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Marked weight loss on liraglutide 3.0 mg: Real-life experience of a Swiss cohort with obesity

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Abstract

Objective: This study investigated the effectiveness of liraglutide 3.0 mg daily in combination with a standardized multidisciplinary intervention on body weight and body composition changes in a real-life setting.

Methods: A prospective, observational cohort study design was used. Adult patients with BMI > 35 kg/m^2, or BMI > 28 kg/m^2 with greater than or equal to one metabolic comorbidity, were included (n = 54, 65% women). Liraglutide treatment was covered by Swiss health insurance. Clinical and biological data were collected at baseline, 4 months, and 10 months. Body composition was assessed by dual-energy x-ray absorptiometry at baseline and 10 months.

Results: At 10 months, mean (SD) percentage weight loss (WL%) was −12.4% (5.5%) or −14.1 (6.6) kg. WL% was ≥5% in 87% of patients at 4 months and in 96% at 10 months. WL% was higher in women (−9.5% [3.1%] vs. men −7.2% [2.5%], p = 0.02) at 4 months and persisted at 10 months (−13.7% [5.2%] vs. −9.6% [5.1%], p = 0.006). WL% was associated with baseline percentage fat mass but not with age or BMI. Body composition showed a decrease in fat mass, visceral adipose tissue, and absolute lean mass.

Conclusions: In a real-world setting, liraglutide 3.0 mg led to beneficial changes in WL and body composition, with a greater impact in women.

INTRODUCTION

Obesity is a major public health issue with increased morbidity and reduced life expectancy. The cumulative prevalence of overweight and obesity in the adult Swiss population in 2017 was 11.3% [1]. Efficacy trials have shown that lifestyle interventions can reduce body weight by 5% to 10%; however, in the real-world setting, effectiveness has not been very successful. Lifestyle modifications with a reduction of food intake and an increase in physical activity have not allowed for consistent weight loss in the long term because of physiological counter-regulatory mechanisms [2, 3]. Thus, new strategies have emerged for prevention and treatment of obesity. Among them, glucagon-like peptide-1 receptor agonists (GLP1RAs) have appeared to be effective and safe for the treatment of obesity by reducing appetite and calorie intake [4, 5].

Body weight loss leads not only to fat mass (FM) reduction, but also to an inevitable decrease in lean mass (LM). LM is an important metabolically active tissue contributing to increased resting energy expenditure and improved muscular strength and body functional capacity [6, 7]. During dietary energy restriction, LM loss is estimated

to be 25% of lost weight [8], and after Roux-en-Y gastric bypass (RYGB) a 10% to 45% decrease in LM has been reported after 1 year [9–16]. Therefore, counseling for dietary protein intake as well as regular physical activity is part of weight-loss management to limit LM loss.

Beyond randomized trials, the beneficial effect of the GLP1RA drug liraglutide 3.0 mg, combined with lifestyle modifications, has been demonstrated in few real-world studies with approximately 60% of the enrolled population experiencing a 5% reduction of initial body weight [17–19]. However, there is little data on body composition changes from real-life studies [20], and it is not known whether there are sex-specific differences in weight loss or in body composition changes. Moreover, in most of the published real-world studies, liraglutide treatment has been paid by the patients, which may affect adherence and induce prescription of lower dosages [18, 19, 21].

Recent recognition of obesity as a disease by various medical associations tends to change the financial implications of health care systems with respect to the management of obesity. Since April 2020, liraglutide 3.0 mg has been reimbursed in Switzerland for a maximum of 3 years for patients with obesity and patients with overweight with metabolic comorbidities. This reimbursement is conditional on intermediate results in terms of weight loss, but the effectiveness of this program has not been documented.

The aim of the current report was to evaluate among real-life patients the effect of liraglutide treatment (3.0 mg/d) in combination with dietary intervention and physical activity counseling from a Swiss obesity clinic to determine (1) clinical effectiveness in terms of weight loss and body composition changes and (2) whether liraglutide effects on weight loss are sex specific.

Study Importance

What is already known?

- The clinical efficacy of liraglutide 3.0 mg has been established in randomized controlled clinical trials and in a few real-world studies with partial or full payment for treatment by patients, which may result in motivational and affordability biases.
- Few studies have examined body composition changes and sex-specific differences with liraglutide 3.0 mg in real-life settings.

What does this study add?

- Multidisciplinary management focusing on eating behavior and full reimbursement of treatment by health insurance resulted in greater weight loss than observed in other real-world studies.
- Sex-specific body composition, with a higher amount of fat mass in women, influences response to treatment with greater weight loss in women.

