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Clinical effectiveness of semaglutide on weight loss, body composition, and muscle strength in Chinese adults

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Abstract. – OBJECTIVE: The aim of this study was to investigate the clinical effectiveness of semaglutide on weight loss, body composition and muscle strength in the Chinese population with obesity.

PATIENTS AND METHODS: Data were retrospectively analyzed for participants prescribed semaglutide in 2021 and 2022 from a Chinese weight management clinic. Changes in weight, body composition, biochemical indicators, calf circumference and handgrip strength were collected. Body fat and skeletal muscle were also measured using the bioelectrical impedance analysis. Paired *t*-test was used to compare the values after 6 months of treatment with the baseline values.

RESULTS: A total of 53 obese patients received 24 weeks of lifestyle intervention plus semaglutide treatment. 10 patients who failed to adhere to the follow-up were excluded, and 43 patients were studied. The average baseline body mass index (BMI) was 33.0 kg/m^2, and the average body weight was 90.0 kg. After 6 months of treatment, the patient's weight was significantly reduced by 9.9 ± 3.9 kg ($p < 0.001$), and the weight loss percentage was 11.2 ± 4.5% ($p < 0.001$). The proportion of patients with weight loss ≥ 5% and ≥ 10% was 93% and 54%, respectively. Fasting blood glucose, fasting insulin, Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) index, blood uric acid and blood lipid levels also decreased after treatment. Body composition analysis showed that the loss of skeletal muscle mass was 1.4 ± 1.3 kg ($p < 0.001$), which was significantly less than the loss of fat mass of 5.6 ± 3.7 kg ($p < 0.001$). By percentage, the fat mass loss was 15.6 ± 10.1%, and the muscle mass loss was 4.8 ± 4.4% ($p < 0.001$). The visceral fat area was significantly reduced by 24.4 ± 17.7 cm ($p < 0.001$). There was no significant change in skeletal muscle index (8.1 ± 1.0 kg/m^2 at baseline and 7.9 ± 1.0 kg/m^2 at 24 weeks). The calf circumference (42.6 ± 3.6 cm at baseline, 41.2 ± 3.8 cm at 24 weeks) and grip strength (33.3 ± 9.5 kg at baseline, 32.3 ± 9.0 kg at 24 weeks) did not decrease significantly. The main adverse reactions were mild gastrointestinal dysfunction (nausea, diarrhea and vomiting), without ketoacidosis.

CONCLUSIONS: In a real-world setting, semaglutide can reduce the weight and fat of obese patients while effectively maintaining muscle mass and muscle strength.

Key Words:
Semaglutide, Obesity, Weight loss, Body composition, Muscle strength.

Introduction

Obesity is a major global public health issues[1]. People who are obese are usually accompanied by various metabolic diseases[2]. Weight loss of over 5% is known to improve health-related quality of life[3]. As lifestyle interventions (diet and exercise) provide moderate efficacy, obesity treatment strategies should be escalated by adding pharmacological and/or surgical interventions. However,

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when obese people successfully lose weight, their muscle mass usually decreases along with body fat reduction[4]. Decreased skeletal muscle mass may be associated with an increased risk of sarcopenia and weakness[5]. Therefore, it is preferable to reduce fat in obese patients without affecting muscle mass and function.

Semaglutide is a new glucagon-like peptide 1 receptor agonist (GLP-1RA) with high homology to human GLP-1. It has a long half-life and can be injected once weekly[6]. A randomized controlled study[7] has proven that 2.4 mg semaglutide per week successfully induced clinically meaningful weight loss compared to a placebo. In June 2021, 2.4 mg semaglutide once-weekly was approved by the Food and Drug Administration (FDA) for the treatment of overweight/obese individuals[8].

At present, obesity has become a serious public health problem endangering the health of Chinese residents. China has the largest number of affected people worldwide, with about 46% of adults and 15% of children being obese or overweight[9]. Orlistat is the only approved drug for weight loss in China. Moreover, anti-diabetic drugs, including GLP-1 receptor agonists, are widely used in adults with obesity in China[10]. However, the changes in body composition and muscle strength associated with the weight loss induced by semaglutide, are unclear. Therefore, in this study, we examined body composition and muscle strength, particularly fat mass, skeletal muscle mass, calf circumference and handgrip strength changes in order to assess the risk of developing sarcopenia, in Chinese obese patients treated with semaglutide.

