of the stomach along its greater curvature was excised, leaving a small gastric remnant for food to travel through to the duodenum [19].

Variables used to calculate ACC/AHA 10-year and lifetime ASCVD risks included age, sex, race (White, African American, or other), total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), systolic blood pressure (SBP),

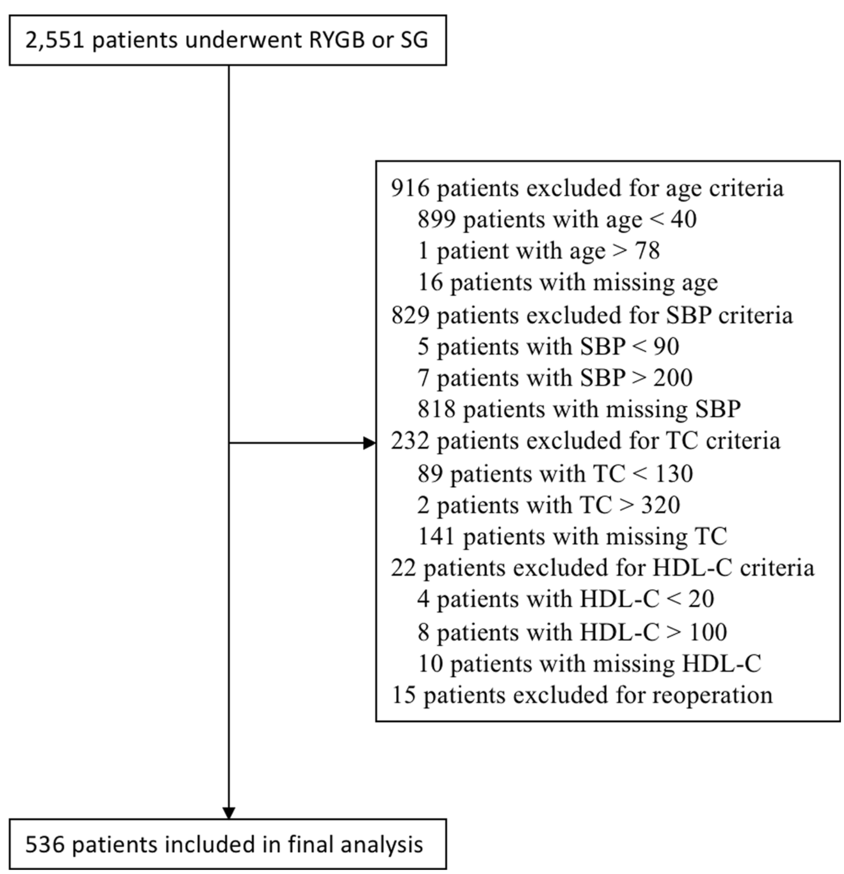

Fig. 1 Patient selection and exclusion criteria. HDL-C, high-density lipoprotein cholesterol, in mg/dL; RYGB, Roux-en-Y gastric bypass; SBP, systolic blood pressure, in mmHg; SG, sleeve gastrectomy; TC, total cholesterol, in mg/dL

the presence of diabetes, hypertension treatment, and tobacco use. Baseline and 1-year measures of these variables and body mass index (BMI) were collected from the existing database and from a review of individual electronic health records. BMI was calculated by weight (kilograms) divided by height (meters) squared. Classifications of obesity were defined using preoperative BMI as follows: super obesity (BMI ≥ 50 kg/m^2), severe obesity (40 kg/m^2 ≤ BMI < 50 kg/m^2), and morbid obesity (35 kg/m^2 ≤ BMI < 40 kg/m^2). Because of an institutional requirement for smoking cessation prior to undergoing bariatric surgery, patients were recorded to be non-smokers at both time points. Diabetes was defined as hemoglobin A1c ≥ 6.5% or use of an anti-diabetic medication. Resolution of diabetes was defined as hemoglobin A1c < 6.5% and not taking any diabetes medications 1 year after surgery. Ten-year and lifetime ASCVD risks were estimated at baseline and 1 year after bariatric surgery using the ACC/AHA Pooled Cohort Risk Assessment Equation [3]. The change in ASCVD risk was calculated by taking the difference between 1-year and baseline risks. For valid calculated risk estimation, variables had to be within the following ranges: age 40–79 years (or 40–59 years for lifetime ASCVD estimation), TC 130–320 mg/dL, HDL-C 20–100 mg/dL, and SBP 90–200 mmHg.

