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ORIGINAL CONTRIBUTIONS

Semaglutide and Tirzepatide for the Management of Weight Recurrence After Sleeve Gastrectomy: A Retrospective Cohort Study

Mohammad Jamal[1,2,3,4] · Mohsen Alhashemi[3,4] · Carol Dsouza[4] · Sara Al-hassani[4] · Wafa Qasem[2,5] · Sulaiman Almazeedi[3] · Salman Al-Sabah[3]

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Abstract

Background Metabolic and bariatric surgery (MBS) is the most effective treatment for obesity and improvement of obesity-associated comorbidities. However, a proportion of these patients may suffer from weight recurrence and recurrence of obesity-associated comorbidities.

Method A retrospective cohort study of patients who underwent SG between January 2008 and August 2022 and sought treatment for weight recurrence with semaglutide or tirzepetide from January 2022 onwards.

Result A total of 115 patients were included, of which 70 had SG and treated for weight recurrence with semaglutide and 45 had SG and treated with tirzepatide. The mean age of patients was 38.8 (10.4) and 80.9% of patients were female. The mean pre-treatment weight and BMI was 94.0 (23.8) kg and 35.1 (6.0) kg/m^2. Following treatment with semaglutide and tirzepatide, the mean post-treatment weight at 6 months was 81.0 (19.0) kg from 90.1 (19.6) kg and 87.6 (28.3) kg from 100.2 (28.5) kg respectively, corresponding to a clinically significant mean weight loss from baseline to 6 months of 10.3 (5.9)% ($p < 0.05$) and 15.5 (6.3)% ($p < 0.05$). Weight loss in tirzepatide patients was significantly greater than the semaglutide patients at 6 months ($p < 0.02$). There were no reported severe adverse events to the treatment.

Conclusion Short-term outcomes show that semaglutide and tirzepatide can be an effective treatment for managing weight recurrence after SG. Studies with longer follow-up are needed to determine the durability, as weight regain after discontinuation of the medication is highly likely, and the high cost of these medications can limit their use.

Keywords Sleeve gastrectomy · Weight recurrence · Weight regain · Bariatric surgery · GLP1 · GIP/GLP1 · Weight loss · Semaglutide · Tirzepatide

Introduction

Metabolic and bariatric surgery (MBS) is the most effective treatment for obesity and improvement of obesity-associated comorbidities [1]. However, a proportion of these patients may suffer from weight recurrence and recurrence of obesity-associated comorbidities [2]. Traditionally, revisional bariatric surgery was offered as a treatment of weight recurrence; however, the weight loss after revisional surgery can be modest and associated with a relatively higher risk of morbidity and mortality [3]. Therefore, an alternative approach that may prove valuable is the use of weight loss medications for long-term weight management after bariatric surgery [4, 5].

The recently introduced anti-diabetic medications, Glucagon-like peptide-1 (GLP-1) receptor agonists, including liraglutide and semaglutide, have shown safe and effective weight loss results, and are associated with improvement of cardiovascular risk profile in patients with type 2 diabetes [6, 7]. Semaglutide have shown better weight loss outcomes compared to liraglutide even in patients without type 2 diabetes [8]. There are a limited number of studies that examined the effect of these medications on weight recurrence

Key Points
- This study adds to the current body of evidence supporting the clinical effectiveness of semaglutide and tirzepatide for weight reduction in patients with obesity, particularly in those with weight recurrence following sleeve gastrectomy (SG).
- Weight loss was significantly greater in the tirzepatide-treated group than the semaglutide-treated group.
- A meaningful weight loss may be achieved with the use of pharmacotherapy in patients with weight recurrence after SG without the need for revisional surgery.
- Pharmacotherapy can be an effective alternative to revisional surgeries with minimum adverse effects.

Extended author information available on the last page of the article

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after bariatric surgery; nonetheless, the results of these studies are promising [8–13].

Tirzepatide is a novel glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 (GIP/GLP-1) receptor agonist that have shown to be the most effective medication for the treatment of obesity with an acceptable safety profile, with results from a randomized clinical trial showing approximately 20% total weight loss with the highest recommended dose of 15 mg weekly injections [14, 15], and it has recently been approved by the US Food and Drug Administration (FDA) for chronic weight management.

To our knowledge, there are no studies reporting on the effectiveness of Tirzepatide for the treatment of weight recurrence after bariatric surgery, and a limited number of studies that examined the use of semaglutide in the same patient population. Therefore, the aim of this study is to report real-world efficacy of semaglutide and tirzepatide as an adjunct for weight recurrence following sleeve gastrectomy (SG).

