Universidade de Évora - Instituto de Investigação e Formação Avançada

Programa de Doutoramento em Motricidade Humana

Tese de Doutoramento

Effects of physical exercise on sarcopenia after bariatric surgery: a randomized controlled trial

Cláudia Sofia Orvalho Mendes

Orientador(es) | Armando Manuel Raimundo
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A tese de doutoramento foi objeto de apreciação e discussão pública pelo seguinte júri nomeado pelo Diretor do Instituto de Investigação e Formação Avançada:

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Efeitos do exercício físico na sarcopenia pós cirurgia bariátrica: um estudo controlado e randomizado

RESUMO

A obesidade é um problema de saúde global e a cirurgia bariátrica destaca-se como uma intervenção eficaz para tratar a obesidade grave e as suas comorbilidades. No entanto, um desafio significativo deste procedimento cirúrgico é a perda de força e massa muscular esquelética, que pode levar à sarcopenia, comprometendo a funcionalidade física e os resultados em saúde. Assim, o sucesso a longo prazo da cirurgia bariátrica depende não só da redução da gordura corporal, mas também da preservação da massa e força muscular. Esta tese tem como objetivo investigar o impacto de um programa de exercício físico na prevenção da sarcopenia após a cirurgia bariátrica, apresentado em nove estudos, organizados na forma de artigos científicos.

O primeiro artigo é uma revisão sistemática que destaca a eficácia de programas de exercícios combinados, que incluem treino aeróbio e de resistência, na manutenção da força e massa muscular. Os artigos seguintes descrevem a metodologia do estudo randomizado e controlado, denominado EXPOBAR, que avalia os efeitos do exercício combinado em indicadores associados à sarcopenia. Os resultados iniciais indicam que a cirurgia bariátrica provoca perdas significativas de massa e força muscular, o que aumenta o risco de sarcopenia, reforçando a necessidade de intervenções de exercício precoces. Um programa de exercício supervisionado de 16 semanas demonstrou melhorias na função muscular e na aptidão física. Além disso, foi observado um efeito positivo do exercício na qualidade de vida dos doentes, o que sublinha os benefícios para além da saúde física. Os últimos artigos abordam as respostas hormonais e inflamatórias relacionadas com o exercício, proporcionando uma compreensão abrangente dos efeitos metabólicos da cirurgia e do exercício neste contexto.

Em suma, esta tese contribui para a compreensão da sarcopenia pós-cirurgia bariátrica e recomenda a integração de intervenções de exercício nos cuidados de saúde, com o objetivo de melhorar os resultados clínicos a longo prazo e os resultados avaliados e reportados pelos pacientes. Além disso, a evidência recolhida suporta a proposta de um programa específico de exercício físico estruturado com base nas sugestões genéricas das actuais recomendações do *American College of Sports Medicine*.

Keywords: bariatric surgery, exercise, leptin, muscle mass, obesity, quality of life, sarcopenia, strength

Effects of physical exercise on sarcopenia after bariatric surgery: a randomized controlled trial

ABSTRACT

Obesity is a global health problem. Bariatric surgery stands out as an effective intervention to treat severe obesity and its comorbidities. However, a significant challenge of this surgical procedure is the loss of skeletal muscle strength and mass, which can lead to sarcopenia, compromising physical function and health outcomes. Thus, the long-term success of bariatric surgery depends, not only on reducing body fat, but also on preserving muscle mass and strength.

This thesis aims to investigate the impact of a physical exercise program on the prevention of sarcopenia after bariatric surgery, presenting nine papers organized in the form of scientific articles.

The first article is a systematic review that highlights the effectiveness of combined exercise programs, which include aerobic and resistance training, in maintaining muscle strength and mass. The next three articles describe the methodology of a randomized controlled trial, called EXPOBAR, which evaluates the effects of combined exercise on indicators associated with sarcopenia. In the fifth paper, initial results indicate that bariatric surgery causes significant losses in muscle mass and strength and increases the risk of sarcopenia, reinforcing the need for exercise interventions. A 16-week supervised exercise program (six paper) demonstrated improvements in muscle function and physical fitness. In addition, a positive effect of exercise on patients' quality of life was observed, underlining benefits beyond physical health (seven paper). The last two articles address exercise-related hormonal and inflammatory responses, providing a comprehensive understanding of metabolic effects of surgery and exercise in this context.

In summary, this thesis contributes to the understanding of post-bariatric surgery sarcopenia and recommends the integration of exercise interventions into healthcare, with the aim of improving patients' long-term clinical and patients reported outcomes. Also, the collected evidence of this work supports the proposal of a specific physical exercise structured program based on the generic suggestions of the current ACSM recommendations.

Keywords: bariatric surgery, exercise, leptin, muscle mass, obesity, quality of life, sarcopenia, strength

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Abbreviations and Acronyms

6MWT: Six-minute walking test

ASMBS: American Society of Metabolic and Bariatric Surgery

ACSM: American College of Sports Medicine

ASMI: Appendicular skeletal muscle index

ASMMI: Appendicular skeletal muscle mass index

BMI: Body mass index

DEXA: Dual-energy X-ray absorptiometry

ESPEN: European Society for Clinical Nutrition and Metabolism

EASO: European Association for the Study of Obesity

FNIH: Foundation for the National Institutes of Health

FITT-VP: frequency, type, intensity, time, duration, volume, and progression

HbA1c: Glycated Hemoglobin

HDL: High-density lipoprotein cholesterol

HIIT: High-intensity interval training

HR: Heart rate

HRQOL: Health-related quality of life

IFSO: International Federation for the Surgery of Obesity

LDL: Low-density lipoprotein cholesterol

LYN: Lymphocyte

NEU: Neutrophil

OSA: Obstructive sleep

PLT: Platelets

PROMS: Patien- reported outcomes measures

RCT: Randomized controlled trial

RPE: Rating of perceived exertion

RYGB: Roux-en-Y gastric bypass

SD: Standard deviation

SII: Systemic Immune-Inflammation Index

SMM: Skeletal Muscle Mass

TWL: Total weight loss percentage

WC: Waist circumference

WHO: World Health Organization

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CHAPTER 1 – GENERAL INTRODUCTION

Obesity is a chronic disease that results in the onset of multiple other clinical conditions in almost all organs and systems, such as diabetes, hepatic steatosis and steatohepatitis, dyslipidemia, hypertension, sleep apnea syndrome, gastroesophageal reflux disease, urinary incontinence and disabling osteoarticular pathology (Endalifer & Diress, 2020; EP Williams, 2015; Sardinha et al., 2012). It has a major impact on mental health, leading to anxiety-depressive disorders, and on the personal sphere, leading to deficits in self-esteem and autonomy da Luz et al., 2018. This pathology occurs in the context of an adverse metabolic environment, where generalized inflammatory changes also coexist. Perhaps because of this proinflammatory environment, the incidence of cancer in individuals with obesity is double that of the general population (Bendor et al., 2020; Crusz & Balkwill, 2015).

The person with obesity is also often the victim of discrimination in society, which can result in an increased level of unemployment and social exclusion. All these problems culminate in a marked reduction in quality of life and longevity (Spahlholz et al., 2016).

The high incidence and prevalence of obesity, combined with the major economic and financial impact of obesity-related diseases, especially diabetes and cancer, have made this disease one of the main determinants of health and disease worldwide, which has led the WHO to consider obesity the epidemic of the 21st century (WHO, 2021).

The multiplicity of factors involved in the development of obesity, especially genetic, epigenetic and hormonal alterations, greatly influences the effectiveness of conventional therapeutic measures, such as lifestyle changes, the implementation of physical activity schemes and the promotion of healthy eating (Baillot et al., 2015; Brazil et al., 2021).

Sarcopenia is a recently recognized disease. It is characterized by a decrease in physical strength and muscle mass. This condition has been studied mainly in old individuals but is increasingly being considered a health conditioner in early age groups and in a growing number of clinical situations, such as chronic disease, cancer and obesity (Batsis et al., 2014; Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, & Zamboni, 2019; Cruz-Jentoft & Sayer, 2019).

The presence of sarcopenia aggravates the impact of these types of illnesses on quality of life, the ability to cope with planned treatments and the onset of complications.

By it self, obesity further affects daily life and worsens the limitations that patients with obesity already have caudes by their excess weight (Beaudart et al., 2016; C. Liu et al., 2023).

