Weight Loss Medications in Older Adults After Bariatric Surgery for Weight Regain or Inadequate Weight Loss: A Multicenter Study

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Weight loss medications are effective to confer additional weight loss after bariatric surgery in the general population, but they have not been evaluated in adults 60 years of age and older. We performed a retrospective study identifying 35 patients who were ≥ 60 years old and had undergone Roux-en-Y gastric bypass (RYGB) or sleeve gastrectomy (SG) from 2000 to 2014, and were subsequently prescribed weight loss medications. Linear regression analyses were performed to determine beta coefficients of certain predictor variables being associated with weight loss. Patients lost weight on medications with an average body mass index (BMI) change of -2.74 kg/m^2 , standard deviation = 2.6 kg/m^2 . RYGB patients lost a greater percentage of BMI on medication than SG (SG; $-1.38 \pm 1.49 \text{ kg/m}^2$ and RYGB; $-3.37 \pm 2.83 \text{ kg/m}^2$, $p = 0.0372$). Patients with hypertension were less likely to lose weight on medications ($\beta = 16.76$, $p = 0.004$, and 95% confidence interval = $5.85-27.67$). Weight loss medications are a useful treatment to confer additional weight loss in adults 60 years of age and older after RYGB and SG.

Keywords: bariatric surgery, weight loss medication, geriatric, older adults

Introduction

OBESITY IS THE MOST COMMON CHRONIC DISEASE in the United States and is linked to comorbidities, including type 2 diabetes, hypertension, obstructive sleep apnea (OSA), non-alcoholic fatty liver disease (NAFLD), and cancer.^{1,2} Over one third of men and women older than 60 years of age, have obesity in the United States³ and as the population ages, the number of people older than 60 years of age with obesity continues to rise. In addition to comorbidities, obesity in older persons is associated with increased dependency on others to carry out activities of daily living.⁴ Older adults with obesity are twice as likely to be admitted to nursing homes, enter nursing homes earlier, and require additional equipment, supplies, and staff.⁵ Bariatric surgery is the most effective treatment for moderate and severe obesity in older patients.⁶⁻⁹ Weight loss surgery in adults older than 60 years of age is effective, safe, and in addition to weight loss, leads

to the resolution or improvement of comorbidities, particularly hypertension and diabetes.¹⁰⁻¹⁴ While there are distinctive hormonal and metabolic changes that occur with surgery, much of the comorbidity improvement seems to be conferred by dramatic weight loss that occurs with surgical treatment compared to other weight loss therapies.^{15,16} Unfortunately, there is a variable response to bariatric surgery and some patients have suboptimal weight loss or experience weight regain after bariatric surgery.^{17,18} These patients are in need of further treatment options to confer additional weight loss or to reach weight loss following bariatric surgery. Pharmacotherapy is a promising treatment method that has been shown to be effective in helping achieve additional weight loss in patients from a wide range of ages following bariatric surgery.¹⁹ In this study, we sought to evaluate the effectiveness of weight loss medications in patients older than 60 years of age, who had Roux-en-Y gastric bypass (RYGB) surgery or sleeve gastrectomy (SG), and

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were subsequently prescribed weight loss medications. We hypothesized that the use of weight loss medications would yield further weight loss following RYGB and SG. The primary consideration in this article is whether medications are beneficial in older patients (≥ 60 years of age) as an adjunct to weight loss surgery for inadequate weight loss or weight regain, as this population tends to have more contraindications to the chronic use of weight loss medications and there is a concern with polypharmacy in this population.

Methods

Sample and data collection

The patients in our study sample came from two major academic medical centers where they underwent RYGB or SG procedures between November 2000 and June 2014. From our sample, all patients who were 60 years of age or older and were subsequently placed on weight loss medications after surgery were considered for inclusion. All patients had at least 12 months of documented postoperative follow-up. Patients were excluded if they did not have sufficient follow-up considered to be at least one annual visit, had additional surgery for complications within 6 months of their initial surgery, or if they required a revision surgery. Two research groups obtained the clinical data from the medical record and the study was approved by the Institutional Review Boards at both academic centers.