Methods

Study Design and Population

The study is reported according to The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) and the principles expressed in the Declaration of Helsinki guidelines. The study protocol was approved by the Research Ethics Committee (Reference Number:2022/2101). This is a retrospective cohort study of a prospectively maintained database of adult (> 18 years old) patients who sought management of weight recurrence after SG with semaglutide or tirzepatide from January 2022, at a single private clinic in Kuwait. Patients who underwent SG between January 2008 and August 2022 were included in the study. Patients were included if they satisfy the criteria for the treatment with weight loss medications as specified in the original studies [8, 14] therefore, patients with BMI greater than 30 kg/m^2 or 27 kg/m^2 with at least one obesity-related complication, and prescribed semaglutide or tirzepetide in increasing dose regimen starting at 0.25 mg and 2.5 mg, respectively, to manage weight recurrence following SG were included in the study. The decision whether to start semaglutide or tirzepatide was taken after discussion with the patient, their preference, and the availability of the medication. The use of tirzepatide was off-label base at the time of the study initiation. Weight recurrence defined a priori as ≥ 10% weight recurrence from the nadir post-SG weight. Exclusion criteria included patients on any other weight loss regimen, had personal history of pancreatitis, personal or family history of medullary thyroid cancer, or they were pregnant or breastfeeding, or if the patient discontinued the treatment in less than 12 weeks. Patients with severe gastroesophageal reflux disease (GERD) symptoms were not offered medical treatment, instead, those patients were offered surgical conversion to Roux-en-Y gastric bypass (RYGB). All patients were assigned to receive a follow-up session with a clinical nutritionist and were encouraged to do at least 10,000 steps per day and to follow a high protein diet with a maximum of 1500 kcal/day. Patients were scheduled for follow-up at 3 and 6 months after initiation of treatment. During each follow-up visit, patients' treatment adherence and tolerability/safety; dietary plan; weight/anthropometric progress; and general clinical status were monitored by assigned clinicians. Health history data, laboratory investigations, and previous treatment data including previous surgical procedures were collected from the patients.

Informed consent was obtained from the patients to participate in the study and to access their electronic medical data for research purposes. Each participant was assigned a unique study identification number, and the research dataset was anonymized and stored securely in a password-protected device accessible only to the research team.

Statistical Analysis

Continuous variables were summarized as means and standard deviations (SDs) and categorical variables were summarized as relative frequencies and percentages. Intergroup differences in weight changes were compared using paired *t*-test for normally distributed data and the Wilcoxon signed-rank test for non-normally distributed data. A one-way ANOVA, paired *t*-test, or Welch's *t*-test was used to compare weight changes across variable categories. *p* values < 0.05 were considered statistically significant. Analysis was conducted using GraphPad Prism 10.0.

Results

Patients Characteristics at Baseline

A total of 115 patients were included in the study, of which 70 had SG and received treatment with semaglutide and 45 had SG and tirzepatide. All patients completed follow-up at 3 and 6 months, except for 10 patients in the SG and tirzepatide group did not complete 6-month follow-up. Baseline characteristics are presented in (Table 1). The mean pre-SG weight and BMI was 116.2 (25.5) kg and 43.0 (8.7) kg/m^2. The mean post-SG nadir weight and BMI was 77.6 (17.6) kg and 29.0 (5.3) kg/m^2, representing a mean total body weight loss percentage of 34.8 (14.6)%. Semaglutide and tirzepatide treatment was initiated at 71.8 (51.1) months after SG. The mean age of patients was 38.8 (10.4) and 80.9% of patients were female. The mean pre-treatment weight and BMI was 94.0 (23.8) kg and 35.1 (6.0) kg/m^2, representing a weight recurrence percentage of 22.0 (18.4)%. The

