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IMPACT OF BARIATRIC SURGERY ON CARDIOVASCULAR RISK REDUCTION: IS THERE STILL ROOM FOR THIS TREATMENT?

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ABSTRACT

Introduction: Obesity is excess body fat, characterized by a BMI ≥30 kg/m², is recognized as a chronic, multifactorial disease, and requires multidisciplinary approaches, associated with health hazards, such as cardiovascular risk, systemic arterial hypertension, type 2 diabetes mellitus, in addition to predisposition to the development of cancer. The increase in cases in the twenty-first century highlights the difficulty in dealing with this issue. **Objective:** To identify an association between bariatric surgery and decreased cardiovascular risk in obese patients and to compare drug treatment. **Methodology:** Articles from 2015-2024 were used in the Google Scholar, Scielo, and Pubmed databases, with the descriptors: "Obesity", "Bariatric surgery", "Cardiovascular risk", "Drug treatment", "Semaglutide", and "Hypertension", and included Gateway studies and the 2019 PRISMA tool. **Results:** In the study by Rabello et al (2016), a ≥30% reduction in the use of antihypertensive drugs was observed, keeping blood pressure controlled in the group of patients undergoing bariatric surgery. In addition, there was an improvement in glycemic and triglyceride levels, with a mean reduction after 3 months, comparing patients undergoing pharmacological treatment, who did not show clinical variation only in glucagon values (18.1±20.7 vs. 16.8±18.4 pg/ml, p<0.001), thus defining surgical treatment as the best option for reducing cardiovascular risk in obese patients. The GATEWAY study, by Shiavon (2018), compared the effects of metabolic surgery in obese and hypertensive patients. The 100 selected women, aged 34 and 53 years, 76% women, were randomly submitted to Roux-en-Y gastric bypass. The result was a reduction of ≥30% total of antihypertensive drugs while maintaining controlled blood pressure. **Conclusion:** Bariatric surgery favors the reduction of visceral fat, control of comorbidities, and prevention of the

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risk of cardiometabolic diseases. The results indicate that metabolic surgery is effective in reducing mortality and complication rates, both macro and microvascular, such as systemic arterial hypertension and dyslipidemia, minimizing adverse cardiovascular outcomes. Although there has been progress in the results of clinical drug treatments, such as tirzepatide, bariatric remains an important and viable therapeutic option to treat obesity and reduce unfavorable cardiovascular clinical outcomes.

Keywords: Obesity. Bariatric Surgery. Cardiovascular Risk.

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INTRODUCTION

Obesity is a chronic clinical condition, of multifactorial etiology, whose treatment involves a multidisciplinary approach, such as nutritional, medication and physical exercise (ZEVE, 2012).

According to the definition of the World Health Organization (WHO 2013), it is the excess of body fat, determining damage to health. Obesity is considered if an individual's Body Mass Index (BMI) is greater than or equal to 30 kg/m2 and the normal weight range varies between 18.5 and 24.9 kg/m2. From the exponential growth of cases involving this condition, more specifically in the twenty-first century, it is tangible that it is difficult for public health to cover this problem in an integral way, which has great potential for predisposition to various conditions, such as systemic arterial hypertension, type 2 diabetes mellitus, metabolic syndrome, non-alcoholic hepatic steatosis, sleep disorders, lung diseases, osteoarticular disorders, mood disorders, dementia and breast, prostate and bowel cancer (SILVA et al, 202; ABESO, 2021).

The WHO also estimates that in 2022, more than 2 billion adults were overweight, with around 650 million considered obese. A complex global health problem that requires an integrated approach. Understanding its epidemiology, risk factors, evolution, early diagnosis, and social and economic implications is crucial to address this growing challenge. In addition, patients with increased body mass index have different comorbidities, including hypertension, which are strongly related to the high cardiovascular risk of this population. In the United States, half of patients with hypertension are obese (SILVA et al, 2021).

Obesity can cause several pathophysiological disorders, such as cardiovascular disorders (systemic arterial hypertension, left ventricular hypertrophy with or without heart failure, deep vein thrombosis, among others), endocrine disorders (type II diabetes *mellitus* , dyslipidemia, hypothyroidism, infertility and others), respiratory disorders (obstructive sleep apnea, hypoventilation syndrome, restrictive lung disease). It can also course with gastrointestinal dysfunctions (hiatal hernia and cholecystitis), dermatological disorders, genitourinary and gestational disorders; musculoskeletal disorders, such as osteoarthritis and postural defects; neoplasms, such as breast or prostate cancer; psychosocial disorders, such as feelings of inferiority and social isolation, among many other conditions whose patients are predisposed to acquire (ZEVE, 2012).

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It is essential for this condition to raise awareness of the health team involved in the therapeutic process of obese patients about the importance of multidisciplinary care, seeking physical, psychic and social improvement, aiming to improve and improve the quality of care offered.

Such conditions have a significant impact on physical and mental well-being, in addition to reducing longevity. Currently, therapeutic methods aim to return and/or increase the quality of life of patients, whether they are medication or not. However, several patients do not respond to clinical and therapeutic maneuvers, requiring a more effective intervention, such as surgery (ZEVE, 2012).

Fundamentally, the treatment of obesity is divided into non-pharmacological and pharmacological measures. Non-pharmacological measures are known as "lifestyle changes", consisting of behavioral therapies, changes in eating habits, physical exercise, and professional intervention in order to reduce caloric and lipid intake. From a BMI greater than or equal to 30 kg/m2, patients adapt to the use of pharmacological measures for weight reduction; or individuals with a BMI greater than 25 kg/m2, who have diseases associated with excessive weight, whose results are not satisfactory with exercise alone diets and behavioral changes (COSTA; DUARTE, 2017; SAINTS; BELO, 2017).