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

- Our results highlight the potential need to adapt weight-loss targets according to sex.
- Although more studies are needed to analyze the long-term clinical and economic outcomes, our results are opening the door for the implication of the health system in the reimbursement of this treatment for obesity.

METHODS

Study design and participants

This prospective, observational cohort study included patients recruited from a single academic center at the Center Hospitalier Universitaire Vaudois (CHUV) in Lausanne, Switzerland. All adult patients who started liraglutide for weight loss between April 2020 and February 2021 were included, and data were collected until February 2022. Exclusion criteria included type 2 diabetes, previous treatment with GLP1RAs, history of bariatric surgery, or use of other treatments for obesity (orlistat). The index date was defined as the date the participant initiated liraglutide. Treatment was started at a dose of 0.6 mg once a day, increasing the dose by 0.6 mg every week to reach the maintenance dose of 3 mg by week 5. A slower dose progression was used if patients exhibited notable side effects. In Switzerland, liraglutide is reimbursed in adults with BMI > 35 kg/m^2, or BMI > 28 kg/m^2 with at least one metabolic comorbidity (hypertension, prediabetes, or dyslipidemia). Reimbursement continues after the first 4 months from the index date if weight loss is ≥7% in patients with BMI ≥ 35 kg/m^2 or if weight loss is ≥5% in patients with BMI ≤ 35 kg/m^2. At 10 months, the reimbursement is continued only if an additional weight loss of ≥5% is observed. The study was approved by the Institutional Ethics Committee of the University of Lausanne in accordance with the Declaration of Helsinki principles, and all participants gave written informed consent.

Patient visits

Clinical and biological data were collected at baseline and at 4 months and 10 months after the index date. Multidisciplinary care with medical, nurse, and dietitian visits was performed (Supporting Information Figure S1). Medical visits occurred 2 to 4 months before liraglutide treatment (M0), at 4 months (M1), and at 10 months (M2). These time points were consistent with the insurance requirements to evaluate weight-loss goals. Four nurse visits were scheduled at day 1 of treatment (index date), 4 weeks, 14 weeks, and 38 weeks to collect clinical data including anthropometric measures (e.g., weight, waist circumference), perform fasting blood sampling, and promote physical activity. All patients were counseled for moderate-intensity physical activity for 150 min/wk. Dietary intervention consisted of group and individual sessions. The objectives

before starting liraglutide were to (1) allocate at least 20 minutes per meal, (2) correctly interpret hunger and satiety, (3) regulate meal schedules, (4) reduce snacking between meals, and (5) avoid liquid calories. To do this, subjects participated in a group intervention consisting of four 2-hour nutrition education sessions prior to therapy in addition to two individual nutrition sessions (D1 and D2). Dietary counseling was also provided at the index date, 8 weeks, 24 weeks, and 38 weeks (D3–D7). Side effects, including gastrointestinal tolerance, were assessed at each visit. Nutritional behavior was assessed by a validated self-questionnaire for the detection of binge-eating (Bulimic Investigatory Test, Edinburgh [BITE]) at each medical visit [22]. BITE scores >9 are suggestive of eating disorder symptoms.

Study variables

Clinical and biological data

In order to assess the improvement in clinical parameters, we performed an overnight fasting metabolic profile at baseline and at 4 months and 10 months of liraglutide for glucose, hemoglobin A_{1c} (HbA_{1c}), insulin, high-sensitivity C-reactive protein (hsCRP), and lipids (low-density lipoprotein [LDL] cholesterol, high-density lipoprotein [HDL] cholesterol, and triglycerides). Standard biological assays were performed in accredited clinical chemistry laboratories in Switzerland. Homeostatic model assessment of insulin resistance (HOMA-IR) was calculated as glycemia (mmol/L) × insulin (U/L)/22.5 [23]. Dyslipidemia was defined as the presence of one or more abnormal plasma lipid concentrations (LDL cholesterol > 3 mmol/L, triglycerides > 2.3 mmol/L) or use of statins [24]. Prediabetes was diagnosed based on HbA_{1c} (5.7%–6.5%) or fasting glycemia (5.6–6.9 mmol/L).

To assess the effect of liraglutide on nonalcoholic fat liver disease (NAFLD), hepatic tests (aspartate transaminase, alanine transaminase, γ-glutamyl transferase, alkaline phosphatase, platelets, albumin) and liver ultrasound (Philips, Epiq 7G) were performed before and after 10 months of treatment. NAFLD fibrosis score was calculated as previously described [25].