Table 1 Patient baseline characteristics and weight loss outcomes

Variable	Total ($n=115$) (%)	Semaglutide ($n=70$) (%)	Tirzepatide ($n=45$) (%)
Mean age			
All [(years (SD)]	38.8 (10.4)	38.1 (10.3)	40.2 (10.5)
< 30	22 (19.1)	15 (21.4)	7 (15.6)
31–40	40 (34.8)	22 (31.4)	18 (40.0)
41–50	36 (31.3)	24 (34.3)	12 (26.6)
> 50	15 (13.0)	9 (12.9)	6 (13.3)
Gender			
Male	22 (19.1)	14 (20.0)	8 (17.8)
Female	93 (80.9)	56 (80.0)	37 (82.2)
Chronic conditions			
Type 2 diabetes	2 (1.7)	1 (1.4)	1 (2.2)
Hypertension	5 (4.3)	4 (5.7)	1 (2.2)
Liver disease	2 (1.7)	2 (2.9)	0 (0.0)
Other chronic conditions	14 (12.2)	12 (17.1)	2 (4.4)
No chronic conditions	92(79.1)	51 (72.9)	41 (91.1)
Maximum dose tolerated (mg)			
< 1.0	-	22 (31.4)	-
> 1.0	-	48 (68.6)	-
< 10.0	-	-	15 (33.3)
> 10.0	-	-	30 (66.7)
Weight			
Pre-SG weight (kg ± SD)	116.2 (25.5)	112.8 (23.5)	122.5 (28.3)
Pre-SG BMI (kg/m^2 ± SD)	43.0 (8.7)	42.0 (9.1)	44.9 (7.6)
Post-SG nadir weight (kg ± SD)	77.6 (17.6)	75.3 (15.9)	81.7 (19.9)
Post-SG nadir BMI (kg/m^2 ± SD)	29.0 (5.3)	28.4 (4.7)	30.1 (6.2)
Pre-treatment weight (kg ± SD)	94.0 (23.8)	90.1 (19.4)	100.2 (28.5)
Pre-treatment BMI (kg/m^2 ± SD)	35.1 (6.0)	33.9 (6.0)	36.9 (7.1)
Weight at 3-month treatment (kg ± SD)	87.3 (22.9)	84.9 (19.3)	91.2 (27.3)
BMI at 3-month treatment (kg/m^2 ± SD)	32.5 (6.4)	31.9 (6.0)	33.5 (6.8)
*Weight at 6-month treatment (kg ± SD)**	83.2 (22.7)	81.0 (19.0)	87.6 (28.3)
*BMI at 6 month treatment (kg/m^2 ± SD)**	31.1 (6.4)	30.4 (6.0)	32.1 (6.9)

SD, standard deviation; *SG*, sleeve gastrectomy; *BMI*, body mass index

*In the tirzepatide group, 10 patients did not complete 6-month follow-up ($n=35$)

following comorbidities were noted in the initial assessment of patients: 2 (1.7)% had Type 2 diabetes, 5 (4.3)% had hypertension, 2 (1.7)% had liver diseases, and 14 (12.2)% patients had other chronic conditions including polycystic ovary syndrome (PCOS), hypothyroidism, high cholesterol, glucose-6-phosphate dehydrogenase deficiency (GP6D), asthma, mild gastroesophageal reflux disease (GERD), and obstructive sleep apnea (OSA).

Weight Loss Outcomes

Weight loss outcomes were obtained after 3 and 6 months of semaglutide and tirzepatide treatment (Table 1). In the semaglutide treatment group, the mean post-treatment weight at 3 months and 6 months was 84.9 (19.3) kg and 81.0 (19.1) kg from 90.1 (19.4) kg, corresponding to a clinically significant mean weight loss from baseline to 3 months of 6.0 (3.6)% and to 6 months of 10.3 (5.9)% ($p<0.05$). Following tirzepatide treatment, the mean post-treatment weight at 3 months and 6 months was 91.2 (27.3) kg and 87.6 (28.3) kg from a mean pre-treatment baseline of 100.2 (28.5) kg, corresponding to a clinically significant mean weight loss from baseline to 3 months of 9.3 (4.3)% and to 6 months of 15.5 (6.3)% ($p<0.05$). Weight loss percentage in tirzepatide patients at 3 and 6 months was significantly greater than the semaglutide patients at 3 months ($p<0.03$) and 6 months ($p<0.001$) (Fig. 1A, B), with statistically significant reduction in weight between 3- and 6-month duration of treatment in both groups ($p<0.05$) (Fig. 1B).

Following a period of 3 months of semaglutide treatment, 62.9% of patients achieved ≥ 5% total body weight loss and

11.4% of patients had ≥ 10%. At 6 months of semaglutide treatment, 80.0% of patients had ≥ 5% total body weight loss, 48.6% of patients had ≥ 10%, and 26.0% achieved > 15% total body weight loss. At 3 months of tirzepatide treatment, 75.5% of patients had ≥ 5% total body weight loss, 44.4% had ≥ 10%, and 8.5% of patients had ≥ 15% weight loss. At 6 months of tirzepatide treatment, 97.1% of patients achieved weight loss ≥ 5%, 74.3% of patients had ≥ 10%, and 57.1% achieved > 15% of total body weight loss (Fig. 1C).

Subgroup analysis of weight loss outcomes stratified by age, sex, BMI category, maximum-tolerated dose, and time from SG was performed (Tables 2 and 3). In the semaglutide treatment group, female patients showed better weight loss at 3 months compared to male patients ($p = 0.02$). A similar trend was also observed at 6 months, with more weight loss among female patients compared to male patients; however, this did not reach statistical significance. Also, although the weight loss was greater in the age group of ≤ 30 at 6 months of treatment, no statistically significant weight change was observed. No statistically significant difference was observed in the other subgroups in either the semaglutide or tirzepatide treatment groups. The percentage post-treatment weight change stratified by subgroup variables is illustrated in Figs. 2 and 3.

