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ORIGINAL ARTICLE

Clinical Trials and Investigations

Semaglutide 2.4 mg/wk for weight loss in patients with severe obesity and with or without a history of bariatric surgery

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Abstract

Objective: This retrospective cohort study aimed to assess the effectiveness of semaglutide 2.4 mg in patients with severe obesity (BMI ≥ 40 kg/m^2) who had previously undergone bariatric surgery (BS) but failed to achieve satisfactory weight loss or experienced weight regain compared with patients without a history of BS with similar BMI.

Methods: The authors analyzed data from 129 patients with a BMI ≥ 40 kg/m^2, including 39 with (BS+) and 90 without (BS−) a history of BS. The patients received semaglutide treatment for 24 weeks starting at 0.25 mg/wk and gradually increasing to reach a final dose of 2.4 mg/wk. The treatment outcomes were assessed based on the percentage of weight loss, changes in BMI, and waist circumference.

Results: Semaglutide treatment resulted in significant 9.1% weight loss in the BS+ group, with no significant difference in weight loss between the BS+ and BS− groups.

Conclusions: This study is the first, to the authors' knowledge, to compare the effectiveness of semaglutide treatment in patients with versus those without a history of BS, providing valuable evidence of its efficacy. By focusing on individuals with severe obesity (BMI > 40 kg/m^2 and associated comorbidities), it fills a gap in the current literature and highlights the potential of semaglutide 2.4 mg as a treatment option for this specific population.

INTRODUCTION

Obesity is a growing public health issue worldwide, affecting more than 650 million adults [1] and leading to a range of serious health complications, including cardiovascular disease (CVD), hepatic steatosis, cancer, and obstructive sleep apnea syndrome (OSA) [2]. Despite the significant impact of obesity on health outcomes, drug therapies for weight control and reduction have proven largely disappointing until recently [3]. Bariatric surgery (BS) has emerged as an effective and risk-controlled strategy for managing obesity, with the potential to reduce weight by up to 30% in the general population and improve metabolic complications [4].

However, not all patients respond to BS, and some may experience weight regain or inadequate weight loss over time. Until recently, few alternative options existed for these patients other than a second BS. The development of glucagon-like peptide-1 (GLP-1) receptor analogs (GLP-1-RAs) has shown promising results in weight loss and management of metabolic complications in patients living with type 2 diabetes mellitus (T2DM) [5–9].

In particular, semaglutide at a dose of 2.4 mg/wk has demonstrated significant effects on weight loss among people living with obesity [10], leading to its approval for the treatment of obesity in individuals with or without diabetes by American and European agencies. However, the efficacy of semaglutide in patients with a body mass index (BMI) ≥ 40 kg/m^2 who have undergone BS and still have obesity-related comorbidities has not yet been fully evaluated. Previous studies have investigated the use of liraglutide [11–13] or semaglutide [14–16] at lower doses after BS, but few have specifically targeted this patient population. These studies show efficacy on weight loss with sometimes superior effects compared with a new BS [11]. None of these studies have specifically considered the population with BMI ≥ 40 kg/m^2, and none have compared this population with patients who have no history of BS.

Semaglutide at a dose of 2.4 mg/wk has been available in France since April 2022 under a temporary authorization for use known as "early access." It is currently eligible for temporary reimbursement by the French social security system for individuals with a BMI ≥ 40 kg/m^2 and associated comorbidities, including treated hypertension, treated dyslipidemia, a history of CVD, or OSA with equipment. Beyond the question of the efficacy of semaglutide in the population with a history of BS, the expected benefit compared with patients with no history of BS has not been clearly established.

The primary aim of our study was to compare the effectiveness of semaglutide treatment in patients who had previously undergone BS versus those who had not and to determine whether there were any differences in weight-loss outcomes. By examining this comparison, we aimed to provide insights into whether the effectiveness of semaglutide is influenced by prior BS, which could have implications for the management of obesity in this specific population.

Study Importance

What is already known?

- Bariatric surgery (BS) is an effective and risk-controlled strategy for managing obesity.
- Some patients do not respond to BS, whereas others experience weight regain or inadequate weight loss over time. Until recently, few alternative options existed for these patients other than another technique of BS.
- Semaglutide at a dose of 2.4 mg/wk has demonstrated significant effects on weight loss among patients living with obesity.

What does this study add?

- Our study supports the effectiveness of semaglutide 2.4 mg/wk in patients with a history of BS.
- After 24 weeks of treatment with semaglutide and gradually escalating the dose to reach 2.4 mg/wk, there was no difference in weight-loss outcomes between patients with and without a history of BS, with both populations being comparable at inclusion.
- The group with a history of BS did not experience an increase in side effects compared with the group without a history of BS.