Bariatric surgery has been established as the most effective therapeutic measure for controlling moderate to severe obesity and improving associated diseases. The significant weight reduction it achieves, together with its long-lasting effect, makes it the treatment of choice for this condition (Bond et al., 2012; Fried et al., 2008; Zlabek et al., 2005).

However, surgical treatment can also have several drawbacks, namely, nutritional problems and difficulties in the adaptation to the lifestyle changes introduced by the surgical intervention itself (Kessler et al., 2020; Shah et al., 2006).

On the other hand, the sharp reduction in food intake resulting from surgical treatment, which is necessary to achieve significant weight loss, results in not only a reduction in fat mass but also a reduction in muscle mass and bone density (Blume et al., 2012). In these circumstances, sarcopenia has a complex relationship with obesity and surgery, since, in addition to already having a high prevalence in patients with obesity, surgical therapy will eventually lead to its worsening. There may even be a vicious cycle in which surgery aggravates existing sarcopenia, and this, in turn, by reducing muscle mass, will compromise basal metabolism, reduce energy consumption and counteract the desired weight loss (Crispim Carvalho et al., 2023; Minniti et al., 2022).

All these variables are important when studying the impact of bariatric surgery. Thus, in addition to studying the specific objectives of surgical treatment, namely, weight control, control of comorbidities and the safety of the intervention, aspects such as changes in the hormonal environment, the psychological sphere, the work sphere and the personal sphere, i.e., quality of life, are also outcomes that should be measured (Balaguera-Cortes et al., 2011; Ionut et al., 2013; Kruljac et al., 2016; Sethi et al., 2018).

Finally, physical activity and exercise are an important determinant of health, playing a significant role in achieving a state of health that counteracts sedentary lifestyles, helps prevent disease and facilitates the implementation of medical treatments. Physical activity also improves quality of life, personal satisfaction and self-esteem (Bond et al., 2012; Brazil et al., 2021; Crowe et al., 2015; Jassil, Richards, Carnemolla, Lewis, Montagut-Pino, et al., 2022).

Its relationship with obesity control seems obvious at first glance. A physically inactive and sedentary lifestyle is one of the conditioning factors for obesity, and physical activity can counteract this lifestyle and contribute to weight control. Unfortunately, once excess weight has occured, it becomes increasingly difficult for patients to adhere to exercise programs, which, of course, must be increasingly intense to achieve results. The use of physical activity as an adjunct to surgical therapy did not show yet its usefulness in achieving higher levels of weight loss (Steffl et al., 2017).

On the other hand, with respect to sarcopenia, physical activity seems to be one of the most valuable tools for improving muscle strength and increasing muscle mass (K. M. Kim et al., 2016; Pekař et al., 2020).

Therefore, if sarcopenia is present in patients with obesity, it seems to be a factor that harms the results of surgical therapy in terms of weight control and improved quality of life. If physical exercise is one of the most useful tools for reversing sarcopenia, the role of exercise in preventing the problems associated with bariatric surgery in patients with obesity and sarcopenia deserves to be studied (Antuña et al., 2022; Beaudart et al., 2016; Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019; Petta et al., 2017).

In this thesis, the complex relationships between obesity, sarcopenia, and bariatric surgical treatment and the role of physical exercise are explored, both as an adjunct to surgical treatment in terms of the effectiveness and prevention of adverse events associated with surgical treatment. To address the main aim of this thesis, all measurements were collected and statistically analyzed to formulate a conclusion. This study involves nine articles: one systematic review, one methodological protocol, one dataset, one study protocol, one observational study and four randomized controlled trials (RCT) that followed the CONSORT guidelines for RCT (http://www.consortstatement.org).

This study begins with a systematic review to identify gaps in knowledge regarding the complex relationships among obesity, sarcopenia, surgical therapy and physical exercise.

This review gives rise to lines of research that were put into practice with the development of a research protocol for which patients with moderate to severe obesity who were candidates for bariatric surgery were selected.

Multiple parameters (anthropometric, clinical pathology, body composition, hormonal and physical fitness parameters were assessed at five time points throughout the perioperative period. Quality of life and sarcopenia screening questionnaires were used. The most up-to-date recommendations for assessing and diagnosing sarcopenia and sarcopenic obesity were applied.

After providing informed consent, patients who were candidates for bariatric surgery were randomized into an intervention group and a control group. The intervention group was given a structured physical exercise program lasting 16 weeks. In the preoperative phase, the patients were assessed from a clinical point of view to consolidate the diagnosis of moderate or severe obesity, identify associated pathologies and define the indication for surgery.

The assessment moments chosen were the preoperative phase; the postoperative period before the exercise program; and three time points after the end of the program, at 6, 12 and 18 months.

The surgical intervention took place following a structured protocol, and gastric bypass surgery was performed in all the patients, using a laparoscopic approach. This surgical procedure consists of trans-sectioning the stomach, resulting in a small gastric reservoir of approximately 50 cc. This gastric reservoir is then connected to a small bowel loop via an anastomosis, which allows gastrointestinal transit to be maintained. A second Roux-en-Y anastomosis was also performed to prevent gastroesophageal reflux.

This intervention has a complex mechanism of action. First, the new gastric reservoir has a reduced capacity, which has a restrictive effect (Karamanakos et al., 2008; Welbourn, Hollyman, et al., 2018). Moreover, a segment of the small intestine is kept away from contact with food, which reduces the absorption of macronutrients. Additionally, the presence of undigested food in the more distal segments of the small intestine increases the release of intestinal hormones with metabolic effects (Courcoulas et al., 2014). GLP-1 plays a prominent role here, as it is a hormone released by the cells of the intestinal mucosa in the presence of food and, among other effects, stimulates insulin production (Battista et al., 2021; Trakhtenbroit et al., 2009). Finally, interference with the mechanisms that produce leptin and ghrelin will also change the previous metabolic and homeostatic balance, altering the mechanisms of hunger and satiety (Rios et al., 2021).

After the postoperative recovery, the patients participated in a structured physical exercise program. This program consisted of combined and interval training following the latest ACSM guidelines (2022).

One of the published studies (article 5) analyzes the outcomes of surgical intervention and its impact on muscle strength, muscle mass, and other parameters before the exercise program. Another study (article 6) analyzes how physical exercise influences the evolution of parameters related to sarcopenia, namely, strength and muscle mass, with validation of evidence for the guidelines to be followed in terms of diagnostic criteria.

Other studies are centered on the impact of physical exercise on the perioperative evolution of ghrelin and leptin, as well as on quality of life, before and after surgery, and pre and post physical exercise intervention. The systemic inflammatory indices, the impact of weight loss resulting from surgical intervention, and the effects of physical exercise are also studied. Data related to bone health, as well as other parameters associated with physical function, are also collected.

Publications related to this thesis

- Articles published in international scientific journals

Paper I: Mendes, C., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2024). Exercise Interventions for the Prevention of sarcopenia after Bariatric Surgery: a Systematic review. Journal of Science in Sport and Exercise. https://doi.org/10.1007/s42978-024-00311-x

Paper II: Santos, C. A., Cinza, A. M., Laranjeira, Â., Amaro, M., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2023). Effects of physical exercise in sarcopenia on patients undergoing bariatric surgery: A protocol for a randomized clinical trial. MethodsX, 10, 102043. https://doi.org/10.1016/j.mex.2023.102043

Paper III: Santos, C. A., Cinza, A. M., Laranjeira, Â., Amaro, M., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2023). A dataset on skeletal muscle mass index, body composition and strength to determine sarcopenia in bariatric patients. *Data in brief*, *46*, 108881. https://doi.org/10.1016/j.dib.2022.108881

Paper IV: Santos, C., Cinza, A. M., Laranjeira, Â., Amaro, M., Carvalho, M., Martins, S., Bravo, J., & Raimundo, A. (2022). The impact of exercise on prevention of sarcopenia after bariatric surgery: The study protocol of the EXPOBAR randomized controlled trial. *Contemporary clinical trials communications*, *31*, 101048. https://doi.org/10.1016/j.conctc.2022.101048

Paper V: Mendes, C., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2025). How Weight Loss After Bariatric Surgery Affects Sarcopenia Parameters and Diagnosis. *Surgeries*, *6*(2), 31. https://doi.org/10.3390/surgeries6020031

Paper VI: Mendes, C., Carvalho, M., Cabo, C., Bravo, J., Martins, S., & Raimundo, A. (2024). Effect of a 16-week Combined Supervised Exercise Program after bariatric surgery on Sarcopenia parameters based on FNIH, EWGSOP2, EASO/ESPEN criteria – The results of the EXPOBAR randomized trial program. Research Square (Research Square). https://doi.org/10.21203/rs.3.rs-4850725/v1 (under review at Obesty Surgery)

