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OBESITY MANAGEMENT - A COMPARATIVE REVIEW OF THE EFFICACY AND SAFETY OF BARIATRIC SURGERY AND TIRZEPATIDE THERAPY

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ABSTRACT

Objective: Obesity is a major global health burden associated with increased morbidity, mortality, and healthcare costs. This review aimed to compare the efficacy and safety of tirzepatide, a novel dual GLP-1/GIP receptor agonist, with bariatric surgery, focusing on their roles in weight reduction, metabolic improvement, and long-term risk–benefit profiles.
Methods: A comprehensive literature search was performed using PubMed and official regulatory and professional society sources (FDA, EMA, MHRA, IFSO). Search terms included "obesity," "bariatric surgery," "tirzepatide," and "GLP-1 and GIP receptor agonist." Only peer-reviewed English-language studies with high levels of evidence, including randomized controlled trials, meta-analyses, systematic reviews, and clinical guidelines, were included.
Key Findings: Bariatric surgery, particularly Roux-en-Y gastric bypass and sleeve gastrectomy, was associated with the most profound and durable weight loss (25–28% short-term; 18–25% long-term), alongside significant remission of type 2 diabetes, hypertension, and dyslipidemia. However, its invasive nature and risk of perioperative and late complications necessitate multidisciplinary follow-up. Tirzepatide demonstrated dose-dependent reductions in body weight (~10–20%), improved glycemic control, lipid profiles, and blood pressure, and enhanced quality of life. Its safety profile was favorable, predominantly gastrointestinal, but long-term data remain limited.
Conclusions: Bariatric surgery remains the gold standard for severe obesity due to its magnitude and sustainability of benefits. Tirzepatide represents a promising, less-invasive pharmacological option, particularly for patients with moderate obesity or contraindications to surgery. Further research is required to establish its long-term efficacy and safety profile.

KEYWORDS

Obesity, Tirzepatide, Bariatric Surgery, GLP-1 and GIP Receptor Agonist

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Introduction

Obesity is a complex and multifactorial disease defined as excessive accumulation of adipose tissue resulting from a long-term imbalance between caloric intake and energy expenditure. Its development is influenced by both genetic predisposition and environmental factors. It may manifest as early as childhood, placing a significant burden on the body throughout life. [1] Risk factors for obesity are divided into modifiable and non-modifiable categories. Non-modifiable factors include genetic predispositions, such as mutations in genes regulating appetite and metabolism, as well as factors related to the intrauterine environment, early development, age, and sex. Modifiable factors, on the other hand, include physical inactivity, excessive calorie intake, insufficient sleep, stress, use of certain medications, endocrine disorders, low socioeconomic status, hormonal imbalances, an unfavorable gut microbiome, and environmental influences such as easy access to unhealthy food and a lack of recreational areas. [2]

Obesity, defined as a body mass index (BMI) exceeding 30, is a growing global health concern. Between 1975 and 2016, the global prevalence of obesity nearly tripled. Currently, approximately 13% of the world's adult population qualifies as obese. [3] Obesity is categorized into three classes based on BMI values: Class I obesity – BMI between 30 and 34.9 kg/m²; Class II obesity – BMI between 35 and 39.9 kg/m²; and Class III obesity – BMI of 40 kg/m² or higher, also known as severe, extreme, or morbid obesity. [4]

Obesity is often associated with a wide range of comorbidities, including hypertension, obstructive sleep apnea and other respiratory disorders, osteoarthritis, type 2 diabetes mellitus (T2DM), dyslipidemia, stroke, non-alcoholic fatty liver disease, cardiovascular diseases, and gallbladder disease. It also increases the risk of certain cancers such as liver, endometrial, gallbladder, prostate, colorectal, breast, ovarian, and kidney cancers. All of these conditions contribute to an increased risk of mortality. [5]

In addition, obesity is associated with a higher incidence of depression and anxiety disorders. An increasing number of studies suggest that the psychological consequences of obesity are due to poor dietary habits, lack of physical activity, and excessive accumulation of visceral fat. [6]