Anthropometric parameters

Patients were weighted barefoot in light clothes (0.2–0.4 kg) with a precision of 0.1 kg and were measured with a fixed-wall stadiometer with a precision of 0.1 cm. Body weight loss was defined as the difference in weight at follow-up compared with baseline weight. Dual-energy x-ray absorptiometry (DXA; GE Healthcare Lunar iDXA) was used to assess body composition before and after 10 months of treatment [10]. Briefly, participants were placed centered on the scanning field in a supine position, with palms down and arms at sides, slightly separated from the trunk. Regions of interest included total body, trunk, android, gynoid, upper limbs, and lower limbs. Total mass, total FM, and total LM were calculated by the GE Lunar iDXA software. Visceral adipose tissue (VAT) was determined using DXA CoreScan software. This software is highly reliable for the measurement of VAT compared with MRI [26]. LM included skeletal muscles and organs. FM and LM were expressed as a percentage of total body weight, and the appendicular lean mass index (ALMI) was calculated as the ratio of the addition of the four limbs LM (kilograms) over height (meters) squared. Fat mass index (FMI) was calculated by dividing total FM (kilograms) by the height (meters) squared.

TABLE 1 Anthropometric data at baseline, after 4 months, and after 10 months of liraglutide treatment

	Baseline	After 4 months	After 10 months
Age (y)	43.6 ± 11.6	–	–
Female	35/54 (65%)	35/54 (68%)	33/49 (67%)
Weight (kg)	115.2 ± 19.6	106.1 ± 18.2*	101.0 ± 18.5§
BMI (kg/m^2)	40.8 ± 5.7	37.5 ± 5.4*	35.8 ± 5.4§
Waist circumference (cm)	116.3 ± 17.5	107.0 ± 15.7*	106.6 ± 22.1§
Weight loss (kg)	–	−10 ± 3.7	−14.1 ± 6.6
Weight loss (%)	–	−8.7 ± 3.1	−12.4 ± 5.5

Note: Data expressed as mean ± SD.
*$p < 0.05$ between baseline and 4 months.
§$p < 0.05$, between baseline and 10 months.

Outcomes

Primary outcomes were absolute and percentage weight change at 4 and 10 months after the index date. Secondary outcomes included percentage of patients achieving weight reduction ≥5% and ≥10% from baseline to 4 and 10 months, change in body composition from baseline to 10 months, and percentage of patients achieving prediabetes, hypertension, dyslipidemia, and NAFLD remission 10 months after the initiation of liraglutide therapy.

Statistical analysis

Continuous variables were expressed as mean (SD). Categorical variables were expressed as percentages. Standard descriptive analyses were used to summarize the study variables. Comparisons between groups (e.g., according to sex or BMI) were assessed using the Mann–Whitney *U* test. Differences between time points (baseline, 4 months, 10 months) were assessed using a paired *t* test. Univariable and multivariable linear regression models were used to find associations between weight loss and explanatory variables such as sex, age, baseline BMI, and baseline FM. Regression analysis was performed based on weight loss at 4 months (when weight loss was more important). Interaction between weight loss and sex was tested by adding an interaction term (baseline FM%) in the multivariable regression. A two-sided *p* value of 0.05 was considered significant. The primary and secondary outcomes (at each time point) were analyzed as per-treatment analysis, so results refer to subjects who actually received the medication.