Paper VII: Mendes, C., Carvalho, M., Bravo, J., Martins, S., Zangão, M. O., & Raimundo, A. (2024). The impact of an exercise program on health-related quality of life (SarQoL) in patients with preoperative sarcopenic obesity after bariatric surgery: a randomized controlled trial. Research Square (Research Square) (under review at Obesty Surgery)

Paper VIII: Mendes, C., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2024). Possible Interaction Between Physical Exercise and Leptin and Ghrelin Changes Following Roux-en-Y Gastric Bypass in Sarcopenic Obesity Patients—A Pilot Study. *Nutrients*, *16*(22), 3913. https://doi.org/10.3390/nu16223913

Paper XI: Mendes, C., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2025). The impact of bariatric surgery and exercise on systemic immune inflammation index in patients with sarcopenia obesity. *Scientific reports*, *15*(1), 5188. https://doi.org/10.1038/s41598-025-89806-3

- Conferences presentations

Oral Presentation: Mendes, C., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2024). Impact of Bariatric Surgery on Sarcopenia Related Parameters and Diagnosis—The Preliminary Results of EXPOBAR Study. Portuguese Society of Obesity Surgery, SPCO Congress. Ílhavo, Portugal - **Best Presentation Award** (APPENDIX 1)

Oral Presentation: Mendes, C., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2024). Interplay of Physical Exercise with Leptin and Ghrelin Alterations After Roux-en-Y-Gastric Bypass in Patients with Sarcopenic Obesity. Portuguese Society of Obesity Surgery, SPCO Congress. Ílhavo, Portugal - **Best Presentation Award** (APPENDIX 2)

Oral Presentation: Mendes, C., Carvalho, M., Cabo, C., Bravo, J., Martins, S., & Raimundo, A. (2024). Effect of a 16-week Combined Supervised Exercise Program after bariatric surgery on Sarcopenia parameters – The results of the EXPOBAR randomized trial program. Portuguese Society of Obesity Surgery, SPCO Congress. Ílhavo, Portugal (APPENDIX 3)

Oral Presentation: Mendes, C. A., Cinza, A. M., Laranjeira, Â., Amaro, M., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2022). Effects of physical exercise in sarcopenia on patients undergoing bariatric surgery: A protocol for a randomized clinical trial and preliminary results. Portuguese Society Mini-Invasive Surgery - XIV SPCMIN Congress. Peniche, Portugal (APPENDIX 4)

E-Poster: Mendes, C., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2024). The impact of bariatric surgery and exercise on Systemic Immune Inflammation Index in patients with sarcopenia obesity. Scientific Reports. Portuguese Society of Obesity Surgery, SPCO Congress. Ílhavo, Portugal (APPENDIX 5)

E-poster: Mendes, C., Carvalho, M., Cabo, C., Bravo, J., Martins, S., & Raimundo, A. (2024). Effects of a randomized 16-week training program in sarcopenia on patients undergone gastric bypass - EXPOBAR results", International Federation of Obesity Surgery, IFSO Congress 2024. Melbourne, Austrália (APPENDIX 6)

E-poster: Santos, C., Cinza, A. M., Laranjeira, Â., Amaro, M., Carvalho, M., Martins, S., Bravo, J., & Raimundo, A. (2022). The impact of exercise on prevention of sarcopenia after bariatric surgery: The study protocol of the EXPOBAR randomized controlled trial. Portuguese Physiological Society (*SPFISIOLOGIA) Congress. Coimbra, Portugal* (APPENDIX 7)

E-poster: Santos, C., Cinza, A. M., Laranjeira, Â., Amaro, M., Carvalho, M., Martins, S., Bravo, J., & Raimundo, A. (2022). Effects of a randomized 16-week training program in sarcopenia on patients undergone gastric bypass - EXPOBAR protocol and primary results. 3th Annual Summit Comprehensive Health Research Centre (CHRC). Evora, Portugal. (APPENDIX 8)

CHAPTER 2 – LITERATURE REVIEW

The rising levels of obesity present a major public health challenge, with obesity recognized as a high-priority condition requiring intervention owing to its considerable increase in incidence. Its prevalence has significantly increased worldwide over recent decades. In 2014, the WHO reported that 20.1% of men and 30.5% of women have obesity, with over 600 million people affected globally. If these trends persist, by 2030, more than 3 billion people will be overweight or have obesity (Hämälaïnen et al., 2020; Morabia & Abel, 2006; Sardinha et al., 2012).

In addition to being classified as a chronic disease, obesity is also a risk factor for numerous other conditions. It is subdivided into various categories on the basis of body mass index (BMI) and is responsible for an average of 3.5 million deaths annually. Type I obesity is identified by a BMI between 30 and 34.9 kg/m², type II obesity is identified by a BMI of 35 to 39.9 kg/m², and morbid obesity is classified as a BMI exceeding 40 kg/m² (DGS, 2017). As the classification of obesity progresses, so do metabolic risk factors, which increase the incidence of cardiovascular events, leading to high morbidity and mortality rates (Soriano-Maldonado et al., 2020).

There is an ongoing challenge in finding the best treatment for obesity, as well as the most effective methods for treating its associated comorbidities, such as hypertension, dyslipidemia, obstructive sleep apnea syndrome, cardiovascular diseases, and musculoskeletal issues. While various nonsurgical approaches exist, studies have revealed that none of these interventions are as effective as surgical procedures (Marshall et al., 2020). Bariatric surgery is a proven method for treating obesity and improving health-related quality of life (Raoof et al., 2015).

Today, obesity can be treated through various medical and surgical therapies. Bariatric surgery is now considered a safe and long-term effective procedure for treating obesity and its associated comorbidities. This type of surgery is becoming the treatment of choice for individuals with obesity and additional associated pathologies (Rozier et al., 2019).

The two most commonly performed bariatric surgeries worldwide are sleeve gastrectomy and Roux-en-Y gastric bypass (RYGB). However, these invasive procedures do not eliminate poor habits; therefore, the success of surgery can be improved through lifestyle changes and adequate physical activity (Bond et al., 2012).

Bariatric surgery is a treatment for severe and morbid obesity, as well as for its associated diseases, with proven success rates (Ribaric et al., 2014). Weight loss, particularly in the first year following surgery, is significant and rapid, affecting body composition, especially muscle mass, with all the consequences that may arise from it (Villa-González et al., 2019).

In this context, physical exercise has shown positive effects on cardiorespiratory fitness, muscle strength, physical function, cardio-metabolic profile, and glucose metabolism (King et al., 2020).

Current evidence and recommendations regarding physical exercise for bariatric surgery patients focus primarily on weight loss, which oversimplifies the evolution process following surgery and overlooks the importance of exercise as a nonpharmacological therapy (Soriano-Maldonado et al., 2020).

In fact, body composition appears to be a key factor for positive outcomes following bariatric surgery and associated comorbidities. We know that weight loss is rapid during the first year, with implications for muscle mass loss. Sarcopenia is a pathological disorder characterized by widespread loss of skeletal muscle mass and function, which has implications for quality of life (H. Yuan et al., 2024). Sarcopenia is also associated with diabetes, metabolic syndrome, and cardiovascular diseases. Additionally, sarcopenia is linked to the severity of fibrosis and steatosis, regardless of metabolic risk factors, in patients with nonalcoholic fatty liver disease (Petta et al., 2017; Voican et al., 2018).

The consequences of significant weight loss after bariatric surgery and the onset or modification of preexisting sarcopenia remain poorly documented and studied. However, early initiation of adequate nutritional support, in combination with physical activity, is an important anabolic stimulus for muscle protein synthesis and prevention of sarcopenia (Voican et al., 2018).

Weight loss associated with bariatric surgery is strongly linked to significant reductions in skeletal muscle and bone mineral mass, leading us to conclude that, after bariatric surgery, patients are at increased risk of developing sarcopenia. In this context, several authors argue that reduced physical activity levels are a contributing factor to the development of sarcopenia and that a combination of aerobic and strength exercises in this population may be effective in preventing sarcopenia (Pekař et al., 2020).

Despite recent WHO recommendations on physical activity and sedentary behavior, few specific programs have been designed for patients with obesity or bariatric surgery populations (Hsu et al., 2012).

The need for preventive programs to mitigate sarcopenia in bariatric surgery patients seems to be one of the key factors for long-term surgical success in bariatric and metabolic surgery. However, the lack of evidence for acute and ongoing programs highlights the need for their development.

