Original article

# Sleeve gastrectomy surgery: when 2 alcoholic drinks are converted to 4

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**Abstract**

**Background:** While it is well established that Roux-en-Y gastric bypass (RYGB) causes a rapid and heightened peak blood alcohol concentration (BAC), results from previous studies on the effects of sleeve gastrectomy (SG) on alcohol pharmacokinetics are conflicting. Data from 2 studies found SG did not affect BAC, whereas another study found SG caused a heightened peak BAC after alcohol ingestion. Moreover, these 3 studies estimated BAC from breathalyzers, which might not reliably estimate peak BAC.

**Objectives:** The aims of this study were to evaluate (1) the effect of SG, relative to RYGB and a presurgery group, on alcohol pharmacokinetics and subjective effects, and (2) whether breathalyzers are reliable in this population.

**Setting:** Single-center prospective nonrandomized trial.

**Methods:** We performed alcohol challenge tests in 11 women who had SG surgery $1.9 \pm .1$ years ago (body mass index = $35.1 \pm 6.6$ kg/m$^2$), 8 women who had RYGB surgery $2.2 \pm .4$ years ago (body mass index = $30.0 \pm 5.2$ kg/m$^2$), and 9 women who were scheduled for bariatric surgery (body mass index = $44.1 \pm 4.0$ kg/m$^2$). BACs were estimated from breath samples and measured by gas chromatography at various times after consuming approximately 2 standard drinks.

**Results:** BAC increased faster, peak BAC was approximately 2-fold higher, and feelings of drunkenness were heightened in both SG and RYGB groups relative to the presurgery group ($P$ values < .001). BAC estimated from breath samples underestimated BAC by 27% (standard deviation = 13%) and missed peak BACs postsurgery.

**Conclusions:** SG, similar to RYGB, causes marked alterations in the response to alcohol ingestion manifested by a faster and higher peak BAC. The breathalyzer is invalid to assess effects of gastric surgeries on pharmacokinetics of ingested alcohol. (Surg Obes Relat Dis 2018;14:277–283.) © 2018 American Society for Metabolic and Bariatric Surgery. All rights reserved.

*Keywords:*  Sleeve gastrectomy; Bariatric surgery; Metabolic surgery; Pharmacokinetics; Ethanol; Alcohol; Breathalyzer

Sleeve gastrectomy (SG) is the most frequent bariatric surgical procedure performed in the United States. Yet, data on its intermediate and long-term effects remain limited. For example, it is unknown whether SG is associated with increased likelihood of developing an alcohol use disorder. However, the increased risk of developing an alcohol use disorder after Roux-en-Y gastric bypass surgery (RYGB) [1–4] and gastrectomy surgery for ulcer disease and gastric cancer [5–7], suggests that attention to this potential serious side effect of SG is critical.

The increase in alcohol use disorder after RYGB and gastrectomy is likely caused, in part, by surgery-related changes in gastric anatomy that alter the pharmacokinetics and subjective effects of ingested alcohol. While it is well established that RYGB [8–11] and gastrectomy [12] accelerate alcohol absorption and cause a rapid, large increase in peak blood alcohol concentration (BAC), results from previous studies on the effects of SG on alcohol pharmacokinetics are conflicting. We are aware of 3 studies that evaluated the effect of SG on BAC achieved after drinking. Of these studies, 2 found SG did not affect BAC [13,14], whereas another study found SG caused a marked increase in peak BAC after alcohol ingestion [15]. However, all 3 studies used breath analysis techniques to estimate BAC.

The use of the breath analysis techniques to estimate BAC in the bariatric population has limitations. First, to ensure that there is no residual mouth alcohol, which could dramatically affect the estimation of BAC, the protocol for breath analysis techniques requires waiting at least 15 minutes after patients finish their drink to take a breath sample. Such a time lag restriction could result in entirely missing peak BAC in conditions when alcohol absorption is significantly faster, such as after RYGB and gastrectomy. Second, we are not aware of any published study that evaluated whether breath-sampling techniques provide a valid assessment of BAC in patients with severe obesity or gastric bypass patients. Notably, BAC estimated from alcohol breath techniques depends on several factors, including lung volume, hematocrit, and body size, and the algorithm currently used to derive BAC estimations is based on data from healthy lean men [16].

