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Alcohol sensitivity in women after undergoing bariatric surgery: a cross-sectional study

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Abstract

Background: Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG), the most common bariatric surgeries performed worldwide, increase the risk to develop an alcohol use disorder. This might be due, in part, to surgery-related changes in alcohol pharmacokinetics. Another risk factor, unexplored within this population, is having a reduced subjective response to alcohol's sedative effects.

Objectives: To assess whether the alcohol sensitivity questionnaire (ASQ), a simple self-report measure, could pinpoint reduced alcohol sensitivity in the bariatric population.

Setting: University medical centers in Missouri and Illinois.

Methods: Women who had RYGB (n = 16), SG (n = 28), or laparoscopic adjustable gastric banding surgery (n = 11) within the last 5 years completed the ASQ for both pre- and postsurgical timeframes, and 45 of them participated in oral alcohol challenge testing postsurgery. Blood alcohol concentration (BAC) and subjective stimulation and sedation were measured before and for 3.5 hours after drinking.

Results: In line with faster and higher peak BACs after RYGB and SG than laparoscopic adjustable gastric banding surgery ($P < .001$), postsurgery ASQ scores were more reduced from presurgery scores after RYGB/SG than after laparoscopic adjustable gastric banding surgery ($-2.3 \pm .3$ versus $-1.2 \pm .2$; $P < .05$). However, despite the dramatic changes in BAC observed when ingesting alcohol after RYGB/SG surgeries, which resulted in peak BAC that were approximately 50% above the legal driving limit, a third of these women felt almost no alcohol-related sedative effects.

Conclusions: Although RYGB/SG dramatically increased sensitivity to alcohol in all participants, meaningful interindividual differences remained. The ASQ might help identify patients at increased

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Key words:

Bariatric surgery; Metabolic surgery; Alcohol; Subjective response; Pharmacokinetics; Sleeve gastrectomy; Roux-en-Y gastric bypass; Laparoscopic adjustable gastric banding surgery; Ethanol

Bariatric surgical procedures provide the most successful long-term treatment for severe obesity [1]. Currently, the most frequently performed procedures worldwide are Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), and laparoscopic adjustable gastric banding (LAGB) [1]. Despite the numerous health benefits of these surgeries, mounting evidence shows an increased risk of alcohol use disorders (AUD) after RYGB [2–6] and SG [7]. One potential mechanism underlying the increase AUD risk is related to surgical changes in the gastrointestinal anatomy that dramatically affect alcohol's pharmacokinetics [8–11].

Nevertheless, while most patients reach significantly higher and faster peak blood alcohol concentration (BAC) when drinking alcohol after undergoing RYGB and SG than presurgery, only a fraction develops symptoms of AUD postoperatively [3,4,7]. Therefore, changes in alcohol pharmacokinetics cannot exclusively explain the increased AUD risk postsurgery. Another factor increasing the risk of AUD in the general population, which could be affected after RYGB and SG, is individual differences in the acute response to alcohol [12–17]. Individuals with attenuated response to sedative or impairing effects of alcohol [16] and those who are more sensitive to the stimulant-like effects of alcohol [12–14] are generally at higher risk for AUD. For example, several studies found that low sensitivity to the effects of alcohol predicts heavy drinking up to 35 years later in both men and women [17] and high sensitivity to the stimulants effects of alcohol in binge drinkers predicts alcohol problems at 2- and 6-year follow-ups [12,14]. However, subjective responses to alcohol in RYGB and SG patients have been relatively unexplored.

The major aims of the present study were 2-fold. First, to evaluate pre-to-postsurgery changes in alcohol sensitivity, as assessed through the alcohol sensitivity questionnaire (ASQ) [18,19], across surgery types and to further explore whether those changes are related to pharmacokinetic observations in subsequently performed alcohol challenge tests, and second, to compare the subjective experiences (i.e., sedation, stimulation) reported during an alcohol challenge test before and after surgery. To this aim, patients completed the ASQ postsurgery and a subsample also completed oral alcohol (and placebo) challenge testing in the laboratory to measure subjective responses to alcohol ingestion.