Patients and Methods

Patients

From November 2021 to November 2022, a total of 53 patients with obesity (BMI $\geq$ 28 kg/m^2) who received 24 weeks of treatment with semaglutide at the Second Affiliated Hospital of Guangxi Medical University were retrospectively recruited for this study. 10 patients were excluded due to a lack of follow-up. Therefore, 43 subjects were studied. All participants provided written informed consent. Inclusion criteria: obesity diagnosed according to the Chinese standard (BMI $\geq$ 28.0 kg/m^2), age $\geq$ 18 years old, and a signed informed consent form. The exclusion criteria were as follows: age under 18 years old, diabetes, a history of allergy to semaglutide, abnormal liver function [serum alanine transaminase (ALT) $\geq$ 3-fold the upper limit of normal], severe renal function impairment (estimated glomerular filtration rate < 45 mL/min/1.73 m^2, calculated using the modification of diet in renal disease equation[11]), acute and unstable heart failure, medullary thyroid carcinoma, multiple endocrine neoplasia, pregnancy, or planning pregnancy, long-term use of drugs such as orlistat and glucocorticoids that affect body weight. The present study design was based on the Declaration of Helsinki and was approved by the Ethical Review Committee of the Second Affiliated Hospital of Guangxi Medical University.

Dose Escalation Schedule of Semaglutide

Within the first two weeks, semaglutide was injected subcutaneously once a week at a dose of 0.25 mg, and then the dose was increased once every two weeks until the dose of 1.0 mg was maintained weekly (if the patient did not tolerate the dose of 1.0 mg, the maintenance dose was reduced) for 24 weeks.

Lifestyle Intervention

Two nutritionists were responsible for guiding the patient's diet. The patients were instructed to eat a low-energy balanced diet (reduce 500 kcal per day) and 150 minutes of physical activity (such as walking, fast walking, etc.) every week.

Blood Sampling

Fasting blood samples were collected at the patient's first visit and 24 weeks after treatment. The glycated hemoglobin (HbA1c) was detected (Automated Glycohemoglobin Analyzer HLC-723G8, Tosoh, Japan). The fasting blood glucose (FPG), oral glucose tolerance test (OGTT), insulin release test (IRT), triglyceride (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL) were evaluated (Automatic Analyzer 7600, Hitachi, Japan). Insulin resistance (IR) was evaluated by the homeostasis model assessment (HOMA), using the following formula: HOMA-IR = fasting plasma glucose (mmol/L) $\times$ fasting plasma insulin (mU/L)/22.5[12].

Body Composition and Muscle Strength Assessment

Bodyweight, BMI, waist circumference, calf circumference, and handgrip strength were measured at every visit. Body composition was assessed by a Bioelectrical Impedance Analysis (BIA) apparatus (InBody S10; Biospace Co., Seoul, Korea). The body fat mass, fat weight percentage, skeletal muscle mass, skeletal weight percentage and visceral fat area were directly

Table I. Baseline characteristics of patients and change in body weight.

	Patient Group	Control Group	*p*
Age (years)	30.4 ± 8.1		
Gender (male/female)	10/33		
Body weight (kg)	90.0 ± 16.8	80.1 ± 16.9	< 0.001
BMI (kg/m^2)	33.0 ± 4.2	29.4 ± 4.4	< 0.001
Waist circumference (cm)	105.2 ± 12.2	98.3 ± 13.2	< 0.001
Hip circumference (cm)	116.6 ± 9.1	109.0 ± 9.4	< 0.001

BMI: body mass index.

obtained. Skeletal muscle index (SMI) was an important index to evaluate the muscle content of the human body. The calculation method used was limb skeletal muscle mass/height square, as described by Janssen et al[13]. Measuring calf circumference and upper limb grip strength is a simple and repeatable method to evaluate muscle mass and muscle strength[14]. An electronic grip strength meter was used to ensure the accuracy of data.

Statistical Analysis

All statistical analyses were performed using SPSS software version 23.0 (IBM Corp., Armonk, NY, USA). The mean ± standard deviation was used to describe variables conforming to a normal distribution, and percentage (%) was used for counting data. A paired sample *t*-test was used to compare the groups before and after treatment. *p*-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics of Patients and Change in Body Weight

Most patients were females (77%), with a mean age of 30.4 years. The average body weight was 90.0 kg, the mean BMI was 33.0 kg/m^2, the average waist circumference 105.2 cm, and the mean hip circumference 116.6 cm. After 24 weeks of treatment with semaglutide, the weight of the patients was significantly reduced (9.9 ± 3.9 kg, $p < 0.001$), and the percentage of weight loss was 11.2 ± 4.5% ($p < 0.001$). In addition, the percentages of subjects that showed ≥ 5% and ≥ 10% body weight reduction were 93% and 53%, respectively. Similarly, the waist circumference was significantly reduced by 6.9 cm, and the hip circumference was reduced by 7.7 cm. The baseline characteristics and body weight changes after semaglutide therapy are provided in Table I.