In 2019, overweight and obesity were responsible for costs representing approximately 2.19% of global GDP. These expenses ranged from about $20 per capita in Africa to $872 per person in the Americas. If current trends continue, the economic burden of these conditions could increase to 3.29% of global GDP by 2060. However, reducing the projected prevalence of overweight and obesity by 5% annually or maintaining it at 2019 levels could save an average of $429 billion or even $2,201 billion globally per year between 2020 and 2060, respectively. [7]

Given the extensive and adverse impact of obesity on patient health, appropriate therapeutic management is crucial. The literature describes several treatment methods, including dietary interventions, pharmacotherapy using glucagon-like peptide-1 (GLP-1) receptor agonists, orlistat, the combination of naltrexone and bupropion (NB), surgical treatment in the form of bariatric surgery [8], and tirzepatide, which acts as an agonist of both the GLP-1 and GIP receptors. [9]

Material and **methods**

This review was conducted through a comprehensive search of scientific literature in the PubMed database. The search strategy employed specific medical subject terms and keywords, including “obesity,” “bariatric surgery,” “tirzepatide,” and “GLP-1 and GIP receptor agonist.” Only peer-reviewed articles published in English were considered. Priority was given to systematic reviews, meta-analyses, randomized controlled trials, and large-scale cohort studies to ensure a high level of evidence. Studies focusing on adult populations and reporting clinical outcomes related to efficacy, safety, and metabolic benefits were included. Exclusion criteria comprised articles without full text availability, case reports, conference abstracts, and studies not directly addressing the comparative role of tirzepatide or bariatric surgery in obesity management.

In addition to PubMed, authoritative sources from international scientific and regulatory organizations, including professional society guidelines and official agency reports (e.g., FDA, EMA, MHRA, IFSO), were also consulted to ensure comprehensive coverage of current recommendations and evidence-based practices.

The primary objective of the search was to identify, synthesize, and critically evaluate available evidence on the efficacy and safety of tirzepatide therapy in comparison to bariatric surgery. By focusing on high-quality studies and official scientific sources, the review aimed to provide a balanced and evidence-based perspective on the therapeutic potential, limitations, and clinical applicability of both approaches in the management of obesity.

Bariatric surgeries

Bariatric surgery is considered a highly effective method for treating obesity, providing significant and long-term weight loss. [10] The goals of surgical obesity treatment include gaining control over metabolic processes, reducing body weight, eliminating numerous comorbid conditions, and improving the patient's quality of life. [11]

Bariatric surgeries are generally categorized into three main types based on their mechanisms of action: restrictive, combined (restrictive and malabsorptive), and primarily malabsorptive procedures. Each type promotes weight loss through distinct physiological pathways. Restrictive procedures limit food intake by reducing the size of the stomach. These include laparoscopic adjustable gastric banding, sleeve gastrectomy, and the now-obsolete vertical banded gastroplasty, which is no longer performed due to a high rate of complications. Malabsorptive procedures primarily reduce nutrient absorption by bypassing a significant portion of the small intestine. One such example, the jejunoileal bypass, is no longer in use due to its association with severe complications like malnutrition and organ failure. Combined procedures incorporate both restrictive and malabsorptive elements. The most common among them are the Roux-en-Y gastric bypass (RYGB) and the biliopancreatic diversion with duodenal switch (BPD/DS), both of which are effective in achieving significant and sustained weight loss. [12]

As part of a global survey, the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) requested all affiliated national societies to submit data on the number and type of surgical and endoscopic procedures performed in 2020 and 2021. Out of 74 societies, 57 (77%) responded, and 24 (42.1%) based their data on national registries. In 2020, a total of 507,806 procedures were performed, increasing to 598,834 in 2021. The most commonly used method remained sleeve gastrectomy (SG). [13]

Laparoscopic surgical treatment of obesity should be considered for patients with a BMI equal to or greater than 40 kg/m². Individuals with a BMI between 35 and 40 kg/m² who have comorbid conditions that

may improve with weight reduction may also qualify for such intervention. Furthermore, bariatric or metabolic surgery may be considered in patients with a BMI of 30–35 kg/m² if they are struggling with type 2 diabetes or hypertension that remains difficult to control despite optimal pharmacological treatment. [14]