Methods*Study design and experimental procedures*

This research is part of an ongoing study evaluating the effects of different bariatric surgical procedures on alcohol pharmacokinetics and pharmacodynamics effects. All participants completed a screening visit consisting of a review of their medical history, standard blood tests, urine pregnancy test, and filling out several validated questionnaires widely used in the field of alcohol research, including the ASQ (see details below and on eAppendix 1). We also assessed patterns of alcohol use and the presence of a family history of alcoholism up to first-degree relatives, by interviewing participants with the alcohol and family history assessment modules of the semistructured assessment of the genetics of alcoholism [20], and participants' fat free mass, by using a dual-energy X-ray absorptiometry scan. Participants were then evaluated in 2 sessions, approximately 1 week apart, in which their response to an alcoholic (.5 g/kg of fat free mass) or nonalcoholic beverage was evaluated using a randomized crossover design. This study was approved by the institutional review board at Washington University School of Medicine in St. Louis, at Carle Foundation Hospital in Urbana and at the University of Illinois at Urbana-Champaign in Illinois. All screened patients gave informed written consent before participation.

Participants

The study population consisted of 55 women, 28 of whom had SG, 16 who had RYGB, and 11 who had LAGB within the last 5 years at Barnes-Jewish Hospital in St. Louis, Carle Foundation Hospital, or Illinois Bariatric Center. We included participants who were regular light drinkers (drink at least 1 standard drink per month but ≤ 7 standard drinks per week and < 4 standard drinks per drinking occasion) and had no evidence of binge drinking 1 month before enrolling in the study [21,22]. Individuals who smoked cigarettes in the last 6 months, were pregnant or breastfeeding, had anemia, liver disease or lifetime alcohol dependence, or were regularly using illicit drugs or medications that could affect alcohol pharmacokinetics were excluded. Of 55 participants who completed the ASQ at screening, 45 completed oral alcohol challenge testing (study flow chart in Supplementary eFig. 1). Data on alcohol

pharmacokinetics from a subsample of these patients have been reported previously [8,10]. The study is registered with the [Clinical Trials.gov](https://clinicaltrials.gov) identifier, NCT02766322 and NCT01843257.

Alcohol sensitivity questionnaire

The ASQ is a validated 15-item, self-report questionnaire to assess sensitivity to a wide range of effects experienced when drinking alcohol ([Supplementary eAppendix 1](#)) [18]. Although to the best of our knowledge the ASQ has not been previously used in bariatric population, the construct validity of the ASQ has been demonstrated in research showing scores on this measure reliably differentiate reports of subjective stimulation, sedation, and intoxication when alcohol is consumed in the laboratory [18]. In addition, the ASQ has consistently showed excellent internal consistency, with Cronbach's alpha generally $>.90$ for both the light- and heavy-drinking effect subscales [18]. To address any change since their surgery, participants were asked to complete the ASQ twice, once recalling their experiences before surgery (hereafter, presurgery ASQ), and a second time with reference to their experiences since surgery (hereafter, postsurgery ASQ). Higher ASQ scores are indicative of lower alcohol sensitivity.

Alcohol and placebo oral challenge tests

Participants were admitted the morning of the study visit after fasting overnight, and remained fasted during the entire procedure. Before each challenge test began, we rechecked nonpregnancy status with a urine pregnancy test. Arterialized heated-hand venous blood samples were obtained before and at various times after drinking either the alcoholic beverage prepared in a noncaloric juice (20% vol/vol) or an equal volume of the noncaloric juice (nonalcoholic, placebo beverage) [8]. Both beverages were sprayed onto the surface of the cup with 2 mL of alcohol to serve as a smell and flavor masks. The beverage was aliquoted into 2 equal volumes, and patients consumed each aliquot within consecutive 5-minute periods ([Supplementary eAppendix 1](#)) [8]. We determined BACs using headspace gas chromatography after a procedure previously described [23]. Participants completed the modified Biphase Alcohol Effects Scale [24,25] and the Addiction Research Center Inventory [26] before (-10 min) and at 10, 45, 90, 180 minutes after drinking each beverage to determine level of "drunkenness," sedation, and stimulation ([Supplementary eAppendix 1](#)).

