COMPARISON BETWEEN BARIATRIC SURGERY AND TIRZEPATIDE (MOUNJARO®) IN REDUCING CARDIOVASCULAR RISK IN OBESE PATIENTS

COMPARAÇÃO ENTRE CIRURGIA BARIÁTRICA E TIRZEPATIDA (MOUNJARO) NA REDUÇÃO DO RISCO CARDIOVASCULAR EM PACIENTES OBESOS

COMPARACIÓN ENTRE LA CIRUGÍA BARIÁTRICA Y TIRZEPATIDA (MOUNJARO) EN LA REDUCCIÓN DEL RIESGO CARDIOVASCULAR EN PACIENTES OBESOS

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ABSTRACT

Obesity is a chronic multifactorial disease associated with high cardiovascular morbidity and mortality, resulting from complex interactions among metabolic, hormonal, and inflammatory factors. In recent decades, surgical and pharmacological therapeutic strategies have been extensively investigated to reduce cardiometabolic risk in individuals with obesity. This study aimed to compare scientific evidence on the effects of bariatric surgery and tirzepatide (Mounjaro®) in reducing cardiovascular risk in obese patients. This is an integrative and comparative review with a qualitative–quantitative approach, developed from articles published between 2015 and 2025 in the PubMed, SciELO, ScienceDirect, and AHA Journals databases. Twenty studies were analyzed, including clinical trials, meta-analyses, and systematic reviews, of which fifteen demonstrated higher methodological relevance and were used in the comparative synthesis of findings. The results showed that bariatric surgery, particularly the Roux-en-Y gastric bypass and sleeve gastrectomy techniques, promotes a significant reduction in cardiovascular mortality, improvement in glycemic and lipid profiles, and a decrease in systemic inflammatory markers. Tirzepatide, in turn, demonstrated a marked impact on weight loss, insulin sensitivity, and improvement of inflammatory and hemodynamic parameters, with a cardioprotective effect comparable to that observed after metabolic surgery. It is concluded that both approaches constitute effective and complementary strategies for the prevention and management of cardiovascular diseases associated with obesity, representing promising perspectives for contemporary metabolic medicine.

Keywords: Bariatric Surgery. Tirzepatide. Obesity. Cardiovascular Risk. Integrative Review.

RESUMO

A obesidade é uma doença crônica multifatorial associada a elevada morbimortalidade cardiovascular, resultante de complexas interações entre fatores metabólicos, hormonais e inflamatórios. Nas últimas décadas, estratégias terapêuticas cirúrgicas e farmacológicas têm sido amplamente investigadas para reduzir o risco cardiometabólico em indivíduos obesos. Este estudo teve como objetivo comparar as evidências científicas acerca dos efeitos da cirurgia bariátrica e da tirzepatida (Mounjaro®) na redução do risco cardiovascular em pacientes com obesidade. Trata-se de uma revisão integrativa e comparativa, com abordagem qualitativo-quantitativa, desenvolvida a partir de artigos publicados entre 2015 e 2025 nas bases PubMed, SciELO, ScienceDirect e AHA Journals. Foram analisados 20 estudos, entre ensaios clínicos, metanálises e revisões sistemáticas, dos quais 15 apresentaram maior relevância metodológica e foram utilizados na síntese comparativa dos

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achados. Os resultados demonstraram que a cirurgia bariátrica, sobretudo as técnicas de bypass gástrico em Y de Roux e gastrectomia vertical, promove redução significativa da mortalidade cardiovascular, melhora dos perfis glicêmico e lipídico e diminuição de marcadores inflamatórios sistêmicos. A tirzepatida, por sua vez, demonstrou impacto expressivo na perda ponderal, na sensibilidade à insulina e na melhora de parâmetros inflamatórios e hemodinâmicos, com efeito cardioprotetor comparável ao observado após a cirurgia metabólica. Conclui-se que ambas as abordagens constituem estratégias eficazes e complementares na prevenção e controle das doenças cardiovasculares associadas à obesidade, representando perspectivas promissoras para a medicina metabólica contemporânea.

Palavras-chave: Cirurgia Bariátrica. Tirzepatida. Obesidade. Risco Cardiovascular. Revisão Integrativa.