The medications that showed the best results and acceptance among patients are currently divided into 7 groups: catecholaminergic drugs, serotonergic drugs, catecholaminergic and serotonergic drugs, thermogenic drugs, fat absorption inhibitors and selective CB-1 antagonist drugs. SGLT-2 inhibitors and GLP-1 agonists, despite focusing on the control of Diabetes Mellitus, have also shown a great impact on weight loss treatment (MARTINS, 2021).

For patients whose previous measurements do not demonstrate success, the possibility of invasive therapy such as bariatric surgery (BC), also called metabolic surgery, becomes possible. In the adult population, this approach is a dynamic and complex field, where techniques, indications, contraindications, complications, and historical evolution are intricately intertwined.

The indications for bariatric surgery were initially brought by the *National Institutes of Health* (NIH) *Consensus Development Panel* in the 90s and then accepted by the Brazilian Multi-Societal Consensus on Obesity Surgery of 2006, being indicated for patients with the following characteristics: BMI equal to or greater than 40 kg/m² without comorbidities or BMI equal to or greater than 35 kg/m² with comorbidities; age between 18 and 60 years;

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undergoing treatment for obesity for more than 5 years; who has previously failed clinical approaches to weight loss; motivated, capable and aware to follow medical and nutritional follow-up after surgery; which does not have important contraindications, such as significant operative risk, limited life expectancy due to the disease (ABESO, 2023).

Patients with obesity who have an indication for surgery should have the right to a multidisciplinary team that includes: surgeon, clinical doctor, endocrinologist, psychiatrist, psychologist, nutritionist and physiotherapist. The multidisciplinary evaluation is one of the key points for the success of the operation, and for a good postoperative improvement (ABESO, 2023).

Previous guidelines recommended that bariatric surgery would be elective only for patients with a body mass index (BMI) above 35 and associated with two other comorbidities. Meanwhile, the innovation tends to cover all people with a body mass index (BMI) above 35 and two associated comorbidities. In the expectation that in the future it will be released for all people with a BMI of 35, without the presence of associated comorbidities (ABESO, 2023).

Last year, the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) in 2023, reorganized the Brazilian guidelines, modifying the indications for metabolic surgery, which was previously indicated for people with grade 1 obesity (BMI of 30 to 35). However, the document ensures the procedure as the best treatment for this group (ABESO, 2023).

Children and adolescents were a group with contraindications to undergo bariatric surgery, and could also benefit when they presented grade 2 obesity, BMI of 35 to 40, associated with other comorbidities. The suggestion was also accepted by the American Academy of Pediatrics. Regarding the elderly population, surgery has shown positive results in older patients in recent decades, including individuals over 70 years of age (MAGALHÃES, 2024; ABESO, 2023).

Bariatric surgery refers to several surgical techniques that promote weight reduction in the medium and long term. The basic mechanisms involved in these techniques are: the restrictive (which induces early satiety by reducing gastric storage) such as "sleeve gastrectomy" or "*sleeve*", the malabsorptive (which aims to delay the absorption of food intake with the reduction of the intestinal absorption surface), such as the "duodenal diversion" or "*duodenal-switch*" techniques" or Scopinaro technique and the mixed

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technique (unites both restrictive and absorptive in a single technique), known as *"gastric bypass*" or "Fobi-Capella" surgery (MARRA et al., 2021; LOPES et al., 2022).

Thus, the objective of this study involves the analysis of therapeutic measures and their impact as medicine advances, seeking evolution and comparison of drug and surgical therapies, aiming at reducing comorbidities and cardiovascular risks.

OBJECTIVES

This study aims to identify the association between bariatric surgery and the reduction of cardiovascular risk in obese individuals and the comparison with other drugs that induce weight loss. In addition, our objective is to demonstrate a reduction in the condition of hypertension in such patients, since bariatric surgery and drug treatment of obesity can contribute to this end.

METHODS

A systematic review of published studies on the impact of bariatric surgery and the reduction of cardiovascular risk was carried out in the Google Scholar, Scielo and Pubmed databases. In addition, Gateway studies, graduate and course completion programs, articles published in magazines and newspapers that have links to topics related to health and endocrinology were included. Our study has characteristics based on the methodological tool PRISMA, in its latest version published in 2019.

For this study, the following descriptors were used: "Obesity", "Bariatric surgery", "Cardiovascular risk", "Drug treatment", "Semaglutide", "Surgical technique" and "Hypertension".

The inclusion criteria comprised primary studies, published in full between 2015 and 2024 and mainly in the following languages: Portuguese, Spanish, and English, which investigate the impact of bariatric surgery on the reduction of cardiovascular risk in obese patients. Studies of integrative, narrative or systematic reviews, with unavailable full text and duplicates, as well as studies that touch on the proposed theme, were excluded.

Potentially relevant studies will be selected for a full review of the text. For data analysis, the titles were read, the selected texts were reviewed, extracting their main information (author, year, title, objective and results), which were shown in Chart 1, after

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the following flowchart (Figure 1). From this, the discussion of the results was made possible, aiming to achieve the objective proposed in this study.

This systematic review will be conducted in accordance with the ethical principles of scientific research, ensuring respect and commitment to the proposed theme.