The objective of this thesis is to study the effects of a 16-week supervised exercise intervention on postbariatric surgery sarcopenia (primary objective). The specific purposes are as follows:

1. To develop new evidence on the effects of exercise on sarcopenia diagnosis after bariatric surgery.
2. To synthesize evidence on the effects of physical exercise on sarcopenia parameters in bariatric surgery patients.
3. To characterize the cardiometabolic profile of bariatric surgery patients.
4. To characterize inflammatory markers before and after bariatric surgery.
5. To understand and characterize the hormonal profile after bariatric surgery.
6. To evaluate noninvasive biomarkers involved in the mechanism of postbariatric surgery.
7. To understand the impact of physical exercise on the quality of life of bariatric surgery patients.
8. To assess the effects of an exercise program applied to bariatric surgery patients.

Article 1: Systematic review

Exercise interventions for the prevention of sarcopenia after bariatric surgery: A Systematic Review

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Abstract

Introduction: Bariatric surgery is a treatment for severe obesity and its associated conditions, that already has ample evidence of its benefits. In addition to the reduction in body fat mass, the weight loss caused by bariatric surgery includes a significant reduction in skeletal muscle and bone mineral mass, which could negatively affect functional capacity and increase the risk of sarcopenia. The need for prophylactic programs that prevent sarcopenia in bariatric surgery patients seems to be one of the crucial points for the long-term surgical success of bariatric and metabolic surgery. This study aims to review the published literature on the effects of physical exercise on the prevention of sarcopenia induced by bariatric surgery.

Methods: We followed the PRISMA checklist for systematic reviews conducted in PubMed/Medline, EBSCO, Web of Science, and Scopus databases. Randomized controlled, controlled clinical, and other types of experimental studies were considered for inclusion. A total of 356 possibly relevant studies were identified with quality considered reasonable and good. Eight studies were included in the review, six of which were randomized experimental studies, one was a pilot study and one a quasi-experimental study.

Results: Structured physical exercise allows significant improvements in body composition, positively affecting functional capacity, muscle strength, cardio-metabolic risk factors, and quality of life in patients with obesity undergoing bariatric surgery, especially with combined exercise in the first weeks after surgery.

Conclusion: A combined, individualized, and supervised exercise program contributes to preventing and reducing sarcopenia after bariatric surgery.

Keywords: exercise, bariatric surgery, muscle mass, sarcopenia

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Introduction

Despite the availability of non-surgical approaches to treat obesity, none of these interventions are as effective as surgery(Marshall et al., 2020). Bariatric and metabolic surgery is currently considered a safe, effective, and successful procedure to treat severe obesity and its associated medical problems assuring long-term results (Rozier et al., 2019). Presently, the dominant procedures are sleeve gastrectomy and gastric bypass, which account for approximately 90% of all operations performed worldwide. Both options have well-researched outcomes in the mid and long-term (Eisenberg et al., 2022; Welbourn, Hollyman, et al., 2018). However, weight loss induced by bariatric surgery represents a significant reduction not only in body fat, but also in muscle strength, muscle mass, and bone mineral mass (Matos et al., 2020). In this setting, patients incur an increased risk of alterations in the skeletal muscle system (Voican et al., 2018).

Body composition changes appear to be one of the key outcomes after bariatric surgery. The potential rapid weight loss in the first year after surgery, associated with low-calorie diets, has been shown to have a significant impact on the reduction of muscle mass (Martínez et al., 2022). The loss of muscle tissue may have negative implications for morbidity, physical performance, and long-term weight regain (Santos et al., 2022).

One of the repercussions of the pronounced weight loss after bariatric surgery may be the onset of sarcopenia or modification of pre-existing sarcopenia. Sarcopenic obesity is a syndrome characterized by the coexistence of excessive body fat, low muscle mass, and reduced muscle strength (Prado et al., 2008; Voican et al., 2018). However, the early establishment of adequate nutritional support in combination with physical activity may be a decisive anabolic stimulus for muscle protein synthesis and sarcopenia prevention (Voican et al., 2018).

The evidence for the effect of the practice of physical exercise in bariatric surgery patients, in general, does not go beyond the objective of weight loss. This narrows the therapeutic process of the person undergoing this type of surgery and the importance of exercise as a non-medical non-pharmacological therapy (Bastos et al., 2013; Soriano-Maldonado et al., 2020; Villa-González et al., 2019), (Donini et al., 2022; Suter et al., 2006). For this reason, some authors propose the need for the implementation of preventive programs to overcome the problem of sarcopenia, that include a combination of aerobic and strength exercises, which seems to be the most effective approach (Bellicha et al., 2021a, 2021; J. Chen et al., 2022; L. Chen et al., 2013; Konopka & Harber, 2014).

Previous reviews addressed the benefits of physical exercise after bariatric surgery, as well as the type and characteristics of the intervention, suggesting that the inclusion of accompanied physical exercise programs may be of great benefit to bariatric surgery patients. It promotes more significant improvements in body composition, namely a decrease in fat mass, and improvements in the skeletal muscle system, bone mineral density and physical fitness (Mendes et al., 2023; O'Leary et al., 2016).

In this context, several authors suggest that reduced levels of physical activity and exercise are potent factors for the development of sarcopenia and that combined exercises in this population can be useful in preventing sarcopenia (C. Amaro Santos et al., 2023; Pekař et al., 2020; C. Santos, Raimundo, et al., 2022; C. A. Santos et al., 2022, 2023; Voican et al., 2018). Prophylactic programs that prevent sarcopenia in bariatric surgery patients seems to be one of the crucial tools that may contribute to the long-term surgical success of bariatric and metabolic surgery.

However, there is still poor evidence, few reviews, and sparse experimental data on the effects of supervised exercise on obesity surgery related outcomes, like sarcopenia, in this specific population, especially in accordance with the FITT-VP principle. To highlight the various aspects to consider when developing an exercise training plan, the American College of Sports Medicine (ACSM) uses the FITT-VP principle of exercise prescription, which includes: Frequency (how often is exercise done each week), Intensity (how hard is the exercise), Time (how long is the exercise duration), Type (what is the mode of exercise), Volume (what is the total amount of exercise), and Progression (how is the exercise program evolves) (Bushman, 2014; Stine et al., 2023). In general, progression is recommended for an exercise prescription to be effective, but there is currently no evidence to make clear recommendations for this in bariatric surgery patients.

The main objective of this review is to analyze the potential effects of exercise on the prevention of sarcopenia (muscle strength, mass and functional capacity) in patients undergoing bariatric surgery. Also, we propose to systematically analyze the available metrics that can be useful to evaluate sarcopenia in this setting and to establish the characteristics of exercise that may be most useful to prevent sarcopenia after bariatric surgery. Secondary metrics are health-related quality of life, physical activity and cardiometabolic conditions.

Methods

Protocol and registration

This systematic review was developed according to the *Preferred items reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA)(Moher et al., 2009; Page et al., 2021). It was also registered in the *International Prospective Register of Systematic Reviews* (PROSPERO), with registration number CRD42022324642 (APPENDIX 9) (C. Santos, Raimundo, et al., 2022).

Search Strategy

The review was conducted in *PubMed*, *Scopus, Web of Science, and Ebsco* databases, and the search terms were subdivided into phases according to the defined criteria.

The following search strategy was used in all databases: (“exercise” OR “physical activity”) AND (“bariatric surgery” OR “gastric bypass” OR “gastric sleeve”) AND (“sarcopenia” OR “skeletal muscle mass” OR “fat-free mass” OR “muscle mass”) (supplementary material - Table 2.1.1).

Using the PICO framework, the research strategy was: “What type (C) of exercise (I) promotes more prevention of sarcopenia (O) in patients undergoing bariatric surgery (P)?”.