RESUMEN

La obesidad es una enfermedad crónica multifactorial asociada a una alta morbilidad y mortalidad cardiovascular, resultado de complejas interacciones entre factores metabólicos, hormonales e inflamatorios. En las últimas décadas, se han investigado ampliamente estrategias terapéuticas quirúrgicas y farmacológicas para reducir el riesgo cardiometabólico en personas obesas. Este estudio tuvo como objetivo comparar la evidencia científica sobre los efectos de la cirugía bariátrica y la tirrizepatida (Mounjaro®) en la reducción del riesgo cardiovascular en pacientes obesos. Se trata de una revisión integrativa y comparativa, con un enfoque cualitativo-cuantitativo, desarrollada a partir de artículos publicados entre 2015 y 2025 en las bases de datos PubMed, SciELO, ScienceDirect y AHA Journals. Se analizaron veinte estudios, incluyendo ensayos clínicos, metaanálisis y revisiones sistemáticas, de los cuales 15 presentaron mayor relevancia metodológica y se utilizaron en la síntesis comparativa de los hallazgos. Los resultados demostraron que la cirugía bariátrica, especialmente las técnicas de bypass gástrico en Y de Roux y gastrectomía en manga, reduce significativamente la mortalidad cardiovascular, mejora los perfiles glucémico y lipídico, y disminuye los marcadores inflamatorios sistémicos. La tirzepatida, a su vez, demostró un impacto significativo en la pérdida de peso, la sensibilidad a la insulina y la mejora de los parámetros inflamatorios y hemodinámicos, con un efecto cardioprotector comparable al observado tras la cirugía metabólica. Se concluye que ambos enfoques constituyen estrategias eficaces y complementarias en la prevención y el control de las enfermedades cardiovasculares asociadas a la obesidad, lo que representa perspectivas prometedoras para la medicina metabólica contemporánea.

Palabras clave: Cirugía Bariátrica. Tirzepatida. Obesidad. Riesgo Cardiovascular. Revisión Integrativa.

1 INTRODUCTION

Obesity is a chronic, multifactorial condition with a high prevalence worldwide, characterized by the excessive accumulation of body fat, resulting in a set of metabolic and inflammatory disorders. This condition is strongly associated with increased risk of cardiovascular disease (CVD), type 2 diabetes mellitus, high blood pressure, and dyslipidemias. Studies show that obesity is one of the main determinants of global CVD mortality, being a modifiable risk factor with great clinical relevance (VAN VELDHUISEN et al., 2022). In addition to contributing to the development of atherosclerosis and insulin resistance, excess adipose tissue induces a chronic pro-inflammatory state and favors structural changes in the myocardium, increasing the risk of heart failure and arrhythmias (FERNANDES CARDOSO SANTOS-FURTADO, 2019).

Bariatric surgery is recognized as one of the most effective strategies for weight control and reversal of comorbidities associated with severe obesity. The most commonly used techniques, such as Roux-en-Y gastric bypass and sleeve gastrectomy, have shown consistent results in reducing body weight and improving cardiometabolic risk factors. Systematic reviews and meta-analyses show that bariatric surgery is associated with a significant reduction in cardiovascular mortality and major adverse events (MACE), including acute myocardial infarction and stroke (CHANDRAKUMAR et al., 2023; DOUMOURAS et al., 2021). In addition, there is a significant improvement in blood glucose, blood pressure, and lipid profile after the procedure, reinforcing the positive impact of this intervention on both primary and secondary prevention of CVD (Pessôa Costa, 2021; OLIVEIRA; ROSÁRIO, 2022).

Recently, the pharmacological treatment of obesity and type 2 diabetes has evolved with the development of incretin agonists, especially tirzepatide, a dual agonist of GIP and GLP-1 receptors. Multicenter clinical trials have shown that the use of tirzepatide promotes a significant reduction in body weight, improved insulin sensitivity, and modulation of inflammatory biomarkers (HANKOSKY et al., 2025; STEFANOU et al., 2024). Studies conducted by Packer et al. (2025) showed that in patients with heart failure with preserved ejection fraction (HFpEF), tirzepatide significantly reduced the composite risk of cardiovascular death and clinical worsening of heart failure. These findings reinforce its potential cardioprotective role, possibly comparable to that observed after metabolic surgery.

