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ORIGINAL ARTICLE

Impact of Glucagon-Like Peptide-1 Receptor Agonists Prior to Bariatric Surgery

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Abstract

Background: With the increase in prevalence of obesity there has been an increase in both surgeries and medications implemented to treat obesity. Weight loss from bariatric surgeries is partially attributed to its impact on endogenous GLP-1, which is the target of the weight loss medication class GLP-1 RA. These medications have been used after surgery to provide additional weight loss but there are no studies analyzing the impact of GLP-1 RA use prior to bariatric surgery. Therefore, the purpose of this study is to assess the impact on weight loss when a GLP-1 RA is used prior to a sleeve gastrectomy.

Methods: This study is a single-site retrospective review of patients receiving a sleeve gastrectomy. Patients who received any GLP-1 RA leading up to surgery were compared to those who did not receive these medications. The weight loss following the surgery was tracked in 3-month intervals for one year following surgery to determine if there is any difference in excess body weight loss between the two groups.

Results: There was an average additional EBWL of 6.8% in the control group compared to the GLP-1 RA group at six months post-surgery which was statistically significant ($p = 0.0313$). However, after 12 months the difference in EBWL was 4.6% greater in control group which was not statistically significant ($p = 0.2737$). In addition, when compared to consultation weight there was minimal difference in EBWL with average EBWL of 69.7% in the GLP-1 RA compared to 71.2% in the control group. The tirzepatide sub-group showed the most weight loss compared to consultation weight, with an average EBWL of 77.3%.

Conclusion: There may be a slight delay in post-surgical weight loss when a GLP-1 RA is used prior to bariatric surgery but no significant difference is seen after 12 months. There does not appear to be any additional weight loss provided when using a GLP-1 RA prior to a sleeve gastrectomy.

Abbreviations

CI: Confidence Interval; BMI: Body Mass Index; GLP-1: Glucagon-Like Peptide-1; GLP-1 RA: Glucagon-Like Peptide-1 Receptor Agonist; EWBL: Excess Body Weight Loss

Introduction

In the United States, obesity rates have steadily increased with an estimated obesity (BMI ≥ 30 kg/m^2) prevalence of 42.4% in 2018 compared to on 33.7% in 2008 [1]. Obesity is related to several chronic disease states, including but not limited to Type 2 diabetes, cardiovascular disease, chronic lung conditions and certain cancers [2]. Therefore, with this increase in prevalence, obesity-related illness has become one of the leading causes of death with over three million deaths attributed to obesity globally [2]. In addition, the associated healthcare cost of someone obese is dramatically higher, with an estimated additional $1,861 spent annually in medical cost for an obese person compared to those at a healthy weight [3]. Despite this, treatment in the primary care setting focuses more on the treatment of the individual chronic diseases, rather than focusing on the underlying cause: Obesity [4].

Recommendations for treatment of obesity in the primary care setting include lifestyle modifications (diet and exercise), but more recently there has been increased demand for medications to help with weight loss [4]. While weight loss medications have been available for several years, the emergence of the glucagon-like peptide-1 receptor agonist (GLP-1 RA) has dramatically

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$$\textit{Excess body weight} = \textit{actual body weight} - \textit{body weight at BMI of } 25$$

Figure 1: Excess body weight calculation.

increased awareness and demand for weight loss medications [4,5]. These medications promote weight loss by mimicking the action of glucagon-like peptide-1 (GLP-1), which leads to delayed gastric emptying and early satiety [5]. In a phase three study of semaglutide, a GLP-1 RA, patients in the treatment group lost 14.9% of body weight after 68 weeks compared to only 2.4% in the placebo group [6]. While these medications have modest effects on weight loss in addition to placebo, bariatric surgeries can provide greater weight lost for a greater duration [7,8].

The American Society for Metabolic and Bariatric Surgery estimates that following bariatric surgery, patients should maintain a percent excess body weight loss (EBWL) of 60% or greater [7]. One meta-analysis showed that bariatric surgeries led to an average difference in weight loss of 22.68 kg and in BMI of 8.18 kg/m^2 when compared to GLP-1 RAs [8]. The prevalence of bariatric surgery has dramatically increased with 173,000 completed in 2012 and 279,967 completed in 2022 [9]. The most common bariatric surgery in the U.S. is the sleeve gastrectomy, with 160,609 surgeries (57% of all bariatric surgeries) completed in 2022 [9]. Within this surgery, approximately 80% of the stomach is removed, limiting the number of calories that can be consumed resulting in weight loss [10]. After a sleeve gastrectomy, there is also a change in hormonal regulation, including GLP-1, that aids in weight reduction [10].