Table 2.1.1. Search strategy

#	***Filters applied: Clinical Trial, Randomized Controlled Trial***	**PubMed**	**Scopus**	**Ebsco**	**Web of Science**
	Phase I				
1	“bariatric surgery”	23190	23887	2560	11628
2	“gastric bypass”	15246	17056	1981	256
3	“gastric sleeve”	310	545	47	439
4	((“#1”) OR (“#2”) OR (“#3”))	30963	31124	3639	1199
	Phase II				
5	“physical function”	20830	282972	35293	27675
6	performance	3678390	1207662	220643	14628
7	strength	430359	29130	9252	6011
8	exercise	502375	941657	110566	516242
9	((“#5”) OR (“#6”) OR (“#7”) OR (“#8”))	5190243	1935422	302884	290820
	Phase III				
10	“skeletal muscle mass”	8315	15102	2081	6273
11	“muscle mass”	20842	46135	4093	4309
12	sarcopen *	13016	19949	1678	588
13	“body composition”	62842	92865	14234	11216
14	((“#10”) OR (“#11”) OR (“#12”) OR (“#13”))	86924	132670	18224	20949
	Phase IV				
27	in the last 10 years ((“#4”))	1725	24285	41	274
28	in the last 10 years ((“#9”))	2829066	942486	217242	3743
29	in the last 10 years ((“#14”))	6031	86816	13569	4873
	Phase VIII				
32	((“#27”) AND (“#28”) AND (“#29”)	57	140	23	106
	TOTAL				326

Eligibility Criteria

In the first phase, the inclusion criteria were defined: (1) studies written in all languages, (2) published after 2011 and based on the latest evidence of exercise recommendation, (3) randomized controlled studies, controlled clinical studies, and other experimental studies were considered. In the next phase, the studies included were: (4) studies in which the population are patients after bariatric surgery, (5) articles that evaluated muscle mass and function after bariatric surgery, and (6) studies in which the intervention is performed after bariatric surgery. Review studies and those that did not assess muscle mass or function were excluded.

Selection of Studies

After applying the first inclusion and exclusion criteria, an analysis of the title and abstract of the articles was screened. Finally, the remaining articles were read and only the articles whose text respected the inclusion criteria for this systematic literature review were selected.

Outcome Measures

The primary outcome in this study was the efficacy of exercise programs on sarcopenia prevention after bariatric surgery. To address that, we studied muscle strength and functional capacity after bariatric surgery. Additionally, we evaluated the type and characteristics of exercise programs according to the FITT-VP principle. Secondary reported evaluations were anthropometric and body composition, physical activity, performance, quality of life, and cardiometabolic assessment and risk.

Data Extraction

The information from the studies is presented in three tables (Table 2.1.2; Table 2.1.3; Table 2.1.4), to systematize the research process.

Table 2.1.2. Main results obtained

Article	Type	objective	Measures and Instruments	Results	Conclusions
In et al., 2021	Pilot Study	Short-term effects on functional capacity and body composition of two home training programs	- Anthropometry (No determined) - Capacity functional (6min walking; 5-time-sit-to-stand) - Quality of life (Beck Depression) - Muscular strength (handgrip)	- <u>Anthropometry and body composition</u> Combined exercise induces greater weight loss, significantly reduces fat mass, increases muscle mass and bone mass at 3 months (FM **p=0.039;** BM **p<0.05;** FFM **p<0.05)**; in both groups there was significant weight loss compared to baseline and a significant reduction in waist and hip measurements (Waist **p<0.05;** Hip **p<0.05)** - <u>Perception exertion; Functional capacity; Quality of life; Physical Activity (IPAQ)</u>	- Exercise promotes a significant improvement in the health of patients, upper body muscle strength

			- Perception exertion (Borg scale) - Physical Activity (IPAQ) - Cardiometabolic assessment (HbA1, Urea, Uric Acid, C - Peptide, Pre-prandial Glucose)	No significant differences (p>0.05) - <u>Muscle strength</u> Hand grip strength significantly increased with the combined exercise (**p<0.05);** 5-time-sit-to-stand - No significant differences (p>0.05) - <u>Cardiometabolic assessment</u> HbA1, Pre-prandial Glucose, blood pressure, decreases in both groups at 3 months; Pre-prandial glucose decreases in the 1st and 3rd month in the combined exercise and only in the 3rd month in the aerobic exercise (p>0.05) C-Peptide and uric acid with significant results at 3 months with combined exercise (**p<0.05)**	
Marc-Hernández et al., 2020	RCT	Effects of supervised and combined exercise, 3 years after gastric sleeve	- Anthropometry (bio impedance, waist, and hip) - Physical fitness (VO_{2max}) - Quality of life (SF-36) Cardiometabolic assessment (blood pressure, glucose) - Cardiovascular risk (score risk)	- <u>Anthropometry and body composition</u> Decreased fat mass, weight regain and waist, increased loss of excess weight and increased muscle mass significantly (BMI ($kg*m^{2}$): GI -0.45; GC 0.62; **p= 0.017** / FFM (Kg): GI 1.4; GC -0.3; p= 0.069 / FM (Kg): GI -2.5; GC 1.8; **p< 0.001** / Waist (cm): GI -1.9; GC 2.8; **p<0.035;** / Hip (cm): GI -0.15; GC 1.01; p=0.305) - <u>Physical fitness</u> Significant improvement of VO2max in the GI ($VO_{2max:}$ GI 19.8; GC 23.2; **p=0.002)** - <u>Quality of life</u> GI has better results in SF-36 and body pain, but not significant (p>0.05) - <u>Blood pressure</u> p>0.05**; Cohen´s=0.31** - <u>Cardiovascular risk</u> Decreased glucose, diastolic pressure, and risk score **(p<0.05; Cohen´s=0.37)**	- Supervised and combined exercise promotes fat mass reduction and muscle mass increase, reduced weight regain, improves physical fitness and quality of life
Noack Segovia et al., 2019	RCT	Effects of resistance exercise over 12 weeks	- Anthropometry (bio impedance) - Muscle strength (1RM, hand grip dynamometer) - Metabolism	- <u>Anthropometry and body composition</u> No significant differences (FFM:GI 49.26; GC 51.17; p>0.05; FM: GI 26.94; GC 21.20; p>0.05; BMI: GI 26.05; GC 24.32; p>0.05) - <u>Muscle strength</u> No significant differences (Hand grip: GI 31.57; GC 31.91; p>0.05) - <u>Metabolism</u> No significant differences (Caloric intake: GI 1974; GC 1331; p>0.05)	- Resistance exercise, for 6 months, has no significance in the development of muscle mass and strength assessed by bioimpedance and dynamometer.
Daniels et al., 2017	RCT	Effect of progressive resistance training	- Anthropometry (air displacement plethysmography) - Muscle strength and quality (1RM leg press/extension) - Muscle cross-sectional area (Magnetic resonance imaging of the right thigh	- <u>Anthropometry and body composition</u> No significant differences (FFM: p>0.05; WL: p=0.398) - <u>Muscle strength and quality</u> Significant differences in muscle strength quality for the quadriceps assessment leg extension and leg press (1RM Leg press (Kg): GI 163.4; GC 222.8; **p<0.001**; **Cohen´s=2.4**; 1RM Leg extension (Kg): GI 32.5; GC 38.3; **p=0.014; Cohen´s=0.86;** Leg muscle quality pressure (Kg/cm^{2}): GI 1.4; GC 2.1; **p<0.001**; **Cohen´s=2.4;** 1RM Leg extension (Kg/cm^{2}): GI 0.62; GC 0.74; **p<0.001)**	- High-intensity resistance training has been shown to be an important enhancer of muscle strength and muscle quality. - This training does not cause an increase in muscle