The contemporary literature suggests that both bariatric surgery and tirzepatide exert beneficial effects on cardiovascular risk, although through different mechanisms. While surgery promotes massive weight loss and hormonal changes that reduce systemic inflammation, tirzepatide acts in a combined way in glycemic regulation, improving

endothelial function, and controlling appetite (KRISHNAN et al., 2025; CAMARGOS BARROS, 2021). However, there are still gaps in the literature regarding the direct comparison between the two strategies in relation to objective cardiovascular outcomes, such as MACE incidence, cardiovascular mortality, and inflammatory markers (CHANDRAKUMAR et al., 2023; BORGES DIAS, 2025). This scarcity of comparative studies justifies the need for investigations that analyze its effects from the perspective of long-term efficacy and safety.

Despite significant advances in the management of obesity and associated cardiovascular diseases, there is still an important gap regarding the direct comparison between the effects of bariatric surgery and tirzepatide on cardiovascular outcomes. Although several studies have shown significant benefits of both approaches, including reduction of major adverse events, improvement of glycemic control, and reduction of systemic inflammation, there are few integrative reviews that systematize this evidence in a critical and comparative manner (CHANDRAKUMAR et al., 2023; PACKER et al., 2025; STEFANOU et al., 2024).

This absence of integrated analyses limits the understanding of which of these strategies offers the greatest impact on reducing global cardiovascular risk, especially in obese patients with different metabolic profiles. In addition, methodological variations between studies make it difficult to extrapolate results to clinical practice, reinforcing the need for an up-to-date, evidence-based synthesis (VAN VELDHUISEN et al., 2022; KRISHNAN et al., 2025).

Thus, the present research is justified by the need to gather and critically discuss the available scientific knowledge about the effects of bariatric surgery and tirzepatide (Mounjaro®) on the reduction of cardiovascular risk in obese patients, identifying convergences, divergences and gaps in the contemporary literature.

Therefore, the objective of this study is to analyze, systematize and compare the scientific evidence published in the last ten years on the efficacy of bariatric surgery and tirzepatide in mitigating risk factors and cardiovascular outcomes in obese individuals**,** contributing to the improvement of clinical practice and the development of evidence-based therapeutic protocols (CHANDRAKUMAR et al., 2023; PACKER et al., 2025; VAN VELDHUISEN et al., 2022).

2 METHODOLOGY

This is an integrative and comparative literature review, with a qualitative-quantitative approach, whose objective was to analyze and synthesize the scientific evidence published

in the last ten years regarding the comparison between the effects of bariatric surgery and tirzepatide (Mounjaro®) on the reduction of cardiovascular risk in obese patients.

The study followed the integrative review method proposed by Mendes, Silveira and Galvão (2008), developed in six stages: definition of the theme and research question, establishment of inclusion and exclusion criteria, search in databases, categorization of studies, critical analysis of the results and final synthesis of the evidence.

This methodology made it possible to integrate and compare findings from different types of studies, allowing a comprehensive and up-to-date understanding of the topic investigated.

2.1 DATABASES AND SEARCH PERIOD

The bibliographic search was carried out in the PubMed/MEDLINE, SciELO (Scientific Electronic Library Online), ScienceDirect and AHA Journals databases, recognized for their relevance and scientific credibility in the health area.

Articles published between January 2015 and December 2025 were selected, a time frame that aims to contemplate recent advances in the use of tirzepatide, introduced in clinical practice as of 2022, as well as innovations in contemporary bariatric surgery techniques. The search took place between October and December 2025, using descriptors in Portuguese and English, combined with Boolean operators.

2.2 SEARCH STRATEGY

The descriptors used followed the terms of **DeCS** (*Health Sciences Descriptors*) and **MeSH** (*Medical Subject Headings*). The following main descriptors were used: **"Bariatric Surgery"; "Tirzepatide" / "Tirzepatide"; "Cardiovascular Risk";** and **"Obesity".**

The combination of the terms was performed using **Boolean operators**, as shown below:

("Bariatric Surgery" AND "Cardiovascular Risk") OR ("Tirzepatide" AND "Cardiovascular Outcomes") AND ("Obesity").

This strategy was applied in a standardized manner in all selected databases, with filters that restricted the results to **original articles, systematic reviews, meta-analyses, and randomized clinical trials**, published in **Portuguese, English, and Spanish**.

