



# ISAPS® PATIENT SAFETY

EMERGING GUIDANCE OF THE INTERNATIONAL SOCIETY  
OF AESTHETIC PLASTIC SURGERY

## THE RISE OF GLP-1 RECEPTOR AGONIST DRUGS AND PLASTIC SURGERY

### Chapter 1: Basic Knowledge and Perioperative Management

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#### INTRODUCTION

The global obesity crisis is an escalating public health concern, with over 650 million obese adults worldwide according to the World Health Organization [1]. In the United States, over 100 million adults are affected by obesity and obesity-associated comorbidities, emphasizing the urgent need for effective treatments [2].

Glucagon-like peptide-1 receptor agonists (GLP-1 RAs), such as semaglutide (Ozempic and Wegovy, manufactured by Novo Nordisk, Bagsværd, Denmark), tirzepatide and liraglutide (Saxenda, Novo Nordisk), have increasingly gained popularity for their groundbreaking efficacy in glycemic control and weight loss. Wegovy and Saxenda are the only injectable medications regulating glucose homeostasis that are Food and Drug Administration (FDA) approved for weight loss. Ozempic and Mounjaro, on the other hand, are only FDA approved for T2 diabetes mellitus (DM) management. Therefore, using Ozempic and Mounjaro for weight loss constitutes an off-label, non-FDA approved use, and the drugs typically cost \$1,000-\$1,200 or more per month. Moreover, Morgan Stanley estimates the number of patients taking GLP-1 RAs could reach 24 million, or nearly 7% of the United States population, by 2035 [4].

The Semaglutide Treatment Effect in People with Obesity (STEP) trials demonstrated significant changes in body weight in non-diabetic patients with obesity after weekly treatment for 68 weeks (-14.9% versus -2.4% in the control group,  $P < 0.001$  for the STEP 1 trial; -16.0% versus -5.7% in the control group,  $P < 0.004$  for the STEP 3 trial). An extension trial evaluating patients one year after stopping the drug found that they regained two-thirds of the lost weight, and the cardiometabolic improvements they made at 68 weeks had reverted back to baseline metrics, demonstrating that this class of medication likely requires indefinite use for sustained results. Weight gain after medication cessation, in addition to the high cost of these drugs, shows that this class of medication is likely not as sustainable as more long-term options for weight management, like bariatric surgery [3].

#### ADVERSE REACTIONS AND POSSIBLE HEALTH IMPAR

These drugs are associated with severe warnings, including risk of thyroid tumors, pancreatitis, hypersensitivity reactions, acute kidney injury, complications associated with diabetic retinopathy and acute gallbladder pathologies. Adverse reactions include nausea, vomiting, appetite suppression, diarrhea, constipation and abdominal pain, among others. When used in the management of DM, weekly injectable GLP-1 RAs are also associated with low risk of diabetic retinopathy and associated complications, with significantly more complications seen with semaglutide use versus other medications [4].

FDA's reviews of the clinical trials, including large outcome studies and observational studies, did not find an association between the use of GLP-1 RAs and occurrence of suicidal thoughts or actions. However, because of the small number of suicidal thoughts or actions observed in both people using GLP-1 RAs and in the comparative control groups, the FDA cannot definitively rule out that a small risk may exist; therefore, the FDA is continuing to look into this issue [6].

Clinical trials have demonstrated that both subcutaneous liraglutide and semaglutide can lead to massive weight loss in overweight or obese adults with semaglutide resulting in significantly greater weight loss compared with liraglutide. Alongside their therapeutic success however, these agents have been associated with unintended facial consequences, including depleted facial volume, accelerated skin aging, and increased sagging and wrinkling.

“Ozempic face”, “Ozempic butt” and “Ozempic body” are now mainstream terms that describe the morphological deflation of tissues due to semaglutide therapy and have been discussed at length by plastic surgeons over social media, podcasts and blogs [5].

## ADDITIONAL BENEFITS

Not all effects of semaglutide are questionable, unknown or potentially harmful. The diabetes literature supports that GLP-1 RAs have a profound positive effect of reducing risk of adverse cardiac outcomes, including cardiovascular death, stroke and myocardial infarction ( $P < 0.0001$ ). These drugs are cardioprotective in non-diabetic patients as well, with demonstrated decrease in plasma lipid levels and lower blood pressure. There is a particularly strong effect on stroke with decreased incidence of both first stroke and any stroke, attributed to the effects of semaglutide on small vessel occlusion. These medications are also associated with decreased all-cause mortality, reduced admissions for heart failure, and decreased incidence of kidney disease and death from renal cause [7].

## PERIOPERATIVE MANAGEMENT

GLP-1 receptor agonism induces physiologic changes with direct implications on patient safety and surgical outcome optimization in the perioperative period. Currently, there are no evidence-based guidelines for preoperatively holding these drugs before surgery. However, the sequelae of delayed gastric emptying and decreased gastrointestinal motility likely increases the risk of general anesthesia and aspiration. This has led the American Society of Anesthesiologists (ASA) to release consensus-based guidelines regarding these drugs [8].

It should take into account patient-specific risk factors for delayed stomach emptying and consider the following guidance for patients at highest risk:

- A. Patients in the escalation phase of GLP-1 drugs (early in treatment) are more likely to have delayed stomach emptying. The escalation phase (when the patient is given increasing doses of the GLP-1 drug) typically lasts four to eight weeks, depending on the drug and the reason it has been prescribed. Elective surgery should be deferred and only proceed once the escalation phase has passed and GI side effects have dissipated.
- B. Patients who have GI symptoms, including nausea, vomiting, abdominal pain, shortness of breath or constipation should wait until their symptoms have dissipated before proceeding with elective surgery.
- C. Patients on a higher dose of the GLP-1 drug typically have more GI side effects and should follow a liquid diet for 24 hours before the procedure.

## CHALLENGES FOR PLASTIC SURGEONS

The rise in the use of GLP-1 agonists like Semaglutide for obesity management has created new challenges for plastic surgeons, particularly in addressing skin laxity, fat redistribution and changes in facial and body contour following significant weight loss. Rapid weight loss has been shown to impair skin's ability to regenerate and maintain elasticity, leading to sagging and wrinkles, especially in areas with high-fat content. Beyond fat loss, it is critical to understand how these medications affect other structural components, including muscles, ligaments and skin. The impact on muscle tone and skin retraction is not yet fully understood, particularly in the context of aesthetic interventions.

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