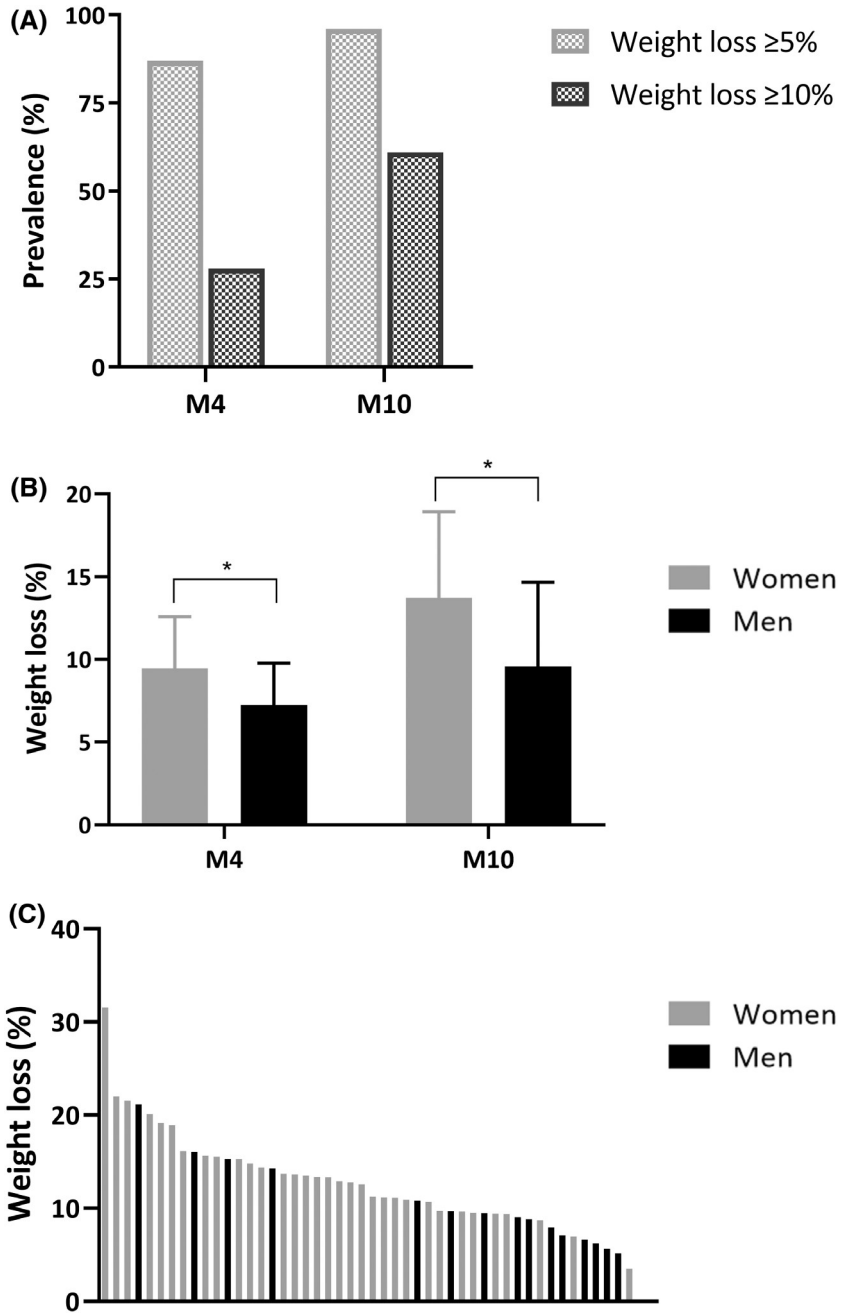

FIGURE 1 Weight loss during the study. (A) Prevalence (%) of subjects achieving ≥5% and ≥10% weight loss at 4 months (M4) ($n = 54$) and 10 months (M10) ($n = 49$). (B) Percentage weight loss according to sex at M4 and M10. (C) Individual percentage weight loss according to sex at 10 months. In panel B, data are expressed as mean ± SE. *$p < 0.05$

RESULTS

Clinical description of the cohort at baseline

The cohort included 54 subjects, 64.8% of whom were female ($n = 35/54$). The mean (SD) age was 43.6 (11.6) years and mean BMI (SD) was 40.8 (5.7) kg/m^2 (Table 1). A total of 85% of subjects had BMI ≥ 35 kg/m^2 ($n = 46/54$). At baseline, 34 subjects (63%) had prediabetes (including 2 subjects treated with metformin for polycystic ovary syndrome), 27 (50%) had dyslipidemia, and 22 (40.7%) had treated hypertension (Supporting Information Table S1).

Liraglutide therapy for 10 months: Effects on weight loss, body composition, and metabolic parameters

The entire cohort completed liraglutide treatment for at least 4 months. A total of 49 participants (91%) continued therapy at 10 months, and 5 subjects discontinued the treatment: 1 for pregnancy (at 3 months) and 4 after failing to meet the weight-loss percentage at 4 months for insurance reimbursement (Supporting Information Figure S2); they had an initial BMI ≥35 kg/m^2 and lost <7%. All patients with an initial BMI ≥28 and ≤35 kg/m^2 ($n = 8$) achieved the required 5% weight loss. At 10 months, 26 of 49 patients (53%) did not reach the additional 5% of weight loss