Results are expressed as medians with interquartile ranges and count frequencies with percentages unless otherwise specified. Continuous variables were analyzed using Wilcoxon signed rank, Mann-Whitney *U*, and Quade's tests, whereas categorical variables were analyzed using the chi-squared test. Logistic regression was used in a sub-group analysis to assess the likelihood of patients achieving a 10-year ASCVD risk < 7.5% 1 year after surgery in the RYGB and SG groups. This metric is clinically relevant, since ACC/AHA guidelines recommend initiation of statin therapy for primary prevention in patients for whom 10-year ASCVD risk ≥ 7.5%. Variables in the logistic regression included preoperative age, sex, BMI, and diabetes. For all statistical analyses, a two-sided p value ≤ 0.05 was considered statistically significant. All analyses were done using SPSS (Version 24.0, IBM Corp., Armonk, NY) and SAS Studio v3.5.

Results

The final analysis included 536 patients, of whom 438 underwent RYGB and 98 underwent SG. The median age was 52 years, 20% were male, and 61% were White. At baseline, 47% had diabetes and 70% took medications for hypertension. Patients undergoing RYGB were more likely to be female (82% vs 71%, $p = 0.021$), had higher baseline BMIs (44.4 ± 8.4 kg/m^2 vs 41.9 ± 8.0 kg/m^2, $p < 0.001$), and greater SBPs (138 ± 28 mmHg vs 132 ± 23 mmHg, $p = 0.004$) relative to patients undergoing SG. Baseline 10-year and lifetime ASCVD risks were comparable between the two groups (4.2 ± 5.9% for RYGB vs 4.4 ± 6.6% for SG, $p = 0.548$; 48 ± 11% for RYGB vs 50 ± 12% for SG, $p = 0.257$, respectively). Table 1 summarizes additional baseline characteristics of the study sample.

After accounting for differences in baseline BMI, sex distribution, and SBP, RYGB still resulted in larger reductions in BMI (− 14.5 ± 5.3 kg/m^2 vs − 8.5 ± 4.1 kg/m^2, $p < 0.001$) and TC (− 16 ± 46 mg/dL vs − 8 ± 45 mg/dL, $p < 0.001$) compared with SG. Patients who underwent RYGB were more likely to experience remission of diabetes relative to patients who underwent SG (80% vs 56%, $p < 0.001$) 1 year after surgery. In addition, more patients stopped their anti-hypertensives after RYGB than SG (71% vs 49%, $p < 0.001$). RYGB and SG were associated with similar increases in HDL-C (10 ± 14 mg/dL vs 8 ± 13 mg/dL, $p = 0.135$) and decreases in SBP (− 10 ± 29 mmHg vs − 3 ± 27 mmHg, $p = 0.164$).

Compared with baseline, 10-year and lifetime ASCVD risks were significantly lower 1 year after bariatric surgery (defined as the aggregate of RYGB and SG, 4.2 ± 6.0% vs. 2.2 ± 3.5%, $p < 0.001$; 50 ± 11% vs. 39 ± 12%, $p < 0.001$, respectively). This is illustrated for 10-year ASCVD risk in Fig. 2. Individually, both RYGB and SG led to statistically significant reductions in 10-year ASCVD risk (4.2 ± 5.9% vs. 1.9 ± 3.2%, $p < 0.001$; 4.4 ± 6.6% vs. 3.2 ± 5.0%, $p < 0.001$, respectively) and lifetime ASCVD risk (48 ± 11% vs. 39 ± 12%, $p < 0.001$; 50 ± 12% vs. 39 ± 10%, $p < 0.001$, respectively). However, after accounting for group differences in BMI reduction and preoperative BMI, sex distribution, and SBP, patients who underwent RYGB had larger reductions in 10-year and lifetime ASCVD risks from baseline to 1 year after surgery than those who underwent SG (1.7 ± 3.5% vs. 0.8 ± 2.4%, $p < 0.001$; 11 ± 23% vs. 0 ± 12%, $p < 0.001$, respectively). This is illustrated for 10-year ASCVD risk in Fig. 3.