Endogenous GLP-1 production will typically increase in response to food, but those who are obese produce less GLP-1 than those who are at a healthy weight [11]. Previous studies have shown that within six days of a sleeve gastrectomy, GLP-1 concentrations increase dramatically [11]. With the increased production of GLP-1, will the addition of medications targeting GLP-1 have the same effect in patients receiving a bariatric surgery? One study shows that when liraglutide was added following a sleeve gastrectomy, there was significantly more weight loss with an additional 14.2% EBWL on average [12]. Another study showed that semaglutide used after surgery had an additional 4.15% weight loss when compared to liraglutide [13]. There are no available studies showing the impact of GLP-1 RAs used prior to surgery. Therefore, this study aimed to look at the impact on weight loss of GLP-1 RA use prior to a sleeve gastrectomy.

Methods

This study was approved by the Institutional Review Board at Saint Joseph Health System. This retrospective study reviewed patients who received a sleeve gastrectomy at Saint Joseph Health System in Mishawaka, IN. Patients were included if their surgeries were completed from 12/20/21 to 2/28/23. All patients completed the minimum 6-month program via Saint Joseph Wellness and Weight Management which consisted of monthly education classes on lifestyle techniques for weight management and provided six months of food logs. Patients were required to complete all follow-ups at 3-month intervals up to month 12 post-surgery to be included. The groups were divided into patients who used any GLP-1 RA (including tirzepatide) prior to surgery and those who did not.

The endpoints used to assess the impact of GLP-1 RA prior to surgery were the excess body weight loss (EBWL) at 3-month intervals up to 12 months. This was compared to both the starting weight at consultation (at least six months prior to surgery) and at pre-surgery weight (within one month of surgery). The equation for excess body weight is shown in Figure 1. The expected excess body weight loss of a bariatric surgery is estimated at 60% [7]. Therefore, if the patient reached this goal within 12 months, this was considered a successful surgery and the rate of successful surgeries was compared between groups. The last endpoint tracked was if a GLP-1 RA was used following surgery, as this could have an impact on weight loss following surgery. Sub-group analysis based on type of GLP-1 RA used, dosing of medication, and duration of use was completed as well. To analyze these endpoints, an unpaired student t-test was used numerical endpoints and the chi-squared test was used to evaluate categorical endpoints. A p-value of < 0.05 was considered statistically significant.

Results

Of the 128 patients who received a sleeve gastrectomy during the specified dates, 100 patients completed all follow-up appointments and were included in this study. Of these 100 patients, half of them received a GLP-1 RA prior to surgery (N = 50) and the other half was considered the control group (N = 50). This patient population were predominantly female (85%), white (76%), and had an average age of 45 years. There are some differences between the two groups. The GLP-1 RA group has a greater average starting weight of (314.8 lbs) compared to the control group (286.9 lbs). There was more weight loss in the GLP-1 RA group with an average weight loss of 26.0 lbs compared to 11.4 lbs in the control group, leading to a more similar pre-surgery weight (288.8 vs. 275.5 lbs). The other difference between the two groups is the medical history with greater incidence of type 2 diabetes in the GLP-1 RA group (42% vs. 22%). All baseline characteristics are included in Table 1. Semaglutide was the most common

Table 1: Baseline characteristics.

	GLP-1 use prior to surgery (N = 50)	Control Group (N = 50)
Age (years)	44.2 ± 14.0	45.8 ± 11.0
Gender	84% female	86% female
Ethnicity	74% White	78% White
	22% Black	16% Black
	4% Hispanic	6% Hispanic
Height (in)	65.5 ± 3.5	66.0 ± 3.0
Consult weight (lbs)	314.8 ± 47.8	286.9 ± 48.6
Consult BMI (kg/m^2)	51.6 ± 6.7	46.1 ± 5.9
Consult EBW (lbs)	162.0 ± 41.2	131.6 ± 40.8
Surgery weight (lbs)	288.8 ± 42.8	275.5 ± 44.2
Surgery BMI (kg/m^2)	47.3 ± 5.3	44.3 ± 5.3
Surgery EBW (lbs)	136.0 ± 35.1	120.2 ± 36.4
Weight loss before surgery (lbs)	26.0 ± 21.9	11.4 ± 33.3
Medical history	T2DM 42%	T2DM 22%
	Pre-DM 30%	Pre-DM 38%
	HTN 52%	HTN 34%
A1C	6.3 ± 1.3%	5.7 ± 0.7%

Table 2: GLP-1 RA dosing and duration.