Figure 1: Flowchart of the selection of studies included in the systematic review - April 2024

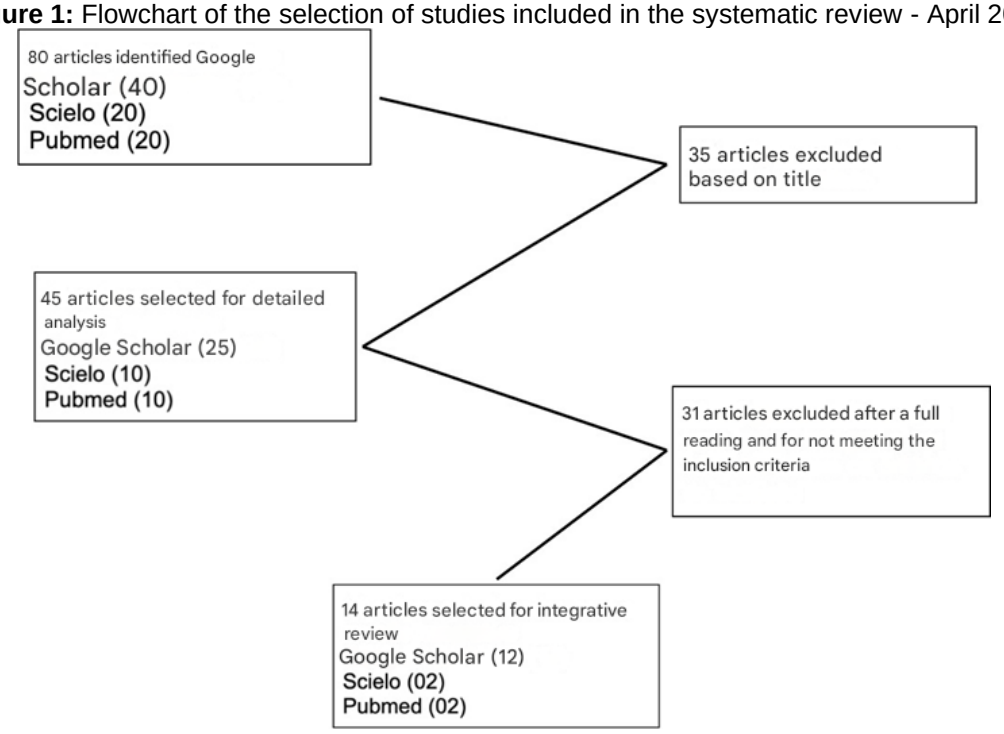

Table 1 - Distribution of the results of the selected articles

Author and Year	Title	Goal	Findings
Carel W. le Roux 2022	Tirzepatide for the treatment of obesity: Rationale and design of the SURMOUNT clinical development	Obesity is a growing global concern compounded by limited availability of	Across trials, participants have a mean age of 44.9 to 54.2 years, are mostly female (50.7% to 69.7%), and have a
	program	effective	mean BMI of 36.1 to
		treatment	38.9.
		options. The	
		SURMOUNT	
		development	

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		Program aims	
		to evaluate the	
		efficacy and	
		safety of	
		tirzepatide as	
		an adjunct to	
		Lifestyle	
		intervention	
		compared with	
		placebo on	
		chronic weight	
		management	
		in adults with	
		BMI ≥ 27	
		kg/m2 with or	
		without type 2	
		diabetes.	
Victor Cury	Risk Reduction	Analyze the	It was observed
Mark	Cardiovascular	impact of	Significant association
2022	Framingham in	surgery	between surgery
	obese patients	bariatric in the	bariatric and reduction
	submitted to	Score of	of the RCF, independent
	Gastrectomy	risk	of the technique used.
	Vertical (Sleeve) and	cardiovascular	
	Gastroplasty in	from	
	Roux-en-Y (Bypass	Framingham	
	gastric) in	BMI of 10	
	An institution	Years	
	toilet	Comparing	
		Pre Data	
		and powders	

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		Operative	
		Those	
		Patients	
		submitted to	
		gastrectomy	
		vertical and	
		Gastroplasty	
		in	
		Roux-en-Y.	
Maria Inês	OBESITY AND	Evaluate the	The absolute values of
Remígio de	SICKNESS	function	Oxygen consumption
Aaron	CARDIOVASCULAR	cardiopulmonary	(VO2 max) if
2015	: IMPACT OF	R and autonomic	showed inferior
	SURGERY	From the heart of	after
	BARIATRIC NA	Patients	Bariatric surgery
	DYSFUNCTION	obese in preschool	Before the procedure
	AUTONOMIC AND	and	(2.37 x 2.21, p=0.007).
	FUNCTION	postoperative	However, when analyzing
	CARDIOPULMONARY	surgery	o VO2 max adjusted
	R.	Bariatric	for body weight,
		through the	An increase was observed
		test	significant after the
		cardiopulmonary	bariatric surgery,
		r of exercise.	suggesting an improvement in
			ability
			related to the
			Surgical procedure

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			(19.7 x 23.9, p<0.001). Despite the VO2 values in VT1 did not show changes before and after bariatric surgery, the moment of onset of VT1 was later after surgery (p=0.001). Regarding the time spent in the reduction of VO2 after exertion, the oxygen kinetics, there was a faster decrease in VO2 after surgery than in the preoperative period (141 x 111.p<0.001), data that suggests physiological and functional improvement of the heart. In correlation analysis, this greater speed in the drop in VO2 after exertion of the operated patients was not related to the change in the body mass index of the patients, suggesting that the functional improvement of the heart may be

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			resulting from the physiological changes associated with surgery and not from the consequent weight reduction.
José Lucas	The Role of Surgery	This review	The results indicate
Moura	Bariatrica at	of literature	than bariatric surgery
Valencia	Reduction of	investigates the	can lead to remission
2024	Obesity and in the	impact of	type 2 diabetes,
	Remission of	surgery	Pressure reduction
	Diseases	bariátrica na	arterial and improvement of
	Metabolic	reduction of	Symptoms of Sleep Apnea
		obesity	sleep. Nevertheless
		and in remission	It is noteworthy the
		of diseases	need for a
		Metabolic	Careful Evaluation
		Associated with	of risks and benefits
		such as diabetes	before the
		type 2,	indication of this
		hypertension	procedure. This
		arterial	review highlights the
		and apnea	Importance of surgery
		sleep. From	bariatric as a
		of a	effective tool in the
		analysis	Treatment of
		Comprehensive	obesity and its
		Studies	Complications
		clinical and	Metabolic
		Observations	offering new
		s,	Perspectives for the
		Identify	management of these