For patients with a baseline 10-year ASCVD risk ≥ 7.5%, the odds of achieving a 10-year risk < 7.5% were 69% lower for those who underwent SG relative to those who underwent RYGB (adjusted OR for SG = 0.31, 95% CI 0.12–0.85, $p = 0.023$) after adjusting for preoperative age, BMI, sex distribution, and diabetes (Table 2). The unadjusted odds for achieving this target (OR = 0.24, 95% CI 0.11–0.56, $p = 0.001$) were similar to the adjusted odds above.

Greater reductions in 10-year ASCVD risk after RYGB compared with SG were observed among female patients (1.5 ± 2.9% vs. 0.5 ± 2.2%, $p < 0.001$), patients who had severe obesity (1.3 ± 2.6% vs. 0.3 ± 2.0%, $p < 0.001$) and morbid obesity (1.7 ± 3.9 vs. 1.4 ± 2.7, $p = 0.05$), and patients who were younger than 60 years of age (1.5 ± 3.1% vs. 0.6 ± 2.3%, $p < 0.001$). Surprisingly, preoperative diabetes status did not significantly impact the comparative effect as both diabetic and non-diabetic patients experienced greater 10-year ASCVD risk reduction if they underwent RYGB (Table 3).

Table 1 Study population baseline characteristics

	All patients $N = 536$	SG $N = 98$	RYGB $N = 438$	*p* value
Age	52 ± 10	54 ± 10	52 ± 11	0.054
< 60—no. (%)	442 (82)	78 (80)	364 (83)	
≥ 60—no. (%)	94 (18)	20 (20)	74 (17)	
Sex				0.021
Male—no. (%)	108 (20)	28 (29)	80 (18)	
Female—no. (%)	428 (80)	70 (71)	358 (82)	
Race/ethnicity				0.728
White—no. (%)	327 (61)	63 (64)	264 (60)	
Black—no. (%)	46 (9)	7 (7)	39 (9)	
Other—no. (%)	163 (30)	28 (29)	135 (31)	
BMI	43.9 ± 8.5	41.9 ± 8.0	44.4 ± 8.4	< 0.001
SBP	136 ± 27	132 ± 23	138 ± 28	0.004
TC	182 ± 46	185 ± 49	180 ± 45	0.417
HDL-C	46 ± 15	48 ± 16	45 ± 14	0.349
DM—no. (%)	254 (47)	43 (44)	211 (48)	0.441
A1c (for diabetic patients)	6.8 ± 1.6	6.9 ± 1.4	6.8 ± 1.6	0.997
HTN treatment (no.)	374 (70)	71 (72)	303 (69)	0.524
Baseline 10-year ASCVD risk	4.2 ± 6.0	4.4 ± 6.6	4.2 ± 5.9	0.548
Baseline lifetime ASCVD risk	50 ± 11	50 ± 12	48 ± 11	0.257

Values for baseline 10-year and lifetime ASCVD risks are given in percentages. Continuous variables are given in count frequency and percentage (in parentheses) or median ± interquartile range

A1c hemoglobin A1c, in %. *BMI* body mass index, in kg/m^2. *DM* diabetes mellitus. *HDL-C* high-density lipoprotein cholesterol, in mg/dL, *HTN* hypertension, *SBP* systolic blood pressure, in mmHg, *TC* total cholesterol, in mg/dL

Postoperative complications occurred in 52 patients—47 who underwent RYGB and 5 SG. For patients who underwent RYGB, complications included clinically significant bleeding requiring a blood transfusion (13), gastrointestinal ulcer (9), wound infection (8), nutritional deficiency (8), arrhythmia (5), pneumonia (5), venous thromboembolism (4), stroke (1), and bowel obstruction/ileus (1). Patients who underwent SG developed venous thromboembolism (3), clinically significant bleeding (1), and nutritional deficiency (1).