How might these results change the direction of research or the focus of clinical practice?

- Our study highlights similar results between groups with and without a history of BS in terms of weight loss. Similarly, there were no differences in terms of side effects. Therefore, this treatment could be an alternative to avoid another BS, as well as a prospect for patients who face difficulty with the failure of a previous treatment. This treatment can also be used as a complement to BS for patients with the highest BMI values.

METHODS

Participants

This retrospective study included all patients who had previously undergone sleeve gastrectomy or gastric bypass and maintained a BMI ≥ 40 kg/m^2 within 6 months prior to initiating semaglutide either due to weight regain or insufficient weight loss, defined as an excess weight loss (EWL) < 50% 18 months post-BS [17, 18]. These patients presented with at least one associated complication among hypertension, dyslipidemia, history of CVD, or OSA with equipment, as required by health insurance in France. Semaglutide was prescribed for the management of obesity with a progressively increasing dose regimen. The treatment started at a dose of 0.25 mg/wk and was escalated in 4-week increments to achieve a target dose of 2.4 mg/wk, administered via subcutaneous injections. The dose escalation schedule was as follows: 0.25, 0.5, 1.0, 1.7, and 2.4 mg/wk, based on the patient's clinical tolerance. Patients with T2DM who were already receiving GLP-1-RA therapy were initiated on semaglutide at an intermediate dose.

All patients included in this study were recruited between April 2022 and October 2022 from the Nutrition-Diabetes Department of the University Hospital of Montpellier in Montpellier, France. They were compared with individuals without a history of BS. Inclusion criteria for all study participants were being at least 18 years old and having a glomerular filtration rate greater than 30 mL/min/1.73 m^2.

All patients included in this retrospective study had previously provided non-opposition consent for the use of their data for research purposes. The patients who had planned BS within 24 weeks of the initiation of treatment or reported plans for pregnancy following their consultation were not eligible for treatment with semaglutide 2.4 mg and therefore were not included in the study.

Side effects were considered when they involved stopping the treatment. We used the last observation carried forward method to

handle missing data for weight at 24 weeks. Patients who completed the 24 weeks of treatment were included in a specific analysis.

Data on age, sex, height (measured using a stadiometer in centimeters), weight (measured in underwear garments on calibrated scales in kilograms), BMI (calculated as weight in kilograms divided by height in meters squared), waist circumference (measured in centimeters at the midpoint between the lower border of the rib cage and the upper border of the iliac crests with a Caperscape V100 following standardized protocols), systolic blood pressure (measured automatically at rest in millimeters of mercury), and heart rate were collected. Additionally, information regarding complications of obesity such as T2DM, treated hypertension, treated dyslipidemia, history of CVD, or OSA with equipment was recorded. The type and time since BS (months) were recorded, as well as the lowest body weight obtained after surgery. All of the aforementioned data were collected by a physician.

Biological data as aspartate transaminase, i.e., serum glutamic-oxaloacetic transaminase (SGOT), glycated hemoglobin (HbA1c), blood lipid parameters (triglyceridemia, calculated or measured low-density lipoprotein [LDL] cholesterol and high-density lipoprotein cholesterol), and C-reactive protein were recorded. Fibrosis-4 (FIB-4) score was calculated according to the following formula: (Age [years] × SGOT [international units per liter])/(platelets [grams per liter] × √[SGPT (international units per liter)]). The biological data were not obtained centrally; rather, each patient visited their local laboratory for these measurements.

The primary endpoint of this study was to compare the percentage of total weight loss at 24 weeks between patients with (BS+) and those without (BS−) a history of BS.

The study was reviewed and approved by the Institutional Review Board of the University Hospital of Montpellier, France (identification number: IRB-MTP_2023_02_202301328).

Statistical analysis

We performed univariate analysis to describe baseline characteristics of the study participants. Categorical variables are presented as numbers and percentages, whereas continuous measures are presented as means and standard deviations. To assess differences between the BS + and BS− groups at baseline, a Student *t* test was used for continuous variables, and a χ^2 test was used for categorical variables.

For data analysis, we used the R package "TableOne." In the event of significant differences between the two groups in various variables (such as age, sex, and BMI) at the time of inclusion, we planned to conduct a matching of participants using the propensity score method.

To compare the measurements at baseline and after 24 weeks of treatment, we performed a paired Student *t* test. Additionally, to examine the weight change dynamics, we employed a mixed-effects linear model. The two groups (BS+ and BS−) were compared using a Student *t* test. The χ^2 test was used to compare differences in proportions between the groups, including the number of withdrawals for adverse events and the percentages of weight loss (5%, 10%, and 15%).