Changes in Blood Metabolic Parameters

The fasting blood glucose, OGTT 2-hour blood glucose and HbA1c levels of patients slightly decreased. Moreover, the level of fasting insulin, HOMA-IR index, blood uric acid, and blood lipids decreased evidently, indicating that insulin resistance was significantly improved (Table II).

Changes in Body Composition, Muscle Mass and Muscle Strength

As shown in Figure 1, the body composition analysis of patients showed that the loss of skeletal muscle mass was 1.4 ± 1.3 kg ($p < 0.001$),

Table II. Changes in blood biochemical indicators of patients.

	Patient Group	Control Group	*p*
Fasting plasma glucose (mmol/l)	5.1 ± 0.5	4.6 ± 0.3	< 0.001
OGTT 2 h glucose (mmol/l)	7.8 ± 2.3	5.7 ± 1.3	< 0.001
HbA1c (%)	5.7 ± 0.4	5.4 ± 0.3	< 0.001
Fasting serum insulin (mIU/L)	18.3 ± 8.7	10.0 ± 5.6	< 0.001
HOMA-IR	4.2 ± 2.1	2.1 ± 1.2	< 0.001
Blood uric acid (umol/l)	400.0 ± 98.0	346.6 ± 66.5	< 0.01
Total cholesterol (mmol/l)	4.7 ± 0.7	4.2 ± 0.6	< 0.01
Triglycerides (mmol/l)	1.9 ± 0.9	1.5 ± 0.8	< 0.01
HDL cholesterol (mmol/l)	1.2 ± 0.3	1.1 ± 0.2	0.212
LDL cholesterol (mmol/l)	3.1 ± 0.6	2.7 ± 0.5	< 0.001

OGTT: oral glucose tolerance test; HOMA-IR: homeostasis model assessment of insulin resistance; HDL: high-density lipoprotein; LDL: low-density lipoprotein.

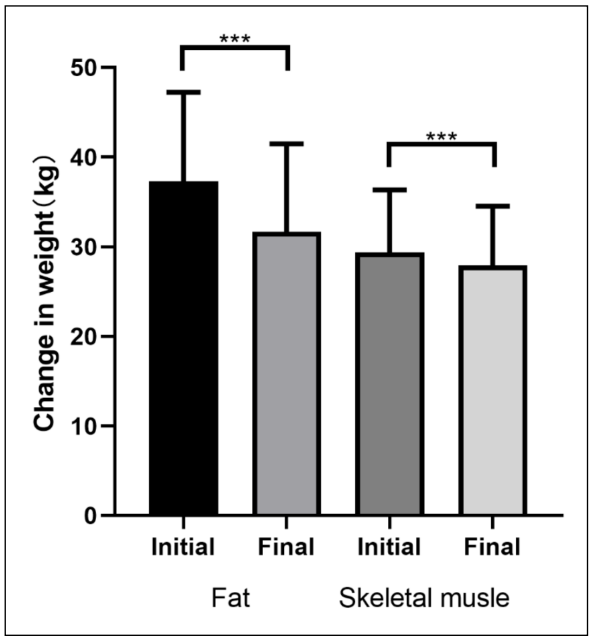

Figure 1. Changes of fat weight and muscle weight by kg during the treatment with semaglutide in obese Chinese patients. ***$p < 0.001$.

which was significantly lower than the loss of fat mass of 5.6 ± 3.7 kg ($p < 0.001$). In Figure 2, the fat mass loss was 15.6 ± 10.1%, while the muscle mass loss was only 4.8 ± 4.4%. The fat mass loss was significantly greater than the muscle mass loss ($p < 0.001$). Body fat mass percentage also decreased significantly (3.2 ± 2.9%, $p < 0.001$), while skeletal muscle mass percentage was increased (2.7 ± 2.6%, $p < 0.001$). The visceral fat area decreased significantly (24.4 ± 17.7 cm, $p < 0.001$) as well. In contrast, SMI was almost unchanged after treatment (8.1 ± 1.0 at baseline, 7.9 ± 1.0 at 24 weeks). In addition, in the analysis of muscle mass and muscle strength, there was no significant decrease in calf circumference (42.6 ± 3.6 cm at baseline, 41.2 ± 3.8 cm at 24 weeks) and grip strength (33.3 ± 9.5 kg at baseline, 32.3 ± 9.0 kg at 24 weeks). The above data are shown in Table III. These results suggest that semaglutide can reduce weight and fat in obese patients, while effectively maintaining muscle mass and muscle strength.