Demographic and clinical factors

We obtained the following data from the medical records of eligible patients: (1) type of surgery (RYGB or SG); (2) date of operation; (3) date of birth; (4) gender; (5) race/ethnicity (Caucasian, Hispanic, Black, Asian, or other); (6) preoperative obesity-related comorbidities (hypertension, type 2 diabetes, OSA, dyslipidemia, and NAFLD); (7) preoperative use of weight loss medications; (8) body mass index (BMI; based on initial height and weight at the following time points: presurgery, at plateau postsurgery, at the start of weight loss medication, at plateau after weight loss medication, and current); (9) time to achieve plateau weight postsurgery; (10) postoperative resolution of obesity comorbidities; (11) continued use of weight loss medication(s); (12) psychiatric comorbidity (anxiety, depression, and bipolar disorder); (13) use of psychotropic medications presurgery; and (14) use of psychotropic medications postsurgery.

Weight loss medications

We collected information on 15 medications that are prescribed by obesity medicine physicians at the two academic centers. We reviewed the entire electronic medical record to determine if there was history of the medication being prescribed and filled at the pharmacy by the patient. The medications included were as follows: (1) phentermine, (2) topiramate, (3) zonisamide, (4) metformin, (5) bupropion, (6) orlistat, (7) sibutramine, (8) liraglutide, (9) exenatide, (10) pramlintide, (11) naltrexone, (12) lorcaserin, (13) phentermine/topiramate, (14) canagliflozin, and (15) bupropion/naltrexone.

Primary endpoints

The primary endpoint was relative change in weight. Additional secondary efficacy endpoints were changes in BMI and the resolution of obesity related comorbidities, which, listed with the criteria that we used to determine resolution, were as follows: (1) hypertension—no longer requiring medication to maintain a normal blood pressure of $<120/80$; (2) type 2 diabetes—no longer requiring medications to maintain a hemoglobin A1c of <6.5 ; (3) OSA—no longer requiring continuous positive airway pressure as assessed by overnight polysomnography; (4) dyslipidemia—normalization of lipid values without lipid-lowering therapy; and (5) NAFLD—normalization of liver function tests. (6) Mental illness—no longer requiring medication or undergoing therapy to treat the condition.

Statistical analysis

The data we collected were used to create variables for analysis. Patient weight histories, including nadir weight after surgery before medical treatment denoted as “nadir-pre,” weight at initiation of weight loss medication treatment, and weight at nadir after weight loss medication treatment denoted as “nadir-post,” were summarized with descriptive statistics overall and broken out by surgery type (RYGB or SG). Baseline demographic characteristics and preoperative baseline characteristics were also included. The treatment period of medications was determined by the time between the date weight loss medications were initiated to the date when nadir-post weight was achieved. Patients were split into two groups based on when weight loss medication treatment was started postsurgery. The distinction between the two groups was whether medication was started at plateau weight or after weight regain had already occurred. Patients were at plateau weight if their weight was no more than 3% greater than their postsurgery nadir-pre weight. Patients who were not within 3% of their postsurgery nadir-pre weight were considered to have started medication after weight regain. The patients in the study did not have to be within 3% of their nadir-pre weight for a certain period of time postoperative because the time to achieve nadir-pre varies among patients as well as by type of surgery. Patients did, however, need to demonstrate at least 3 months of weight stability.

Linear regression analyses were performed to build a model with medications used over the treatment period as our candidate predictor variables for weight loss. We adjusted for the type of surgery performed and patient BMI at the start of weight loss medication treatment by including them as covariates in our model. These variables were controlled for because they have influenced weight loss using weight loss medication in other studies.¹⁹ We then performed linear regression analyses with candidate predictor variables based on our demographic and baseline characteristics. Beta coefficients (β) and corresponding p values were estimated. Negative beta coefficients were indicative of increased weight loss and positive beta coefficients were indicative of decreased weight loss. All analyses were performed in Stata Version 11.