All statistical analyses were conducted by both intention-to-treat and per-protocol approaches. The intention-to-treat analysis included all 129 participants. The last observation carried forward was used to handle missing data for weight at 24 weeks. Sensitivity analyses using alternative missing data approaches, including multiple imputation, were conducted to validate the robustness of the results. For quantitative variables with less than 5% missing data, missing values were replaced by the mean. All statistical hypothesis tests were two-tailed with $p < 0.05$ considered significant. Statistical analyses and graphs were produced with R software (version 3.4.2).

RESULTS

From April 2022 to October 2022, we initially included 132 patients with a BMI of 40 kg/m^2 or higher and associated comorbidities (such as hypertension, dyslipidemia, history of CVD, or OSA with equipment) in our study. However, two patients who became pregnant (1 in the BS+ group and 1 in the BS− group) and one woman who underwent BS during the follow-up period were subsequently excluded. Consequently, a total of 129 patients were included in the final analysis. Unfortunately, one patient passed away 2 days after the first injection, which was reported to pharmacovigilance and determined not to be related to semaglutide (OSA with non-use of a positive airway pressure device at night for several months leading to major hypoxia, followed by cardiac arrest and death). Furthermore, during the course of treatment, 12 out of 129 patients (9.3%) experienced adverse events (2/39 in the BS+ group [5.1%] and 10/90 in the BS− group [11.1%]) and discontinued the treatment, 4 were considered as "lost to follow-up" (1/39 in the BS+ group [2.6%] and 3/90 in the BS− group [3.3%]), and 2 out of 90 patients from the BS− group (2.2%) discontinued the treatment due to lack of efficacy. Therefore, the final analysis of those who completed the full 24 weeks of semaglutide treatment was conducted on 111 patients. This group comprised 36 patients with (BS+) and 75 patients without (BS−) a history of BS (Figure 1). Among the 18 patients who discontinued the treatment before the 6-month period, the only statistically significant difference we observed in the rate of cessation was based on sex. Specifically, 12 out of these 18 patients were men, accounting for 66.6% of the discontinuations, in comparison with 6 women ($p < 0.01$). There was no significant difference in the incidence of side effects or early discontinuation between the BS+ group ($n = 3$, 7.7%) and the BS− group ($n = 15$, 16.7%; $p = 0.3$).

The demographic characteristics of the study population are given in Table 1. Among the patients in the BS+ group, 28 (71.8%) had a sleeve gastrectomy, whereas the remaining patients had undergone gastric bypass surgery. The mean BMI for this group was 45.7 ± 7.8 kg/m^2. The lowest mean weight after BS (nadir) was 96.1 ± 23.8 kg, with an average weight regain of 29.2 ± 17.0 kg. Eight patients (20.5%) had a nadir corresponding to a BMI > 40 kg/m^2. The percentage of EWL was higher among patients with a nadir corresponding to a BMI < 40 kg/m^2 (23.2% vs. 12.3%; $p = 0.01$). Among the patients in the BS− group, the mean BMI was 47.5 ± 8.7 kg/m^2.

The description of the populations who completed the 24 weeks of treatment is available in Table S1.

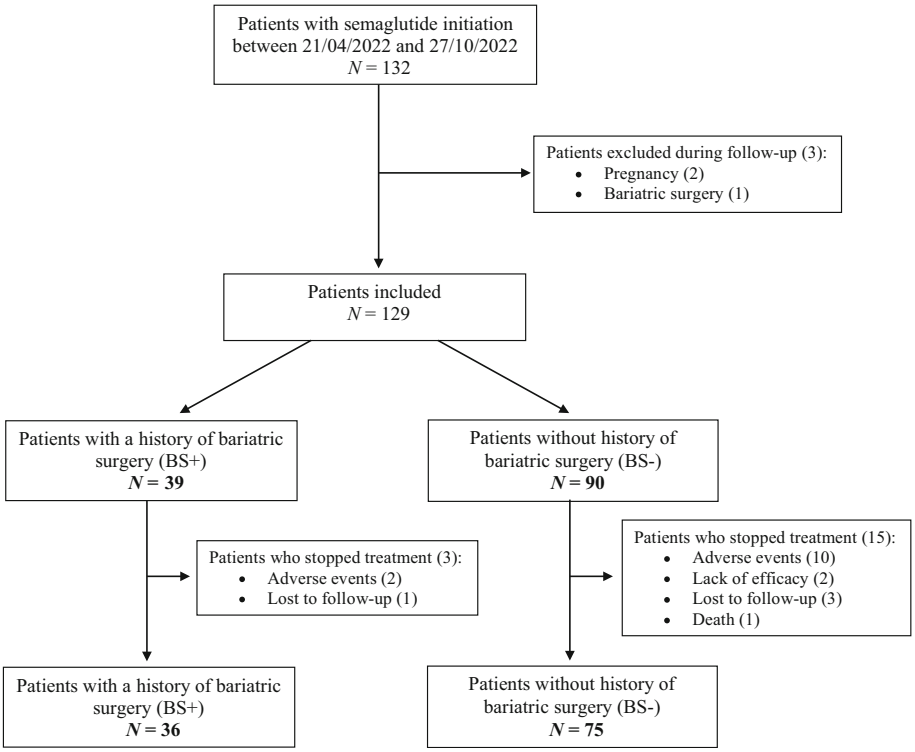


FIGURE 1 Study flowchart.