	Mean Dose (mg)	Mean Duration (months)	Mean Weight Loss (lbs)
Semaglutide (N = 23)	0.55 ± 0.35	5.3 ± 3.3	18.2 ± 13.4
Dulaglutide (N = 13)	2.31 ± 0.99	7.3 ± 4.1	10.9 ± 9.6
Tirzepatide (N = 12)	7.50 ± 1.51	4.5 ± 1.4	31.9 ± 17.8
Liraglutide (N = 2)	2.40 ± 0.85	9.0 ± 2.3	61.0 ± 54.6
All Medications (N = 50)	N/A	5.8 ± 3.4	26.0 ± 21.9

GLP-1 RA used in the trial, but several other GLP-1 RAs were used. The dosing, duration and weight loss significantly differed between agents and is included in Table 2.

Comparison to pre-surgery weight

In the GLP-1 RA group, there is less EBWL at each of the 3-month intervals (full results in Table 3). The only statistically significant difference is at the 6-month interval where there was a difference of EBWL of 6.8% (p = 0.0313). At 12 months after surgery, there is a difference in average EBWL between the GLP-1 RA group (64.2%) and the control group (68.8%) but was not statistically significant (p = 0.2737). There was similar number of successful surgeries in both groups (p = 0.534) with 60% in the GLP-1 RA and 66% in the control group. There were more patients who were prescribed a GLP-1 RA following surgery in the GLP-1 RA group (32%) than in the control group (14%), which was statistically significant (p = 0.0325).

Comparison to consultation weight

The EBWL from consultation was not significantly different between the GLP-1 RA group (69.7%) and the control group (71.2%) 12 months post-surgery. There was also no difference in reaching EBWL of ≥ 60% between the two groups. Full results can be found in Table 3.

Sub-group analysis

Sub-group analysis was completed for each of the GLP-1 RAs which was compared to the control group (available in Table 4). Compared to pre-surgery and consultation weight, both the semaglutide group (N = 23) and the dulaglutide group (N = 13) had a lower average EBWL when compared to the control group. However, neither of these results were statistically significant. In the tirzepatide group (N = 12), there was a greater percentage of EBWL when compared to the control group but this was not statistically significant.

When dosed for 6 months or greater, there was less weight loss when compared to pre-surgery weight in the GLP-1 RA group (61.1% EBWL) than the control group (68.8% EBWL) but was not statistically significant (p = 0.1424). When looking at efficacy dosing and high dosing (defined in Table 4) there is greater weight loss in the control groups but not a statistically significant difference when compared to both pre-surgery and consultation weight.

Table 3: Primary results.

	GLP-1 use prior to surgery (N = 50)	Control Group (N = 50)	Mean Difference (95% CI)	p-value
Compared to pre-surgery weight				
EBWL at 3 months	36.7 ± 11.5%	40.9 ± 11.1%	4.2 (-0.3 to 8.7)	0.0662
EBWL at 6 months	51.2 ± 15.0%	58.0 ± 16.1%	6.8 (0.6 to 13.0)	0.0313
EBWL at 9 months	59.4 ± 16.4%	65.8 ± 18.9%	6.4 (-0.6 to 13.4)	0.0736
EBWL at 12 months	64.2 ± 19.5%	68.8 ± 22.2%	4.6 (-3.7 to 12.9)	0.2737
Goal EBWL of ≥ 60% reached	30 (60%)	33 (66%)		0.534
Use of GLP-1 agent after surgery	16 (32%)	7 (14%)		0.0325
Compared to consult weight				
EBWL at 12 months	69.7 ± 16.9%	71.2 ± 20.9%	1.5 (-6.0 to 9.0)	0.694
Goal EBWL of ≥ 60% reached	36 (72%)	41 (82%)		0.2351

Table 4: Sub-group analysis.