Tolerability of Semaglutide and Tirzepatide

More than half of patients (68.6%) tolerated semaglutide dose ≥ 1 mg while 63.8% patients tolerated tirzepatide ≥ 10 mg. Of these, 30.0% reported mild adverse events related to treatment with semaglutide and 34.0% with tirzepatide, however none of these patients discontinued the treatment until 6 month of the study. Most of the adverse events occurred when patients increased their dose and the effects decreased over time. In some cases, the dose was reduced, and the patient continued with decreased dosage. The reported adverse events were nausea, fatigue, vomiting, constipation, diarrhea, hair loss, heartburn, and local reaction at the injection site. None of the patients discontinued the medication due to worsening symptoms of GERD. However, none of the patients in the semaglutide group received a dose of more than 2 mg. In the tirzepatide group, 11 patients received a maximum dose of 15 mg/week.

Discussion

In this study, treatment with semaglutide and tirzepatide for weight recurrence after SG yielded meaningful short-term weight loss in this cohort. Patients who received semaglutide had mean weight loss of 10.3% at 6 months from pre-treatment weight, while those who received tirzepatide achieved a greater mean weight loss of 15.5% at 6 months. This is equivalent to more than 50% of the total weight recurrence after SG. This was associated with good tolerability of the treatment with no significant adverse events.

Sleeve gastrectomy is the most common bariatric surgery performed worldwide, and it is considered a very effective treatment for morbid obesity [16]. However, a significant proportion of patients undergoing SG require revisional surgery, mainly for weight recurrence [16, 17]. We have previously reported the outcomes of conversion of SG to one anastomosis gastric bypass (OAGB) for weight recurrence, and showed a total weight loss of 9.8%, 14.1%, and 28.8% at 3, 6, and 12 months, respectively, with remission

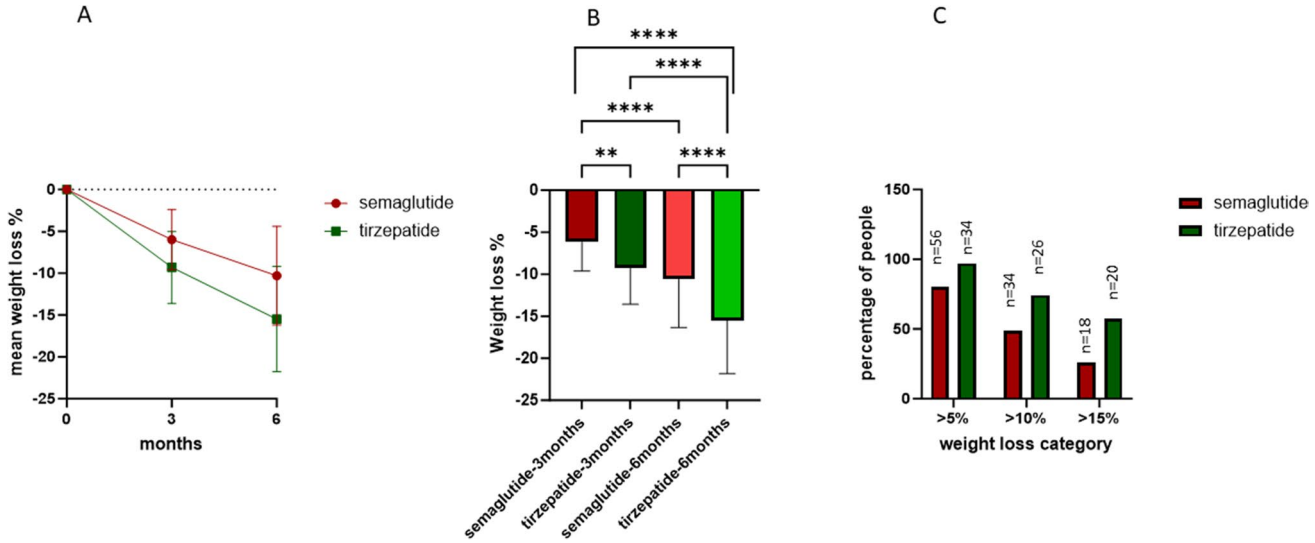

Fig. 1 Weight loss percentage. **A** Weight loss over time following adjunct treatment with semaglutide and tirzepatide, **B** comparison of weight loss by treatment, and **C** percentage of people who achieved weight loss at 6 months of at least ≥ 5%, ≥ 10%, and ≥ 15%