TABLE 1 Characteristics of the population at baseline

	Total ($N = 129$)		BS+ group ($n = 39$)		BS− group ($n = 90$)		*p* value
Age (y)	51.1 (13.4)		53.6	(10.8)	50.0	(14.5)	0.13
Male, *n* (%)	45 (34.9)		15	(38.5)	30	(33.3)	0.70
Body weight (kg)	128.0 (26.2)		125.2	(23.6)	129.1	(27.3)	0.40
BMI (kg/m^2)	46.9 (8.4)		45.7	(7.8)	47.5	(8.7)	0.30
Waist circumference (cm)	132.5 (14.9)		132.4	(15.8)	132.6	(14.6)	0.90
Dyslipidemia, *n* (%)	57 (44.2)		19	(48.7)	38	(42.2)	0.60
Established CVD, *n* (%)	20 (15.5)		9	(23.1)	11	(12.2)	0.20
OSA, *n* (%)	75 (58.1)		21	(53.8)	54	(60.0)	0.60
Family history of T2DM, *n* (%)	30 (23.3)		13	(33.3)	17	(18.9)	0.12
Family history of obesity, *n* (%)	70 (54.3)		24	(61.5)	46	(51.1)	0.40
T2DM, *n* (%)	25 (19.4)		9	(23.1)	16	(17.8)	0.60
BS							
Type, *n* (%)							
SG			28	(71.8)			
RYGB			13	(33.3)			
Nadir (kg)			96.1	(23.8)			
Weight regain			29.2	(17.0)			
Length of time since last BS (y)			8.4	(4.4)			
Weekly dosage of semaglutide (mg)	0.37 (0.37)		0.39	(0.37)	0.37	(0.38)	0.79

Note: Data are means (standard deviation) unless otherwise noted. The *p* value column represents the comparison between the BS− and BS+ groups using a two-sample Student *t* test.

Abbreviations: BS, bariatric surgery; BS+, patients with a history of BS; BS−, patients without a history of BS; CVD, cardiovascular disease; OSA, obstructive sleep apnea syndrome; RYGB, Roux-en-Y gastric bypass; SG, sleeve gastrectomy; T2DM, type 2 diabetes mellitus.

The mean weekly dose of semaglutide was 2.35 ± 0.32 mg/wk at week 24 for the BS+ group and 2.33 ± 0.30 mg/wk for the BS− group ($p = 0.76$). Results regarding weight change, BMI evolution, and waist circumference measurements for the entire population are available in Table 2. For those who completed 24 weeks of treatment, these results, along with the evolution of biological variables, are presented in Table 3 and in Table S2.

In the BS+ group, semaglutide treatment resulted in a weight loss of 9.8% ± 5.7% and an EWL of 23.2% ± 14.9% ($p < 0.001$). The change in waist circumference was 9.2 ± 5.8 cm ($p < 0.01$). A total of 72% of patients in the BS+ group lost at least 5% of their initial body weight, 36% lost at least 10%, and 8% lost at least 15% (Figure 2). There was no difference in weight-loss outcomes between patients with a history of sleeve gastrectomy or gastric bypass ($p = 0.42$). All changes in the characteristics of the BS+ group before and after 24 weeks of treatment are available in Table 3.

In the BS− group, semaglutide treatment resulted in a weight loss of 8.7% ± 5.4% ($p < 0.001$) and an EWL of 19.7% ± 12.4%

TABLE 2 Evolution of anthropometric characteristics from baseline to 24 weeks

	Total ($N = 129$)	BS+ group ($n = 39$)		BS− group ($n = 90$)		p value
Weight loss (%)	−9.1 (5.5)	−9.8	(5.7)	−8.7	(5.4)	0.27
EWL (%)	−20.8 (13.3)	−23.2	(14.9)	−19.7	(12.4)	0.23
Change in BMI (kg/m^2)	−4.2 (2.6)	−4.3	(2.4)	−4.1	(2.7)	0.70
Change in body weight (kg)	−11.3 (7.2)	−11.6	(6.3)	−11.2	(7.6)	0.70
Change in waist circumference (cm)	−8.3 (6.0)	−9.2	(5.8)	−7.8	(6.0)	0.30

Note: Data are means (standard deviation). The p value column represents the comparison between BS− and BS+ using a two-sample Student t test. Change scores within each group (BS+ and BS−) were statistically significant for all variables from baseline to 24 weeks using a paired Student t test ($p < 0.001$).
Abbreviations: BS, bariatric surgery; BS+, patients with a history of bariatric surgery; BS−, patients without a history of bariatric surgery; EWL, excess weight loss.