Classical pharmacokinetic measures

From the raw BAC data, we determined peak BAC, time-to-peak BAC, and area under the BAC time curve. We estimated disappearance rate of alcohol (β_{60}), total amount of alcohol eliminated from the body per hour

(β_{60}), and the alcohol elimination rate (R), for each participant, after procedures previously described ([Supplementary eAppendix 1](#)) [27].

Statistical analysis

To determine significant differences among surgery groups on postsurgery ASQ scores, we conducted a 1-way analysis of covariance using presurgery ASQ scores as a covariate. To evaluate differences in alcohol effects that were independent of surgery-related changes in alcohol pharmacokinetics, we used a tertile split of postsurgery ASQ scores of those women who underwent RYGB and SG. Subject characteristics among surgery groups and between extreme ASQ groups (high sensitive [HS] ASQ range scores: 1–1.4 and low sensitive [LS] ASQ range scores: 2.1–4.1) were compared using separate 1-way analyses of variance or Kruskal-Wallis test by rank and Mann-Whitney U test (for data not normally distributed). To analyze effects of type of surgery and postsurgery ASQ groups on alcohol pharmacokinetics and subjective responses separate mixed analyses of variance were conducted. When differences in values were statistically significant ($P \leq .05$), a post hoc Fisher's least significant difference analysis was conducted. All analyses were performed with STATISTICA 13.3 (TIBCO Software Inc., Palo Alto, CA, USA).

Results

Participant characteristics

There were no significant differences in age, body composition, or reported alcohol use between surgery groups ([Table 1](#)). However, compared with women in the LAGB group, women in RYGB/SG groups were evaluated more proximal to their surgeries (ranges for RYGB: .3–4.9 yr; SG: .3–4.3 yr; and LAGB: 1.6–4.5 yr; $P = .01$; [Table 1](#)). When comparing ASQ groups, the LS group was younger, taller, heavier, and reported drinking more alcohol and drinking more frequently over the last 6 months than the HS group ([Table 2](#)). There were no significant differences between ASQ groups in their pattern of alcohol consumption during the 12-month period in their lifetime when they drank the most, in the proportion of individuals with a family history of alcoholism, or in the type of bariatric surgery they underwent ([Table 2](#)).

ASQ

Presurgery ASQ scores did not differ between surgical groups ($P > .5$, [Fig. 1A](#)). However, while postsurgery ASQ scores decreased for all participants, scores of women who underwent RYGB and SG decreased more than those of women who underwent LAGB surgery ($P < .01$; [Fig. 1A](#)). These results remained the same when "time from surgery" was included as a co-variate in the analysis ($P = .05$).