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		Consistent	chronic conditions.
		Evidence of the benefits of bariatric surgery in promoting sustained weight loss and improving metabolic comorbidities in obese patients.	
Ana Miranda Abi-Ackel 2020	Impact of bariatric surgery on the prognosis of patients with type 2 diabetes mellitus	To evaluate the possible changes that bariatric surgery can generate in the prognosis of type 2 diabetes mellitus and, in addition, to act on the reduction of cardiovascular risk factors.	Bariatric surgery has better results in relation to the prognosis of the disease. It also generates benefits in the control of hypertension and hyperlipidemia, thus reducing cardiovascular risk factors.

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Marcos Eduardo Mezzomo da	HYPERTENSION AND BARIATRIC SURGERY: A	The obesity epidemic is a crisis	Bariatric surgery has been shown to be the most effective therapy for

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2021	REVIEW OF THE CURRENT LITERATURE AFTER THE RANDOMIZED SCHIAVON TRIAL	that is undeniably intensifying. Many of the comorbidities associated with obesity are facilitated by or contribute to an extremely high prevalence of hypertension in the obese population. In this context, the objective of the present study was to analyze the theme of bariatric surgery and hypertension and to review the current scientific literature after the study carried out by Schiavon	patients with severe obesity, achieving greater weight loss than that obtained with conventional treatment and favoring the remission of obesity-related comorbidities. The scientific literature lacks studies on hypertension remission as a primary outcome. Finally, so far, bariatric surgery represents an effective strategy for blood pressure control in a broad population of patients with obesity and hypertension.

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		et al. to evaluate the impact of bariatric surgery on the improvement of hypertension in patients with obesity.	
Cristiane Maria Araújo Tavares de Sá 2023	Body composition assessed by dual-energy x-ray absorptiometry on metabolic profile and cardiovascular risk in obese patients prior to bariatric surgery.	This study aimed to evaluate the influence of body mass components on the metabolic profile and cardiovascular risk in the preoperative period of bariatric surgery.	A total of 60 patients were analyzed, 86.7% of whom had comorbidities, 33.3% had moderate/high cardiovascular risk, and 71.4% had vitamin D insufficiency/deficiency. Lower lean body mass (adjusted PR 3.24; 95%CI 1.19–5.77) was independently associated with the severity of obesity. The body mass index and waist circumference were negatively correlated with lean body mass (r=-0.52; p<0.01)/r=-0.36; p<0.01). Lean body

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			mass was negatively correlated with fat mass (r=-0.26; p<0.05), trunk FAT (r=-0.29; p<0.05), Fasting glucose (r=-0.26; p<0.05), and Bone mineral density (r=-0.26; p<0.05). The total of 84.2% of individuals with less trunk fat tended to have low cardiovascular risk (p=0.05). However, physical inactivity (adjusted PR 2.14; 95%CI 1.19–5.54) and the risk of alcohol dependence (adjusted PR 2.41; 95%CI 1.76–4.15) were the only variables independently associated with cardiovascular risk.
Carlos Aurelio Schiavon 2018	Effects of Bariatric Surgery in Obese Patients With Hypertension	Recent research efforts on bariatric surgery have focused on metabolic	We included 100 patients (76% female, mean age 43.8±9.2 years, mean body mass index 36.9±2.7 kg/m2), and 96% completed

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		and diabetes mellitus resolution. Randomized trials designed to assess the impact of bariatric surgery in patients with obesity and hypertension are needed.	follow-up. Reduction of ≥30% of the total number of antihypertensive medications while maintaining controlled blood pressure occurred in 41 of 49 patients from the gastric bypass group (83.7%) compared with 6 of 47 patients (12.8%) from the control group with a rate ratio of 6.6 (95% confidence interval, 3.1–14.0; P<0.001). Remission of hypertension was present in 25 of 49 (51%) and 22 of 48 (45.8%) patients randomized to gastric bypass, considering office and 24-hour ambulatory blood pressure monitoring, respectively, whereas no patient submitted to medical therapy was free of antihypertensive drugs at 12 months. A post hoc analysis for the primary end point

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			considering the SPRINT (Systolic Blood Pressure Intervention Trial) target reached consistent results, with a rate ratio of 3.8 (95% confidence interval, 1:4–10:6; P=0.005). Eleven patients (22.4%) from the gastric bypass group and none in the control group were able to achieve SPRINT levels without antihypertensives. Waist circumference, body mass index, fasting plasma glucose, glycohemoglobin, low-density lipoprotein cholesterol, triglycerides, high-sensitivity C-reactive protein, and 10-year Framingham risk score were lower in the gastric bypass than in the control group.
Fernanda Reis de Azevedo Rabello	Effect of bariatric surgery on clinical parameters,	Analyze the behavior of	Currently Pre-intervention The individuals in the group