The primary goals of the present study were to evaluate the effect of SG, relative to RYGB and a presurgery group, (1) on alcohol pharmacokinetics, by measuring BAC with gas chromatography, the gold standard technique, as well as by breath analysis; and (2) on alcohol subjective effects, by using the drunkenness scale of the Addiction Research Center Inventory, a validated questionnaire. A secondary aim of this study was to determine whether breath analysis, which is normally used to estimate BAC, is a reliable technique to study the effects of RYGB or SG on alcohol pharmacokinetics.

## Methods

### Patients

There were 11 women who had SG (SG group) and 8 women who had RYGB (RYGB group) within the last 1 to 5 years, and 9 women who were scheduled to have RYGB at Barnes-Jewish Hospital in St. Louis, MO (presurgery group) who participated in this study (Table 1). The study was approved by the Washington University institutional review board. All patients provided written informed consent.

Patients were recruited by reviewing their medical record to determine initial eligibility followed by a personal interview conducted at the Bariatric Surgery Clinic. We only studied women because most patients who have bariatric surgery are women [17] and sex can affect alcohol pharmacokinetics [18]. All patients completed a comprehensive medical evaluation, including history, physical examination, blood tests, and urine pregnancy test. Subject's alcohol use patterns were assessed with the Alcohol Module of the Semi-Structured Assessment for the Genetics of Alcoholism [19]. To be eligible for the study, patients had to be regular, light drinkers and not have evidence of risky drinking, according to the National Institute of Alcohol Abuse and Alcoholism guidelines 1 month before enrolling in the study. Patients with lifetime alcohol dependence, current regular use of drugs other than alcohol, or current use of medications that can affect alcohol pharmacokinetics were excluded. In addition, patients who smoked cigarettes in the last 6 months, were pregnant, breastfeeding, or not using an effective birth control method, anemic, or had liver disease were excluded. Data from a subsample of these patients have been reported previously [9]. The study is registered with the Clinical Trials.gov identifier: NCT01843257.

### Study design and experimental procedures

The study was conducted in the Clinical Research Unit at Washington University School of Medicine. Using a randomized crossover design, all patients were evaluated in 2 sessions, approximately 1-week apart. Body fat-free mass (FFM) was assessed in the Clinical Research Unit by using dual-energy x-ray absorptiometry. Patients consumed either .5 g of alcohol per kg of FFM (equivalent to ~2 standard alcoholic beverages: alcohol condition) or a non-alcoholic placebo beverage (control condition) at each visit. The dose of alcohol consumed was based on each subject's total FFM because FFM, not weight, correlates closely with alcohol volume of distribution [20].

### Alcohol and placebo challenge tests

For each session, patients were admitted to the Clinical Research Unit after an overnight fast and remained fasted

Table 1
Characteristics of study participants

| Characteristics | Mean (SD) | | |
| --- | --- | --- | --- |
| | Presurgery (n = 9) | RYGB surgery (n = 8) | SG surgery (n = 11) |
| Age, yr | 41.1 (9.3) | 42.5 (7.9) | 48.4 (8.3) |
| Weight, kg | 120.2 (18.7)[*] | 80.8 (14.1)[†] | 96.7 (17.1)[†] |
| BMI, kg/m$^2$ | 44.1 (4.0)[*] | 30.0 (5.2)[†] | 35.1 (6.6)[‡] |
| FFM, kg | 54.3 (6.0) | 49.4 (5.7) | 49.3 (5.1) |
| Time from surgery, yr | – | 2.2 (1.2) | 1.9 ± .1 |
| Alcohol-related variables | | | |
| Age, yr | | | |
| First drink | 17.9 (3.0) | 17.4 (2.3) | 17.8 (1.5) |
| Regular drinking | 20.2 (2.8) | 25.4 (10.6) | 24.9 (7.6) |
| N° of Drinking d/mo (in last 6 mo) | 2.8 (2.6) | 4.7 (3.3) | 3.4 (3.9) |
| N° of Drinks per drinking d (in last 6 mo) | 2.8 (1.5) | 1.9 (1.7) | 1.8 (.9) |
| N° of standard drinks given on alcohol challenge test[§] | 1.9 (.2) | 1.8 (.2) | 1.7 (.1) |

SD = standard deviation; RYGB = Roux-en-Y gastric bypass; SG = sleeve gastrectomy; BMI = body mass index (calculated as weight in kilograms divided by height in meter squared); FFM = fat free mass.