Table 2 Weight outcomes before and after semaglutide treatment

Variable	Mean weight (kgs) pre treatment *Mean (SD)*	Mean weight (kgs) at 3-month treatment *Mean (SD)*	Percentage (%) weight change at 3-month treatment *Mean (SD)*	Mean weight (kgs) at 6 months of treatment *Mean (SD)*	Percentage (%) weight change at 6 month treatment *Mean (SD)*	*p*-value*
All patients	90.1 (19.4)	84.9 (19.3)	− 6.0 (3.6)	81.0 (19.1)	− 10.3 (5.9)	*< 0.05*
Age						
< 30	97.2 (21.3)	90.7 (20.1)	− 6.7 (3.7)	85.6 (21.7)	− 12.2 (7.1)	
31–40	89.6 (21.7)	84.8 (22.0)	− 5.7 (3.8)	83.0 (22.9)	− 9.4 (5.9)	
41–50	87.1 (15.1)	81.8 (16.1)	− 6.4 (3.6)	78.3 (16.1)	− 10.3 (5.8)	
> 50	87.4 (17.0)	83.1 (17.4)	− 5.2 (2.5)	77.1 (17.3)	− 9.2 (4.4)	
Sex						
Male	110.9 (23.8)	106.3 (22.5)	− 4.4 (2.7)	102.1 (23.4)	− 8.6 (4.2)	
Female	85.2 (14.2)	79.7 (14.3)	− 6.7 (3.4)	75.8 (14.1)	− 11.3 (5.8)	*0.02 at 3 months*
BMI category						
< 35	81.0 (11.1)	75.8 (11.2)	− 6.5 (3.3)	72.4 (11.0)	− 10.7 (5.0)	
35–40	100.0 (11.3)	94.9 (11.8)	− 5.8 (3.7)	90.1 (12.7)	− 11.0 (5.8)	
> 40	120.4 (18.4)	114.4 (19.2)	− 5.1 (4.0)	109.1(21.5)	− 9.7 (8.4)	
Max-tolerated dose						
High (> 1 mg)	94.3 (20.0)	-	-	81.2 (25.1)	− 10.0 (5.6)	
Low (< 1 mg)	81.7 (15.2)	-	-	72.3 (19.1)	− 10.3 (6.4)	
Time from SG						
> 5 years	90.3 (19.1)	85.1 (20.1)	− 6.1 (3.6)	82.2 (21.2)	− 10.0 (6.1)	
< 5 years	90.5 (20.0)	85.0 (18.8)	− 6.0 (3.5)	80.6 (18.1)	− 10.7 (5.9)	

*p-value < 0.05 is reported

SD, standard deviation; *SG*, sleeve gastrectomy; *BMI*, body mass index

of comorbidities such as diabetes and hypertension [18]. In a randomized clinical trial by Hany et al., comparing outcomes of revisional procedures after SG to either OAGB or RYGB, the authors showed similar weight loss outcomes, with BMI reduction from 44.9 and 45.1 kg/m^2 pre-revision to 27.8 and 27.4 kg/m^2 at 2 years after revision surgery in the RYGB and OAGB groups, respectively [19]. A systematic review and meta-analysis of retrospective studies comparing the outcomes of OAGB and RYGB after SG, showed percentage of total body weight loss ranging between 15.8 and 39.5% among all the included studies, with better outcomes observed after OAGB [20].

Although revisional surgeries have shown a variable but definite success in the treatment of weight recurrence after SG, they do come at a price of increased morbidity compared to primary procedures in terms of risk of marginal ulcers, anastomotic leak, bleeding, and post-operative mortality [17–23]. Salama et al. compared OAGB to single anastomosis duodeno-ileal switch (SADI-S) as revisional procedures after SG in 91 patients, and although showed better weight loss outcomes at 5 years in the SADI-S vs the OAGB groups (30 vs 19.4%, respectively), they have also reported a complication rate of 28.6% in the OAGB group, with 10.2% requiring conversion to another procedure, while the SADI-S cohort had a complication rate of 21.4% [22]. Poublon et al. also compared the outcomes of OAGB and RYGB as revisional surgeries after failedSG or gastric banding, and reported major complications rate in terms of leak, bleeding, intra-abdominal abscess, and perforation to 1.1% in the OAGB group and 4.9% in the RYGB group, with one mortality in each group, and 5.4% rate of surgical intervention in the OAGB due to bile reflux, and 4.9% rate of surgical intervention in RYGB due to internal hernia [23].