Safety and Side-Effect

The major adverse events after semaglutide treatment were gastrointestinal disorders (nausea, diarrhea, and vomiting). Five patients had nausea, four had diarrhea, four had vomiting, and one had weakness. No ketoacidosis occurred. Most gastrointestinal events were mild-to-moderate in severity. None of the patients dropped out of the study because of adverse events.

Discussion

As far as we know, there are few reports on the clinical efficacy of semaglutide in obese people in China. In this study, the baseline BMI of patients was 33.0 kg/m^2, and the baseline weight was 90 kg. After lifestyle intervention and semaglutide treatment for 24 weeks, the average weight loss of patients was 9.9 kg, and the percentage of weight loss was 11.2%. Moreover, 93.0% of subjects showed a ≥ 5% clinically meaningful weight loss[1,15] and 53.5% of subjects achieved a weight loss of at least 10%, whereas a randomized controlled trial[16] reported 86.4% of patients achieving a ≥ 5% weight loss and 69.1% of patients losing 10% body weight. Recently, a Canadian real-world data study[17] also reported 64.1% of participants achieving a ≥ 5% weight loss and 34.5% of participants losing 10% body weight. Thus, weight loss was evident in real-world Chinese populations as well, which is consistent with clinical trial settings and real-world Western data.

In our study, the baseline mean BMI was 33.0 kg/m^2, which was lower than the previous study[16]

Table III. Changes in body composition, calf circumference and grip strength of patients.

	Patient Group	Control Group	*p*
Fat mass (kg)	37.3 ± 9.9	31.7 ± 9.8	< 0.001
Skeletal muscle mass (kg)	29.4 ± 7.0	27.9 ± 6.6	< 0.001
Body fat rate (%)	41.0 ± 6.7	37.8 ± 7.3	< 0.001
Body skeletal muscle rate (%)	33.1 ± 10.1	35.8 ± 11.3	< 0.001
SMI (kg/m^2)	8.1 ± 1.0	7.9 ± 1.0	< 0.01
Visceral fat area (cm^2)	165.5 ± 44.6	141.1 ± 47.4	< 0.001
Calf circumference (cm)	42.6 ± 3.6	41.2 ± 3.8	< 0.001
Handgrip strength (kg)	33.3 ± 9.5	32.3 ± 9.0	0.095

SMI: skeletal muscle index.

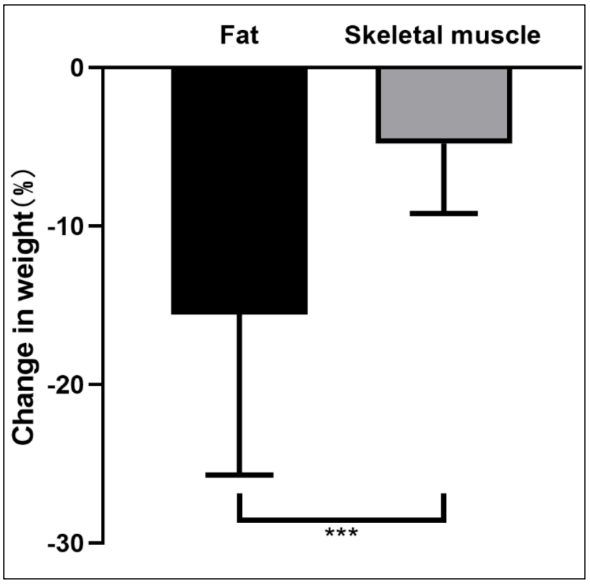

Figure 2. Changes of fat weight and muscle weight by percentage during the treatment with semaglutide in obese Chinese patients. ***$p < 0.001$.

of semaglutide for Western obese populations, which had an average BMI of over 38 kg/m^2. In the Asian population, people with relatively low BMI may be obese; thus, China uses BMI ≥ 24.0 kg/m^2 and ≥ 28.0 kg/m^2 to diagnose adults as overweight and obese, respectively[18]. This study indicates that weight loss was still evident in real-world settings despite the lower BMI criteria for Chinese populations.

The weight loss mechanism of semaglutide is to inhibit appetite, increase satiety and delay gastric emptying[19]. In our study, weight loss from semaglutide was accompanied by significant improvement in cardiometabolic risk factors, including reductions in waist circumference, glycosylated hemoglobin level and lipid levels. Waist circumference measurement is a widely accepted, simple, and non-invasive method to assess central obesity compared to BMI[20]. The optimal waist circumference cut-off for visceral obesity in the Chinese population is 90 cm and 85 cm in men and women, respectively[21]. In our study, the patients' waist circumference decreased by 6.9 cm on average.