TABLE 2 Clinical outcomes after 10 months of liraglutide treatment

	n	Baseline	After 10 months
Metabolic comorbidities			
Hypertension	48	20/48 (42%)	18/48 (37%)
Dyslipidemia	47	24/47 (51%)	16/47 (34%)
Prediabetes	48	30/48 (62%)	4/48 (8%)*
Hepatic steatosis	20	20/20 (100%)	12/20 (60%)*
Metabolic parameters			
Glucose (mmol/L)	43	5.8 ± 0.8	5.2 ± 0.4*
HbA_{1C} (%)	45	5.5 ± 0.4	5.2 ± 0.3*
Insulin (mU/L)	32	31.1 ± 22.3	19.8 ± 11.8*
HOMA-IR	32	8.5 ± 7.4	4.6 ± 3.0*
Total cholesterol (mmol/L)	45	4.6 ± 0.8	4.5 ± 0.7
HDL (mmol/L)	44	1.3 ± 0.4	1.3 ± 0.2
Triglycerides (mmol/L)	45	1.6 ± 1.0	1.3 ± 0.7*
LDL (mmol/L)	44	2.7 ± 0.6	2.6 ± 0.7
hsCRP (mg/dL)	33	7.6 ± 5.3	4.6 ± 4.4*
AST (U/L)	44	23.4 ± 11.1	19.7 ± 7.7*
ALT (U/L)	44	33.2 ± 20.7	26.1 ± 18.4*
γ-GT (U/L)	43	37.2 ± 27.2	26.5 ± 18.5*
NAFLD fibrosis score	26	−1.5 ± 1.0	−2.33 ± 1.1*
Body composition			
Fat mass (%)	36	49.6 ± 6.1	46.3 ± 6.4*
Fat mass (kg)	36	54.4 ± 11.8	44.0 ± 10.6*
VAT (g)	36	2247 ± 1157	1717 ± 1002*
Lean mass (%)	36	49.3 ± 6.0	51.8 ± 7.2*
Lean mass (kg)	36	55.0 ± 10.6	51.7 ± 11.3*
FMI (kg/m^2)	36	19.6 ± 4.5	16.1 ± 3.8*
ALMI (kg/m^2)	36	9.5 ± 1.3	9.0 ± 1.1*

Note: Data expressed as mean ± SD.
Abbreviations: ALT, alanine aminotransferase; ALMI, appendicular lean mass index; AST, aspartate aminotransferase; FMI, fat mass index; HDL, high-density lipoprotein; HOMA-IR, homeostatic model assessment of insulin resistance; hsCRP, high-sensitivity C-reactive protein; LDL, low-density lipoprotein; NAFLD, nonalcoholic fatty liver disease; VAT, visceral adipose tissue; γ-GT, γ-glutamyl transferase.
*$p < 0.05$, as compared with baseline.

required to continue insurance reimbursement. Of those patients, only two subjects had an initial BMI ≥28 and ≤35 kg/m^2.

Effects on weight loss

Overall mean weight change at 4 months was −8.7% (3%) or −10 (3.7) kg. At 10 months, overall mean weight loss was −12.4% (5.5%) or −14.1 (6.6) kg (Table 1, Figure 1). No significant weight changes were depicted at 4 months between patients with BMI > 35 kg/m^2 and patients with BMI ≤ 35 kg/m^2, either in absolute or relative values (−8.5% [2.7%] vs. −9.6% [4.9%], $p = 0.9$; −10.3 [3.5] kg vs. −8.5 [4.8] kg, $p = 0.15$, respectively). Similarly, patients with BMI > 35 kg/m^2 had similar weight loss compared with patients with lower BMI (−11.8% [4.6%] vs. −15.0% [8.5%], $p = 0.4$; −14.3 [6.1] kg vs. −13.5 [8.8] kg, $p = 0.3$). Between 4 and 10 months, the weight loss (absolute and relative) was lower compared with the weight loss achieved during the first 4 months of treatment (−3.6% [4.5%] and −3.6 [4.7] kg vs. −10.0% [3.7%] and −8.7 [3.1] kg) in the 49 patients who completed the 10-month treatment. The prevalence of subjects with ≥5% weight loss was 87% ($n = 47/54$) at 4 months and 96% at 10 months ($n = 47/49$). At 4 months, 28% of patients had ≥10% weight loss, and this percentage increased to 61% at 10 months (Figure 1). Percentage weight loss was significantly higher in women than in men at 4 months (9.5% [3.1%] in women vs. −7.2% [2.5%] in men, $p = 0.02$) and at 10 months (−13.7% [5.2%] in women vs. −9.6% [5.1%] in men, $p = 0.006$; Figure 1).

Effects on body composition

As expected, women displayed higher FM and lower LM compared with men (Supporting Information Table S2). Body composition analysis by DXA showed a significant decrease in absolute and relative FM, FMI, absolute LM, and VAT at 10 months (Table 2, Figure 2). LM loss at 10 months was −2.7 (1.9) kg and this represented 23% (13.9%) of total weight loss. Because it was less than FM loss, LM% was higher at 10 months compared with baseline. LM loss relative to total mass loss was not significantly different according to sex (22.5% [14.7%] in women vs. 24.5% [12.8%] in men, $p = 0.7$).