2.3 INCLUSION AND EXCLUSION CRITERIA

- **Inclusion criteria:**

a) Original articles, systematic reviews, integratives, and meta-analyses on **bariatric surgery** and/or **tirzepatide (Mounjaro®)** related to **cardiovascular risk reduction in obese patients**;

b) Studies conducted in ; **adult populations (BMI ≥ 30 kg/m²)**

c) Publications **indexed in recognized databases** (PubMed, SciELO, ScienceDirect and AHA Journals);

d) Works **published between 2015 and 2025**, available in full in **Portuguese, English or Spanish**.

• **Exclusion Criteria:**

a) Duplicate studies between databases;

b) Work **with paediatric, animal or in vitro samples**;

c) Articles **not directly related to cardiovascular outcomes** (e.g., studies focused only on weight loss or gastrointestinal effects);

d) **Case reports, editorials, letters to the editor, dissertations and conference proceedings.**

2.4 STUDY SELECTION PROCESS

The screening of the studies was conducted in two sequential stages. In the first, the titles and abstracts were read, with the objective of excluding articles outside the thematic scope of the research. In the second stage, the selected texts were read in full, in order to confirm eligibility according to the previously established criteria.

After the selection process, **20 scientific articles** were included, including randomized clinical trials, observational studies, systematic reviews, and meta-analyses, which met the inclusion criteria. Screening was carried out independently by two reviewers, and any discrepancies were resolved by consensus, ensuring traceability, transparency, and methodological reliability.

However, **of the 20 articles analyzed, 15 were considered more relevant and methodologically consistent**, and were used to support the discussion and conclusions of this study. The others, although eligible, had sampling limitations or secondary scope in relation to the central theme, and were included only in the initial descriptive analysis.

2.5 DATA ANALYSIS AND SYNTHESIS

The selected articles were organized in Microsoft Excel spreadsheets**, including information on** the author, year of publication, country of origin, type of study, sample size, intervention investigated, cardiovascular outcomes evaluated, and main results**.**

Subsequently, the data were grouped according to the defined analytical variables, considering:

a) Type of intervention**: bariatric surgery or pharmacological treatment with tirzepatide;**

b) Type of cardiovascular outcome**: Major *Adverse Cardiovascular Events* (MACE), mortality, systemic inflammation, blood glucose, and lipid profile;**

c) Study methodology**: clinical trials, cohort studies, systematic reviews and meta-analyses.**

The analysis was conducted in a descriptive and comparative manner, focusing on the identification of patterns of evidence, convergences, divergences, and gaps in the scientific literature. This approach enabled the elaboration of a critical and interpretative synthesis, aimed at evaluating the relative impact of the two therapeutic strategies, bariatric surgery and tirzepatide, on the reduction of cardiovascular risk in obese individuals.

2.6 ETHICAL CONSIDERATIONS

As this is a literature review, the present study did not involve experimentation with humans or animals, and, therefore, submission to a Research Ethics Committee was waived.The principles of academic integrity, scientific transparency and methodological rigor were fully observed, ensuring the proper citation and recognition of original sources, as established by NBR 6023:2018 of the Brazilian Association of Technical Standards (ABNT)

3 RESULTS AND DISCUSSION

We analyzed **20 scientific articles** published between 2015 and 2025, of which **15 had greater methodological relevance** and were used in the comparative synthesis of the findings. The studies predominantly addressed the effects of **bariatric surgery** and **tirzepatide (Mounjaro®)** on cardiovascular outcomes in obese individuals, including mortality, endothelial function, glycemic and lipid profiles, and systemic inflammatory markers.

In general, studies related to bariatric surgery have shown significant reductions in cardiovascular mortality, improved metabolic control, and partial reversal of cardiac structural abnormalities. On the other hand, studies investigating tirzepatide have highlighted significant reductions in body weight, improved insulin sensitivity, and decreased inflammatory biomarkers, reflecting a cardioprotective profile similar to that observed after surgery.

The consolidated results demonstrated that **both surgical and pharmacological approaches promote substantial benefits in reducing cardiovascular risk in obese**

patients, although they act by different pathophysiological mechanisms and present different magnitudes and durability of therapeutic response.

3.1 EFFECTS OF BARIATRIC SURGERY ON CARDIOVASCULAR RISK REDUCTION

The studies analyzed in this review consistently demonstrate that bariatric surgery, especially Roux-en-Y gastric bypass and sleeve gastrectomy, is associated with a significant reduction in cardiovascular mortality and the occurrence of major cardiovascular events (MACE). In addition to substantial and sustained weight loss, there is a significant improvement in the glycemic, lipid and pressure profiles, accompanied by a decrease in systemic inflammatory markers, elements closely related to the mitigation of global cardiometabolic risk.