Values are represent in means (SD). Means in the same row that do not share symbol (*, †, ‡ or §) differ in Fisher's post hoc tests at $P < .05$

[§]One standard drink contains about 14 g of pure alcohol (~17.7 mL of alcohol)

during the entire testing procedure. After a urine pregnancy test was performed to recheck pregnancy status, an intravenous catheter was inserted into a hand vein, which was heated to 50°C by using a thermostatically-controlled box, to obtain arterialized venous blood [21]. Blood samples were obtained before and at 5, 15, 25, 35, 50, 65, 80, 95, 110, 125, 140, 170, and 200 minutes after the women had consumed an alcoholic beverage, [20% vol/vol solution of 190-proof ethanol mixed with an unsweetened fruity flavored juice (Kool-Aid; Kraft Heinz Company, Chicago, IL, USA) sweetened with Splenda (Heartland Consumer Products, Carmel, IN, USA)] or an equal volume of the fruity juice. The beverage was aliquoted into 2 equal volumes, and patients consumed each aliquot within consecutive 5-minute periods. During both conditions, 2 mL of alcohol were sprayed onto the surface of the cup to serve as a flavor mask [22]. An assessment of BAC estimated from breath samples (BrAC) was performed by using an Alco-Sensor IV (Intoximeters, Inc., St. Louis, MO, USA). BrAC were obtained at the same time points as the blood samples with the exception that BrAC were not obtained until 15 minutes after the patients finished the consumption of the beverage, as recommended by the manufacturer.

*Subjective effects of alcohol*

Before and at 15, 45, 90, and 180 minutes after ingesting each beverage, patients completed the Addiction Research Center Inventory. The Addiction Research Center Inventory, a true–false questionnaire designed to differentiate among different classes of psychoactive drugs, consists of several scales, including the Drunk Scale that measures drunkenness [23].

*Analysis of BAC*

BAC was determined by using gas chromatography after a procedure previously described [24].

*Classical pharmacokinetic measures*

For the pharmacokinetic calculations, we used a first-order absorption and Michaelis-Menten or zero order elimination, after the methods of Mumenthaler et al. [25]. From the raw BAC data, we determined time-to-peak BAC, peak BAC, alcohol disappearance rate ($\beta_{60}$), and area under the BAC time curve (AUC; g/L/hr). We estimated $\beta_{60}$ for each subject from the slope of the linear least-squares regression lines within the apparent linear portion of the descending limb of the BAC versus time curve. As customary for $\beta_{60}$ estimation, to exclude the upper distribution phase and lower first-order elimination phase of the apparent lineal portion of the curve, we used the first value taken .5 hours after the peak BAC and all subsequent readings ≥.20 g/L. The total amount of alcohol eliminated from the body per hour, $b_{60}$, was calculated as $b_{60} = (\beta_{60} \times$ total body water [TBW])/$B_w$, taking TBW into account with TBW = (.1069 × height [cm]) + (.2466 × weight [kg]) − 2.097 and $B_w$ = .80. This standardized anthropometric equation estimates TBW for women with a precision of ±9 to 11% [26]. The alcohol elimination rate (R), expressed as the amount of alcohol eliminated per kilogram of the body per hour, was calculated as R = $b_{60}$/weight. AUCs were calculated by using the trapezoid method.

*Statistical analysis*

To analyze effects of type of surgery on alcohol pharmacokinetics and drunkenness feelings, separate

analysis of the variances with group (SG, RYGB, and presurgery) as the between-subject factor and time since beverage consumption (when applicable) as the within-subject factors were conducted. To analyze effects of groups on drunkenness, we first calculated the differences between responses on the alcohol and placebo conditions at each time point and then analyzed these differences using a mixed analysis of the variance design. When differences in values were statistically significant, a post hoc Fisher's Least Significant Difference analysis was conducted. One woman in the RYGB group did not complete the questionnaires during the alcohol condition because she was nauseated, and 2 women in the presurgery group did not complete the control condition visit due to technical problems with placement of the intravenous line (n = 1) and loss to follow-up (n = 1). To include data on the subjective effects of alcohol recorded in these 2 women presurgery, the mean value for the group on the placebo condition for the drunkenness scale was used. Therefore, data on alcohol subjective effects included a total of 7 women in RYGB group and 9 women in the presurgery group. The analysis of the data excluding the 2 presurgery patients showed similar results.