Univariable analysis showed that weight-loss percentage was significantly associated with baseline FM% and sex but not with age or baseline BMI (Figure 3, Supporting Information S3). After adjusting for baseline FM%, the multivariable analysis showed no effect of sex on weight loss (Supporting Information Table S3). By adding an interaction analysis in the regression model, percentage weight loss according to baseline FM% was not different in women compared with men (Supporting Information Table S4).

Effects on metabolic parameters

Prevalence of prediabetes and hepatic steatosis was significantly lower after 10 months of liraglutide compared with baseline (Table 2). No difference in terms of prevalence of hypertension or dyslipidemia was found. Significant improvement in glucose profile, triglycerides, and hsCRP was observed (Table 2). NAFLD fibrosis score significantly decreased after 10 months of treatment. No significant changes in total cholesterol, LDL, or HDL were observed. BITE score was significantly lower at 10 months compared with baseline (7.7 [4.4] vs. 3.7 [3.2], $p < 0.01$). Similarly, significant improvements were also observed at 4 months (Supporting Information Table S1). At baseline, men exhibited higher HOMA-IR and hepatic tests and lower hsCRP compared with women (Supporting Information Table S2). After 10 months of liraglutide, HOMA-IR and hsCRP were similar between the two groups, whereas hepatic tests were still higher in men.

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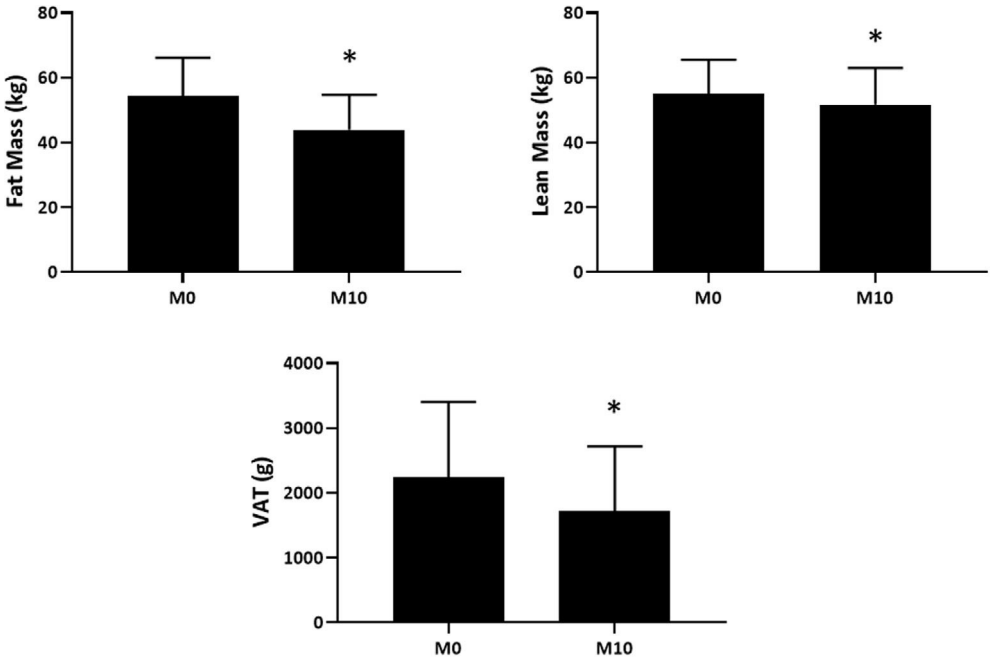

FIGURE 2 Body composition evolution at baseline (M0) vs. 10 months (M10). Data are expressed as mean ± SE. *$p < 0.05$. VAT, visceral adipose tissue