Table 1
Subject characteristics and alcohol related outcomes by surgery groups

Characteristic	LAGB	RYGB	SG	P value
Participants, n	11	16	28	
Age, yr	42.2 (13.9)	41.8 (8.6)	42.1 (9.3)	.99
Weight, kg	92.9 (18.5)	80.2 (14.8)	89.3 (16.2)	.10
Height, cm	164.4 (6.7)	163.7 (8.6)	165.1 (5.5)	.82
BMI, kg/m ²	34.4 (7.0)	30.1 (5.9)	32.7 (5.6)	.16
FFM, kg	50.2 (6.2)	49.3 (5.8)	49.4 (5.5)	.91
Time from surgery, yr*	2.4 (.5)[†]	1.2 (.6)[‡]	1.8 (.3)^{†,‡}	.01
Family history of alcoholism (FHP/FHN)	2/9	2/14	12/16	.40
<i>Alcohol-related variables</i>				
Age, yr				
First drink*	17.0 (1.0)	17.0 (1.0)	17.0 (1.5)	.89
Regular drinking*	21.0 (2.0)	21.0 (1.8)	21.0 (3.6)	.13
Age first got drunk*	18.0 (2.0)	18.0 (1.0)	18.0 (1.6)	.91
Drinking over the past 6 mo				
Number of drinking days per month*	5.0 (3.8)	2.0 (2.8)	2.0 (.6)	.35
Number of drinks per drinking day*	2.0 (.8)	1.5 (.5)	2.0 (.8)	.37
Drinking over the 12-mo period when drank the most				
Number of drinking days per month*	8.3 (9.5)	14.5 (2.1)	12.4 (7.8)	.08
Number of days per month with ≥5 drinks*	1.9 (2.7)	6.8 (5.9)	3.5 (6.2)	.27
Number of days drunk per month*	.9 (.9)	2.9 (3.8)	1.9 (4.0)	.24
<i>Classical alcohol pharmacokinetics</i>				
Participants, n	8	15	19	
Peak BAC, g/L	.67 (.20)[‡]	1.15 (.20)[‡]	1.03 (.22)[†]	.00
Time to reach peak BAC, min [§]	35.0 (12.8)[‡]	15.4 (1.5)[†]	18.9 (4.8)[†]	.00
Area under the BAC time curve, g/L/hr	1.16 (.19)[‡]	1.56 (.29)[†]	1.36 (.24)[‡]	.00
<i>Alcohol elimination measures</i>				
Disappearance rate, β ₆₀ , g/L/hr	.16 (.05)	.17 (.04)	.18 (.04)	.39
Total eliminated, b ₆₀ , g/hr	7.65 (2.60)	7.49 (1.57)	8.89 (2.23)	.13
Elimination rate, R, g/kg weight/hr	.09 (.02)	.09 (.02)	.10 (.02)	.57
Number of standard drinks given on alcohol challenge test	1.7 (.21)	1.8 (.2)	1.8 (.2)	.89

LAGB = laparoscopic adjustable gastric banding surgery; RYGB = Roux-en-Y gastric bypass surgery; SG = sleeve gastrectomy surgery; BMI = body mass index; FFM = fat free mass; FHP = family history of alcoholism positive; FHN = family history of alcoholism negative; BAC = blood alcohol concentration.

Significant group effects are indicated by boldface. Values are means (standard deviations).

* Show values as medians (semi-interquartile range).

[†] Values in the same row that do not share symbol († or ‡) differ in post hoc tests at P < .05.

[‡] Values in the same row that do not share symbol († or ‡) differ in post hoc tests at P < .05.

[§] From the time of the first sip of alcoholic beverage, consumed over 10 minutes.

^{||} One standard drink contains ~14 g of pure alcohol (~17.7 mL of alcohol).

Presurgery ASQ scores were higher in the LS group than in the HS group (Table 2) and the change on postsurgery ASQ scores relative to presurgery ASQ scores was smaller in the LS group than in the HS group (−35.6 ± 6.1% [95% confidence interval −48.8 to −22.4] versus −61.6 ± 3.4% [95% confidence interval −69.0 to −54.1]; P = .001; Supplementary eFig. 2).

Alcohol pharmacokinetics

Compared with the LAGB group, RYGB and SG groups reached peak BAC sooner and their peak BACs were approximately 2-fold higher (Fig. 1B; Table 1). Alcohol area under the BAC time curve was greater in the RYGB group than in the SG and LAGB groups, but β₆₀, b₆₀, and R were similar among surgery groups (Table 1).

Peak BAC, time-to-peak BAC, and alcohol area under the BAC time curve did not differ significantly between HS and LS groups (Table 2 and Fig. 2). However, while HS and LS groups eliminated a similar total amount of alcohol per hour (b₆₀), due to anthropometric differences between the ASQ groups the alcohol disappearance rate (β₆₀), and the alcohol elimination rate (g/kg weight/hr, R) were lower in LS group than in HS group (Table 2).