Pharmacotherapies have evolved over the years and are approved for long-term management of obesity in combination with lifestyle modification [24]. There is growing evidence that compared to revisional surgery, weight recurrence after bariatric procedures can be effectively managed with pharmacotherapy, with long-term weight loss benefits, lower risks of adverse events, and is associated with resolution of comorbidities like hypertension and dyslipidemia [25]. Previous studies by Lautenbach et al. and Bonnet et al. both reported a weight reduction of 10.3 and 9.8%, respectively, after 6 months of semaglutide treatment, whereas Murvelashvili et al. reported a weight loss of 12.9% and 8.8% after 12 months of semaglutide 1.0 mg and liraglutide 3.0 mg treatment, respectively [5, 9, 13]. Wharton et al. in a retrospective analysis of patients treated with Liraglutide 3.0 mg after different types of bariatric surgery also showed a significant weight loss that was maintained for more than 1 year

Table 3 Weight outcomes before and after tirzepatide treatment

Variable	Mean weight (kgs) pre treatment *Mean (SD)*	Mean weight (kgs) at 3-month treatment *Mean (SD)*	Percentage (%) weight change at 3-month treatment *Mean (SD)*	Mean weight (kgs) at 6-months of treatment *Mean (SD)*	Percentage (%) weight change at 6-month treatment *Mean (SD)*	*p*-value
All patients	100.2 (28.5)	91.2 (27.3)	−9.3 (4.3)	87.6 (28.3)	−15.5 (6.3)	*< 0.05*
Age						
< 30	103.3 (37.9)	91.3 (30.0)	−10.9 (4.3)	84.9 (29.2)	−17.7 (5.5)	
31–40	102.3 (31.3)	93.3 (32.5)	−9.8 (4.6)	88.7 (34.7)	−15.5 (6.9)	
41–50	97.9 (25.0)	91.1 (25.7)	−7.5 (4.0)	90.9 (21.5)	−12.8 (5.1)	
> 50	88.8 (4.4)	81.9 (6.3)	−7.8 (3.4)	76.7 (7.7)	−13.8 (4.9)	
Sex						
Male	139.3 (32.7)	128.5 (31.0)	−7.8 (4.5)	123.1 (31.0)	−11.8 (6.0)	
Female	91.8 (19.2)	82.8 (18.4)	−9.6 (4.2)	77.1 (16.9)	−16.6 (6.0)	
BMI category						
< 35	81.2 (11.9)	73.3 (12.2)	−10.0 (4.2)	68.4 (12.0)	−16.8 (8.0)	
35–40	92.6 (6.1)	83.3 (6.4)	−10.0 (3.6)	77.4 (8.1)	−17.1 (5.9)	
> 40	130.0 (21.2)	120.8 (23.2)	−7.5 (4.3)	115.2 (25.4)	−12.6 (6.6)	
Max-tolerated dose						
High (> 10 mg)	102.5 (30.0)	-	-	86.5 (28.4)	−16.2 (6.3)	
Low (< 10 mg)	89.7 (19.0)	-	-	79.0 (15.6)	−11.2 (4.0)	
Time from SG						
> 5 years	102.9 (32.5)	93.4 (30.9)	−9.6 (4.2)	90.6 (33.9)	−16.9 (5.8)	
< 5 years	96.1 (22.0)	87.3 (20.8)	−9.3 (4.4)	82.5 (19.4)	−14.8 (6.7)	