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2016	Laboratory and cardiovascular risk factors	Laboratory, clinical and structural variables related to the development and progression of atherosclerosis in diabetic individuals submitted to bariatric surgery.	surgical and were different in relation to BMI, Blood Glucose and Triglycerides, so the results obtained were adjusted minimizing the impact of these differences. After the For a 3-month follow-up, the surgical group showed a significant reduction in weight and BMI (33.4±2.6 vs. 27.4±2.8 kg/m2, p<0.001), HbA1c (9.26±2.12 vs. 6.18±0.63%, p<0.001), CT (182.9±45.4 vs. 139.8±13 mg/dl, p<0.001), HDL (33.1±7.7 vs. 38.4±10.6 mg/dL, p<0.001), TG (369.5±324.6 vs. 130.8±43.1 mg/dL, p<0.001), Proinsulin (12.72±9.11 vs. 1.76±1.14 pM, p<0.001), RBP-4 (9.85±2.53 vs. 7.3±1.35 ng/ml, p<0.001) and CCK

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			(84.8±33.2 vs. 79.9±31.1, ng/ml, p<0.001), there was also a significant increase in HDL-cholesterol levels (33.1±7.7 vs.38.4±10.6 mg/dL, p<0.001), Glucagon (7.4±7.9 vs. 10.2±9.7 pg/ml, p<0.001) and FGF-19 (74.1±45.8 vs. 237.3±234 pg/ml, p=0.001). An interesting fact was that the values of Proinsulin, RBP-4, HbA1c and HDL-cholesterol levels in the surgical group reached values similar to those of the control group three months after the intervention, and the FGF-19 was twice as high as that found in the group of healthy individuals (237±234 vs. 98±102.1 pg/ml). The clinical group did not showed variation in clinical variables,

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			only in glucagon values with significant reduction in the post-intervention period (18.1±20.7 vs. 16.8±18.4 pg/ml, p<0.001).
Célio Alves	DIAGNOSIS	Analyze the	69 were approached
Cavalcanti	NUTRITIONAL AND	diagnosis	patients, among them
Grandson	RISK	nutritional and	Pre and post volunteers
2023	CARDIOVASCULAR	risk	bariatric surgeries, between 22 and
	IN	cardiovascular	64 years old.
	PRE-E PATIENTS	of patients	91.3% of participants
	POSTOPERATIVE	Pre and	were of the same
	SURGERY	postoperative	female. The average of the
	BARIATRIC	surgery	age was 44 and the grade
	IN	Bariatric	of obesity more
	FOLLOW-UP	accompanied	evident was the III
	Or	s by the team	obtaining the percentage of
	MULTIPROFESSION	Multiprofession	69.2% among the
	AL	Al in one	pre-patients
		Teaching Hospital	while the
		of the Northeast	degree of obesity
		of Brazil.	zero represented the
			postoperative patients
			Result totaling
			35.3% characterized
			how
			overweight. When evaluating
			the most comorbidities

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			frequent among the
			patients was SAH, resulting in 65.4% of patients pre-bariatric and 17.7% post-bariatric. Waist circumference (WC) showed significant values in both sexes before gastroplasty and abrupt fall after gastroplasty. When examining the episodes of regurgitation, it was since 32.7% of preoperative patients confirm occurrences at the same time as 58.8% of the post-bariatric patients affirm such episodes.

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Maria Carolina Alves Zanatta 2023	Semaglutide applied to the treatment of obesity: clinical perspectives in the literature	Obesity is a chronic disease defined by an excessive concentration of body fat, which	The 21 selected articles were submitted to a complete reading, seeking convergences and divergences in the observed results. Most articles (20) demonstrated the

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		Comes affecting more than 1 billion individuals worldwide. This disease is usually related to other metabolic disorders, such as type 2 diabetes (DM2), cardiovascular diseases (CVD), nonalcoholic fatty liver disease (NAFLD), chronic kidney disorder (CKD), in addition to some types of cancers. From this perspective, this work aims to analyze	efficacy of semaglutide and an acceptable safety profile for its use, associated with combined and specific therapy for each patient. No increased risk was pointed out due to adverse effects. Semaglutide is characterized as a promising alternative in the treatment of obesity, proving to be effective in significantly reducing body weight in a sustained way.

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		studies involving Semaglutide as an anti-obesity agent, since the use of glucagon-like peptide-1 receptor agonists (GLP-1 RA) are being indicated as one of the most positive procedures in the treatment of obesity.	
Jhonatan Picinin Ribeiro 2024	Cobalamin deficiency after bariatric surgery: a narrative review	The present study aims to describe the relationship between bariatric surgery and the development of cobalamin deficiency.	Bariatric surgery is a therapeutic option for cases of morbid obesity, sustainably reducing weight, comorbidities, and mortality. However, the procedure can cause complications in the long term. term, such as the

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			cobalamin (vitamin B-12) deficiency. Such a picture deficiency is influenced by the type of procedure and the vitamin reserves before surgery, and can cause serious complications to the patient, such as neurological manifestations, increased cardiovascular risk and development of megaloblastic anemia. Thus, the adoption of preventive conducts during the pre- and postoperative periods allow for lower negative outcomes.
Thinzar Min 2020	The Role of Tirzepatide, Dual GIP and GLP-1 Receptor Agonist, in the Management of Type 2 Diabetes: The SURPASS Clinical	Glucagon-like peptide 1 (GLP-1) based therapy is an established treatment option for the management of type 2	Pre-clinical trials and phase 1 and 2 clinical trials indicate that tirzepatide has potent glucose lowering and weight loss with adverse effects comparable to those of established GLP-1

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	Trials	diabetes	receptor agonists. The
		Mellitus	long-term efficacy,
		(T2DM) and is	safety and
		recommended	cardiovascular
		early in the	outcomes of
		treatment	Tirzepatide will be
		algorithm	investigated in the
		owing to	SURPASS phase 3
		glycaemic	Clinical Trial Programme.
		efficacy,	In this paper,
		weight	we will review the
		reduction and	pre-clinical and phase 1
		Favourable	and 2 trials for
		cardiovascular	Tirzepatide in the
		outcomes.	management of T2DM
			and give an overview of
			the SURPASS
			clinical trials.