TABLE 3 Evolution of anthropometric and biological characteristics from baseline to 24 weeks of patients who actually benefited from the treatment for 24 weeks

	BS+ group ($n = 36$)		BS− group ($n = 75$)		p value
Weight loss (%)	−9.8%	(5.7)[a]	−8.8%	(5.3)[a]	0.37
EWL (%)	−23.2	(14.9)[a]	−20%	(12.4)[a]	0.23
Change in anthropometric characteristics					
BMI (kg/m^2)	−4.3	(−5.1 to −3.5)	−4.2	(−4.8 to −3.6)	0.77
Body weight (kg)	−11.6	(−13.8 to −9.5)	−11.3	(−13.1 to −9.6)	0.83
Waist circumference (cm)	−9.2	(−11.1 to −7.2)	−8.0	(−9.4 to −6.5)	0.30
Systolic blood pressure (mm Hg)	0.13	(−5.8 to −6.0)	−1.69	(−5.3 to 1.9)	0.58
Heat rate (beats/min)	1.5	(−3.6 to 6.5)	6.8	(3.0 to 10.6)	0.10
Change in biological characteristics					
HbA1c (percentage points)	−0.44	(−0.65 to −0.23)	−0.42	(−0.55 to −0.29)	0.89
SGOT (UI/L)	−10.6	(−20.7 to −0.5)	−3.3	(−5.5 to −1.1)	0.16
SGPT (UI/L)	−12.6	(−27.1 to 1.9)	−6.0	(−10.4 to −1.4)	0.38
HDL cholesterol (mmol/L)	−0.02	(−0.07 to 0.03)	−0.04	(−0.09 to 0.02)	0.33
LDL cholesterol (mmol/L)	−0.1	(−0.59 to −0.05)	−0.19	(−0.31 to −0.06)	0.42
Triglycerides (mmol/L)	−0.25	(−0.43 to −0.08)	−0.15	(−0.27 to −0.03)	0.32
C-reactive protein (nmol/L)	9.9	(−1.28 to 3.25)	3.5	(−1.83 to 2.53)	0.68
Change in FIB-4	−0.16	(−0.28 to −0.04)	−0.08	(−0.19 to 0.02)	0.36
Weekly dosage of semaglutide at 24 wk (mg)	2.35	(0.32)	2.33	(0.30)	0.76

Note: Data are means (standard deviation or 95% confidence interval). The p value column represents the comparison between the BS− and BS+ groups using a two-sample Student t test.
Abbreviations: BS, bariatric surgery; BS+, patients with history of BS; BS−, patients without history of BS; EWL, excess weight loss; FIB-4, fibrosis-4; HbA1c, glycated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein; SGOT, serum glutamic-oxaloacetic transaminase; SGPT, serum glutamate-pyruvate transaminase.
[a]Denotes that change from the baseline is statistically significant according to a Student t test and $p < 0.001$.

($p < 0.001$). The change in waist circumference was 7.8 ± 6.0 cm ($p < 0.01$). A total of 62% of patients in the BS− group lost at least 5% of their weight, 31% lost at least 10%, and 8% lost at least 15% (Figure 2). All changes in the characteristics of the BS− group before and after 24 weeks of treatment are available in Table 3.

There was no significant difference in mean weight loss, EWL, BMI change, or waist circumference change between patients in the BS+ and BS− groups from baseline to 24 weeks (Table 2). Additionally, our analysis using the mixed-effects linear model did not reveal any significant difference in the dynamics of weight loss between the two groups over the entire treatment period, including baseline, 12 weeks, and 24 weeks (Figures 3 and 4, Figures S1 and S2). We also did not find any differences in the dynamics of weight loss between patients with a history of sleeve gastrectomy or gastric bypass (Figures S3 and S4). The proportion of patients who achieved a weight loss of at least 5%, 10%, and 15% did not differ between the BS+ and BS− groups ($p = 0.29$, $p = 0.59$, and $p = 0.98$, respectively; Figure 2).

For patients who completed 24 weeks of treatment, HbA1c was lower in both the BS+ and BS− groups after 24 weeks. We have the same observation for blood levels of LDL cholesterol, triglycerides, and SGOT. We noted a decrease in FIB-4 score in the overall population ($p < 0.01$) and in the BS+ group ($p = 0.01$), but not in the BS− group ($p = 0.1$). There was no difference in the evolution of metabolic data between the BS+ and BS− groups (Table 3).