These findings reinforce that bariatric surgery acts as a multifactorial metabolic intervention, whose impact goes beyond the mere reduction of body weight. The hormonal modulation resulting from the procedure, marked by an increase in GLP-1 (glucagon-like peptide-1) and PYY (peptide YY), and a decrease in ghrelin, contributes to improving insulin sensitivity, reducing glycotoxicity, and attenuating the chronic low-grade inflammatory state characteristic of obesity. Such physiological changes favor the improvement of endothelial function, reduce arterial stiffness, and delay the progression of atherosclerosis, consolidating the metabolic cardioprotective effect of the surgery.

From the hemodynamic point of view, there is also a reduction in circulating plasma volume and cardiac overload, which contributes to the regression of left ventricular hypertrophy and to the improvement of diastolic function. These effects are widely documented in individuals with severe obesity and have a direct impact on the decrease in the incidence of heart failure and arrhythmias.

The findings of this review corroborate the results described by Chandrakumar et al. (2023) and Doumouras et al. (2021), who identified reductions of up to 50% in the relative risk of acute myocardial infarction and stroke after bariatric surgery. Similarly, Van Veldhuisen et al. (2022) reported a significant reduction in cardiovascular and overall mortality, evidencing the maintenance of long-term benefits. National research, such as those by Pessoa Costa (2021) and Oliveira and Rosário (2022), corroborate these findings, indicating an improvement in blood pressure and serum lipid levels, as well as metabolic homeostasis.

In recent meta-analyses, bariatric surgery has been identified as the most effective non-pharmacological intervention for reducing cardiovascular risk in individuals with grade III obesity, surpassing the effects obtained with drug therapies alone. However, the literature still lacks direct comparative clinical trials between different surgical techniques and long-term

evaluations in specific populations, such as patients with advanced type 2 diabetes or established heart failure.

These gaps highlight the need for prospective multicenter studies that allow for a more precise measurement of the relationship between the magnitude of weight loss, hormonal changes, and real reduction in cardiovascular risk. Despite this, the available evidence consolidates bariatric surgery as a high-impact therapeutic strategy for the prevention and control of cardiovascular diseases in patients with severe obesity, with benefits that go beyond the metabolic axis and achieve functional and structural remodeling of the cardiovascular system.

3.2 EFFECTS OF TIRZEPATIDE (MOUNJARO®) ON CARDIOMETABOLIC MODULATION

The studies included in this review indicate that tirzepatide (Mounjaro®), a double agonist of glucose-dependent insulinotropic peptide (GIP) and glucagon-like peptide type 1 (GLP-1) receptors, has stood out as one of the main pharmacological innovations in the management of obesity and cardiovascular risk. Multicenter clinical trials conducted between 2022 and 2025 demonstrate that tirzepatide promotes an average weight reduction of 15% to 20% of body weight, in addition to a significant improvement in insulin sensitivity, glycemic control, and lipid profile, with a positive impact on endothelial function and inflammatory biomarkers.

These results reinforce the role of tirzepatide as a multifunctional pharmacological intervention, whose action is not limited to glycemic control, but extends to metabolic and systemic inflammatory modulation. By simultaneously stimulating GIP and GLP-1 receptors, the drug promotes improved glucose-dependent insulin secretion, reduced hepatic glucose production, increased satiety, and delayed gastric emptying, culminating in a negative energy balance and long-lasting metabolic control. These mechanisms combined contribute to the reduction of insulin resistance, improvement of endothelial dysfunction and reduction of vascular inflammation, key factors for the prevention of cardiovascular events.

The findings of this review are in line with the results presented by Packer et al. (2025) and Hankosky et al. (2025), who showed a significant reduction in cardiovascular risk estimated at ten years among obese patients treated with tirzepatide. In addition, Stefanou et al. (2024) observed substantial improvement in cardiac function and reduced hospitalizations for heart failure with preserved ejection fraction (HFpEF), reinforcing the cardioprotective potential of the drug. Additional studies, such as the one by Krishnan et al. (2025), report a reduction in inflammatory biomarkers, including C-reactive protein and

interleukin-6, which suggests that part of the beneficial effect of tirzepatide stems from the attenuation of systemic inflammation associated with obesity.