DISCUSSION

CARDIOVASCULAR RISK

Cardiovascular diseases have been the leading cause of death in the world for some time. It is known that cardiovascular risk is dependent on the continuous exposure of individuals to risk factors represented by metabolic diseases (diabetes mellitus, insulin resistance, hypertension, dyslipidemia) and lifestyle habits (smoking, atherogenic diet and sedentary lifestyle). The control of cardiovascular risk factors represents the main strategy for the primary prevention of these diseases. The adoption of a healthy lifestyle, including diet, exercise and abstinence from smoking, is the most powerful tool to combat cardiovascular risk factors in primary prevention (RABELLO, 2016).

The earlier changes observed in the cardiovascular system of patients who underwent bariatric surgery result not only in a decrease in BMI, but also important metabolic changes, which help in cardiovascular improvement (AGUIAR, 2015).

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Among the comorbidities associated with obesity, systemic arterial hypertension (SAH) is one of the most important for public health because it has an extensive epidemiology. However, bariatric surgery has been shown to be efficient in reducing blood pressure in patients who had both SAH and obesity. In these patients, a significant decrease in the need for antihypertensive medication after bariatric surgery is evident, in addition to presenting patients who can reach blood pressure levels within the expected without the need for additional pharmacological therapy (VASCONCELOS et al, 2024).

In addition to SAH, a significant remission of blood glucose was also observed in patients with Diabetes Mellitus (DM). Bariatric surgery is more effective than intensive medical therapy alone in decreasing, and in some cases, resolving hyperglycemia. The results are even better when associated with surgery and a change in lifestyle, however, among the modalities of surgery, the best results were found in the Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SGBS) modalities (ABI-ACKEL et al, 2020).

OBESITY

Obesity is a chronic condition that is characterized by the excessive accumulation of fat in the body. Its incidence has increased significantly in recent decades, especially in developing countries. Its origin is multifactorial, resulting from the interaction of genetic, metabolic, social, behavioral and cultural factors (TAVARES, 2010).

Obesity, marked by excess body fat, is linked to several metabolic and cardiovascular complications, such as type 2 diabetes, high blood pressure, cholesterol problems, heart disease, and sleep apnea (VASCONCELOS, 2024).

In fact, increased levels of leptin and resistin, hormones released by adipose tissues, appear to be associated with increased heart rate, hypertrophy, and hyperplasia of the inner layers of blood vessels, which are mechanisms involved in the development of atherosclerosis. The continuous release of tumor necrosis factor and interleukin-6 (TNF and IL-6) by adipose tissue and the increase in C-reactive protein (CRP) levels in obese individuals contribute to the dysfunction of small blood vessels, decreasing nitric oxide production and impairing the dilation function of the arteries. Another mechanism involved in cardiovascular diseases associated with obesity is dysfunction of the autonomic nervous system. The cause of this imbalance, which results in an increase in sympathetic tone and a decrease in parasympathetic tone, is not yet completely understood. Continuous

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stimulation of the sympathetic nervous system leads to hypertrophy of the heart muscle, apoptosis of myocytes, and fibrosis of the heart (AGUIAR, 2015).

According to the Ministry of Health, obesity represents a serious public health problem, with its prevalence increasing epidemically in recent years, affecting both children and adolescents. It is estimated that more than half of adults are overweight, with a higher incidence in the female public. This situation is attributed to several factors in the modern world, such as a sedentary lifestyle, unbalanced diet, globalization, and genetic predisposition (RIBEIRO, 2024).

Despite the government's priority efforts to promote healthy eating habits and prevent obesity, the prevalence of this morbid condition continues to grow, requiring more stringent treatment measures. Consequently, the number of bariatric surgeries performed worldwide has increased significantly in recent years, making it possible to reverse the condition of excess weight in patients who were unsuccessful with lifestyle changes (RIBEIRO, 2024). Nutritional assessment and monitoring of cardiovascular risks in patients before and after surgery are extremely important due to the implications that these factors have on the quality of life of these individuals. When not evaluated regularly and by a multidisciplinary team, these patients are at risk of developing food intolerance, recurrence of obesity, cardiovascular diseases, and complications related to the emergence or worsening of comorbidities (NETO, 2023).

Among obese patients, systemic arterial hypertension (SAH) is the most common comorbidity, indicating that weight gain is an influential factor in the onset of this condition, along with an inadequate diet and excessive consumption of sodium-rich foods (NETO, 2023). It is known that obesity is associated with dyslipidemia, characterized by increased levels of lipids in the blood, which accumulate in the arteries forming plaques, which can obstruct blood flow and lead to the development of atherosclerosis, heart attacks, strokes and other circulatory problems. However, there is a high possibility of reversing these problems for those who adopt a healthy food-based diet (NETO, 2023).

DRUG TREATMENT

For the pharmacological treatment of obesity, a complete analysis of the patient is necessary, with detailed studies on dietary and morbid history, laboratory analyses with hematological, biochemical, hormonal indicators, as well as cardiological, psychological and metabolic studies, enabling a careful and individual evaluation. The purpose of

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pharmacotherapy is to improve the quality of life, prevent and minimize complications that excess weight causes to health, and the use of drugs alone is not indicated. This pharmacotherapy is used when the patient is obese, or for patients who are overweight and have orbidities due to excess weight, such as hypertension, type II diabetes or dyslipidemias, who did not obtain results with diet and physical exercise (TAMARGO, 2016).

According to Oliveira et al (2009), the main pharmacological classes used in the treatment of individuals with obesity or overweight are: catecholaminergic drugs, serotonergic drugs, catecholaminergic and serotonergic drugs, thermogenic drugs, fat absorption inhibitors and selective CB antagonist drugs (OLIVEIRA, 2021).