	Subgroup	Control Group (N = 50)	Mean Difference (95% CI)	p-value
	Semaglutide (N = 23)			
EBWL at 12 months (pre-surgery)	64.1 ± 16.7%	68.8 ± 22.2%	4.7 (-5.7 to 15.1)	0.3695
EBWL at 12 months (consult)	69.6 ± 13.6%	71.2 ± 20.9%	1.6 (-7.9 to 11.1)	0.7384
	Dulaglutide (N = 13)			
EBWL at 12 months (pre-surgery)	60.9 ± 22.0%	68.8 ± 22.2%	7.9 (-5.9 to 21.7)	0.2567
EBWL at 12 months (consult)	64.7 ± 19.2%	71.2 ± 20.9%	6.5 (-6.3 to 19.3)	0.3143
	Tirzepatide (N = 12)			
EBWL at 12 months (pre-surgery)	71.2 ± 21.0%	68.8 ± 22.2%	-2.4 (-16.5 to 11.7)	0.7353
EBWL at 12 months (consult)	77.3 ± 19.3%	71.2 ± 20.9%	-6.1 (-19.4 to 7.2)	0.361
	Duration ≥ 6 months (N = 24)			
EBWL at 12 months (pre-surgery)	61.1 ± 17.6%	68.8 ± 22.2%	7.7 (-2.6 to 18.0)	0.1424
EBWL at 12 months (consult)	66.4 ± 15.8%	71.2 ± 20.9%	4.8 (-4.8 to 14.4)	0.3228
	Efficacy dosing* (N = 42)			
EBWL at 12 months (pre-surgery)	64.2 ± 20.5%	68.8 ± 22.2%	4.6 (-4.3 to 13.5)	0.3081
EBWL at 12 months (consult)	69.4 ± 18.0%	71.2 ± 20.9%	1.8 (-6.4 to 10.0)	0.6624
	High dosing** (N = 28)			
EBWL at 12 months (pre-surgery)	64.1 ± 18.0%	68.8 ± 22.2%	4.7 (-5.1 to 14.5)	0.3416
EBWL at 12 months (consult)	69.8 ± 16.5%	71.2 ± 20.9%	1.4 (-7.7 to 10.5)	0.7613

*Efficacy dosing defined as semaglutide 0.5 mg, dulaglutide 1.5 mg, tirzepatide 5 mg and liraglutide 1.2 mg; **High dosing defined as: Semaglutide 1 mg, dulaglutide 3 mg, tirzepatide 7.5 mg and liraglutide 1.8 mg.

Discussion

Based on a literature search, this is the first study completed reviewing the impact of GLP-1 RA prior to bariatric surgeries. The results, when compared to pre-surgery weight, seem to show a greater impact on weight in the immediate months following the surgery compared to the 1-year follow-up. This is based on the statistically significant result at 6-months with an 6.8% additional EBWL in the control group whereas

at 12 months it is only at 4.6% difference and was not statistically significant. This could be related to the impact on endogenous GLP-1 following surgery. Post-prandial GLP-1 increases within six days of surgery and levels are increased when measured six months post-surgery [11,14]. However, after 12 months, there does not appear to be similar increases in GLP-1 in response to food in these studies [14]. The other possible cause of this difference is the use of GLP-1 RA following surgery. There were 32% of patients using GLP-1 RA in the GLP-1 RA group, compared to only 14% in the control group. These medications were typically restarted six or more months after surgery when patients were not at their EBWL goal, which could also cause this difference.

The addition of a GLP-1 RA to a sleeve gastrectomy does not appear to have an additive impact on EBWL when compared to the surgery alone. This is based on the comparison to consultation weight as there was no significant difference between the two groups, with the control group even having slightly higher EBWL compared to the GLP-1 RA group. This information would then support reduced prescribing of GLP-1 RA for weight loss prior to bariatric surgery as these agents are expensive and do not provide additional value in terms of total weight lost. The exception to this may be the use of tirzepatide prior to surgery. This sub-group was the only group to have greater EBWL in the GLP-1 RA group compared the control group. Based on randomized clinical trials, tirzepatide does appear to produce more weight loss than other agents such as semaglutide [15]. In this study, there was not a statistically significant difference, as it was likely underpowered with a sample of only 12 patients for comparison.

There are several key limitations of this study that limit external application. Primarily, the lack of randomization leads to patients who are already struggling to lose weight to be assigned to the GLP-1 RA group. In order to meet weight goals prior to surgery either for insurance or safety based on surgeon recommendations, GLP-1 RA are often initiated for those who are gaining weight prior to surgery. These patients may struggle to obtain weight loss after surgery if the struggled to gaining weight prior to srugery. The lack of randomization also led to some difference in baseline characteristics. This included a greater portion of people with diabetes who are more likely to be on weight promoting medications such as insulin or sulfonylureas. There was a greater starting weight in the GLP-1 RA group but would not expect this to majorly impact results as EBWL accounts for differences in weight.