Results

Participants

Baseline characteristics of study patients are noted in Table 1. Of the 5110 patient records that were reviewed, 35

TABLE 1. DEMOGRAPHIC DATA AND BASELINE CHARACTERISTICS FOR PATIENTS >60

Variable	All patients n=35	Surgery type	
		Sleeve gastrectomy n=11 (31.4%)	RYGB n=24 (68.6%)
Gender, n (%)			
Female	26 (74.3)	8 (72.7)	18 (75)
Male	9 (25.7)	3 (27.3)	6 (25)
Age at surgery (years), n (%)			
60–64	19 (54.3)	5 (45.5)	14 (58.3)
65–69	14 (40)	5 (45.5)	9 (37.5)
70+	2 (5.7)	1 (9.0)	17 (74)
Race/ethnicity, n (%)			
White	29 (82.8)	10 (90.9)	19 (82.8)
Hispanic	1 (2.9)	0	1 (2.9)
African American	4 (11.4)	1 (9.1)	1 (4.2)
Asian	0	0	0
Other/declined to state	1 (2.9)	0	1 (2.9)
Preoperative characteristics, mean (SD)			
Weight (lbs)	273 (43)	274 (45)	273 (43)
BMI (lbs/inches ²)	44.3 (6.2)	43.2 (4.3)	44.8 (6.9)
Obesity class, n (%)			
Class I (BMI 30–34.9)	0	0	0
Class II (BMI 35–39.9)	10 (29)	3 (27)	7 (29)
Class III (BMI ≥40)	25 (72)	8 (73)	17 (71)
Comorbid conditions (individual), n (%)			
Hypertension	27 (77)	9 (33)	18 (67)
Type II diabetes	18 (51)	4 (22)	14 (78)
OSA	12 (34)	5 (42)	7 (58)
Dyslipidemia	28 (80)	8 (29)	20 (71)
NAFLD	25 (71)	7 (28)	18 (72)
Mental illness ^a	18 (51)	6 (33)	12 (67)
No. of comorbid conditions, n (%)			
None	1 (3)	1 (100)	0 (0)
1	2 (6)	1 (50)	1 (50)
2	6 (17)	1 (17)	5 (83)
3	10 (28)	3 (30)	7 (70)
4	14 (40)	4 (29)	10 (71)
5	2 (6)	1 (50)	1 (50)

^aBased on variable Psychiatric Comorbidity—Yes/No.

BMI, body mass index; NAFLD, non-alcoholic fatty liver disease; OSA, obstructive sleep apnea; RYGB, Roux-en-Y gastric bypass; SD, standard deviation.

(0.6%) met criteria for inclusion. Almost three quarters of patients were female ($n=26$; 74.3%) and a little over one quarter of patients were male ($n=9$; 25.7%). All patients were 60 years of age or older at the start of medication therapy with 19 (54.3%) patients between 60 and 64 years of age, 14 (40%) patients between 65 and 69 years of age, and 2 (5.7%) patients being 70 years of age or older. Patients were predominantly white, 19 (82.8%) of the patients identified as Caucasian, 1 (2.9%) identified as Hispanic, 4 (11.4%) identified as African American, and 1 (2.9%) declined to answer or identified as a different race. At the time of surgery, RYGB patients had a slightly higher mean BMI (44.8 kg/m²; standard deviation [SD]=6.9) versus (43.2 kg/m²; SD=4.3). Before surgery, the RYGB group also had higher percentages of obesity-related comorbidities and took longer to reach their weight plateau after surgery. At the start of medication, as denoted in Table 2, the mean weight and BMI of RYGB (BMI=34.7 kg/m²; SD=5.8) and SG (BMI=36.6 kg/m²; SD=3.6) were similar, but RYGB patients had a longer time

elapse between surgery (38.5 months; SD=28.6) and the start of medication compared with patients who had SG (26.2 months; SD=13.2). At the nadir-post weight achieved after weight loss medication, the mean BMI for patients in the RYGB group was also similar to that of the SG group, RYGB (BMI=31.3 kg/m²; SD=5.7) and SG (BMI=35.2 kg/m²; SD=3.8).

Weight loss medications and response

Both the RYGB and SG groups were often trialed on several medications over the course of treatment. The average number of medications was 2.2 (SD=1.3) (Table 3). Patients were more likely to be prescribed medications after weight regain (71.4%; $n=25$) had occurred than at plateau (28.6%; $n=10$) (Table 4). Overall, the patients in this cohort lost weight on medication, with an average BMI change of -2.74 kg/m², SD=2.6 kg/m². Patients prescribed medications at their plateau weight saw a slightly greater (-3.53 ± 3.39 kg/m²) decrease in BMI compared to patients who were prescribed medication