				- Muscle cross-sectional area No significant differences (p=0.345; p=0.070	mass or changes in the cross-section of the muscle.
Herring et al., 2017	RCT	To evaluate the results of supervised exercise for 12 weeks, after 12-24 months of bariatric surgery	- Anthropometry (bio impedance, waist, and hip circumference) - Muscle strength (hand grip dynamometer) - Functional capacity (shuttle walk test and sit -to-stand) - Physical activity (IPAQ-SF, accelerometer) - Food (24h registration) Cardiometabolic assessment (blood pressure, HR reserve)	- Anthropometry and body composition Fat mass was significantly lower at 12 and 24 weeks, and muscle mass at 24 weeks. Waist and hip without significant differences at 24 weeks 12 weeks - BMI ($kg*m^{2}$)): GI -0.9; GC 0.4; **p= 0.003** / FFM (Kg): GI -0.3; GC 0.2; p= 0.391 / FM (Kg): GI -2.1; GC 0.9; **p= 0.002** / Waist (cm): GI -7.53; GC -0.59; **p<0.001** / Hip (cm): GI -6.3; GC -0.1; **p=0.026** 24 weeks - BMI ($kg*m^{2}$)): GI -1; GC 1; **p= 0.004** / FFM (Kg): GI -0.8; GC 0.8; **p= 0.034** / FM (Kg): GI -1.9; GC 2.1; **p= 0.009** / Waist (cm): GI -3.9; GC 0.5; p<0.123 / Hip (cm): GI -7.7; GC -0.6; p=0.067 - Muscle strength Performance had improved at 12 weeks on the exercise group (12 weeks - Handgrip (Kg): GI 2.5; GC -0.9; **p=0.036**; 24 weeks - Handgrip (Kg): GI 2.8; GC 0.8; p=0.201) - Functional capacity 12 weeks - STS (%): GI -3.8; GC 0.2; **p=0.010** / ISWT (m): GI - 3.8; GC 0.2; **p= 0.010** 24 weeks - STS (%): GI -4.2; GC 0.2; **p=0.003** / ISWT (m): GI - 3.8; GC 0.2; **p= 0.010; Cohen´s=2.2** - Physical activity (No significant differences) 12 weeks - Sedentary behaviour (min/day): GI -38.3; GC -13; p= 0.562 24 weeks - Sedentary behaviour (min/day): GI -15.5; GC -5.6; p= 0.905 - Food (No significant differences) 12 weeks – Intake caloric (Kcal): GI -96.2; GC -262.5; p= 0.212 24 weeks - Intake caloric (Kcal): GI -209.2; GC 152.4; p= 0.103 - Cardiometabolic assessment Blood pressure and HRR with significant differences at 12 weeks; blood pressure with significant differences at 24 weeks and HRR without significant differences at 24 weeks. 12 weeks - Resting heart rate ($B*min^{-1}$)): GI -11.3; GC -2.8; **p= 0.021**; Systolic blood pressure (mmHg): GI -7.4; GC 3.7; **p= 0.012**; Diastolic blood pressure (mmHg): GI -5.3; GC 3.3; **p= 0.002** 24 weeks - Resting heart rate ($B*min^{-1}$)): GI -5; GC -3.4; p= 0.672; Systolic blood pressure (mmHg): GI 6.9; GC 0.4; **p= 0.036**; Diastolic blood pressure (mmHg): GI -5.2; GC -2.7; p= 0.001)	- Supervised exercise leads to improvement in muscle mass and functional capacity.
Hassannejad et al., 2017	RCT	Impact of aerobic and strength exercise on	- Anthropometry (bio impedance) - Muscle strength (1RM-handgrip)	- Anthropometry and body composition There is no significant difference in weight loss between the groups that exercised, but there is in relation to the control	- Exercise preserves muscle mass. - Combined exercise allows better

		weight loss and body composition after bariatric surgery	- Functional capacity (12min walk run test and sit-to-stand) - Physical activity (self-reported) - Food (24h registration) - Perception exertion (Borg scale)	group; Muscle mass and fat-free mass was better in the combined exercise group: BMI ($kg*m^{2)}$: (GI aerobic -2.2; GC -0.6; p= 0.279); (GI aerobic+strength -1.9; GC -0.9; p= 0.487); (GI aerobic+strength -1.2; GI aerobic 1.8; p= 0.722) FFM (Kg): (GI aerobic -0.9; GC 5.8; p= 0.155); (GI aerobic+strength 0.2; GC -7.3; **p= 0.038);** (GI aerobic+strength -2.3; GI aerobic 4.9; p= 0.473) FM (Kg): (GI aerobic -9.7; GC -1.1; **p=0.014);** (GI aerobic+strength -10.6; GC -1.9; **p= 0.006);** (GI aerobic+strength -5.3; GI aerobic 3.7; p= 0.728) SMM (Kg): (GI aerobic -1.7; GC 1.3; p= 0.799); (GI aerobic+strength -1.3; GC 1.8; p= 0.757); (GI aerobic+strength -1.1; GI aerobic 2.0; p= 0.580) - Muscle strength Handgrip: (GI aerobic -0.9; GC 2.5; p=0.348)**;** (GI aerobic+strength 0.9; GC 4.6; **p= 0.004);** (GI aerobic+strength 0.2; GI aerobic 3.7; **p= 0.031**) Functional capacity STS: (GI aerobic -2.4; GC 8.4; p=0.267)**;** (GI aerobio+strength -1.5; GC -10.2; p= 0.142)**;** (GI aerobio+strength -3.9; GI aerobic 6.6; p= 0.608) 12min walk run test: (GI aerobic 23.5; GC 198; **p= 0.014**); (GI aerobic+strength 56.8; GC 243.9; **p= 0.002**); (GI aerobic+strength -42.6; GI aerobic 121.9; p= 0.337) - Physical activity: No significant differences (p> 0.05) - Food: No significant differences (p=0.120)	preservation of muscle mass and improves 1RM.
Huck, 2015	- quasi-experi mental	Effects of supervised resistance exercise for 12 weeks in patients undergoing bariatric surgery	- Anthropometry (bio impedance, waist, and hip) - Physical fitness (VO_{2max}) - Evaluation cardiometabolic (blood pressure, RH reserve) - Muscle strength (5RM >1RM chest press/leg press; hand grip dynamometer) - Capacity functional (sit-to-stand - STS) - Activity physics (self-report: BRFSS Physical Activity Questionnaire 2001)	- Anthropometry and body composition (No significant differences): BMI ($kg*m^{2)}$: GI -3.3; GC -1.9; p= 0.200 FFM (Kg): GI -1.8; GC -1.5; p= 0.810 FM (Kg): GI -1.8; GC -1.5; p= 0.810 Waist (cm): GI - 9.6; GC -8.6; p=0.795 - Physical fitness (No significant differences): VO_{2max} ($ml*Kg^{-1}*min^{-1)}$: GI 0.91; GC 0.46; p=0.347) - Evaluation cardiometabolic (No significant differences): Resting heart rate ($B*min^{-1)}$: GI -3.6; GC -0.88; p= 0.519 Systolic blood pressure (mmHg): GI 6.9; GC -0.25; p= 0.321 Diastolic blood pressure (mmHg): GI 1.4; GC -1.75; p= 0.493 - Muscle strength (No significant differences): 1RM leg pressure (Kg): GI 114.70>148.07; **p=0.001;** GC did not perform this test 1RM chest pressure (Kg): 28.15>39.63; **p=0.001;** GC did not perform this test Handgrip (Kg): GI 11.3; GC 11.6; p=0.419 - Functional capacity Better in intervention group (STS (%): GI 44; GC 11.4; **p= 0.006)** - physical activity Self-Report ($METhrs*wk^{-1}$): GI 23.3; GC 6.2; **p = 0.026**	- Exercise benefits the improvement of body composition. - Supervised endurance exercise improves physical and functional capacity

Shah et al., 2011	- RCT	Feasibility of a high-volume, moderate-intensity program after bariatric surgery; The secondary objective is to evaluate weight loss, comorbidities, and quality of life.	- Anthropometry (DEXA, waist, and hip) - Physical fitness (VO $_{2max}$) - Quality of life (SF-36) - Cardiometabolic assessment (lipids, lipoprotein, insulin, glucose) - Physical activity (indirect calorimetry, pedometer) - Food (24h registration) - Perception exertion (Borg scale)	- Anthropometry and body composition Muscle mass decreased less in GI but without significant differences; Waist and hip with significant differences between groups: FFM (Kg): GI 54.4; GC 50.4; p= 0.94 / FM (Kg): GI 44.1; GC 44.5; p= 0.57 / Waist (cm): GI 112.6; GC 105.6; p=0.30 / Hip (cm): GI 126.8; GC 122.9; p=0.37 - Physical fitness Better in intervention group (VO2max _ **p<0.05)** - Quality of life (No significant differences) p=0.41 - Cardiometabolic assessment (No significant differences) p>0.05 - Physical activity (PA) Moderate levels with significant differences at 12 weeks, but not in low levels. No difference in calorimetry - Food (No significant differences) Energy intake: GI 1.21; GC 1.03; p=0.47 - Perception exertion (not described)	High-volume, moderate-intensity exercise is about 50% feasible to improve physical fitness and improve postprandial glycaemic response.