The other major limitation is the inconsistency between the type, dosing, and duration of the GLP-1 RA. With this inconsistency, it is difficult to assess the full impact as they have varying impacts on weight loss. The sub-group analyses were underpowered based on small sample size and were not able to obtain statistically significant difference. In order to appropriately detect a difference, there would need to be randomized, controlled trials assessing individual agents at standard dosing patterns. With tirzepatide being the only agent in the sub-group analysis to produce greater EBWL than the control group, this would potentially be the preferred agent to study as it may be the most likely to provide additive weight loss.

Conclusion

The use of a GLP-1 RA prior to a sleeve gastrectomy may delay post-surgical weight loss within the first 6 months of surgery but does not have an impact after 12 months. The total weight loss from using a GLP- 1 RA prior to a sleeve gastrectomy does not appear to be greater than that of the surgery alone. These results suggest that it may be prudent to limit GLP-1 RA prescribing specifically for weight loss prior to surgery. Randomized, controlled studies would be needed to assess the true impact of GLP-1 RA against use prior to surgery as this study has several major limitations that prevents this information from being widely applicable. Based on sub-group analysis, tirzepatide may be able to provide additive weight loss when used prior to surgery but further studies are needed to confirm this finding.

References

1. Purnell JQ (2000) Definitions, classification, and epidemiology of obesity.
2. Djalalinia S, Qorbani M, Peykari N, Kelishadi R (2015) Health impacts of obesity. Pak J Med Sci 31: 239-242.
3. Centers for Disease Control and Prevention (2022) Adult obesity facts.
4. Tucker S, Bramante C, Conroy M, Fitch A, Gilden A, et al. (2021) The most undertreated chronic disease: Addressing obesity in primary care settings. Curr Obes Rep 10: 396-408.
5. Chakhtoura M, Haber R, Ghezzawi M, Rhayem C, Tcheroyan R, et al. (2023) Pharmacotherapy of obesity: An update on the available medications and drugs under investigation. EClinicalMedicine 58: 101882.
6. Wilding JPH, Batterham RL, Calanna S, Davies M, Gaal LFV, et al. (2021) Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med 384: 989-1002.
7. Eisenberg D, Shikora SA, Aarts E, Aminian A, Angrisani L, et al. (2022) 2022 American society for metabolic and bariatric surgery (ASMBS) and international federation for the surgery of obesity and metabolic disorders (IFSO): Indications for metabolic and bariatric surgery. Surg Obes Relat Dis 18: 1345-1356.
8. Sarma S, Palcu P (2022) Weight loss between glucagon-like peptide-1 receptor agonists and bariatric surgery in adults with obesity: A systematic review and meta-analysis. Obesity (Silver Spring) 30: 2111-2121.
9. American Society for Metabolic and Bariatric Surgery (2024) Estimate of Bariatric Surgery Numbers, 2011-2022.
10. Hutch CR, Sandoval D (2017) The Role of GLP-1 in the Metabolic Success of Bariatric Surgery. Endocrinology 158: 4139-4151.

11. Gudbrandsen OA, Dankel SN, Skumsnes L, Flolo TN, Folkestad OH, et al. (2019) Short-term effects of Vertical sleeve gastrectomy and Roux-en-Y gastric bypass on glucose homeostasis. Sci Rep 9: 14817.

12. Thakur U, Bhansali A, Gupta R, Rastogi A (2021) Liraglutide augments weight loss after laparoscopic sleeve gastrectomy: A randomised, double-blind, placebo-control study. Obes Surg 31: 84-92.

13. Murvelashvili N, Xie L, Schellinger JN, Mathew MS, Marroquin EM, et al. (2023) Effectiveness of semaglutide versus liraglutide for treating post-metabolic and bariatric surgery weight recurrence. Obesity (Silver Spring) 31: 1280-1289.

14. Çalık Başaran N, Dotan I, Dicker D (2024) Post metabolic bariatric surgery weight regain: The importance of GLP-1 levels. Int J Obes (Lond).

15. Frías JP, Davies MJ, Rosenstock J, Manghi FCP, Lando LF, et al. (2021) Tirzepatide versus semaglutide once weekly in patients with type 2 diabetes. N Engl J Med 385: 503-515.