


# Implications of Ozempic and Other GLP-1 Receptor Agonists for Facial Plastic Surgeons

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## Abstract

Obesity is a growing global health concern. Glucagon-like peptide-1 (GLP-1) receptor agonists, such as Ozempic, have emerged as potential treatments. GLP-1 receptor agonists regulate appetite and can promote weight loss. Some GLP-1 receptor agonists, though Food and Drug Administration (FDA)-approved for diabetes, are also used off-label for weight loss alone. Rapid weight and fat loss with these medications can lead to what has been called “Ozempic Face” on social media and in the lay press, where facial volume and fat are depleted, resulting in wrinkles and sagging skin. Prescribers rarely counsel patients about the potential impact on the face, and the plastic surgery community faces a challenge in managing the facial changes associated with rapid weight loss. Dermal fillers, skin tightening techniques, and surgical interventions are useful for both restoration of facial volume and to manage excess skin. Discontinuation of GLP-1 receptor agonists should be considered prior to general anesthesia due to delayed gastric emptying while on these medications. As the popularity of GLP-1 receptor agonists grows, facial plastic surgeons must be aware of both the impact on facial appearance and perioperative considerations.

## Keywords

- ▶ facial aging
- ▶ weight loss
- ▶ fat loss
- ▶ semaglutide
- ▶ Ozempic face

Obesity is increasing worldwide, leading to significant health consequences including comorbidities like diabetes. Weight loss medications, such as semaglutide, have emerged as a potential solution. There are three semaglutide products approved by the U.S. Food and Drug Administration (FDA): Ozempic, Wegovy, and Rybelsus (Novo Nordisk, Denmark). Ozempic and Rybelsus are indicated for lowering blood sugar in adults with type 2 diabetes, while Wegovy is approved for weight loss in individuals over the age of 12 who are obese or overweight with medical-related illnesses.<sup>1</sup> These medications belong to the glucagon-like peptide-1 (GLP-1) receptor agonist class of drugs, mimicking the action of the endogenous hormone GLP-1. The activation of GLP-1 receptors in the central nervous system plays a crucial role in appetite regulation and weight loss.<sup>2</sup> Medications containing semaglutide are gaining widespread attention for their efficacy in reducing body weight and improving metabolic parameters. While Ozempic is currently FDA-approved only for people with type 2 diabetes, it is also used off-label to aid nondiabetic patients in weight loss.

Clinical trials have demonstrated the effectiveness of these products in promoting weight loss, reducing hemoglobin A1c levels, and improving cardiovascular outcomes. The Semaglutide Treatment Effect in People with Obesity (STEP) program is investigating the use of a once-weekly semaglutide injection to promote weight loss.<sup>1</sup> For people with type 2 diabetes, the recommended dose is 2 mg or less, administered through weekly injections into the thigh, upper arm, or abdomen. In the weight loss clinical trials, a dose of 2.4 mg per week was used, gradually titrated up over a 16-week period. Initial reports from the STEP-1 randomized controlled trial comparing semaglutide with a placebo revealed that participants on semaglutide had better outcomes in terms of waist circumference, systolic blood pressure, and physical function scores.<sup>2</sup> The STEP-1 study revealed that individuals who were administered semaglutide for 68 weeks experienced a weight loss of 14.9%, whereas patients who received a placebo alongside lifestyle interventions only lost 2.4% of their body weight.<sup>2</sup> In the STEP-4 study, two groups of

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patients initially began taking semaglutide, but one group was randomly assigned to discontinue the medication and switch to a placebo.<sup>3</sup> Throughout the 68-week trial period, an impressive 64% of patients on semaglutide achieved a weight loss of at least 15%, and 40% achieved a weight loss of at least 20%. The patients who continued to take the semaglutide exhibited a remarkable weight loss of 17.4%, while those on the placebo gradually regained weight, demonstrating that the effect of a semaglutide can be lost once it is discontinued. Therefore, a semaglutide should be prescribed with the expectation that it will be a lifelong medication.<sup>1</sup>

The rapid weight and fat loss observed with certain GLP-1 receptor agonists is attributed to its effects on delayed gastric emptying and appetite suppression. Consequently, this medication carries multiple gastrointestinal-related side effects, including diarrhea, constipation, indigestion, nausea, vomiting, and abdominal pain. These effects raise concerns, particularly prior to surgery, as delayed gastric emptying can increase the risk of vomiting and aspiration during intubation. Although there is a lack of scientific data describing how GLP-1 agonists specifically affect patients undergoing surgery and interact with anesthesia, anecdotal evidence suggests an increased incidence of vomiting. In response to these concerns, the American Society of Anesthesiologists has established new guidelines for individuals taking GLP-1 receptor agonists such as semaglutide. They recommend discontinuing the medication 1 day prior to surgery for patients who use it daily and 1 week prior for those who use it weekly. If a patient experiences symptoms such as nausea, vomiting, or abdominal pain on the day of surgery, the surgeon should consider canceling the elective procedure. In cases where patients have not followed the guidelines and stopped a GLP-1 agonist prior to surgery but lack symptoms, an ultrasound to assess stomach contents could be considered.<sup>4</sup> Additionally, apart from the gastrointestinal effects, these medications also carry risks of headaches, dizziness, vision complications, renal failure, pancreatitis, and thyroid tumors.<sup>1</sup>