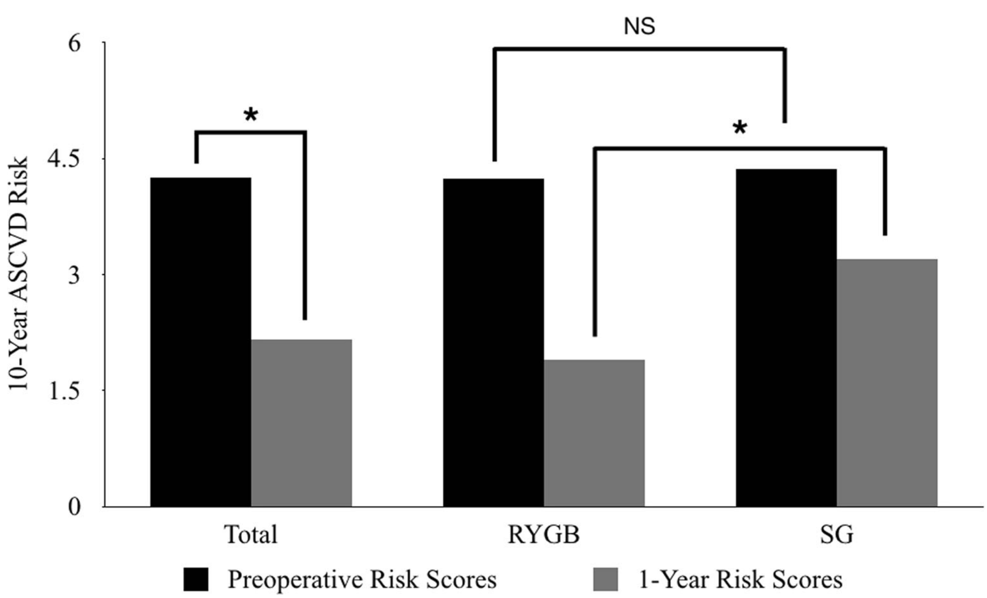

Fig. 2 Median 10-year ASCVD risk at baseline and 1-year after surgery, total and by surgery type. NS, non-significant difference between baseline 10-year ASCVD risk for RYGB and SG. Asterisk symbol indicates significant difference between 10-year ASCVD risk 1 year after RYGB versus SG. ASCVD, atherosclerotic cardiovascular disease; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy

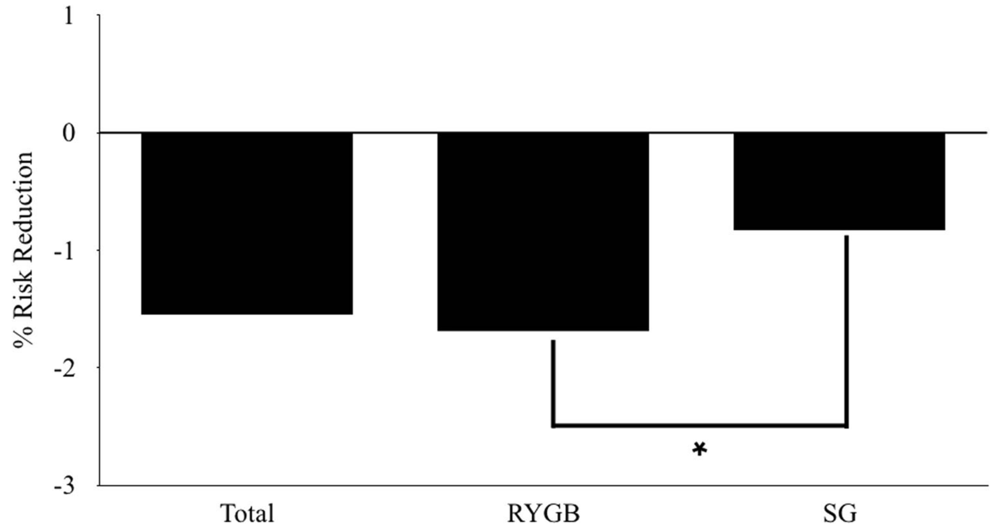

Fig. 3 Median 10-year ASCVD risk reduction, total and by surgery type. Asterisk symbol indicates significant difference in 10-year ASCVD risk reduction after RYGB versus SG. ASCVD, atherosclerotic cardiovascular disease; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy

Discussion

The purpose of this study was to assess the comparative effectiveness of RYGB and SG on 10-year and lifetime ASCVD risks, as defined by the ACC/AHA Pooled Cohort Risk Assessment Equation, 1 year after surgery. While both RYGB and SG were associated with significant reductions in the 10-year and lifetime risks of ASCVD, RYGB was associated with greater reductions than SG. Greater reductions in risk among patients who underwent RYGB vs. SG were largely driven by patients who were female, had BMIs 35–50 kg/m^2, and were younger than 60 years of age, although sub-group analyses should be interpreted cautiously due to small sample sizes. Notably, patients with elevated baseline 10-year ASCVD risk were more likely to achieve a 10-year

Table 2 Multivariable logistic regression demonstrating odds of achieving ASCVD risk < 7.5% after surgery

	β	Odds ratio	95% CI	*p* value
Surgical procedure				
Gastric bypass	Reference			
Sleeve gastrectomy	− 1.164	0.312	(0.115, 0.849)	0.023
BMI classification				
35–40	Reference			
40–50	1.049	2.855	(1.002, 8.13)	0.050
50+	− 0.046	0.955	(0.284, 3.207)	0.940
Age				
Age < 60	Reference			
Age > 60	− 2.450	0.086	(0.032, 0.231)	< 0.001
Sex				
Male	Reference			
Female	2.073	7.946	(3.018, 20.92)	< 0.001
Preoperative DM				
No DM	Reference			
DM	− 0.815	0.443	(0.163, 1.205)	0.111

Event modeled is the odds that a patient who qualified for statin therapy prior to surgery (i.e., 10-year ASCVD risk ≥ 7.5%) has a 10-year ASCVD risk < 7.5% after surgery such that statin therapy is no longer indicated. Variables in the logistic regression include preoperative age, sex, BMI, and diabetes. *P* values correspond to differences in odds between test and reference value for each variable

ASCVD atherosclerotic cardiovascular disease, *BMI* body mass index, in kg/m^2 , *DM* diabetes mellitus, *RYGB* Roux-en-Y gastric bypass, *SG* sleeve gastrectomy

Table 3 Sub-group analysis of median 10-year ASCVD risk reduction, stratified by surgery type

		RYGB *N* = 438		SG *N* = 98	
	N	Risk reduction	*N*	Risk reduction	*p* value
BMI classification					
35–40	81	1.3 ± 2.6	39	0.3 ± 2.0	0.003
40–50	256	1.7 ± 3.9	47	1.4 ± 2.7	0.044
50+	101	2.3 ± 4.4	12	1.3 ± 3.5	0.110
Age					
Age < 60	364	1.5 ± 3.1	78	0.6 ± 2.3	< 0.001
Age ≥ 60	74	3.3 ± 5.7	20	2.1 ± 5.6	0.101
Sex					
Male	80	3.5 ± 6.0	28	1.9 ± 6.7	0.068
Female	358	1.5 ± 2.9	50	0.5 ± 2.2	< 0.001
Preoperative DM					
No DM	184	1.0 ± 1.6	43	0.3 ± 1.5	0.001
DM	254	3.6 ± 4.8	55	1.8 ± 3.9	0.002

Ten-year ASCVD risk reduction is given as median ± interquartile range (%). *P* values correspond to differences between 10-year ASCVD risk reduction after RYGB versus SG within each defined sub-group

ASCVD atherosclerotic cardiovascular disease, *BMI* body mass index, in kg/m^2 , *DM* diabetes mellitus, *RYGB* Roux-en-Y gastric bypass, *SG* sleeve gastrectomy

ASCVD risk < 7.5% 1 year after surgery if they underwent RYGB rather than SG. Postoperative complications were more likely after RYGB than SG, although no patients suffered a postoperative myocardial infarction.