On the other hand, Tirzepatide, a GLP-1 analogue class, a drug that has been gaining prominence in the medical community in recent years due to its therapeutic effects in patients with DM2, has a pharmacological character of reducing serum glucose and delaying gastric emptying, helping patients lose weight and consequently control glycemic goals. Given the increasing prevalence of obesity, it is more important now than ever to find effective treatments that provide substantial and sustainable outcomes for people with obesity. The extensive evaluation of weekly subcutaneous administration of this drug in the SURMOUNT program will provide relevant evidence on its safety and efficacy in weight reduction and maintenance in adults with obesity. We anticipate that the results of the SURMOUNT program have demonstrated that tirzepatide represents an innovative and effective pharmacological intervention with positive outcomes for adults with obesity (ROUX, 2022).

However, more active habits on a daily basis are still recommended by professionals who monitor pre-bariatric patients, with the aim of reducing surgical complications, formation of lean mass and reducing the risk of obesity recurrence, since a sedentary lifestyle is also directly linked to the consumption of fatty foods with a large amount of sugar. However, it is a difficult process for this population due to the musculoskeletal, cardiorespiratory, and psychological repercussions caused by obesity that make it difficult to perform this habit frequently, unlike those who have already undergone the procedure (NETO, 2023).

SURGICAL TREATMENT

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It can be said that obesity has become a constantly growing global epidemic, representing one of the greatest public health challenges of the twenty-first century. Defined by the accumulation of body fat excessively, it is associated with several metabolic and cardiovascular complications, such as type 2 diabetes, hypertension, dyslipidemia, cardiovascular disease, and sleep apnea, among others. These comorbidities significantly increase the risk of morbidity and mortality, resulting in a substantial reduction in quality of life and an increase in healthcare costs (VASCONCELOS, 2024).

Faced with this new challenge, bariatric surgery was developed as an intervention that has been shown to be effective in the treatment of severe obesity and its associated comorbidities, including techniques such as gastric bypass, sleeve gastrectomy and adjustable gastric banding, which have demonstrated the promotion of significant and sustained weight loss in obese patients, especially when compared to other non-surgical approaches (VASCONCELOS et al, 2024).

In addition to the benefits in weight reduction, studies have shown the positive impact of bariatric surgery on the remission of metabolic diseases, particularly high blood pressure, type 2 diabetes, and sleep apnea. The study by Schauer et al. (2017) compared the outcomes between patients undergoing bariatric surgery and those who received intensive medical therapy for type 2 diabetes, demonstrating a higher rate of disease remission in the group undergoing surgery. Similar results were observed in relation to hypertension and sleep apnea, where bariatric surgery proved to be effective in reducing the need for medication and improving respiratory symptoms (VASCONCELOS et al, 2024).

The *GATEWAY* study, led by Shiavon (2018), returned comparisons to the effects of metabolic surgery only in obese patients with hypertension, including patients using 2 or more medications at maximum doses or more than 2 moderate doses, in addition to body mass index (BMI) between 30.0 and 39.9 kg/m2. The 100 selected patients, aged 34.6 and 53 years, including 76% of whom were women, were randomly submitted to *Roux-en-Y* gastric *bypass*, either in conjunction with medication or medication alone. The primary endpoint was 30% or more reduction of the total number of antihypertensive drugs while maintaining systolic and diastolic blood pressure less than 140x90 mmHg at 12 months (SHIAVION, 2018).

The parameters used in the study (waist circumference, body mass index, fasting plasma glucose, glycohemoglobin, low-density lipoprotein cholesterol, triglycerides, high-

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sensitivity C-reactive protein, and *Framingham* risk score) were lower in the gastric bypass group than in the control group. Thus, bariatric surgery can be seen as an effective strategy for blood pressure control in a large population of hypertensive and obese patients (SHIAVION, 2018).

Despite the high relevance of the results of the *GATEWAY* study, some questions related to the effect of bariatric surgery on hypertension are still awaiting answers. First, little is known about the medium (3-5 years) and long (> 5 years) effects of bariatric surgery on hypertension remission. Regarding hypertension, observational studies indicate that blood pressure also worsens after the first year after surgery, in parallel with weight regain. On the other hand, it would also be of great interest to identify preoperative predictors of hypertension remission after bariatric surgery. This information would help the doctor who prescribed the bariatric surgery and the patient in order to meet real expectations before the procedure. Thus, the number of antihypertensive drugs before surgery was inversely related to the remission of hypertension after the procedure (SILVA, 2021).

Finally, it would also be necessary to evaluate the differential effect of the various bariatric surgery techniques on the remission of hypertension. In this regard, the use of sleeve gastrectomy has increased in the last ten years due to its technical simplicity and similar short-term results to those of *Roux-en-Y* gastric *bypass*, in terms of weight loss and remission of comorbidity.

These advantages placed *the Sleeve* as the most used bariatric surgery technique worldwide for the first time in 2014 (SILVA, 2021).

RESULTS

The analysis of the literature on how bariatric surgery influences the reduction of obesity and the control of metabolic diseases showed that there is significant evidence supporting the importance of this procedure in promoting health and improving the quality of life of obese patients. These studies highlighted the effectiveness of bariatric surgery in facilitating lasting weight loss and reducing metabolic comorbidities, such as type 2 diabetes, hypertension, and sleep apnea (VASCONCELOS et al, 2021).