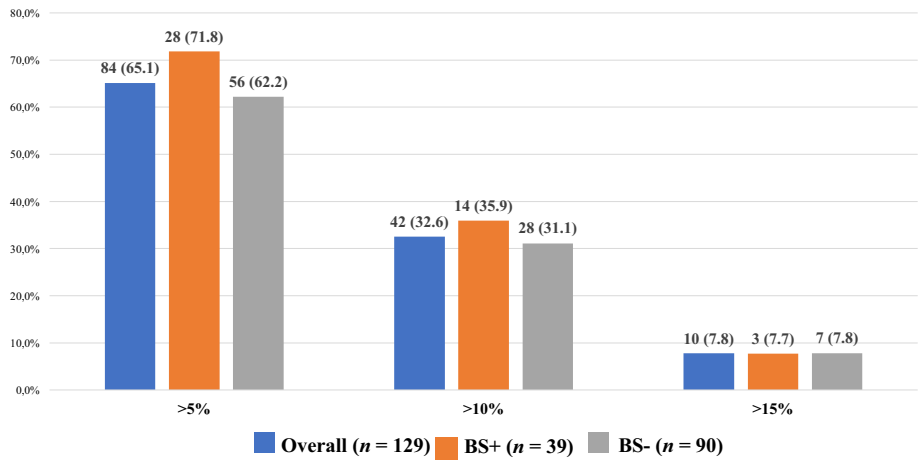
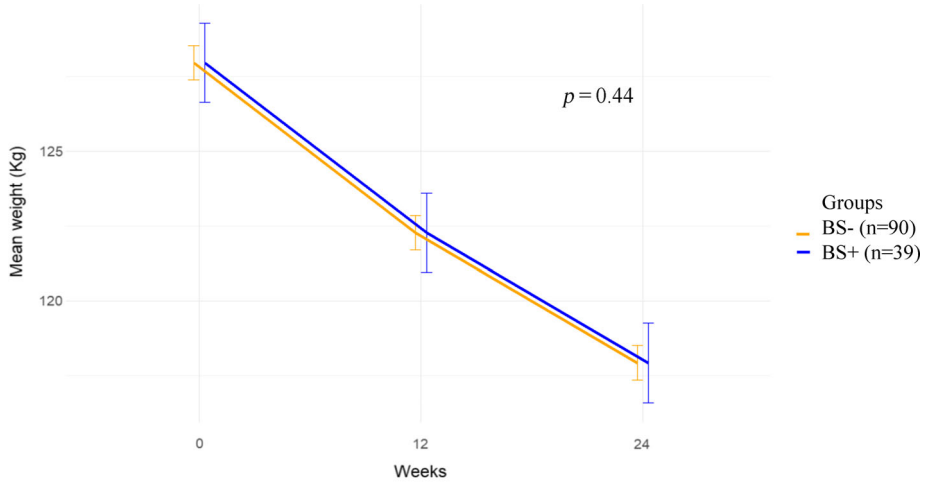
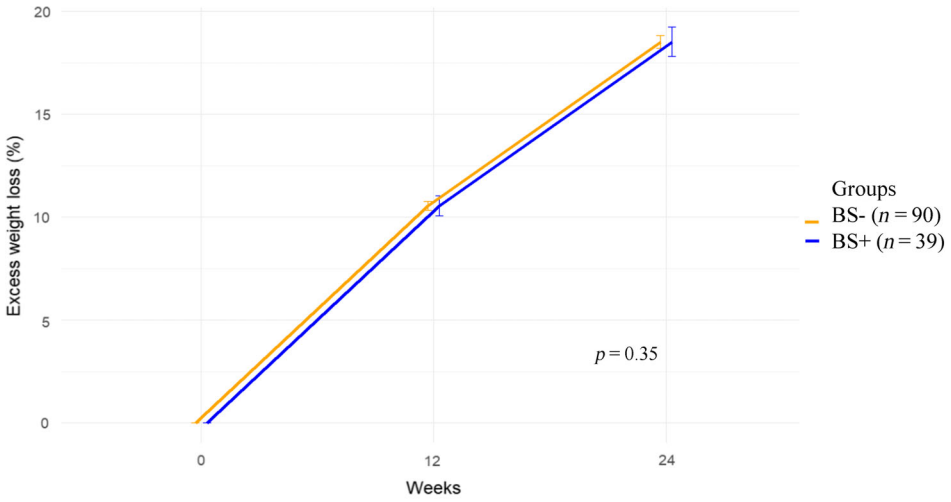


FIGURE 2 Weight-loss thresholds at week 24 after initiation of treatment with semaglutide. Intention-to-treat analysis. Data are presented as number (percentage). BS, bariatric surgery; BS+, patients with a history of BS; BS−, patients without a history of BS. [Color figure can be viewed at wileyonlinelibrary.com]



Note: P-value represents the comparison between BS- and BS+ obtained using a mixed-effects linear model.