TABLE 2. POSTOPERATIVE PATIENT CHARACTERISTICS AND WEIGHT HISTORY AFTER SURGERY, BEFORE MEDICATIONS, AND AFTER TREATMENT

	<i>All patients</i>	<i>Sleeve gastrectomy</i>	<i>RYGB</i>
Comorbid conditions (individual), <i>n</i> (%)	35	11 (31.4)	24 (68.6)
Hypertension, <i>n</i> (%)			
Preoperative patients (<i>n</i> =27) who achieved resolution (%)	9 (33.3)	2/9 (22.2)	7/18 (39.8)
Type II diabetes, <i>n</i> (%)			
Preoperative patients (<i>n</i> =18) who achieved resolution (%)	7 (39.8)	2/4 (50)	5/14 (35.7)
OSA, <i>n</i> (%)			
Preoperative patients (<i>n</i> =12) who achieved resolution (%)	7 (53.3)	0/5 (0)	7/7 (100)
Dyslipidemia, <i>n</i> (%)			
Preoperative patients (<i>n</i> =28) who achieved resolution (%)	15 (53.6)	2/8 (25)	13/20 (65)
NAFLD, <i>n</i> (%)			
Preoperative patients (<i>n</i> =25) who achieved resolution (%)	18 (72)	4/7 (57.1)	14/18 (77.8)
Mental illness, ^a <i>n</i> (%)			
Preoperative patients (<i>n</i> =17) who achieved resolution (%)	15 (88.2)	5/5 (100)	10/12 (83.3)
Postoperative nadir weight before medication, <i>n</i> (%)	35	11 (31.4)	24 (68.6)
BMI (lbs/inches ²), mean (SD)	33.0 (5.4)	35.1 (3.6)	32.1 (5.9)
Time to achieve nadir (months), mean (SD)	12.6 (6.8)	10.4 (7.5)	13.6 (6.3)
Average weight loss at nadir weight (lbs), mean (SD)	70.0 (28.7)	52.4 (28.2)	78.0 (25.5)
At start of medication, mean (SD)			
Weight (lbs) ^b	217.9 (35.6)	231.1 (30.1)	211.9 (36.9)
BMI (lbs/inches ²)	33.3 (5.3)	36.6 (3.6)	34.7 (5.8)
Time elapsed between surgery and start of medication (months)			
Mean (SD)	34.6 (25.3)	26.2 (13.2)	38.5 (28.6)
Minimum	12.3	12.3	13.1
Maximum	133.4	51.3	133.4
Postmedication treatment—at nadir weight, mean (SD)			
Weight (lbs)	201.3 (38.4)	222.2 (29.5)	191.8 (38.6)
BMI (lbs/inches ²)	32.6 (5.5)	35.2 (3.8)	31.3 (5.7)
Weight gain between nadir and medication initiation (BMI)	2.33 (2.86)	1.55 (3.80)	2.69 (2.33)
Weight loss with medications at new nadir (BMI)	2.80 (2.59)	1.53 (1.34)	3.37 (2.83)

^aMissing data for one patient.^b*n*=35.

after weight regain ($-2.43 \pm 2.27 \text{ kg/m}^2$) ($p=0.2730$), but this difference was not found to be significant (Table 4).

The most frequently prescribed medications were topiramate, phentermine, metformin, bupropion, zonisamide, lorcaserin, and liraglutide (Table 5). In our model, which was adjusted for type of surgery and BMI at the start of medication, beta coefficients are shown in Table 5 for each medication as a predictor of weight loss. A significant beta

coefficient was observed for liraglutide, ($\beta=-16.07$, $p=0.009$, confidence interval [CI]= -25.17 to 3.57).

Predictors of weight loss medication response

RYGB patients had greater BMI decreases on medication than SG that were statistically significant, (SG; $-1.38 \pm 1.49 \text{ kg/m}^2$, RYGB; $-3.37 \pm 2.83 \text{ kg/m}^2$, $p=0.0372$) (Table 4).