Bariatric surgery is considered the most effective long-term treatment for severe obesity. It not only allows for significant weight reduction but also for lasting improvement in obesity-related comorbidities. Although outcomes may vary depending on the type of surgery, most patients maintain a significant portion of their weight loss for many years. [15]

A systematic review and meta-analysis published in 2024 assessed the effectiveness and safety of bariatric surgery by analyzing clinical studies conducted between January 2013 and May 2023. The review included a total of 1,984 adult patients who underwent one of four treatment modalities: Roux-en-Y gastric bypass (RYGB, n = 843), sleeve gastrectomy (SG, n = 540), gastric banding (GB, n = 151), or conservative medical therapy (MT, n = 420).

To evaluate the sustainability of treatment outcomes, the results were categorized into short-term (1–2 years post-intervention) and long-term (3–10 years post-intervention) follow-up periods. In the short-term analysis, all surgical procedures demonstrated significant reductions in body weight compared to medical therapy. Patients who underwent RYGB lost an average of 28.5% of their initial weight, those who received SG lost 25.8%, while GB patients achieved a 17.1% weight reduction. In contrast, patients managed with medical therapy experienced a modest weight loss of 6.7%.

Long-term results confirmed that the effects of surgery were largely sustained over time. Average weight loss remained at 25.4% for RYGB, 18.7% for SG, and 12.9% for GB, whereas the MT group maintained only a 5.1% reduction. A similar pattern was observed for changes in body mass index (BMI). In the short term, BMI decreased by 28.5% following RYGB, 24.9% after SG, and 16.7% after GB, compared to 6.0% in the MT group. Long-term follow-up showed BMI reductions of 25.0% for RYGB, 19.5% for SG, 12.6% for GB, and only 4.0% for patients receiving medical therapy. Importantly, the consistency of findings across the included studies was very high, as indicated by an I^2 value of 0.00%, suggesting no relevant statistical heterogeneity. These results strongly support the long-term effectiveness of bariatric surgery—particularly RYGB and SG—in achieving and maintaining clinically meaningful weight loss and BMI reduction, outperforming non-surgical interventions across all measured time points. [16]

Studies show that surgical treatment of obesity yields tangible health benefits. Analyses indicate a clinically significant reduction in the incidence of major obesity-related comorbidities. Observed benefits include a 63% relative risk reduction for cardiovascular diseases, a 33% reduction in cancer risk, and a lower prevalence of depressive disorders. There is also a strong correlation between bariatric surgery and remission of type 2 diabetes, hypertension, and hyperlipidemia. Although mental health issues remain a challenge regardless of surgery, bariatric procedures combined with appropriate specialist care, such as psychotherapy and pharmacological treatment, can significantly improve patient well-being, especially as they begin to see the effects of weight loss. [17]

Numerous meta-analyses confirm that bariatric surgery contributes to a significant decrease in the severity and frequency of depressive and anxiety symptoms. [18] However, in young women with obesity, the effectiveness of bariatric surgery in alleviating anxiety symptoms may be limited. Therefore, a comprehensive psychological assessment should be a crucial step before surgery for all patients considering this intervention. [19]

Complications following bariatric surgery are not uncommon and play an important role in the decision-making process for both patients and surgeons. They are divided into intraoperative, early (within 30 days post-surgery), and late (beyond 30 days). [20]

Short-term complications include anastomotic leakage, strictures, bleeding, infections, marginal ulcers, gastroesophageal reflux disease (GERD), and dumping syndrome. Effective treatment requires timely diagnosis and intervention tailored to the type of complication and the patient's overall condition.