Compared to other GLP-1 agonists, tirzepatide is more effective in weight reduction and metabolic improvement, possibly due to its dual hormonal pathway. This characteristic differentiates the drug from agents such as semaglutide and liraglutide, whose exclusive action on the GLP-1 receptor results in less pronounced effects on lipid metabolism and insulin resistance.

In addition, follow-up studies indicate that the continuous use of tirzepatide promotes sustained improvement in systolic blood pressure and reduction in abdominal circumference, indicators of favorable metabolic remodeling in the medium term.

Despite the promising results, the current literature still lacks long-term clinical trials that evaluate actual cardiovascular mortality and the effects of therapeutic interruption on the maintenance of the benefits obtained. There is also a need for direct comparisons between tirzepatide and surgical interventions to elucidate the therapeutic equivalence and potential synergistic effects between pharmacological and metabolic approaches.

From a clinical point of view, tirzepatide represents a relevant advance in the pharmacological therapy of obesity and cardiovascular risk, offering a less invasive alternative, with high metabolic efficacy and a favorable safety profile. Its combined effects on weight, blood glucose, and inflammation position the drug as a strategic option in the integrated management of obese patients at high cardiometabolic risk, especially those with surgical contraindications or in the early stages of cardiovascular disease.

3.3 COMPARISON BETWEEN THE TWO APPROACHES: EFFICACY, MECHANISMS AND CLINICAL APPLICABILITY

The comparison between bariatric surgery and tirzepatide (Mounjaro®) reveals that both therapeutic strategies exert substantial and complementary effects on the reduction of cardiovascular risk in obese patients, although they act by different mechanisms and with different temporal magnitudes. While bariatric surgery produces profound anatomical and hormonal changes, resulting in immediate and sustained metabolic improvement, tirzepatide acts pharmacologically and progressively, promoting gradual hormonal and metabolic regulation.

The cardiovascular benefits of surgery derive predominantly from combined structural and metabolic mechanisms, including reduced insulin resistance, improved leptin sensitivity, increased endogenous GLP-1, and decreased chronic vascular inflammation. Tirzepatide, on the other hand, achieves similar results through exogenous stimulation of GIP and GLP-1

receptors, mechanisms that partially mimic the hormonal changes induced by surgery. This physiological similarity suggests that tirzepatide may pharmacologically reproduce some of the beneficial metabolic effects of bariatric surgery, especially on blood glucose, lipids, and systemic inflammation.

In terms of magnitude, surgical results remain more significant in the short and medium term, particularly in patients with morbid obesity (BMI ≥ 40 kg/m²) and associated comorbidities, such as type 2 diabetes resistant to medical treatment. On the other hand, recent studies with tirzepatide show continuous and sustainable gains, with significant weight reduction, improved glycemic control, and decreased estimated cardiovascular risk, achieving benefits comparable to those of surgery in patients with class I or II obesity (Packer et al., 2025; Krishnan et al., 2025).

From the point of view of clinical applicability, the choice between the two approaches should be guided by individual patient characteristics, including degree of obesity, presence of comorbidities, surgical risk, therapeutic adherence, and access to specialized care. Bariatric surgery is more indicated for severe cases that are refractory to drug treatment, while tirzepatide emerges as a viable alternative for patients who are not candidates for the surgical procedure or who seek less invasive and reversible options.

It is important to highlight that the synergistic effects between surgical and pharmacological interventions have been increasingly explored. Recent studies suggest that the use of tirzepatide in the postoperative period can enhance the maintenance of weight loss and reduce metabolic recurrence, contributing to optimize long-term results. This hybrid approach, which combines anatomical and pharmacological modulation, reflects the advancement of personalized medicine and the emerging concept of integrated metabolic treatment.

In the pathophysiological context, both treatments converge in the improvement of energy homeostasis and in the reversal of endothelial dysfunction, although by different pathways. Surgery induces structural changes in the gastrointestinal tract, altering the secretion of intestinal hormones and bile metabolism, while tirzepatide acts directly on endocrine receptors, simulating postprandial responses and reducing caloric intake. This complementarity of mechanisms reinforces the idea that the two strategies are not concurrent, but potentially complementary in the management of cardiovascular risk associated with obesity.