Subjective responses to alcohol

For all surgery groups, alcohol consumption increased scores on the stimulant- and sedative-like subscale of the Biphasic Alcohol Effects Scale, and on the Pentobarbital-Chlorpromazine-Alcohol Group (a measure of sedation) and Drunkenness scales of the Addiction Research Center

Table 2
Subject characteristics and alcohol related outcomes by postsurgery ASQ groups

Characteristic	High sensitive	Low sensitive	P value
Participants, n	15	15	
Age, yr	45.5 (7.4)	38.3 (9.6)	.03
Weight, kg	82.0 (13.2)	94.7 (16.8)	.03
Height, cm	162.2 (6.1)	168.6 (5.1)	.00
BMI, kg/m ²	31.3 (5.1)	33.3 (5.9)	.31
FFM, kg	48.0 (5.8)	51.2 (5.4)	.13
Time from surgery, yr*	1.4 (.4)	1.6 (.4)	.51
Family history of alcoholism (FHP/FHN)	4/11	4/11	.99
Type of surgery (RYGB/SG)	6/9	4/11	.91
<i>Alcohol-related variables</i>			
Age, yr			
First drink	17.4 (1.8)	16.6 (1.7)	.25
Regular drinking*	21.0 (2.0)	21.0 (4.0)	.62
Age first got drunk*	18.0 (1.0)	17.0 (2.0)	.47
Drinking over the past 6 mo			
Number of drinking days per month*	1.0 (.8)	2.5 (5.7)	.00
Number of drinks per drinking day*	1.0 (.5)	2.3 (2.0)	.05
Drinking over the 12-mo period when drank the most			
Number of drinking days per month	10.6 (6.5)	13.8 (7.3)	.21
Number of days per month with ≥ 5 drinks*	2.9 (6.2)	4.1 (5.8)	.55
Number of days drunk per month*	.9 (4.1)	1.9 (1.9)	.54
ASQ scores presurgery [†]	3.3 (1.1)	4.9 (2.1)	.01
<i>Classical alcohol pharmacokinetics</i>			
Participants, n	12	11	
Peak BAC, g/L	1.09 (.26)	1.02 (.22)	.51
Time to reach peak BAC, min [‡]	18.1 (4.6)	17.8 (4.8)	.89
Area under the BAC time curve, g/L/hr	1.44 (.34)	1.41 (.28)	.83
<i>Alcohol elimination measures</i>			
Disappearance rate, β_{60} , g/L/hr	.20 (.05)	.16 (.03)	.05
Total eliminated, b_{60} , g/hr	8.71 (2.39)	8.18 (2.12)	.58
Elimination rate, R, g/kg weight/hr	.11 (.03)	.08 (.01)	.01
Number of standard drinks given on alcohol challenge test [§]	1.7 (.2)	1.9 (.2)	.09

ASQ = alcohol sensitivity questionnaire; BMI = body mass index; FFM = fat free mass; FHP = family history of alcoholism positive; FHN = family history of alcoholism negative; RYGB = Roux-en-Y gastric bypass surgery; SG = sleeve gastrectomy surgery; BAC = blood alcohol concentration.

ASQ scores postRYGB/SG were divided into tertiles to compare responses during alcohol challenge testing between the extreme groups, high versus low sensitive.

Significant group effects are indicated by boldface at $P < .05$. Values are means (standard deviation).

* Show values as medians (semi-interquartile range).

[†] Two patients, 1 in each postsurgery ASQ group, did not complete the ASQ for presurgical time frame; $n = 14$ for each group.

[‡] From the time of the first sip of alcoholic beverage, consumed over 10 minutes.

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

Inventory (Supplementary eFig. 3). In line with BAC profiles, participants who underwent RYGB and SG felt more drunk than participants who underwent LAGB 10 minutes after drinking alcohol ($P = .05$; Supplementary eFig. 3). However, feelings of sedation and stimulation did not differ significantly between surgery groups (all P values $> .2$).

Compared with the HS group, the LS group felt less sedated after drinking alcohol ($P < .001$; Fig. 2), but the groups did not differ on feelings of drunkenness ($P = .10$) or stimulation ($P > .29$; Fig. 2).