Over the long term, different bariatric procedures are linked to specific late complications that must be considered in patient care. Laparoscopic adjustable gastric banding (LAGB) may result in issues such as slippage of the band, erosion, and dilation of the esophagus. Vertical sleeve gastrectomy (VSG) can cause marginal ulcers, nutritional deficiencies, and gallstone formation. Roux-en-Y gastric bypass (RYGB) is associated with nutritional shortfalls, late dumping syndrome, anastomotic strictures, ulcers, hernias, and potential weight regain. Biliopancreatic diversion with duodenal switch (BPDDS) presents risks, including significant nutritional deficiencies, intestinal obstructions, and hepatic complications. [21]

Drastic changes in body weight and physiology after surgery can trigger emotional distress, body image concerns, and identity changes, potentially contributing to the development of mental health disorders. Rapid

weight loss may also cause mood swings and cognitive fluctuations, affecting psychological well-being. Additionally, nutritional deficiencies following surgery can negatively impact brain function, exacerbating psychiatric symptoms. Clinicians caring for these patients should be aware of such potential complications, conduct appropriate screening, provide treatment, and refer for further care when necessary. [22]

Tirzepatide

Tirzepatide is a modified peptide consisting of 39 amino acids, showing structural similarity to glucose-dependent insulinotropic polypeptide (GIP). It acts as an agonist for both the GIP receptor and the GLP-1 (glucagon-like peptide 1) receptor. Treatment with thiothiazolidinedione leads to an increase in insulin secretion, a decrease in glucagon secretion and a slowing of gastric emptying. The effect of these mechanisms is to lower blood glucose levels - both fasting and after meals - and improve tissue sensitivity to insulin. In addition, tirzepatide contributes to appetite suppression and weight loss. [23] In addition, thirzepatide therapy has a marked effect in lowering fasting blood triglyceride levels. [24] Thirzepatide has been approved for the treatment of obesity and overweight in the United States (Zepbound), the European Union (Mounjaro) and the United Kingdom (Mounjaro), among others. Eligibility conditions for treatment are BMI≥30 or BMI≥27 with at least one comorbid condition, such as hypertension, type 2 diabetes or high cholesterol. Therapy should be given in parallel with a low-calorie diet and increased physical activity. Tirzepatide is administered once a week by subcutaneous injection, and the dose should be gradually increased over a period of four to twenty weeks until the target dose is reached: 5 mg, 10 mg or 15 mg once a week. The maximum allowable dose of the drug is 15 mg per week. [25, 26, 27]. A total of 12 randomized controlled trials including 11, 758 patients were analyzed, and the meta-analysis demonstrated that, compared to GLP-1 receptor agonists, placebo, and insulin, tirzepatide significantly reduced patients' body mass index (BMI) [MD = −1.71, 95% CI (−2.46, −0.95), $p < 0.00001$], [MD = −3.99, 95% CI (−3.69, −2.45), $p < 0.00001$], [MD = −4.02, 95% CI (−4.72, −3.31), $p < 0.00001$]. Regarding waist circumference, tirzepatide showed a more pronounced effect [MD = −4.08, 95% CI (−5.77, −2.39), $p < 0.00001$], [MD = −7.71, 95% CI (−10.17, −5.25), $p < 0.00001$], [MD = −9.15, 95% CI (−10.02, −8.29), $p < 0.00001$]. In terms of body weight, tirzepatide led to a significantly greater reduction compared to the control groups [MD = −5.65, 95% CI (−7.47, −3.82), $p < 0.001$], [MD = −10.06, 95% CI (−12.86, −7.25), $p < 0.001$], [MD = −10.63, 95% CI (−12.42, −8.84), $p < 0.001$]. Compared to placebo, tirzepatide had a marked advantage in achieving weight loss of ≥20% and ≥25% [RR = 30.43, 95% CI (19.56, 47.33), $p < 0.00001$], [RR = 37.25, 95% CI (26.03, 53.30), $p < 0.00001$]. Subgroup analysis indicated a dose-dependent therapeutic effect. [28]. Importantly, tirzepatide has been shown to be highly effective in reducing blood pressure, blood glucose levels, and improving lipid profiles. [29] In the SURMOUNT-4 study, overweight or obese adults who continued treatment with tirzepatide at the maximum tolerated dose showed a significant and sustained improvement in health-related quality of life (HRQoL) compared to patients who were switched to placebo. [30] Tirzepatide has a safety profile similar to that of known GLP-1 agonists. The most commonly reported adverse reactions are gastrointestinal in nature and include decreased appetite, nausea, diarrhea, and, less commonly, vomiting, reflux, and constipation. In isolated cases, sinus tachycardia has been observed, the severity of which may be modified by other medications used. Acute kidney injury has also been reported, mainly secondary to dehydration as a result of gastrointestinal symptoms, highlighting the importance of monitoring patient hydration. Hypersensitivity reactions at the injection site are rare and comparable to those observed with other incretin medications. Like other drugs in this class, tirzepatide may be associated with a risk of acute pancreatitis and asymptomatic increases in pancreatic enzymes. Cases of cholelithiasis and cholecystitis have also been observed, which may be associated with rapid weight loss. In patients with previously diagnosed diabetic retinopathy, temporary worsening may occur as a result of rapid improvement in glycemic control. A small but clinically significant risk of hypoglycemia occurs mainly in people treated simultaneously with insulin or sulfonylureas, which requires appropriate monitoring and patient education. [31] Another limitation concerns the scarcity of long-term data on tirzepatide treatment. Most studies had relatively short follow-up periods, which may restrict the ability to fully assess the drug's long-term safety and efficacy. Since obesity often requires chronic management, it is essential to understand both the sustained benefits and potential risks of prolonged tirzepatide use. Future research should focus on extended follow-up to provide a clearer picture of its long-term effects [32]