Some patients who lose weight while taking GLP-1 receptor agonists such as semaglutide are known to experience rapid fat loss throughout the body including the face. The term “Ozempic face” was coined by celebrity dermatologist Dr. Paul Jarrod Frank in the United States to describe the characteristic gaunt facial appearance of these patients. Volume in key areas makes a face look youthful, and much of this volume comes from fat. With rapid fat loss in patients taking semaglutide or similar GLP-1 receptor agonists, wrinkles become more prominent and the skin starts to sag in areas such as the temples, cheeks, tear troughs, jawline, marionette lines, and nasolabial folds. Apart from fat loss, GLP-1 receptor agonists such as semaglutide can also cause changes in the size of the lips, cheeks, and chin that disrupt the balance of facial features. Patients appear gaunt not only due to volume loss but also due to changes in the facial skin where there is a loss of collagen, elastin, and essential nutrients. These effects are particularly noticeable in an elderly population with already reduced elastin and collagen in their skin. Additionally, the loss of fatty acids can affect the skin barrier, leading to dryness and a lackluster appearance.

Rapid depletion of vitamins and nutrients during weight loss can cause malnutrition, exacerbating the above issues; thus, closely monitoring one's diet to ensure it meets appropriate nutritional requirements is advisable and beneficial.<sup>1</sup> Clinical trials assessing the use of GLP-1 receptor agonist products for weight loss rarely report facial fat loss as an adverse effect. Because of this, providers prescribing these medications are unlikely to counsel patients pretreatment about the potential for undesirable changes in facial appearance. The characteristic features of “Ozempic face” are not exclusive to patients using semaglutide and other GLP-1 receptor agonists; similar changes are often seen in any patient with rapid weight loss or malnourishment.

The undesirable facial appearance and diminished self-esteem that sometimes follows the initiation of treatment with GLP-1 receptor agonists such as semaglutide pose a new challenge for the plastic surgery community. Weight loss is a top priority for many individuals to improve both their health and appearance, and GLP-1 receptor agonists have gained popularity despite their cost. However, a dilemma arises as the reduction in body weight accelerates facial aging. Patients who experience massive weight loss appear up to 5 years older than those of similar ages without a history of extensive weight loss.<sup>5</sup> While discontinuing a GLP-1 receptor agonist is an option, it will likely lead to weight regain, even with ongoing lifestyle interventions.<sup>3</sup> Further, during weight gain, fat often does not redistribute as it did prior to starting the medication, resulting in persistent signs of facial aging. As facial plastic surgeons, we can offer treatments to restore volume and mitigate the hollowed facial appearance caused by semaglutide and other GLP-1 receptor agonist products. Typical signs of facial aging such as temporal hollowing, lower orbital rim prominence, midface volume deflation, central face laxity, and heavy jowls are exaggerated in patients with rapid and marked weight loss.<sup>6</sup> Dermal fillers, such as hyaluronic acid, poly-L-lactic acid, autologous fat grafting, or collagen stimulators like poly-L-lactic acid and calcium hydroxyapatite, should be targeted to these areas of the face. Energy-based skin tightening techniques such as radiofrequency microneedling and CO2 laser treatments can revive the skin's surface and stimulate collagen and elastin production. Surgical treatments should be considered as well. A lower facelift can effectively improve the appearance of wrinkles and eliminate excess skin. In cases of massive weight loss, however, patients may require longer incisions and wider skin undermining, necessitating the use of the extended superficial musculoaponeurotic system or deep plane techniques to achieve optimal results in this population.<sup>6</sup> When contemplating surgical management for weight loss patients, it becomes crucial to take into account the potential loss of essential nutrients, including iron, vitamin B12, fat-soluble vitamins, and protein, all of which play a significant role in wound healing.<sup>6</sup> Therefore, surgical interventions should typically be postponed until a patient achieves his or her weight loss goal, is successfully maintaining that weight, and nutrition is optimized. For most patients, a combination of surgical procedures, skin treatments, and volume restoration will yield the best

outcomes. When discussing any available treatment options for facial consequences resulting from weight loss, it is essential to provide patients with comprehensive information about associated extended costs, potential complications, and the time commitment involved.

Ozempic (semaglutide) is an FDA-approved drug for type 2 diabetes with demonstrated off-label efficacy for weight loss. Semaglutide and other GLP-1 receptor agonists are likely to flourish in the market as they are increasingly being used among a wider population to effectively facilitate weight management. With an oral formulation of this weight loss drug on the horizon that will eliminate the need for less convenient injections, popularity of GLP-1 receptor agonists will continue to increase.<sup>7</sup> This is the first report in the medical literature regarding the facial effects of semaglutide and other GLP-1 agonists despite the term “Ozempic face” returning over 36 million results on a recent Google search (12/8/23). Although none of the published clinical trials to date have measured the effect of GLP-1 receptor agonists on the face, the authors and other facial plastic surgeons have cared for numerous patients taking these medications seeking treatment for aging changes due to decreased facial volume. Facial plastic surgeons must be familiar with semaglutide and other GLP-1 receptor agonists both due to the unique perioperative considerations as well as to this undesirable impact they can have on the facial appearance. Injectables, fat grafting, skin treatments, and surgery are all viable options for treating “Ozempic face” and improving self-esteem in these patients.

#### Conflict of Interest

None declared.

#### Disclaimer

This article is not intended to guide clinicians when using semaglutide for the treatment of type 2 diabetes or obesity. For this information, please refer to prescribing information at FDA.gov for specific medications.

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