Discussion

The primary finding of this study is that although RYGB and SG were associated with a dramatic increased sensitivity to alcohol in all participants, meaningful interindividual differences remained, which could be observed with ASQ scores. In agreement with previous findings [8,10], but with a larger sample, we found both RYGB and SG, but not LAGB [28], profoundly affect the pharmacokinetics of ingested alcohol. In line with the measured changes in BAC, the number of drinks participants

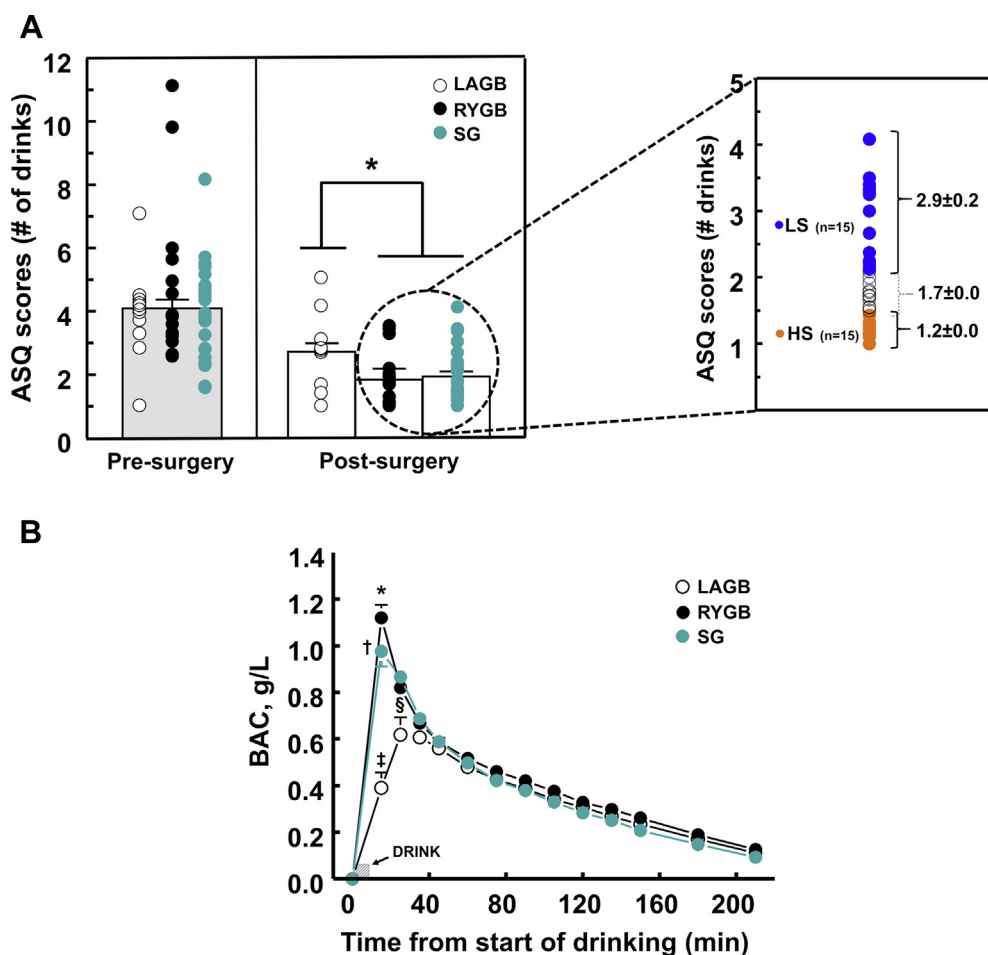


Fig. 1. (A) Scores in the alcohol sensitive questionnaire (ASQ) for both pre- and postsurgical periods and (B) blood alcohol concentrations (BAC) after alcohol ingestion (.5-g/kg fat free mass; ~2 standard drinks) in women who had undergone sleeve gastrectomy surgery (SG; turquoise symbols), Roux-en-Y gastric bypass surgery (RYGB; black symbols), or laparoscopic adjustable gastric banding surgery (LAGB; white symbols). The right inlet on (A) shows individual differences in postsurgery ASQ scores for RYGB and SG groups. From the postsurgical ASQ scores tertile approach, blue dots show scores of participants in the low-sensitive group (LS) and orange dots those in the high-sensitive group (HS) with their respective means \pm standard error of the mean. Empty dots on the inlet show participants whose postsurgery ASQ scores fell in between HS and LS groups. *, †, ‡ $P < .05$ surgery groups significantly different within a timepoint; § $P < .05$ LAGB group is different from both RYGB and SG groups within a timepoint.