Despite the promising results, there is still a lack of direct comparative studies between tirzepatide and bariatric surgery on harsh clinical outcomes, such as mortality and hospitalization for cardiovascular events. Most of the available data derive from secondary

analyses of clinical trials or observational studies, limiting comparability between interventions. Thus, there is an urgent need for multicenter randomized controlled trials that evaluate in a controlled manner the relative efficacy and cost-effectiveness of both approaches.

In summary, both bariatric surgery and tirzepatide demonstrate proven efficacy in reducing cardiovascular risk, but differ in terms of response time, degree of invasiveness, and safety profile. Surgery continues to be the option with the greatest metabolic impact, while tirzepatide is consolidated as a promising pharmacological strategy, with the potential to expand the therapeutic spectrum of obesity and its cardiovascular complications. Scientific advancement is therefore moving towards a rational integration of these approaches, with a focus on therapeutic individualization and the sustainability of clinical results.

3.4 LIMITATIONS AND GAPS IN THE CURRENT LITERATURE

Despite significant advances in the field of obesity and cardiovascular risk, the scientific literature on the comparison between bariatric surgery and tirzepatide (Mounjaro®) still has methodological limitations and important gaps that compromise the generalization of the available results.

One of the main limitations observed is the heterogeneity between the studies analyzed, both in relation to the methodological design and the inclusion criteria for participants. The available clinical trials and systematic reviews vary widely in terms of follow-up time, sample size, and type of cardiovascular outcome assessed, which makes it difficult to consolidate robust and comparable evidence. This diversity of designs results in selection bias and differences in the interpretation of the magnitude of the observed effects.

In addition, most publications on tirzepatide are still relatively recent, focusing on short-term trials, with a predominant focus on intermediate outcomes, such as weight reduction, improvement of the glycemic profile, and reduction of inflammatory markers, without consolidated data on cardiovascular mortality or major clinical events (MACE). This time limitation restricts the ability to assess the durability and safety of long-term metabolic effects, especially compared with the already consolidated evidence from bariatric surgery.

Another critical point is the absence of direct comparative studies between the two approaches. Although there are meta-analyses and retrospective analyses that address both separately, there is a paucity of randomized controlled trials comparing bariatric surgery and tirzepatide under the same experimental protocol, evaluating efficacy, cost-effectiveness, and real cardiovascular impact. This methodological gap prevents definitive conclusions about which intervention offers the best risk-benefit ratio in different obese patient profiles.

In addition, there is little standardization of cardiovascular assessment parameters among studies. Some use the Framingham risk score, others use composite metabolic indices or inflammatory biomarkers, with no consensus on which measure best reflects actual cardiovascular risk in patients undergoing metabolic interventions. The lack of standardization compromises the comparability between studies and makes it difficult to perform robust quantitative meta-analyses.

Another aspect that is often overlooked is the influence of genetic, behavioral, and socioeconomic factors on the observed outcomes. Most studies focus on specific populations, limiting the extrapolation of results to diverse ethnic groups and clinical contexts, such as developing countries. In addition, there is a lack of longitudinal data evaluating the maintenance of metabolic and cardiovascular benefits over horizons longer than five years, both for tirzepatide and for surgical techniques.

These gaps reinforce the need for multicenter, randomized, long-term clinical trials capable of establishing direct and standardized comparisons between surgical and pharmacological interventions. Such studies should include harsh clinical outcomes, such as mortality, reinfarction, and hospitalizations for heart failure, as well as cost-effectiveness and impact analyses on quality of life. The development of unified assessment protocols and integrated international databases could contribute to overcoming current limitations and formulating more accurate and personalized clinical recommendations.

In summary, although current evidence points to significant benefits for both bariatric surgery and tirzepatide, the body of literature is still in the scientific maturation phase. The consolidation of high-quality comparative data is essential for the advancement of knowledge and for the definition of more effective, safe, and sustainable therapeutic strategies to reduce the cardiovascular risk associated with obesity.

3.5 IMPLICATIONS FOR CLINICAL PRACTICE AND FUTURE PROSPECTS

The comparative analysis between bariatric surgery and tirzepatide (Mounjaro®) shows that both represent effective and complementary therapeutic strategies in the management of obesity and in the reduction of cardiovascular risk. The findings of this review indicate that the impact of these interventions goes beyond the sphere of weight loss, reaching metabolic, hormonal, and inflammatory dimensions, which are fundamental for the restoration of cardiovascular homeostasis in obese individuals.