IG: intervention group: CG: control group; FM: fat mass; BM: bone mass; FFM: fat free mass; BMI: body mass index; WL: weight loss; PA: physical activity

Table 2.1.3. Main characteristics of interventions

Author	Sample	Start	Duration	Type, Frequency and Progression	Intensity	Assessments
In et al., 2021	N=35 (25 women; 10 men) IG=17 (aerobic) IG=18 (aerobic + resistance)	1-month post-surgery	- 12 Weeks of 1h/session aerobic training - 8 weeks combined training (after 1-month aerobic training) of 1h/session - Core at session start and end - Heating - dynamic stretching	Aerobic training: 1h walk/3 sessions/week Combined training: - 3 sessions/week - Exercises at home (elastic bands) - 30-35 minutes 1st week - 50-55 minutes remaining weeks - Week 1 – 1set/8 reps - Week 2 - 2set/8 reps - Week 3/4 - 3set/8 reps - Week 5/6 - 3set/10 reps - Week 7/8 - 3set/12 reps	Combined training: - 500-750Kcal - Women: Green Elastic Band 4/7 - Men: Blue Elastic Band 5/7 Aerobic training: - 1st month – 40-50% heart rate reserve - 2/3 months 60-80% of heart rate reserve	1st - Before the surgery 2nd – Before the intervention 3rd – After the intervention
Marc-Hernández et al., 2020	N=21 (16 women; 2 men) IG=10 (8 women) GC=8 (8 women)	37 months after surgery	- 20 weeks of training - 50min/session - 4min dynamic stretching	Resistance training: - 2 days/week - 4-7 exercises - 10-20 repetitions - 8-28min Endurance training: - 2 days/week - 20min	Resistance training: 50-75%RM Endurance training: 60-80% HRmax	1st - 1 month after surgery 2nd - 7 month after surgery 3rd - 13 months after surgery 4th - 19 month after surgery 5th - 37 months after surgery (beginning of the program) 6th - 42 months after surgery (end of program) 7th - 44 month after surgery (6 months after program)

Noack Segovia et al., 2019	N=43 (32 women; 11 men) IG=21 GC=22	1-month post-surgery	- 24 weeks of moderate intensity - 60-80min/session - 5-10min warm-up - 5-10min dynamic stretching	- 3 sessions/week - 90 minutes with 30 minutes of aerobic training on the treadmill - Number of repetitions based on 1RM - 2 weeks of adaptation	- 54-59% heart rate reserve - Progressive strength training - 1RM	1st – Preoperative 2nd – Before the intervention 3rd – After the intervention
Daniels et al., 2017	N=16 women IG=8 GC=8	8 weeks post-surgery	- 12 weeks of resistance training - 60-80min/session - 5-10min warm-up - 5-10min dynamic stretching	Period 1: - 1-2 weeks – adaptation - 3 sessions/week - 8-10 Exercises - 1 set exercise - 10-15 Reps Period 2: - 3-7 Weeks – Progressive - 3 sessions/week - 8-10 Exercises - 3-4 Set exercise - 10-15 Reps Period 3: - 8-12 Weeks – resistance - 3 sessions/week - 8-10 Exercises - 3-4 Set Exercises - 8-12 Reps	Period 1: 50-70% 1RM Period 2: 70-80% 1RM Period 3 :> 80% 1RM	1st - Before the intervention (baseline) 2nd - 12 Weeks
Herring et al., 2017	N=21 (19 women; 2 men) IG=11 (1 man) GC=10 (1 man)	12 – 24 months post-surgery	- 12 Weeks of resistance training and aerobic training	- 3 sessions/week - 60 minutes (warm-up, moderate aerobic + resistance, stretching) Aerobic 35min (1-2 weeks) 45min (3-12 weeks) Resistance: 3 sets 12 repetitions 30-60 seconds rest	Aerobic: 64-77% 1RM Endurance: 60% 1RM	1st - Before the intervention (baseline) 2nd - 12 Weeks 3rd – 24 Weeks
Hassannejad et al., 2017	N=60 (45 women; 15 men) – initial recruitment N final = 49 IG=18 (aerobic) IG=16 (aerobic + strength) GC=15 (control)	After surgery, depending on the evolution of the patients	- 12 weeks of aerobic and strength training	Aerobic - 3 sessions/week - 20-30 minutes - Start from the 5th to the 12th week - Elastic bands - Pictures of the exercises Aerobic + strength - 1st-4th week – walking/150min/week - 5th-12th week - walking/150-200min/week - 3 to 5 days/week	- 1st-4th week: Progressive intensity up to 150min/week - 150-200min/week - Borg scale between 12-14	1st – Before the surgery 2nd – 12 weeks or after intervention
Huck, 2015	N=15 (12 women; 3 men) IG=7 (6 women) GC=8 (6 women)	12 months post-surgery	- 12 weeks of resistance training - 60 minutes (10min warm-up, 45min resistance training, 5min stretching)	- 2 Sessions/week (1st-6th week) - 3 Sessions/week (6th-12th week) - 8-12 Reps - 1 set (1st-2nd week) - 2 sets (3rd-7th week) - 3 sets (8th-12th week) - 60s rest between sets	- progressive intensity - 60%-75% 1RM	1st – Before the intervention (baseline) 2nd – 12 weeks
Shan et al., 2011	N=33 (30 women; 3 men) – initial recruitment N final = 28 IG=20 GC=8	3 months post-surgery	- 12 weeks of high-volume training	- 5 days/week (1-2 days/gym) - Monitoring with cardiac monitor or diary) - Caloric calculation/week by walking duration and distance in relation to weight or by recording on treadmill machines or cycle ergometer	->2000Kcal/week of moderate exercise. initial 500kcal and increasing by 500kcal each week - 60-70% VO_2max	1st - Before the intervention (baseline) 2nd – 6 Weeks (Except Dexa, glucose tolerance test, VO_2max) 3rd - 12 Weeks

IG: intervention group: CG: control group; RM: repetition maximum; HR: heart rate; VO_2max: maximal oxygen consumption.

Table 2.1.4. Evaluation variables and effects of different types of exercise

Measures and results	Number of assessment tools per study	Combined Training	Resistance Training	Aerobic Training
Anthropometry	Scale Measuring tape - Waist and hip (4 studies) Air displacement plethysmometer (1 study)	(+)(+)(+) (+)(+)	(-)(-) (-)(-) (-)	(NA)
Body composition	Bioimpedance (8 studies) DEXA	(+)(+)(+)(+)	(-)(-)(-)(-) (-)	
Associated comorbidities and clinical analysis	Resting Heart Rate, Basal arterial blood (4 studies) Cardiovascular risk score (1 study)	(+)(-)(+) (+)	(-) (NA)	(NA) (NA)
Self-reported Quality of life and Inventory Depression	Short-Form Health Survey (SF-36) (2 studies) Beck Depression (1 study)	(-) (-)	(-) (NA)	(-) (NA)
Functional capacity	Six-Minute Walk Test (6MWT) (1 study) Incremental Shuttle Walk Test (ISWT) (1 study) 12 min walking test (1 study) Sit-to-stand (4 studies)	(-) (+) (+) (+)(-)(-)(+)	(NA) (NA) (NA) (+)	(NA) (NA) (NA) (NA)
Level of physical activity	IPAQ: International Physical Activity (2 studies) Accelerometer (1 study) Pedometer (1 study) Calorimetry (1 study) Self-reported (2 studies)	(+)(-) (-) (NA) (NA) (-)	(NA) (NA) (-) (-) (+)	(NA) (NA) (NA) (NA) (NA)
Fitness physical	VO_2max (3 studies)	(+)	(-)(-)	(NA)
Muscle quality	Magnetic resonance imaging of the right thigh (1 study)		(-)	(NA)
Muscle strength	1 repetition maximum chest press (1 study) 1 repetition maximum leg extension (2 studies) Handgrip (5 studies)	(NA) (+) (+)(+)(+)	(+) (+) (-)(-)	(NA) (NA) (NA)
Perception of exertion	Borg scale (2 studies)	(-)	(NA)	(NA)

(+) significant effect; (-) no significant effect; (NA) not available

Selection and Quality of the Studies

One of the authors performed the search strategy (CM), after which the three reviewers (CM, SM, and MC) screened the title and abstract of the articles independently, assessing their eligibility according to the inclusion criteria. Divergences were settled by another author (AR). The assessment of the quality of these studies was done by four authors (CM, MC, AR, JB) using the "*Quality Assessment of Controlled Intervention Studies",* obtained from the website *"The NIH Quality Assessment",* in the various existing dimensions (Moher et al., 2007, 2009)**.** This tool defines the classification of studies according to their risk of bias. The general recommendations indicate that an individual evaluation of each study should be carried out. Thus, the studies are categorized as “Good,” “Fair,” or “Poor,” and the general classification of *GOOD was considered* for six of the eight evaluated studies (table 2.1.5).