*p-value < 0.05 is reported

SD, standard deviation; *SG*, sleeve gastrectomy; *BMI*, body mass index

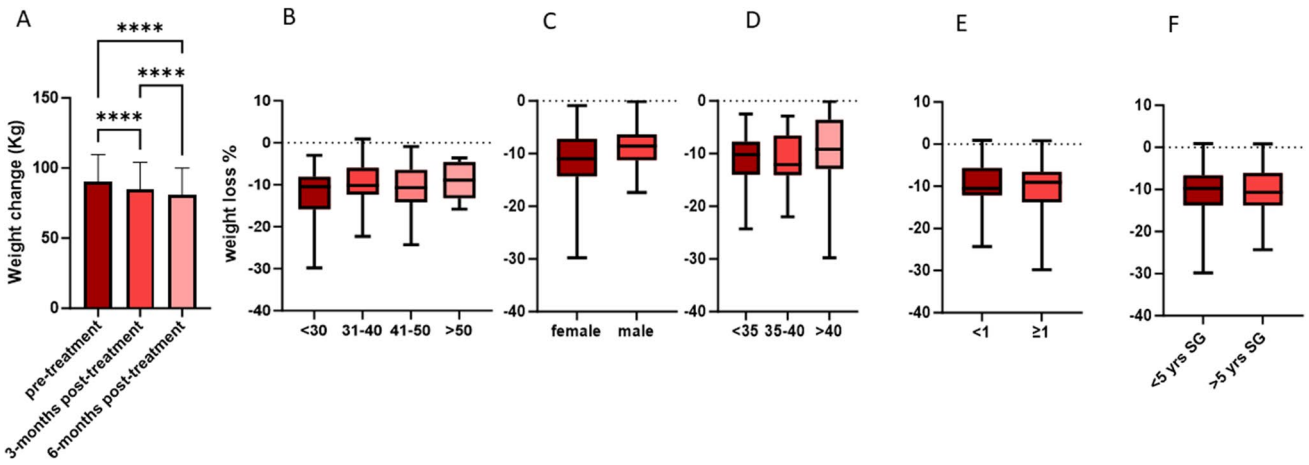

Fig. 2 Post-treatment weight change at 6 months of semaglutide patients. **A** For all patients, **B** by age groups, **C** by gender the duration of treatment, **D** by BMI, **E** by maximum-tolerated dose, and **F** by SG duration

[26]. Finally, in the BARI-OPTIMISE randomized clinical trial comparing liraglutide 3.0 mg vs placebo for the management of poor weight loss following metabolic surgery, Mok et al. showed a mean total body weight loss of around 9% after 24 weeks of treatment with liraglutide compared to placebo [27]. We previously published our experience with the use of daily liraglutide for weight recurrence post sleeve gastrectomy. The cohort had a similar total body weight recurrence to the current study of 23.6%. After 3 months of treatment with liraglutide, a mean weight loss of 6.2% was achieved. Those who tolerated a daily dose of 2.4 mg or above achieved a higher weight loss of 8.1% [10].

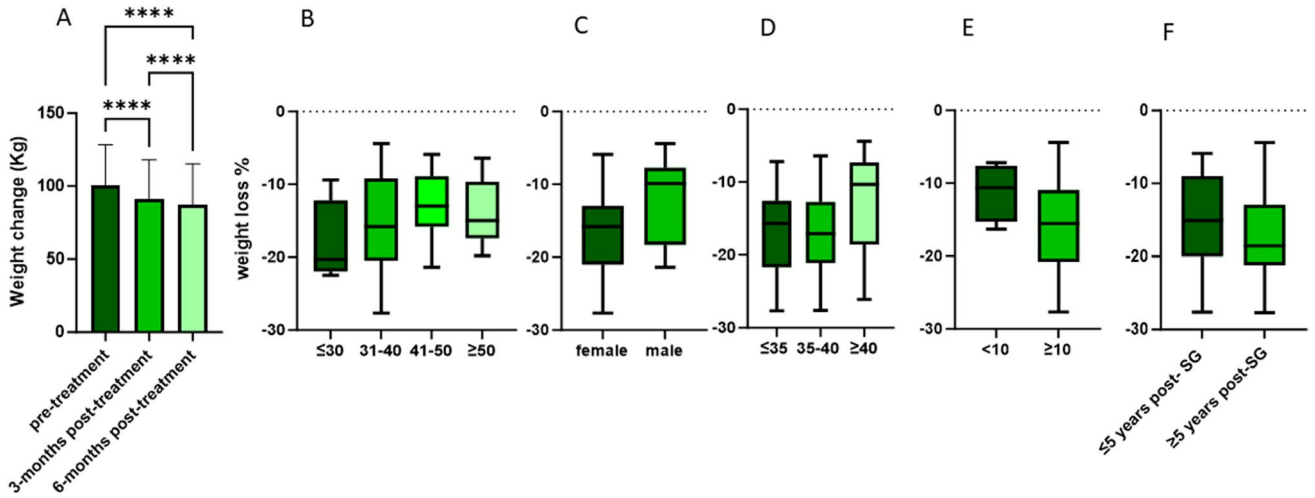

Fig. 3 Post-treatment weight change at 6 months of tirzepatide patients. **A** For all patients, **B** by age groups, **C** by gender the duration of treatment, **D** by BMI, **E** by maximum-tolerated dose, and **F** by SG duration

Tirzepatide has been shown in randomized controlled trials to result in the most significant weight loss in the treatment of obesity compared to other available medications [15]. A post hoc comparative analysis of the results of the STEP1 and SURMOUNT1, comparing tirzepatide 10 mg and 15 mg to semaglutide 2.4 mg found that patients treated with tirzepatide are more likely to achieve 5% weight loss in comparison to semaglutide [28]. Currently, none of the available weight loss medications is approved for the treatment of weight recurrence after bariatric surgery specifically, despite the growing evidence that postoperative pharmacotherapy can maximize weight loss, improve metabolic outcomes, and lower the risk of weight recurrence [29]. Therefore, this remains an underutilized intervention with great potential benefit for this population of patients.