To analyze whether breath-analysis techniques that estimate BAC were valid in the bariatric population, linear regression analysis were conducted with BAC as the independent and BrAC as the dependent variable. In addition, the statistical method of Bland and Altman was used [27] to compare the agreement between 2 measurements techniques. This includes plotting the differences between the 2 techniques (i.e., BAC-BrAC) against the values measured by the technique considered to be the gold standard. Then, horizontal lines are drawn at the mean difference, and at the limits of agreement, which are defined as the mean difference $\pm1.96$ times the standard deviation of the differences. Data in the table and figures are presented as means $\pm$ standard deviation unless otherwise indicated. All analyses were performed with STATISTICA 13.0 (Dell Inc. Tulsa, OK, USA) and criterion for statistical significance was $P \leq .05$.

## Results

### Alcohol pharmacokinetics and subjective effects

BAC increased faster ($F_{(2,25)} = 18.21$, $P < .001$), peak BAC was approximately 2-fold higher ($F_{(2,25)} = 19.69$, $P < .001$), and total AUC was approximately 1.5 times larger ($F_{(2,25)} = 15.15$, $P < .001$) in SG and RYGB groups relative to the presurgery group (Table 2). As shown in Fig. 1A, BAC differed among groups across time ($F_{(22,275)} = 17.69$, $P < .001$). BAC for SG and RYGB groups were higher than presurgery group during the first
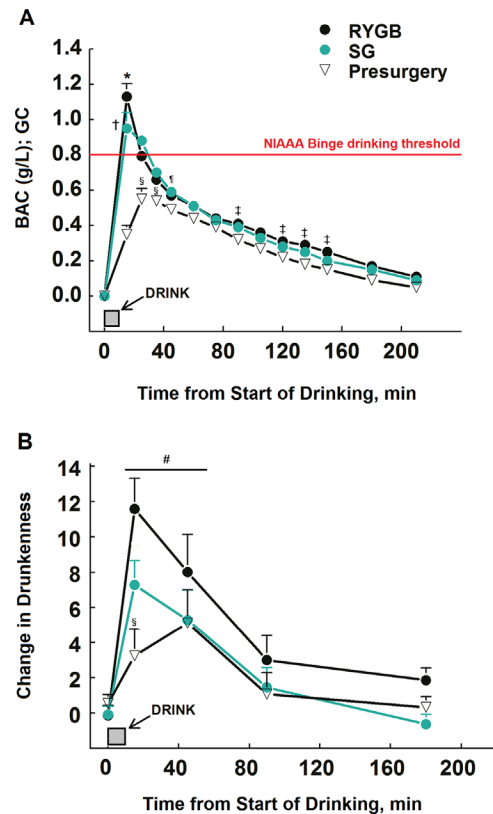


Fig. 1. Blood alcohol concentrations (BAC) (A) and subjective feelings of drunkenness (B) after alcohol ingestion (.5-g/kg fat free mass, which is equivalent to ~2 standard drinks) in women who had sleeve gastrectomy (SG) surgery (n = 11) or Roux-en-Y gastric bypass (RYGB) surgery (n = 8) 1 to 5 years ago, and in nonoperated controls (presurgery, n = 9). For each time point, scores on feelings of drunkenness on the alcohol day were subtracted from scores on the placebo day. *$P < .05$ SG group versus both RYGB and presurgery groups within a time point; †$P < .05$ RYGB group versus presurgery group within a time point; §$P < .05$ presurgery group versus both RYGB and SG within a time point; #$P < .05$ from baseline. Shown in red, the BAC threshold for binge drinking defined by the National Institute on Alcohol Abuse and Alcoholism, which is also the BAC limit for driving in the United States.

35 minutes from start of drinking. BAC for SG did not differ from the other groups thereafter, with the exception that at 45 minutes, BAC was higher than in the presurgery group. In addition, BAC for RYGB was higher than in presurgery group at 90, 120, 135, and 150 minutes. $\beta_{60}$ and R were similar among groups, but the total amount of alcohol eliminated per hour ($b_{60}$) was greater in presurgery than in the other groups ($F_{(2,25)} = 6.29$, $P < .01$; Table 2).