TABLE 3. WEIGHT LOSS MEDICATIONS USE

	<i>All patients</i>	<i>Surgery type</i>	
	<i>n</i> = 35	<i>Sleeve gastrectomy</i>	<i>RYGB</i>
		<i>n</i> = 11 (31.4%)	<i>n</i> = 24 (68.6%)
No. of medications trialed over treatment course, <i>n</i> (%)			
One	15 (43)	3 (20)	12 (80)
Two	8 (23)	2 (25)	6 (65)
Three	6 (17)	4 (67)	2 (33)
Four	4 (11)	2 (50)	2 (50)
Five	1 (3)	0 (0)	1 (100)
Six	1 (3)	0 (0)	1 (100)
No. of medications prescribed over treatment period, mean (SD)	2.2 (1.3)	2.4 (1.1)	2.0 (1.4)

TABLE 4. MEAN BODY MASS INDEX CHANGE AFTER TREATMENT BY SUBGROUP

Subgroup	BMI change		p	95% CI
	BMI, mean (SD)	%, Mean (SD) ^a		
All patients (n=35)	-2.74 (2.6)	-8 (7)	0.2730 ^c	-3.6 to -1.8
Patients prescribed medication at weight plateau (n=10, 28.6%) ^b	-3.53 (3.39)	-9 (8)		
Patients prescribed medication at weight regain (n=25, 71.4%) ^b	-2.43 (2.27)	-7 (7)		
Surgery type			0.0372 ^c	-2.39 to -0.38
Sleeve gastrectomy (n=11)	-1.38 (1.49) ^d	-3.7 (4)		
RYGB (n=24)	-3.37 (2.83) ^d	-9.5 (7)		

^aCalculated this number as $[(\text{BMI at nadir postmedications}) - (\text{BMI at start of medication})]/(\text{BMI at start of medication}) \times 100$.

^bPlateau defined as weight that is within 3% above or below nadir weight postoperatively before medication. If above 3% patient defined as starting medication at weight regain.

^cTwo-sample *t*-test of means conducted for posttreatment weight change (BMI).

^dCalculated by postmedication BMI at nadir—preoperative BMI.
CI, confidence interval.

We also evaluated other specific predictors of response to weight loss medications as summarized in Table 6. No statistically significant difference in beta values was found for gender, age range, weight when medications were prescribed, race, BMI at baseline preoperatively, BMI at start of medications, or time to achieve nadir-pre weight after surgery before medications were prescribed. The number of comorbidities at the time of surgery did not yield statistically significant changes to beta values; however, hypertension at the time of surgery did have a significantly large beta value ($\beta = 16.76$, $p = 0.004$, $CI = 5.85-27.67$, $R^2 = 0.3485$).

Discussion

The use of weight loss medications has been shown to help patients across a broad range of ages lose additional weight after bariatric procedures, but the use of weight loss medications in patients 60 years of age and older has not been thoroughly studied.¹⁹⁻²³ Our study demonstrates the utility of weight loss medications for additional weight loss in patients 60 years of age or older, following RYGB and SG. The mean BMI change achieved with medications was -2.74 ± 2.6 kg/m². Figure 1 depicts a representative example of a 72-year-old patient included in our study, who achieved weight loss with the use of pharmacotherapy after RYGB surgery. We did not find a statistically significant difference in BMI de-

crease when medications were prescribed at weight plateau (-3.53 ± 3.39 kg/m²) versus at weight regain (-2.43 ± 2.27 kg/m²; $p = 0.2730$), which is in line with previous findings on weight loss medication use postsurgery.¹⁹⁻²³ While further prospective studies are needed, response to pharmacotherapy after weight loss surgery may be governed by a threshold paradigm that has been observed in other weight loss therapies where higher starting BMIs result in anabolic responses due to adiposity-related signals that occur at a higher threshold.²⁴ Thus, initiating pharmacotherapy at the initial nadir-pre weight instead of following weight regain after surgery may be the ideal time to commence therapy to achieve maximal overall weight loss; however, our research did not prove this as the differences in weight loss observed were not statistically significant.