reported needing to experience alcohol effects postsurgery was roughly half as many as they reported needing presurgery. Remarkably, despite the dramatic changes in BAC observed when ingesting alcohol after RYGB/SG surgeries, some women felt almost no alcohol-related sedative effects. This finding is clinically relevant, as relative insensitivity to the sedative effects of alcohol, which can signal when to stop drinking, increases the chance of consuming greater amounts of alcohol and, therefore, the risk for AUD [14,16].

Another phenotype that predicts alcohol problems is increased sensitivity to alcohol’s stimulant effects [12,14]. Although, on average, alcohol consumption increased feelings of stimulation, there were no significant differences between surgery groups or ASQ groups on the stimulant-like effects of alcohol. This lack of differences between groups on the stimulant-like effects of alcohol (which generally

are perceived during the early, rising limb of the BAC curve) may be due to the rapidity of rise of BAC after RYGB/SG, which might prevent detection of stimulant-like effects using the Biphasic Alcohol Effects Scale. Future studies could use shorter questionnaires and assess the stimulant-like effects of alcohol even sooner post drinking. Additionally, data from both human and rodent studies suggest calorie restriction enhances the rewarding/stimulant effects of drugs [29,30]; therefore, although LAGB did not change alcohol pharmacokinetics, women in this group might be as sensitive to the stimulant effects of alcohol as their SG and RYGB counterparts because they were also calorie restricted.

An important limitation of the study is that, due to its cross-sectional design, it is unknown whether the dampened sedation in the LS group was due to an acquired response to alcohol ingestion after undergoing RYGB/SG