The changes in self-reported drunkenness paralleled the changing BAC. All groups felt drunk for 45 minutes from start of drinking ($F_{(4,96)} = 28.83$, $P < .001$). However, feelings of drunkenness were greater in both SG and RYGB groups than in the presurgery group at 5-minutes postalcohol consumption ($F_{(8,96)} = 2.61$, $P < .05$; Fig. 1B).

Table 2
Classic alcohol pharmacokinetics

| | Mean (SD) | | |
|---|---|---|---|
| | Presurgery (n = 9) | RYGB surgery (n = 8) | SG surgery (n = 11) |
| Peak BAC, g/L | .59 (.15)[*] | 1.12 (.16)[†] | 1.01 (0.23)[†] |
| Time to reach peak BAC, min[‡] | 35.6 (12.3)[*] | 15.0 (.00)[†] | 18.7 (5.2)[†] |
| Area under the BAC time curve, g/L/h | .97 (.24)[*] | 1.53 (.22)[†] | 1.42 (.22)[†] |
| Alcohol elimination measures | | | |
| Disappearance Rate, $\beta_{60}$, g/L/h | .21 (.07) | .17 (.03) | .20 (.04) |
| Total Eliminated, $b_{60}$, g/h | 12.09 (3.88)[*] | 7.43 (1.35)[†] | 9.73 (2.22)[*,†] |
| Elimination Rate, R, g/kg weight/h | .10 (.03) | .09 (.01) | .10 (.03) |

SD = standard deviation; RYGB = Roux-en-Y gastric bypass; SG = sleeve gastrectomy; BAC = blood alcohol concentration.
Values are represent in means (SD). Means in the same row that do not share symbol (* or †) differ in Fisher's post hoc tests at $P < .05$
[‡]From the time of the first sip of alcoholic beverage, consumed over 10 min.

### *Breath-analysis techniques*

BrAC was highly and linearly correlated with direct measurement of arterialized BAC ($r^2 = .93$; $P < .05$; data not shown), however the BrAC underestimated measured arterial BAC by 27 ± 13% (Figs. 2A, 2B). In addition, because of the 15-minute lag between end of alcohol ingestion and first breath sample, the breath analysis technique missed the true peak BAC in RYGB and SG groups, which occurred within a few minutes after alcohol consumption (Fig. 1A and Table 2).

### Discussion

The primary finding of this study is that SG, similar to RYGB, is associated with a more rapid delivery of ingested alcohol into systemic circulation, which results in higher and faster peak BAC and more intense feelings of drunkenness. In addition, our findings that BrAC underestimated BAC by 27% (standard deviation = 13%) and that peak BAC after SG and RYGB occur within a few minutes after alcohol consumption underscore the peak BAC levels

estimated by breathalyzer will not be accurate in this population.

Our study is not able to determine the mechanism underlying a higher and faster peak BAC after alcohol ingestion in patients who underwent SG or RYGB surgeries. However, the rapid delivery of the ingested alcohol into the systemic circulation observed in the present study for these groups is consistent with results from previous studies that show increased gastric emptying after SG [28] and RYGB [29] surgeries. An important consequence of such accelerated gastric emptying after SG and RYGB surgeries for alcohol pharmacokinetics is a decrease in the first-pass metabolism (FPM). FPM is the fraction of a given dose of a drug that is metabolized in its passage through the gut and liver before reaching the systemic circulation [30,31]. Despite controversy about the site where alcohol FPM occurs (i.e., liver and/or stomach), it is clear that FPM decreases under circumstances in which the alcohol-absorption phase is shortened [20]. Consistent with the hypothesis that SG and RYGB reduce alcohol FPM, here we found that despite negligible differences in the rates of alcohol
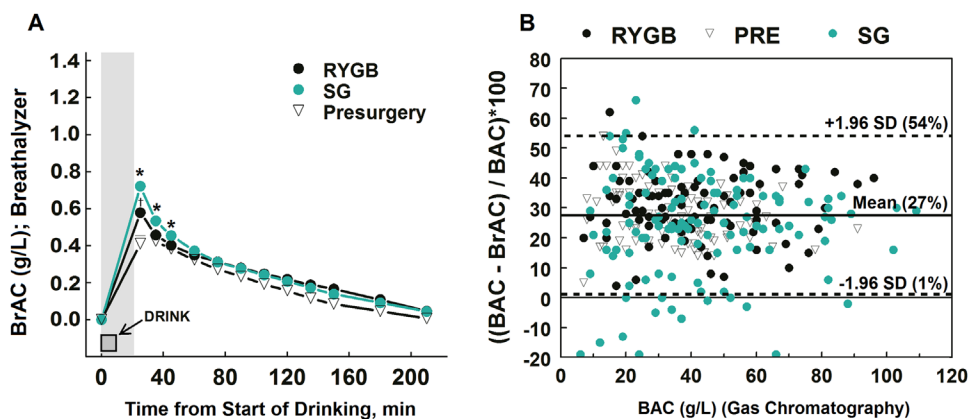