FIGURE 3 Weight change at 12 and 24 weeks. Intention-to-treat analysis. BS, bariatric surgery; BS+, patients with a history of BS ($n = 39$); BS−, patients without a history of BS ($n = 90$). [Color figure can be viewed at wileyonlinelibrary.com]



Note: P-value represents the comparison between BS- and BS+ obtained using a mixed-effects linear model.

FIGURE 4 Excess weight loss under semaglutide at 12 and 24 weeks. Intention-to-treat analysis. BS, bariatric surgery; BS+, patients with a history of BS ($n = 39$); BS−, patients without a history of BS ($n = 90$). [Color figure can be viewed at wileyonlinelibrary.com]

DISCUSSION

Our study uniquely provides real-world evidence of the effectiveness of semaglutide in patients with a history of BS who have not achieved sufficient weight loss or who have experienced weight regain. Notably, our research is distinctive in its approach of comparing the efficacy of semaglutide between patients with and without a history of BS, which is an element not specifically addressed in previous studies [11–16]. Moreover, this is the first study of its kind, to our knowledge, to exclusively focus on individuals with severe obesity, defined as having a BMI greater than 40 kg/m^2 and associated comorbidities (hypertension, dyslipidemia, history of CVD, or OSA with equipment). After 24 weeks of treatment with semaglutide and gradually escalating the dose to reach 2.4 mg/wk in the final 2 months, we revealed, for the first time, that there was no difference in weight-loss outcomes between patients with and without a history of BS, with both populations being comparable at the initiation of treatment.

We observed a significant weight loss of 9.1% across the entire study population and 9.8% specifically in patients with a history of BS. In comparing our results obtained in a real-world setting to previous randomized controlled trials (RCTs), the weight loss achieved with semaglutide at 24 weeks in our study was consistent with the weight loss reported in RCTs investigating the efficacy of semaglutide [10, 19, 20]. For example, the Semaglutide Treatment Effect in People with Obesity (STEP) 1 and STEP 5 studies reported a weight loss of approximately 10% with semaglutide 2.4 mg at 24 weeks [10, 19]. Importantly, our study population had a higher BMI compared with the participants in these RCTs, which adds to the significance of our findings in a specific population of patients with severe obesity.

Furthermore, statistical analysis showed no significant difference in weight-loss outcomes between patients with and without a history of BS. These findings align with prior studies that have examined the efficacy of GLP-1-RAs in managing obesity [11–16]; however, our study is distinctive as the first, to our knowledge, to employ the higher dose of semaglutide, which is currently recommended for individuals living with obesity. This outcome implies that post-BS alterations in hormonal secretions or changes in gut microbiota do not significantly influence the response to GLP-1-RAs [21]. This insight is important given that one might initially presume that individuals with a history of BS, especially those who have experienced significant weight regain, would exhibit a diminished response to pharmacotherapy. As such, clinicians can anticipate similar efficacy from semaglutide treatment whether or not a patient has a history of BS.

Although our study's primary objective did not focus on evaluating the impact of weight loss on obesity-related comorbidities, we observed notable improvement in HbA1c, liver transaminases, and LDL cholesterol levels within the overall population, as well as in both the groups with and without a history of BS. These findings align with established knowledge regarding the benefits of GLP-1-RAs [22]. Importantly, we also observed a significant improvement in the FIB-4 score within the entire population and among patients with a history of BS, although not among those without such a history. GLP-1-RA therapies have emerged as a promising avenue of research for the treatment of nonalcoholic steatohepatitis (NASH) and associated diseases [23], and previous results have shown improvement in NASH, but not in liver fibrosis [24, 25]. Our results suggest that clinicians can anticipate similar metabolic improvements in patients with a history of BS compared with those without such a history.

In our study, the mean weekly dose of semaglutide at week 24 for those who completed the 24 weeks of treatment was 2.3 ± 0.3 mg/wk in both the BS+ and BS− groups. This finding indicates that both groups were mostly able to tolerate the recommended dose for obesity treatment of 2.4 mg without significant issues. Importantly, our study demonstrated that the BS+ group did not experience an increase in side effects compared with the BS− group, providing reassurance about the safety and tolerability of semaglutide

in this specific population. These findings are consistent with previous studies that have reported the generally favorable tolerability profile of GLP-1-RAs, with the most reported side effects being of gastrointestinal nature and generally not severe.