In order to emphasize our analysis of the significant improvement in the effect of bariatric surgery to reduce cardiovascular risks, the following study was analyzed, whose methodology is the inclusion of 100 patients (76% women, with a mean age of 43.8 ± 9.2

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years and a mean body mass index of 36.9 ± 2.7 kg/m2), Of whom 96% completed follow-up, a ≥30% reduction in total antihypertensive medications was observed, keeping blood pressure under control. This was evidenced in 41 of the 49 patients in the gastric bypass group (83.7%), compared with only 6 of the 47 patients (12.8%) in the control group, with a rate ratio of 6.6 (95% confidence interval, 3.1–14.0; P<0.001). Remission of hypertension was observed in 25 of 49 patients (51%) and 22 of 48 patients (45.8%) randomized to gastric bypass, considering both in-office and 24-hour outpatient blood pressure monitoring, respectively.

In contrast, no patient undergoing medical therapy was free of antihypertensive medications after 12 months. A post-hoc analysis for the primary outcome, taking into account the goal of the *Systolic Blood Pressure Intervention Trial (SPRINT*), yielded consistent results, with a rate ratio of 3.8 (95% confidence interval, 1.4–10.6; P=0.005). Eleven patients (22.4%) in the gastric bypass group were able to achieve *SPRINT* levels without the need for antihypertensives, compared to no patients in the control group (SHIAVION, 2018).

The remission of type 2 diabetes after bariatric surgery marks a transformation in the treatment of this chronic disease, offering many patients the chance to decrease or even eliminate the need for medication and considerably improve their quality of life. In addition, bariatric surgery has been shown to be effective in reducing blood pressure in patients with hypertension and improving sleep apnea symptoms, contributing to reducing the risk of cardiovascular and respiratory complications (VASCONCELOS et al, 2021).

Despite the promising results, it is crucial to recognize that bariatric surgery is not a universal solution for all patients with obesity and associated medical conditions. Careful patient selection, detailed evaluation of risks and benefits, and multidisciplinary follow-up are essential to ensure positive long-term results. In addition, more research is needed to better understand the mechanisms by which bariatric surgery produces its beneficial effects and to identify strategies that optimize outcomes and reduce complications related to the procedure (VASCONCELOS et al, 2021).

Randomized clinical studies conducted by Mingrone et al. (2012) and Schuer et al. (2017) demonstrated significant remission of type 2 diabetes in obese patients after undergoing bariatric surgery, consequently leading to improvements in insulin sensitivity and normalization of glucose levels, which has a significant impact on reducing the risk of chronic complications. as cardiovascular disease. In addition, studies such as the one by

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Lkramuddin et al. (2013) have reported a significant reduction in the use of antihypertensive drugs after bariatric surgery, without the need for additional pharmacological therapy.

According to the study carried out by Rabello et al. (2016), there was an improvement in blood glucose and triglyceride levels of patients undergoing bariatric surgery, equivalent to a statistically mean reduction in fasting blood glucose and triglycerides after 3 months, compared to patients using pharmacological treatment, in view of the drug Semaglutide which, according to article 10 by Reis et al. (2022), it should be prescribed only for T2DM and does not have therapeutic responses in the treatment of obesity, and consequently does not present responses in reducing cardiovascular risk

These statistical data were confirmed by the study by Rabello et al. (2016) in which it was analyzed that statistical data of patients in the surgical and clinical group were different in relation to BMI, Blood Glucose and Triglycerides. After the 3-month follow-up, the surgical group showed a significant reduction in weight values, BMI (33.4±2.6 vs. 27.4±2.8 kg/m2, p<0.001), HbA1c (9.26±2.12 vs. 6.18±0.63%, p<0.001), CT (182.9±45.4 vs. 139.8±13 mg/dl, p<0.001), HDL (33.1±7.7 vs. 38.4±10.6 mg/dL, p<0.001), TG (369.5±324.6 vs. 130.8±43.1 mg/dL, p<0.001), Proinsulin (12.72±9.11 vs. 1.76±1.14 pM, p<0.001), RBP-4 (9.85±2.53 vs. 7.3±1.35 ng/ml, p<0.001) and CCK (84.8±33.2 vs. 79.9±31.1, ng/ml, p<0.001), there was also a significant increase in HDL-cholesterol levels (33.1±7.7 vs.38.4±10.6 mg/dL, p<0.001), Glucagon (7.4±7.9 vs. 10.2±9.7 pg/ml, p<0.001) and FGF-19 (74.1±45.8 vs. 237.3±234 pg/ml, p=0.001). An interesting finding was that the values of Proinsulin, RBP-4, HbA1c and HDL-cholesterol in the surgical group reached values similar to those of the control group three months after the intervention, and FGF-19 was twice as high as that found in the group of healthy individuals (237±234 vs. 98±102.1 pg/ml). The clinical group did not show variation in clinical variables, only in glucagon values with a significant reduction in the post-intervention period (18.1±20.7 vs. 16.8±18.4 pg/ml, p<0.001). As a result, we can observe more significant results in the surgical group that are not observed as effectively in the clinical group.

CONCLUSION

In summary, bariatric surgery emerges as an essential instrument in the treatment of obesity and its metabolic comorbidities, resulting in substantial benefits for the health and quality of life of patients. However, it is vital that the decision to undergo such a procedure

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be thoroughly considered in consultation with qualified healthcare professionals, taking into account the individual needs and preferences of each patient.

The current study reveals that, despite being an invasive procedure, such surgery offers tangible benefits in reducing visceral fat, controlling comorbidities, and decreasing the risk of developing metabolic and cardiovascular diseases. The results obtained indicate that metabolic surgery surpasses intensive medical therapy alone, being effective in reducing mortality and complication rates, both macrovascular and microvascular, such as systemic arterial hypertension and dyslipidemia. Among the different types of techniques, Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy (SGBV) stand out for presenting the best results in reducing cardiovascular risk.

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