Fig. 2. Blood alcohol concentrations (BAC) estimated from breath samples (BrAC) in women who had sleeve gastrectomy (SG) surgery or Roux-en-Y gastric bypass (RYGB) surgery 1 to 5 years ago, and in nonoperated controls Presurgery (A). The area shown in gray is the lag period from beginning of drinking until approximately 15 minutes passed from the end of drinking to obtain the first BrAC. *$P < .05$ SG group versus both RYGB and presurgery groups within a time point; †$P < .05$ RYGB group versus presurgery group within a time point. Bland-Altman plot (panel B) for comparing BAC measured by gas chromatography and BrAC estimated from breath samples including the mean percent difference between the 2 methods (27%, solid line) and the 95% limits of agreement (dashed lines).

clearance among groups, total AUC was approximately 1.5 times larger in SG and RYGB groups relative to the presurgery group. The larger AUC with equal rates of alcohol clearance after RYGB (and SG) probably explains results from previous studies that after RYGB, patients had a longer time to reach zero BAC after drinking the same amount of alcohol than control patients [11].

It is important to clarify that the underestimation of BAC by breath analyzers is not unique to the bariatric population; similar differences have been reported in lean nonsurgical candidates when a BAC:BrAC ratio <2300:1 is used [32–34]. Although the BAC:BrAC ratio varies widely among people (from 1800:1 to 3200:1), and changes as a function of time after drinking alcohol, breath analyzers use a constant ratio [35]. The Alco-Sensor IV, which like most breath analyzers is used to provide evidence of whether a driver has consumed alcohol over the legal limit to drive, uses a ratio of 2100:1. A ratio of 2300:1 would be more accurate, but the 2100:1 ratio has been selected because very few individuals have a BAC:BrAC ratio <2100:1; consequently, the BrAC is almost always lower than the real BAC. Therefore, a person is not at a disadvantage by providing an evidential BrAC instead of venous blood [33]. However, there is another more important issue for the validity of this technique in investigation of the effect of gastric surgeries on alcohol pharmacokinetics – the recommended lag period of approximately 15 minutes from the end of drinking to obtaining the first BrAC. This recommendation is to avoid contamination of the sample with alcohol in oral tissue. However, because peak BAC after RYGB and SG occurs within minutes of drinking, waiting 15 minutes for the first sample means the peak BAC levels will be missed using breathalyzers.

The results of this study should be considered alongside some limitations. First, our study used a cross-sectional design and, considering the large variability in individual differences in sensitivity to the subjective effects of alcohol, a longitudinal study is the most robust design to evaluate changes in these responses after bariatric surgery. Second, we included only women to assure a more homogeneous sample and because 81% of the patients undergoing bariatric surgery are women [17]. However, given the well-known sex differences on alcohol's pharmacokinetics [18], future studies including men are warranted.

## Conclusion

SG, similar to RYGB, causes marked alterations in the response to alcohol ingestion manifested by a faster and higher peak BAC when BAC is measured with the gold standard technique of gas chromatography. Remarkably, although all groups consumed approximately 2 standard drinks, only women who underwent SG or RYGB met the National Institute on Alcohol Abuse and Alcoholism definition of binge drinking by virtue of consuming an amount of alcohol that raises BAC to $\geq.8$ g/L and is associated with alcohol problems [36]. Therefore, clinicians should recognize the altered alcohol pharmacokinetics after these bariatric surgeries so that potential serious consequences of moderate alcohol consumption are discussed not only with RYGB patients but also with SG patients.

## Disclosures

## Acknowledgments

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