Overall, these findings were attributable to greater ASCVD risk factor reduction in the RYGB group. Compared with SG, RYGB not only caused a larger reduction in TC, but also resulted in greater remission of diabetes and decreased utilization of anti-hypertensives. Patients who underwent RYGB also experienced more weight loss than those who underwent SG, although the group differences in ASCVD risk reduction were persistent after accounting for this finding. As previously described, RYGB may have a greater effect on weight loss and metabolic syndrome remission due to bypass of the proximal small intestine leading to decreased nutrient contact with the duodenum and proximal jejunum. This is thought to prevent secretion of an unidentified "anti-incretin," a signal that otherwise promotes insulin resistance [20].

The results of this study demonstrate a 54% and 30% relative reduction in 10-year ASCVD risk after RYGB and SG, respectively, and are comparable with results from prior studies that have examined the effect of bariatric surgery on the Framingham risk score [21], which estimates the 10-year risk of myocardial infarction, coronary death, and adverse cardiovascular events. For example, Torquati et al. [22] estimated that RYGB led to a reduction in 10-year cardiovascular risk, as defined by the Framingham risk score, from 5.4 to 2.7% (50% relative risk reduction) 1 year after surgery. Similarly, two large prospective cohort studies [23, 24] found that the incidence of myocardial infarction and coronary death over an average of 7–10 years was reduced by ~50% after RYGB compared with medical management. While cardiovascular risk after SG has not been well studied, a prospective cohort study of 140 Spanish patients by Benaiges et al. [25] found that 10-year cardiovascular risk, as measured by the Framingham risk score, decreased from 5.6 to 3.4% (equivalent to a 39% relative risk reduction) 1 year after SG.

To our knowledge, this study is first to quantify changes in ASCVD risk for bariatric patients in a way that can be used to inform clinical decisions and patient-provider discussions in current practice. Since the 2013 ACC/AHA cholesterol guideline [1] recommended use of the Pooled Cohort Equation to estimate 10-year and lifetime ASCVD risks, it has become integrated into clinical practice as a quantitative way to effectively risk stratify patients when determining statin eligibility. Currently, patients with 10-year ASCVD risk ≥ 7.5% are considered eligible for statin therapy. No previous studies have analyzed the impact of bariatric surgery—specifically, RYGB and SG—on ACC/AHA 10-year and lifetime ASCVD risks. Understanding the impact of these common procedures on a clinically relevant risk assessment tool and in a high-risk population is important for understanding the role of bariatric surgery in the prevention and treatment of ASCVD. Our results demonstrate that RYGB may be more effective than SG in reducing overall ASCVD risk, particularly in lower risk sub-groups.

There are several limitations to the present study. First, patients were recorded to be non-smokers prior to and following bariatric surgery based on institutional requirements. Although patients were asked preoperatively and during follow-up to confirm smoking cessation and were deemed non-operative candidates if they were suspected to have continued smoking, it is possible that some patients continued smoking without provider knowledge. Second, due to the observational study design, it is possible that the observed differences in ASCVD risk reduction following RYGB and SG may be due to residual confounding not accounted for by our analyses, and it is not possible to ascertain causality. Third, a significant proportion of patients were excluded for values outside the range of ASCVD risk estimation, which limits the external validity of our findings. Fourth, this study only includes follow-up data for 1 year after bariatric surgery. In the future, it will be important to conduct similar investigations using longer term outcomes.

Conclusion

RYGB and SG are both associated with significantly lower 10-year and lifetime cardiovascular disease risk 1 year after surgery, but patients undergoing RYGB experienced greater cardiovascular risk reduction than those undergoing SG. Randomized controlled trials are needed to evaluate the comparative effect of different bariatric procedures on ASCVD risk and events.

Authors' Contribution V.R. performed data analysis and wrote the manuscript. L.G. assisted with data analysis and reviewed the manuscript. D.M. contributed to the research design and revised the manuscript. J.M. provided the data and critical review of the manuscript. J.M. and D.M. conceived of study. All authors agree with the contents of this manuscript.

Compliance with Ethical Standards Data were collected from patients who provided written informed consent, and approval for this study was provided by the Stanford University Institutional Review Board.

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

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