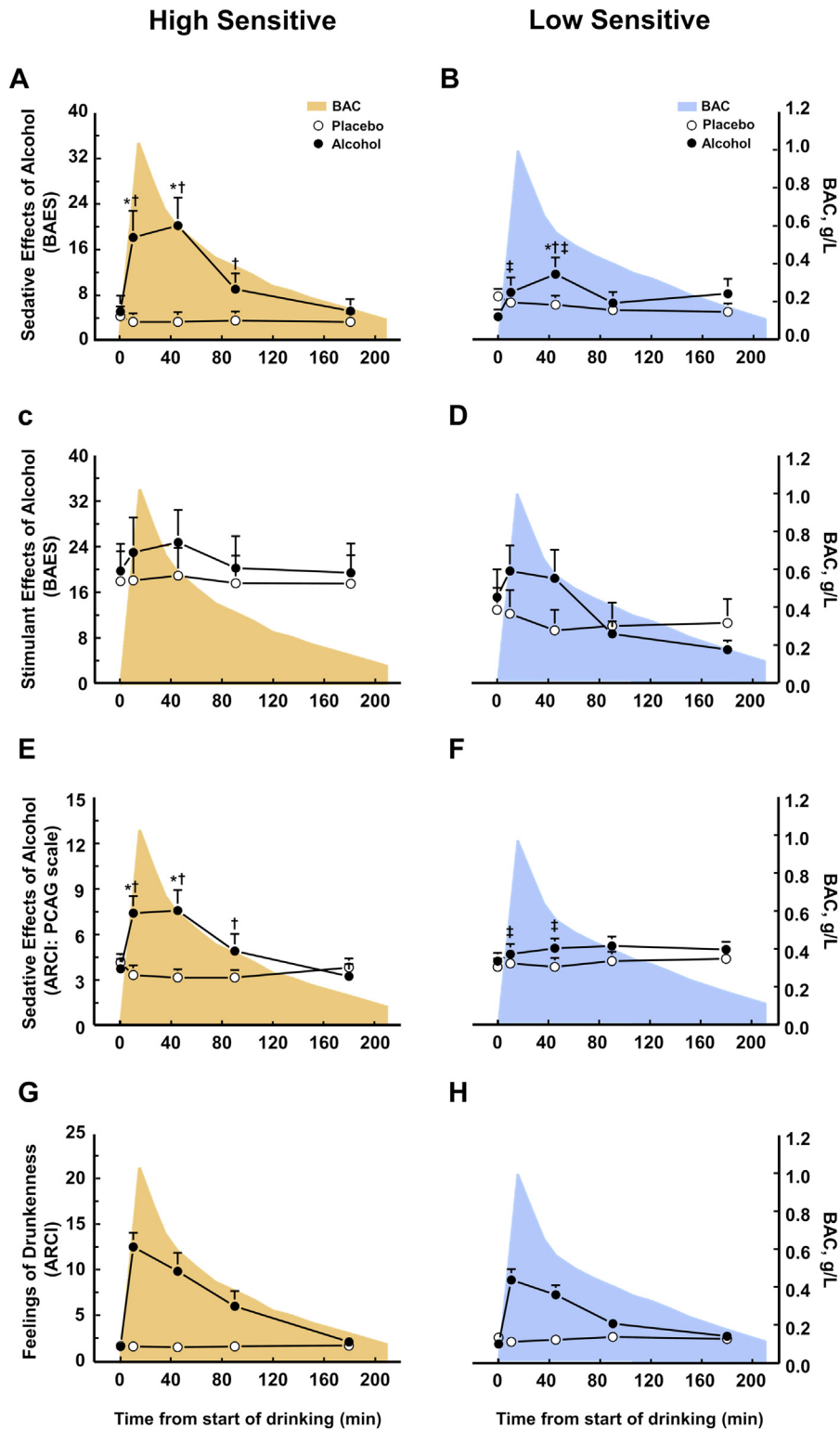


Fig. 2. Self-reported effects of drinking alcohol (black symbols) and placebo (white symbols; left y-axis) in women in the high-sensitive (left panels) and in the low-sensitive (right panels) group based on their scores on the postsurgical alcohol sensitive questionnaire. (A–D) Subjective effects obtained with the Biphasic Alcohol Effects Scale (BAES) and (E–H) subjective effects obtained with the Addiction Research Center Inventory (ARCI) scales (Pentobarbital-Chlorpromazine-Alcohol Group scale, a measure of sedation, and the Drunkenness scale). The shaded area illustrates blood alcohol concentrations (BAC; right y-axis). At time zero, women ingested alcohol (.5-g/kg fat free mass; ~2 standard drinks) within 10 minutes. Values are mean \pm standard error of the mean. * $P < .05$ from own baseline (0 min), † $P < .05$ from placebo at a given time. ‡Low-sensitive group is significantly different from high-sensitive group at a given time.

surgery or an inherent predisposition present in these individuals presurgery. Also unknown is whether differences between HS and LS groups were explained by different drinking patterns presurgery. Nonetheless, although subject to recall bias, groups did not differ in characteristics that have been associated with increased risk for AUD, such as age of drinking initiation or drinking patterns over the 12-month period when they drank the most in their lifetime. Other important limitations of our study are the exclusion of men, the range period at which we evaluated participants postsurgery, which sometimes was too proximal to surgery (~3 mo postRYGB/SG), and the fact that participants were asked to recall their experience before surgery on the ASQ. Future longitudinal studies, including both sexes and longer periods from surgery, are needed.

Conclusions

In summary, the ASQ might be a helpful tool to identify postbariatric patients with low sensitivity to alcohol. The identification of low sensitivity to the sedative effects of alcohol early postsurgery could help deliver more effective strategies to avoid alcohol misuse in patients with increased vulnerability for AUD; as successfully used for college students with low levels of response for alcohol [31,32].

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Disclosures

The authors have no commercial associations that might be a conflict of interest in relation to this article.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.1016/j.soard.2020.01.014>.

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