Liraglutide was the only medication to show a significant negative beta coefficient in our linear regression analysis using medication as a predictor of weight loss ($\beta = -16.07$, $p = 0.009$, and $CI = -27.76$ to -4.38). It is important to note that after Bonferroni correction, the *p*-value adopted for this analysis is 0.005 and therefore, Liraglutide seems to be approaching a significant beta coefficient, but still remains the only medication in this analysis that comes close to a *p*-value of 0.005. The negative beta coefficient may portend a higher likelihood of weight loss when using Liraglutide in this older cohort. Liraglutide is an acylated glucagon-like peptide-1

TABLE 5. LINEAR REGRESSION ANALYSIS WITH MEDICATION AS PREDICTOR

Medication	No. of patients (%)	Treatment period weight loss		
		β	p	95% CI
Topiramate	20 (57.1)	-6.56	0.230	-17.47 to 4.35
Phentermine	10 (28.6)	3.35	0.558	-8.19 to 14.9
Metformin	14 (40.0)	-6.72	0.193	-17.02 to 3.57
Bupropion	4 (11.4)	-7.54	0.343	-23.49 to 8.42
Zonisamide	8 (22.9)	0.59	0.924	-11.93 to 13.12
Lorcaserin	5 (14.3)	-10.80	0.136	-25.17 to 3.57
Liraglutide	7 (20.0)	-16.07	0.009	-27.76 to -4.38
Qsymia	1 (2.9)	-7.96	0.614	-39.84 to 23.91
Naltrexone	3 (8.6)	-7.67	0.458	-28.49 to 13.15
Bupropion/naltrexone	3 (8.6)	3.05	0.745	-15.91 to 22

TABLE 6. LINEAR REGRESSION BY PREDICTOR VARIABLE

Predictor	Treatment period weight loss			
	β	p	95% CI	R ²
Surgery type				
Gastrectomy (reference)	Ref.			
RYGB	-11.29	0.043	-22.21 to -0.37	0.0915
RYGB ^a	-12.38	0.029	-23.42 to -1.34	0.1012
RYGB ^b	-11.64	0.046	-23.03 to -0.24	0.0652
Gender				
Male (reference)	Ref.			
Female	-5.69	0.349	-17.88 to 6.5	0.0266
Female ^c	-5.41	0.351	-17.04 to 6.23	0.0886
Age (every 1 year increase)	0.34	0.661	-1.21 to 1.88	0.0059
Weight when medications prescribed				
At plateau (reference)	Ref.			
At regain	4.30	0.465	-7.55 to 16.16	0.0163
At regain ^{a,d}	2.98	0.607	-8.73 to 14.68	0.0702
Race/ethnicity				
Caucasian (reference)	Ref.			
All other	-3.27	0.644	-17.55 to 11.01	0.0065
BMI class—at baseline preoperatively				
For 1 unit increase	-0.65	0.133	-1.51 to 0.21	0.0671
Class II (reference)	Ref.			
Class III	-6.80	0.246	-18.5 to 4.91	0.0406
Comorbidities—No. present at preoperative ^d				
0 (Reference)	Ref.			
1	3.60	0.841	-32.85 to 40.05	0.3183
2	-6.16	0.707	-39.37 to 27.05	
3	-6.13	0.697	-38.08 to 25.82	
4	7.81	0.619	-24.01 to 39.63	
5	2.42	0.894	-34.55 to 39.39	
Type of comorbidity ^d				
Hypertension	16.76	0.004	5.85 to 27.67	0.3485
Diabetes	0.50	0.923	-10.08 to 11.09	0.1839
OSA	-0.03	0.996	-11.15 to 11.1	0.1422
Dyslipidemia	5.22	0.419	-7.79 to 18.23	0.1604
NAFLD	-0.76	0.897	-12.61 to 11.08	0.1427
Mental illness	1.42	0.782	-8.94 to 11.78	0.1444
Time to achieve nadir weight postoperative before medications ^{d,e}				
≤12 Months (reference)	Ref.			
13–36 Months	-1.48	0.781	-12.22 to 9.27	0.1444
>36 Months	NA			
BMI at start of medications (every 1 unit increase)	-0.37	0.466	-1.4 to 0.66	0.0162

^aAdjusted for BMI at start of medications.^bAdjusted time elapse between surgery date and start of medications.^cAdjusted for type of surgery by including as covariate.^dAdjusted for type of surgery and gender.^en=35.

NA, not applicable.

analogue that has a different mechanism of action than many of the other weight loss medications trialed.²⁵ Furthermore, in a previous study of multiple weight loss medications used in a broader age range of patients, topiramate appeared to confer the highest weight loss potential.¹⁹ Therefore, the question of whether Liraglutide is particularly efficacious in older populations of patients following bariatric surgery needs further study.