A 5% reduction in body weight is considered as clinically significant threshold for weight loss success and is associated with improved quality of life and glycemic control, while weight loss greater than 10–15% is more clinically effective in the control of other obesity-associated comorbidities including hypertension, obstructive sleep apnea, polycystic ovarian syndrome, and depression [30]. In this study, after 6 months of treatment with semaglutide, 80% of patients achieved weight loss ≥ 5%, 48.6% of patients achieved ≥ 10% weight loss, and 26% achieved ≥ 15% weight loss, whereas with tirzepatide treatment for 6 months, 97.1% of patients achieved weight loss ≥ 5%, 74.3% of patients achieved ≥ 10% weight loss, and 57.1% achieved ≥ 15% weight loss. More than half of patients (68.6%) tolerated semaglutide dose ≥ 1 mg and none received a dose higher than 2 mg while 63.8% patients tolerated tirzepatide ≥ 10 mg, with 11 patients (24%) receiving the maximum dose of 15 mg. Several patients reported minor adverse events including headache, mild GERD, constipation, diarrhea, nausea, and vomiting but none stopped the medical therapy due to adverse outcomes and no severe adverse events were reported. There was no statistically significant difference between weight loss and patients-associated variables including age, BMI, time since the SG, and max-tolerated dose in both the groups. However, there was a more pronounced weight loss among female patients, which was statistically significant at 3 month in the semaglutide group. Female sex and age group of ≤ 30 years showed greater weight loss in both the groups at 6 month; however, it did not reach statistical significance. These results are in line with multiple previous studies demonstrating greater weight loss with GLP-1 agonists among female patients [31]. The lack of significant associations between weight loss and other patient characteristics contrasts with prior research that found a range of sociodemographic, clinical, and other patient-level factors to be major predictors of clinical efficacy and effectiveness [10, 14, 32]. However, these differences may not have been captured in this cohort due to the relatively small sample size.

The current study has several strengths and limitations. First, although retrospective study provides real-world data on the effectiveness of weight loss medications for the treatment of weight recurrence, it may include inherent biases that are not accounted for in the results. Second, the relatively small sample size and lack of control group may limit the generalization of the study results. Furthermore, the patients included in the study had the SG at different centers and by different surgeons at various times, and therefore, variations in technique and initial outcomes after surgery may contribute to their response to the treatment with weight loss medications. The superiority of tirzepatide to semaglutide cannot be fully ascertained since the semaglutide dose was not escalated to the maximum FDA-approved dose of 2.4 mg. Lastly,

the results of this study should be interpreted with caution. Although the weight loss outcomes at 6 months were comparable to previously published results of revisional surgeries at the same timepoint, these results only represent very early outcomes with short course of treatment, and the durability of these results with longer treatment or longer follow-up is not yet known. This is especially a concern since the results of the STEP 4 [33] trial, STEP 1 [34] trial extension, and the SURMOUNT-4 [35] study all showed significant weigh regain after withdrawal of semaglutide or tirzepatide treatment. This confirms the chronicity of obesity and the need for lifelong treatment. However, GLP-1 medications are costly and can represent a significant financial burden, and limits access to these medications and long-term compliance.

Nevertheless, despite these limitations, to our knowledge is the first study which provide real-world evidence regarding the effectiveness of semaglutide and tirzepatide in the treatment of weight recurrence after SG.

Conclusion

A meaningful weight loss was observed with the use of pharmacotherapy at 6 months in patients with weight recurrence after sleeve gastrectomy which was comparable to the weight loss after revisional surgeries without any of the patients discontinuing therapy due to adverse events. The study indicates that pharmacotherapy can be an effective alternative to weight recurrence or bariatric surgery with minimal adverse effects. However, weight regain after discontinuation of the medication is highly likely, and the high cost of these medications can limit their use. Further studies with larger sample sizes and longer follow-up periods are needed to strengthen the evidence on the benefits and safety of the treatment approach.

Data Availability The data supporting the findings of this study are available through the corresponding authors upon request.

Declarations

Conflict of Interest The authors declare no competing interests.

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Authors and Affiliations

Mohammad Jamal[1,2,3,4] · Mohsen Alhashemi[3,4] · Carol Dsouza[4] · Sara Al-hassani[4] · Wafa Qasem[2,5] · Sulaiman Almazeedi[3] · Salman Al-Sabah[3]

✉ Mohammad Jamal
mohammad.jamal@mail.mcgill.ca; u22mohjam@gmail.com

[1] Department of Organ Transplant, College of Medicine, Health Sciences Center, Kuwait University, Kuwait City, Kuwait

[2] The Clinic, Kuwait City, Kuwait

[3] Department of Surgery, Jaber Hospital, Kuwait City, Kuwait

[4] Department of Surgery, College of Medicine, Health Sciences Center, Kuwait University, Kuwait City, Kuwait

[5] Mubarak Hospital, Kuwait City, Kuwait