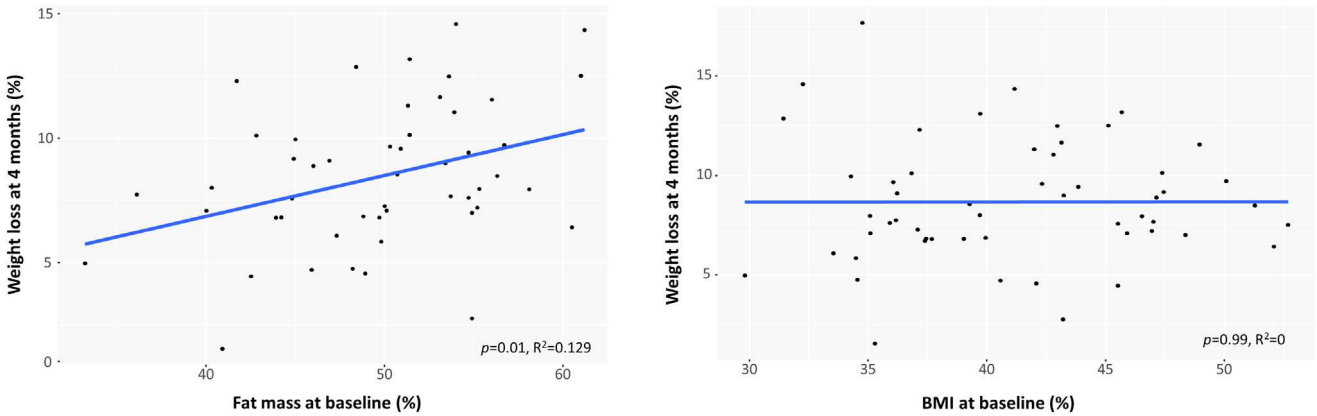

FIGURE 3 Univariable linear regressions between percentage weight loss at 4 months (%) as outcome variable and baseline fat mass percentage (left) or baseline BMI (right) as explanatory variables. R^2, Spearman coefficient [Color figure can be viewed at wileyonlinelibrary.com]

Adverse events and follow-up

The prevalence of adverse events is shown in Table 3. During the first 16 weeks, two patients had abdominal pain with modest increased lipase levels with no evidence of pancreatitis on abdominal tomography. These patients temporarily discontinued liraglutide until lipase decreased, then resumed and completed the 10-month study without further issues. At 4 months, 53 subjects were receiving the full 3.0 mg dose of liraglutide, with only 1 subject taking a reduced 2.4 mg dose because of gastrointestinal side effects. At 10 months, 48 subjects were receiving the full 3.0 mg dose, with only 1 subject receiving a reduced 1.2 mg dose of liraglutide because of a desire to stop treatment.

TABLE 3 Prevalence of side effects at 4 months and at 10 months of liraglutide 3.0 mg treatment

Side effect	4 months ($n = 54$), n (%)		10 months ($n = 49$), n (%)	
Constipation	13	26	3	6
Nausea	7	13	2	4
Dizziness	2	4	1	2
Reflux	6	11	–	–
Vomiting	1	2	–	–
Bloating	2	4	–	–
Diarrhea	4	7	1	2
Cutaneous reactions	3	5	1	2
Lipase elevation	2	4	–	–

DISCUSSION

Our real-life study showed that liraglutide 3.0 mg/d as an adjunct to a structured multidisciplinary intervention for patients with obesity or overweight led to significant weight loss of 10.0 to 14.1 kg (8.7%–12.4%) at 4 and 10 months of treatment, respectively. Furthermore, after 10 months of therapy, 96% of patients had ≥5% weight loss, and 61% had ≥10% weight loss. These results are superior to the SCALE randomized clinical trial, in which 13-month treatment with liraglutide 3.0 mg resulted in a proportion of 63.2% patients losing at least 5% of their body weight and 33.1% achieving >10% weight loss [4].

Compared with other real-life studies, the percentage of patients reaching ≥5% or ≥10% weight loss was higher. Spanish [19], Canadian [17], and Italian [18] real-life studies on populations with obesity or overweight demonstrated 64% to 68% of subjects exhibited >5% weight loss and 20% to 35% of subjects exhibited >10% weight loss at 4 to 7 months of treatment [17–19]. A Korean study with 6-month follow-up described 52.0% and 18.1% of subjects showing ≥5% and ≥10% body weight reduction, respectively [20]. Recently, Haase et al. reported that 42% and 12% of subjects reduced their weight by ≥5% and ≥10%, respectively, after 4 months but with a median dose of liraglutide of only 1.5 mg/d [21]. The improved performance of liraglutide treatment in the current study may be influenced by the impact of early multidisciplinary management and by the dietary intervention approach focusing on eating sensations and behavior rather than caloric restriction. This may improve the effect of liraglutide and reduce the incidence and intensity of digestive side effects that may lead to treatment discontinuation. Indeed, no patient discontinued treatment because of digestive side effects. The regular follow-ups after initiation with a focus on protein intake and physical activity may also explain these results. The Swiss insurance reimbursement schema could be another factor contributing to the increased success of the current study, especially compared with the other real-world studies in which patients self-paid for the treatment [18, 19, 21]. The approximate monthly cost of the treatment is 200 Swiss francs (225 euros, 220 US dollars), thus providing a strong incentive for weight loss.