We did not find the number of comorbidities present before weight loss surgery to influence weight loss postsurgery. However, the presence of hypertension before weight loss surgery

resulted in a significant positive beta coefficient ($\beta = 16.76$, $p = 0.004$, and $CI = 5.85-27.67$), which suggests that the presence of hypertension before surgery may decrease the likelihood of weight loss with medication therapy. Patients with hypertension do present a clinical challenge as many weight loss medications that might be considered might worsen hypertension or be a relative or absolute contraindication to their use. This is particularly germane to the use of stimulant medications such as phentermine. Research is limited, but this result is paradoxical to findings in a study by Shantavasinikul where hypertension was correlated with sustained weight

FIG. 1. Graphical representation of weight loss medication after bariatric surgery in a 72-year-old RYGB patient. Note: The patient's weight loss from RYGB was from a BMI of 46–31 (class 1: mild obesity). She regained weight to a BMI of 35 (class 2: moderate obesity). She lost weight after starting on topiramate to a current BMI of 28. BMI, body mass index; EBWL, excess body weight loss; RYGB, Roux-en-Y gastric bypass; TBWL, total body weight loss.

loss after bariatric surgery.²⁶ Prospective research studies regarding comorbidities and response to weight loss medication following bariatric surgery are needed to further explore this issue.

There are many limitations to our study due to its retrospective nature. Limitations include missing patient data, no control group, an inability to account for the length of time that patients were on weight loss medications, and confounding factors, including concurrent treatment with weight promoting medications, as well as weight loss medications being evaluated for weight loss potential when they may have been prescribed for other indications. We were also unable to measure the effect of diet and exercise and some medications were prescribed more than others. Despite these limitations, our study data came from two large academic study sites performing the two most common weight loss procedures in the United States, and included a long duration of follow-up, which gave us the ability to assess the long-term efficacy of weight loss medication after bariatric surgery. In addition, patients in our study received multiple weight loss medications, which helped us explore the efficacy of weight loss medications as well as the individual variability of responses to different medications.

Conclusions

Weight loss medications are a useful tool to confer additional weight loss in adults 60 years of age and older following inadequate weight loss or weight regain after RYGB and SG. RYGB patients in this age group appear to respond better to weight loss medications, but medication is still effective for conferring additional weight loss in SG patients.

Liraglutide may be particularly useful for additional weight loss in adults 60 years of age and older following bariatric surgery, and further studies are needed to confirm this. The presence of hypertension before bariatric surgery may lower the likelihood of achieving weight loss on medications and further studies are needed to explore this finding.

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References

1. Kyrrou I, Randeva HS, Tsigos C, Kaltsas G, Weickery MO. Clinical problems caused by obesity. In: De Groot LJ, Chrousos G, Dungan K, Feingold KR, Grossman A, Hershman JM, Koch C, Korbonits M, McLachlan R, New M, Purnell J, Rebar R, Singer F, Vinik A (eds). *Endotext* [Internet]. South Dartmouth, MA: MDText.com, 2000–2018.
2. Guh DP, Zhang W, Bansback N, Amarsi Z, Birmingham CL, Anis AH. The incidence of co-morbidities related to obesity and overweight: a systematic review and meta-analysis. *BMC Public Health* 2009;9:88.
3. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity among adults: United States, 2011–2012. *NCHS Data Brief* 2013;(131):1–8.