Conclusions:

Bariatric surgery and tirzepatide therapy are two important and effective methods of treating obesity, differing in their mechanisms of action, scope of intervention, and risk-benefit profile. Available data indicate that bariatric surgery—in particular procedures such as Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SG)—provides the greatest and most sustained weight loss, averaging 25–28% in the short term and 18–25% in the long term. In addition, surgical procedures lead to significant improvements in metabolic health, including remission of type 2 diabetes, hypertension, hyperlipidemia, and a reduced risk of cardiovascular and cancerous diseases, making them the standard of care in cases of morbid obesity or obesity resistant to conservative treatment. However, it should be noted that these are invasive procedures associated with the risk of intraoperative, early, and late complications, such as anastomotic leaks, nutritional deficiencies, postprandial syndromes, or psychological complications, which require comprehensive interdisciplinary care. Tirzepatide, as an incretin drug with a dual mechanism of action on GIP and GLP-1 receptors, is also highly effective in reducing body weight, achieving weight losses of up to 10–20% in clinical trials, with the effect being dose-dependent. Pharmacological therapy is also associated with an improvement in metabolic parameters – glycemia, lipid profile, and blood pressure – as well as an improvement in quality of life, especially in the mental and psychosocial spheres. Its safety profile is generally favorable, although adverse effects on the gastrointestinal tract and the risk of acute pancreatitis and gallstones predominate. Unlike bariatric surgery, tirzepatide does not require surgical intervention, making it a less invasive therapeutic alternative, especially for patients with moderate obesity or contraindications to surgery. However, it should be emphasized that tirzepatide is a relatively new drug, and data on its long-term efficacy and safety are still limited, so it is necessary to continue monitoring patients and conducting observational studies over a longer time horizon. In summary, bariatric surgery remains the gold standard in the treatment of severe obesity due to the scale and durability of its effects, tirzepatide is a promising, modern pharmacological treatment option, especially in the context of personalised therapy and the need to reduce surgical risk, while taking into account the need for further evaluation of its long-term efficacy and safety profile.

Disclosure:

Authors contribution:

Conceptualization - Wojciech Gąska, Michał Lenart and Weronika Tuszyńska;
methodology - Izabela Lekan, Alicja Sodolska;
software - Joanna Mazurek, Barbara Teresińska;
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data curation - Ignacy Rożek, Agnieszka Brzezińska;
writing - rough preparation - Wojciech Gąska, Alicja Sodolska;
writing - review and editing - Izabela Lekan, Joanna Mazurek, Agnieszka Brzezińska;
visualization - Wojciech Gąska, Weronika Tuszyńska, ;
supervision - Wojciech Gąska, Alicja Sodolska, Izabela Lekan;
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