In this study, women lost more weight compared with men. As expected, body composition analysis showed that women displayed higher FM compared with men. LM loss was not significantly different according to sex, suggesting that women preferentially reduced their FM. Moreover, regression analysis found that greater baseline FM% and female sex, but not BMI, were significantly associated with a higher percentage weight loss. After adjusting for baseline FM%, weight-loss percentage was not significantly associated with sex. Taken together, these data suggest that sex-specific body composition, with a higher amount of FM in women, influences response to treatment. A previous study on exposure-response of liraglutide 3.0 mg demonstrated that women had greater weight loss, and only about 50% of this difference could be explained by higher pharmacological levels in women [27]. Consistently, sex-specific dimorphism in effectiveness of GLP1RAs was also observed in real-world settings with exenatide [28]. In contrast, the Korean real-life study did not show any differences in terms of weight loss according to sex [29]. A difference in ethnicity might explain these different results. However, the overall data across the multiple studies highlight the potential need to differentiate objectives in terms of weight according to sex.

In contrast to a previous study, we did not find a difference in weight loss in patients with higher BMI compared with lower BMI [30]. Thus, it is questionable whether the difference in terms of weight loss criteria according to BMI imposed by the Swiss insurance program may be pertinent. Moreover, despite an adequate weight loss over the entire 10 months of therapy, a notable proportion of patients (44%) did not reach the weight-loss target for reimbursement at 10 months, which is pursued only if an additional weight loss of ≥5% is observed between the fourth and the tenth month of treatment. This suggests that total weight loss after 10 months should be taken into account by insurance. As expected, after 10 months on liraglutide, FM was significantly reduced, as well as FMI and VAT. In this study, LM loss was about 22% of total lost mass. However, LM% increased after 10 months of treatment, suggesting higher FM loss and a beneficial body composition change. Although ALMI was statistically lower at 10 months compared with baseline, this change was not clinically relevant as the difference was small (9.5 ± 1.3 vs. 9.0 ± 1.1 kg/m^2) and ALMI values remained normal/high. GLP1RAs act on murine skeletal muscle cells by promoting muscle tissue synthesis and suppressing muscle tissue breakdown [31, 32]. However, data regarding the impact of liraglutide on LM are discordant, ranging from no change to 65% of LM loss, measured either with DXA or bioelectrical impedance [33–41]. These differences are probably due to different population characteristics and diseases (i.e., obesity, diabetes, and polycystic ovary syndrome), various dietary restriction interventions, different techniques for body composition assessment, and different dosages of liraglutide.

Improvement in cardiometabolic markers and hepatic steatosis (as assessed by ultrasound or by NAFLD fibrosis score) was consistent with previous studies [42, 43]. Metabolic comorbidities were not significantly different according to sex. However, men displayed higher insulin resistance and transaminase levels compared with women, as previously shown [44, 45]. Sex-specific differences in body fat distribution and in sex hormones, with the well-known protective role of estrogens, may explain the difference in insulin resistance markers. It was demonstrated that the amount and the distribution of FM may influence CRP with a greater magnitude in women compared with men [46]. Consistently, greater values of hsCRP were found in women compared with men at baseline.

Gastrointestinal secondary effects are common during liraglutide treatment and are known to be transient. In our study, there were two reports of increased lipase with no evidence of pancreatitis, consistent with previous studies [20]. These patients were able to resume liraglutide treatment after a brief break allowing lipase normalization. In contrast to other reports [19, 20], nausea was not the most common side effect. Careful preparation before starting treatment with specific work on slowing down food intake may explain the low prevalence of nausea in our study.

Our study has several strengths. This is the first study, to our knowledge, evaluating real-life data of liraglutide treatment covered by a national insurance system without financial burden if patients met the weight-loss criteria. Patients had a standardized dietary and behavioral preparation before starting treatment, with no strict hypocaloric diet that could potentially affect short-term weight loss. Additionally, body composition data were obtained by DXA, which is an accurate and validated technique for body composition assessment [10]. It will be very important to follow prospectively the patients who discontinued therapy after 10 months. The weakness of the study that potentially reduced the power of the results included the absence of a control group and the modest sample size. The results were not controlled for physical activity, given the lack of objective data.

In conclusion, both 4 and 10 months' treatment with liraglutide 3.0 mg in a real-world setting led to positive changes in terms of weight loss, body composition, and metabolic parameters, with a greater impact on weight loss observed in women. Future research on clinical and economic outcomes of this reimbursed treatment over the long term, and the impact of discontinuing reimbursement of treatment as currently proposed in Switzerland, will need to be evaluated.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

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