Several limitations should be acknowledged in our study. First, the retrospective nature of our analysis, although providing real-world insights, may introduce inherent biases that could impact the interpretation of our findings. Second, the relatively small sample size of our study, particularly in the gastric bypass group ($n = 13$), is a major weakness that might limit the generalizability of our results and reduce the statistical power to detect differences between groups. We would like to emphasize that the difference in weight loss between the BS+ and BS− groups was minimal both in percentage and in absolute value. Therefore, if a larger sample size could make it possible to show a statistically significant difference, it is important to note that the clinical significance of these differences in weight loss would remain uncertain. The impact of a larger sample size on the findings and conclusions may therefore be limited.

Furthermore, although we collected biological data, it is important to note that these measurements were obtained from local laboratories visited by each patient, introducing the potential for variability in measurement procedures; therefore, caution should be exercised in interpreting these data.

Nevertheless, despite these limitations, our study yields valuable real-world evidence regarding the effectiveness of semaglutide 2.4 mg in a specific population of patients living with severe obesity (BMI greater than 40 kg/m^2) who have undergone BS. This information is of paramount importance because there is a paucity of data on the use of semaglutide 2.4 mg in this specific population, and our results contribute to the knowledge base informing both research and clinical practice.

One important consideration is that the full effect of semaglutide treatment may not have been reached within the relatively short duration of our study, which lasted for 6 months. This is particularly relevant because the dose of semaglutide was progressively escalated over the course of 5 months, with patients reaching the maximum dose of 2.4 mg/wk for only 2 months. Therefore, it is crucial to acknowledge that the observed weight loss effects may not reflect the complete potential of semaglutide in this specific population. Longer-term follow-up studies extending beyond 1 year are warranted to fully evaluate the sustained and optimal effects of semaglutide treatment in patients with a history of BS.

Additionally, it is important to highlight that we did not collect detailed information on the previous weight dynamics of patients with a history of BS, which could have provided further insights into the influence of prior weight loss and regain on the response to semaglutide treatment. Future studies addressing this aspect could enhance our understanding of the impact of previous weight dynamics on treatment outcomes.

Our study provides valuable evidence supporting the efficacy of semaglutide at a dose of 2.4 mg/wk as a potential treatment option for patients with a history of BS who have not achieved satisfactory weight loss or have experienced weight regain and who maintain a BMI of 40 kg/m^2 or higher. These findings contribute to the growing body of knowledge on the use of semaglutide and highlight the potential of GLP-1-RA therapies as valuable treatment options for individuals living with obesity, particularly those with a BMI greater than 40 kg/m^2.

Our study provides compelling evidence supporting the efficacy of semaglutide at a dose of 2.4 mg/wk as a promising treatment option for patients with a history of BS who have struggled to achieve satisfactory weight loss or have experienced weight regain, even among those with a BMI greater than 40 kg/m^2. These findings contribute significantly to the existing knowledge on semaglutide and emphasize the potential of GLP-1-RA therapies in addressing the complex challenge of obesity management.

These results have important clinical implications because they suggest that semaglutide could be an effective alternative for individuals with a history of BS who require additional support in their weight-loss journey. Furthermore, the comparable weight-loss outcomes between patients with and without a history of BS highlight the potential of semaglutide as a viable treatment option for severe obesity, irrespective of previous surgical interventions.

However, further research is warranted to validate and expand upon our findings. RCTs comparing semaglutide with other treatment modalities, including a second BS, in patients with a history of BS and inadequate weight loss or weight regain would provide valuable insights. Additionally, longer-term follow-up studies are needed to evaluate the durability of the observed weight-loss outcomes.

In conclusion, our study contributes novel real-world evidence supporting the effectiveness of semaglutide in patients with a history of BS who face challenges in weight management. These findings have the potential to inform clinical decision-making and guide future research efforts aimed at improving outcomes in this specific patient population. As the global prevalence of obesity continues to rise, it is imperative to identify and evaluate innovative therapeutic approaches, and our study sheds light on the promising role of semaglutide in this context.O

AUTHOR CONTRIBUTIONS

Research idea and study design: Jean-Baptiste Bonnet, Sarah Tournayre, Ariane Sultan, and Antoine Avignon; Data acquisition: All authors; Data analysis/interpretation: Jean-Baptiste Bonnet, Sarah Tournayre, and Jean Anitcheou; Statistical analysis: Jean Anitcheou; Supervision or mentorship: Ariane Sultan and Antoine Avignon. Each author contributed important intellectual content during manuscript drafting or revision and agrees to be personally accountable for the individual's own contributions.

CONFLICT OF INTEREST STATEMENT

The authors declared no conflict of interest.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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