In clinical practice, bariatric surgery should continue to be indicated as the therapy of choice for patients with severe obesity (BMI ≥ 40 kg/m²) or obesity associated with difficult-to-control comorbidities, such as type 2 diabetes and resistant hypertension. The

accumulating evidence demonstrates that the surgical procedure offers consistent cardiometabolic benefits, including reduced cardiovascular mortality, improved blood pressure control, decreased systemic inflammation, and partial reversal of endothelial dysfunction. However, its invasive nature and the risk of postoperative complications require careful evaluation of the patient's eligibility, multidisciplinary support, and prolonged follow-up.

On the other hand, tirzepatide emerges as an innovative and highly effective pharmacological alternative, with the potential to expand access to intensive metabolic treatment in less complex clinical contexts. Its dual action profile (GIP/GLP-1) provides robust metabolic control, significant reduction in body weight and improvement of endothelial function, consolidating the drug as a promising tool for pharmacological cardiovascular prevention. The possibility of outpatient use and the low risk of serious adverse events make tirzepatide a valuable option for patients with surgical contraindications or with mild to moderate obesity.

In the contemporary therapeutic scenario, the integration between surgical, pharmacological, and behavioral approaches tends to configure the ideal model for the treatment of obesity and metabolic syndrome. The rational combination of these strategies can enhance results, minimize recurrences, and provide long-term sustainable cardiovascular control. In this context, the role of tirzepatide as an adjuvant therapy to bariatric surgery deserves to be highlighted, as preliminary studies suggest that the combined use can potentiate weight loss, improve glycemic control, and prevent postoperative weight regain.

Future perspectives point to the consolidation of personalized metabolic medicine, based on metabolic phenotyping, risk stratification, and genomic analysis, in order to direct the most appropriate type of intervention for each patient. The development of long-term comparative clinical trials, with harsh cardiovascular outcomes and cost-effectiveness analyses, will be decisive to define integrated clinical protocols that combine safety, accessibility and sustainability.

Finally, it is evident that the effective coping with obesity and its cardiovascular complications requires multidisciplinary and individualized approaches, involving nutritional education, behavioral change, pharmacotherapy, and metabolic surgery. The scientific advance represented by tirzepatide and the consolidation of bariatric surgery as a reference treatment converge towards the same objective: to reduce the global burden of cardiovascular disease associated with obesity, promoting longevity and quality of life for the population at risk.

4 CONCLUSION

The findings of this integrative and comparative review show that both bariatric surgery and tirzepatide (Mounjaro®) are effective and clinically relevant strategies to reduce the cardiovascular risk associated with obesity. Although they have different mechanisms of action, both approaches promote significant improvement in metabolic, hormonal, and inflammatory markers, contributing to the restoration of cardiovascular homeostasis and to the reduction of mortality from cardiometabolic diseases.

Bariatric surgery stands out for its more robust and long-lasting impact on body weight reduction and global metabolic modulation, especially in individuals with severe obesity and difficult-to-control comorbidities. Tirzepatide, on the other hand, represents a promising pharmacological innovation, with the potential to achieve benefits comparable to those of surgical intervention, especially in patients with moderate obesity or surgical contraindication, offering a less invasive alternative and more accessible clinical management.

The comparative analysis allows us to infer that the rational integration between metabolic, surgical and pharmacological therapies may represent, in the future, the most efficient and sustainable strategy for the control of obesity and its cardiovascular outcomes. This integrated approach has the potential to broaden the therapeutic spectrum, enhance the beneficial effects on energy and inflammatory metabolism, and allow the individualization of treatment according to the risk profile of each patient.

However, there is a clear need for multicenter, randomized, long-term clinical trials that directly and standardise the comparative efficacy of tirzepatide and bariatric surgery, as well as their possible combined effects. Future studies should prioritize hard clinical outcomes, cost-effectiveness analyses, and impact on quality of life, in order to support integrated clinical protocols and public policies aimed at cardiovascular prevention and the global treatment of obesity.

Finally, it is concluded that both bariatric surgery and tirzepatide represent significant advances in the management of obesity from a cardiometabolic perspective. Consolidating high-quality comparative evidence is essential to strengthen evidence-based clinical practice, guide medical decision-making, and contribute to reducing the global burden of obesity-associated cardiovascular disease.

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