Contrary to fat reduction, reducing skeletal muscle is not good for obese patients. Usually, skeletal muscle loss occurs after diet control and bariatric surgery[22]. The decrease in skeletal muscle mass may be related to the increased risk of sarcopenia and weakness in elderly patients[23]. Compared to Western populations, Asian populations are more prone to abdominal obesity, low muscle mass, and increased insulin resistance[24], all of which are known risk factors for sarcopenia. Therefore, when achieving weight loss, it is better to mainly reduce fat without significantly reducing muscle mass[25].

In this study, the body fat rate decreased from 41% to 37.8%, while the body skeletal muscle rate increased from 33.1% to 35.8%. Skeletal muscle index (SMI) reduced from 8.1 to 7.9, with little change. It shows that skeletal muscle mass was preserved after semaglutide treatment. Analyses from the Bioelectrical Impedance Analysis (BIA) suggested that semaglutide led to a greater reduction in fat mass (15.6%) than skeletal muscle mass (4.8%), which is consistent with a previous study[19] with 1.0 mg semaglutide administered to obesity patients. Moreover, in a Japanese study[26], liraglutide 0.9 mg per day reduced body fat (-10.9%), but the skeletal muscle index did not change. In another Italian study[27], after treatment with liraglutide at a dose of 3.0 mg, a decrease in fat mass (-1,498 g) and an increase in skeletal muscle index (+0.03 kg/m^2) from baseline were observed.

The Asian Working Group for Sarcopenia (AWGS) defined sarcopenia based on low muscle strength, low muscle mass, and/or low physical performance, with low muscle strength defined as handgrip strength < 28 kg for men and < 18 kg for women, with low muscle mass defined as calf circumference < 34 cm for males and < 33 cm for females[28]. Among the anthropometric parameters, calf circumference has proven[29] to be an effective method for measuring skeletal muscle mass. Muscle strength is commonly evaluated using handgrip strength, which is an easy, reliable, and inexpensive method[30]. In our study, the patient's grip strength was reduced from 33.3 kg to 32.3 kg ($p = 0.095$), and calf circumference was reduced from 42.6 cm to 41.2 cm ($p < 0.001$). On the basis of significant weight loss, there was no significant decrease in muscle mass and muscle strength. Few studies on the associations of handgrip strength and calf circumference with weight loss have been conducted in China. Therefore, we believe that semaglutide can reduce the risk of muscle mass loss and muscle function decline in obese patients during weight loss.

Andreozzi et al[31] reported that glucagon-like peptide-1 receptor agonists (GLP-1RAs) exenatide and liraglutide can activate glucose delivery in skeletal muscle through an AMP-activated protein kinase (AMPK). Li et al[32] also reported that liraglutide enhances glucose transporter 4 translocation *via* regulation of AMPK signaling pathways

in mouse skeletal muscle cells. GLP-1 also mediates the increase of blood flow in muscle, which indicates that it increases the transport of glucose to tissues, thus increasing muscle synthesis and reducing muscle decomposition[33]. In addition, the increase of skeletal muscle mass has positive effects on insulin resistance and fat metabolism through several molecular mechanisms[34]. Moreover, GLP-1RAs can activate the GLP-1 receptor of muscle cells, and inhibit the expression of myostatin and other cytokines of muscle atrophy, such as F-box only protein 32 (atrogin-1) and muscle RING-finger protein-1 (MuRF-1), and delay muscle atrophy through protein kinase A (PKA) and protein kinase B (PKB) signaling pathways[35]. Therefore, we believe that semaglutide can reduce the risk of muscle mass loss and muscle function decline in obese patients. Further studies are needed to verify the effect of semaglutide on muscles.

Semaglutide, in combination with lifestyle interventions, was well tolerated in this study. The adverse reactions mainly focused on gastrointestinal events, such as nausea, vomiting, and diarrhea, which are similar to those reported[36] with liraglutide at a dose of 3.0 mg. Usually, the incidence of gastrointestinal adverse events decreases over time. There was no hypoglycemia, no adAll participants provided written informed consent..

Conflict of Interest
The authors declare that they have no conflict of interests.

Informed Consent
All participants provided written informed consent.

Ethics Approval
The study was approved by the Ethical Review Committee of the Second Affiliated Hospital of Guangxi Medical University (#2022-KY0763).

Availability of Data and Materials
The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

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Authors' Contributions
This study was designed by NX and YZL, as the principal investigator. Data collection and analysis was conducted by JX, XYD, WZ, JZ, YSZ, and ZML. The manuscript was written by Jie Xiang and Yuzhen Liang. All the authors have read the manuscript and approved this submission.

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