4. Pajecski D, Santo MA, Kanagi AL, Riccioppo D, de Cleva R, Ceconello I. Functional assessment of older obese patients candidates for bariatric surgery. *Arq Gastroenterol* 2014;51:25–28.
5. Marihart CL, Brunt AR, Geraci AA. The high price of obesity in nursing homes. *Care Manag J* 2015;16:14–19.
6. Abbas M, Cumella L, Zhang Y, Choi J, Vemulapalli P, Melvin WS, *et al.* Outcomes of laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass in patients older than 60. *Obes Surg* 2015;25:2251–2256.
7. Buchwald H, Avidor Y, Braunwald E, Jensen MD, Pories W, Fahrbach K, *et al.* Bariatric surgery: a systematic review and meta-analysis. *JAMA* 2004;292:1724–1737.
8. Sjostrom L, Peltonen M, Jacobson P, Ahlin S, Andersson-Assarsson J, Anveden A, *et al.* Association of bariatric surgery with long-term remission of type 2 diabetes and with microvascular and macrovascular complications. *JAMA* 2014;311:2297–2304.
9. Chang SH, Stoll CR, Song J, Varela JE, Eagon CJ, Colditz GA. The effectiveness and risks of bariatric surgery: an updated systematic review and meta-analysis, 2003–2012. *JAMA Surg* 2014;149:275–287.
10. Pajecski D, Santo MA, Joaquim HD, Morita F, Riccioppo D, de Cleva R, *et al.* Bariatric surgery in the elderly: results of a mean follow-up of five years. *Arq Bras Cir Dig* 2015; 28(Suppl 1):15–18.
11. Musella M, Milone M, Maietta P, Bianco P, Coretti G, Pisapia A, *et al.* Bariatric surgery in elderly patients. A comparison between gastric banding and sleeve gastrectomy with five years of follow up. *Int J Surg* 2014;12(Suppl 2):S69–S72.
12. McGlone ER, Bond A, Reddy M, Khan OA, Wan AC. Super-obesity in the elderly: is bariatric surgery justified? *Obes Surg* 2015;25:1750–1755.
13. Giordano S, Victorzon M. Bariatric surgery in elderly patients: a systematic review. *Clin Interv Aging* 2015;10:1627–1635.
14. Gebhart A, Young MT, Nguyen NT. Bariatric surgery in the elderly: 2009–2013. *Surg Obes Relat Dis* 2015;11:393–398.
15. Wolfe BM, Kvach E, Eckel RH. Treatment of obesity: weight loss and bariatric surgery. *Circ Res* 2016;118:1844–1855.
16. Grams J, Garvey WT. Weight loss and the prevention and treatment of type 2 diabetes using lifestyle therapy, pharmacotherapy, and bariatric surgery: mechanisms of action. *Curr Obes Rep* 2015;4:287–302.
17. Ochner CN, Teixeira J, Geary N, Asarian L. Greater short-term weight loss in women 20–45 versus 55–65 years of age following bariatric surgery. *Obes Surg* 2013;23:1650–1654.
18. Contreras JE, Santander C, Court I, Bravo J. Correlation between age and weight loss after bariatric surgery. *Obes Surg* 2013;23:1286–1289.
19. Stanford FC, Alfari N, Gomez G, Ricks ET, Shukla AP, Corey KE, *et al.* The utility of weight loss medications after bariatric surgery for weight regain or inadequate weight loss: a multi-center study. *Surg Obes Relat Dis* 2017;13: 491–500.
20. Schwartz J, Suza A, Wehr AM, Foreman KS, Mikami DJ, Needleman BJ, *et al.* Pharmacotherapy in conjunction with a diet and exercise program for the treatment of weight recidivism or weight loss plateau post-bariatric surgery: a retrospective review. *Obes Surg* 2016;26:452–458.
21. Jester L, Wittgrove AC, Clark W. Adjunctive use of appetite suppressant medications for improved weight management in bariatric surgical patients. *Obes Surg* 1996;6: 412–415.
22. Pajecski D, Halpern A, Cercato C, Mancini M, de Cleva R, Santo MA. Short-term use of liraglutide in the management of patients with weight regain after bariatric surgery. *Rev Col Bras Cir* 2013;40:191–195.
23. Zilberstein B, Pajecski D, Garcia de Brito AC, Gallafrio ST, Eshkenazy R, Andrade CG. Topiramate after adjustable gastric banding in patients with binge eating and difficulty losing weight. *Obes Surg* 2004;14:802–805.
24. Ferrannini E, Rosenbaum M, Leibel RL. The threshold shift paradigm of obesity: evidence from surgically induced weight loss. *Am J Clin Nutr* 2014;100:996–1002.
25. Jacobsen LV, Flint A, Olsen AK, Ingwersen SH. Liraglutide in type 2 diabetes mellitus: clinical pharmacokinetics and pharmacodynamics. *Clin Pharmacokinet* 2016;55:657–672.
26. Shantavasinkul PC, Omotosho P, Corsino L, Portenier D, Torquati A. Predictors of weight regain in patients who underwent Roux-en-Y gastric bypass surgery. *Surg Obes Relat Dis* 2016;12:1640–1645.

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