Table 2.1.5. Results of the analysis of the quality of studies - Controlled intervention studies

Rating criteria	(In et al., 2021)	(Noack Segovia et al., 2019)	(Marc-Hernández et al., 2020)	(Herring et al., 2017)	(Hassannejad et al., 2017)	(Daniels et al., 2017)	(Huck, 2015)	(Shan et al., 2011)
1. Described as RCT?	no	yes	yes	yes	yes	yes	no	yes
2. Appropriate randomization method?	NA	yes	yes	yes	yes	yes	NA	yes
3. Effective randomization?	NA	yes	yes	yes	yes	yes	NA	yes
4. Double blind participants?	no	yes	yes	yes	yes	yes	no	yes
5. Double-blind investigators?	no	no	yes	yes	no	no	no	no
6. Similar groups?	yes	yes	yes	yes	yes	yes	yes	yes
7. Overall dropout < 20%?	yes	yes	no	yes	yes	yes	yes	yes
8. Dropout among groups < 15%?	yes	yes	yes	yes	yes	yes	yes	yes
9. High adherence to protocols?	yes	yes	yes	yes	yes	yes	yes	yes
10. Other similar interventions?	yes	yes	yes	yes	yes	yes	yes	yes
11. Definition of dependent variables?	yes	yes	yes	yes	yes	yes	yes	yes
12. Valid and reliable measurements?	no	no	yes	yes	yes	yes	yes	yes
13. Sample size 80% power?	NA	yes	NA	yes	yes	no	NA	NA
14. Subjects analysed in your group?	yes	yes	yes	yes	yes	yes	yes	yes
Result	**7/14**	**12/14**	**12/13**	**14/14**	**12/14**	**12/14**	**8/12**	**12/14**
Classification	**Fair**	**Good**	**Good**	**Good**	**Good**	**Good**	**Fair**	**Good**

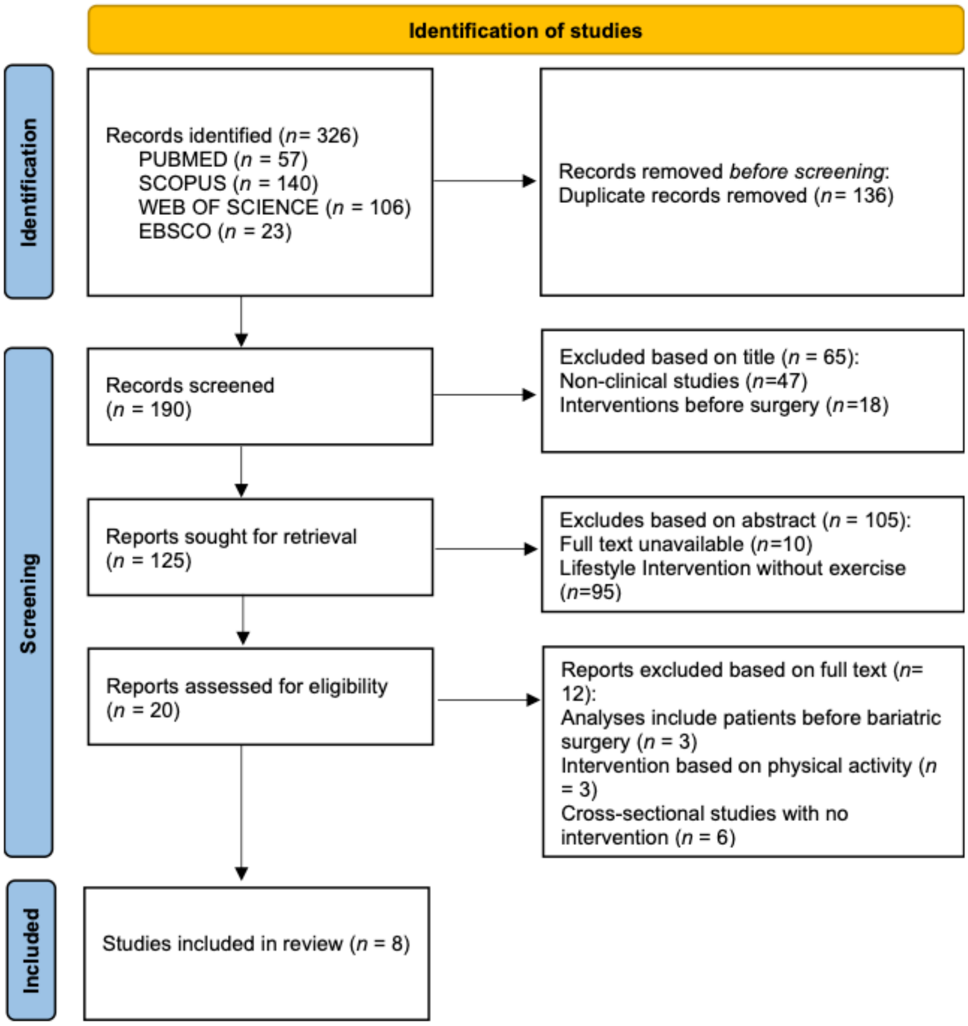
NA-Not available

Results

Literature Research

In the initial search, 326 studies were found, 57 in Pubmed, 140 in Scopus, 106 in Web of Science, and 23 in Ebsco. The exclusion criteria were applied. After removing the excluded studies, 20 possibly relevant studies remained, but 12 were excluded after analysis of the full texts. All studies were experimental, six studies were *randomized controlled trials* (RCT), one was quasi-experimental, and one was a pilot study. In six of the studies, there was an intervention group and a control group. One study considered two intervention groups and a control group (Hassannejad et al., 2017) and there were two intervention groups with different types of exercise (In et al., 2021). Finally, eight studies were collected and analyzed, as seen in the diagram in Figure 2.2.1. Summarizing the research, by adapting the PRISMA-P diagram:

Figure 2.1.1. Diagram of the study selection process for the systematic literature review



Types of Studies

The search strategy included publications in all languages and our time interval corresponded to a period between 2011 and 2022. However, we only have one study from 2011, and six of the eight studies evaluated were published after 2017, with analyses limited to the immediate postoperative period. Only one study carried out the exercise program in a more extended postoperative period, up to 3 years after surgery (Marc-Hernández et al., 2020).

The age range of subjects in almost all studies is 18 to 65 years old. Samples included 15 and 60 subjects divided into an experimental group (GI) and a control group (CG). Only one study used two intervention groups and a control group; in this study, the largest sample have n=49 (Hassannejad et al., 2017). It should be noted that, in this case, the structured exercise was prescribed to the subjects and the monitoring was self-reported; there was no face-to-face monitoring.

The experimental studies were based on exercise programs that started after bariatric surgery. Only one study started a program at a later stage, 37 months after surgery (Marc-Hernández et al., 2020).

The studies were based on structured physical exercise programs, lasting between 12 and 24 weeks, starting mainly between 1 and 3 months after surgery. All studies had evaluations before the intervention which, in most cases, were done before surgery (Hassannejad et al., 2017; Herring et al., 2017; Huck, 2015; In et al., 2021; Noack-Segovia et al., 2019; Shah et al., 2011). All had evaluations after the program.

The objective was to evaluate the effect of structured physical exercise, aerobic, resistance or combined exercise, on body composition. The pilot study evaluated two types of exercise, aerobic and aerobic combined with resistance, and its short-term effects on functional capacity and body composition. These exercise programs were not applied face-to-face but were carried out at home, with self-registration and monitoring (In et al., 2021). Training plans with elastic bands were provided in the study with three groups.

Anthropometry and body composition

Anthropometric and body composition assessments were carried out with bioimpedance (Hassannejad et al., 2017; Herring et al., 2017; Huck, 2015; Marc-Hernández et al., 2020; Noack-Segovia et al., 2019) or with Dual-energy X-ray absorptiometry (DEXA) (Daniels et al., 2018); in half of the studies waist and hip measurements were also evaluated (Herring et al., 2017; Huck, 2015; Marc-Hernández et al., 2020; Shah et al., 2011).

Combined exercise resulted in significant improvements in all body composition metrics, including a significant increase in muscle mass, in addition to improvements quality of life, physical fitness and decreased weight regain (Hassannejad et al., 2017; Herring et al., 2017; In et al., 2021; Marc-Hernández et al., 2020).

All studies showed different results in the intervention group when compared to the control group, regardless of the type of exercise, although in only some of them were there significant differences, namely, significant, in the decrease in fat mass($p=0.039$ (In et al., 2021); $p<0.001$ (Marc-Hernández et al., 2020); $p=0.002$ (Herring et al., 2017)), the increase in muscle mass ($p=0.038$ (Hassannejad et al., 2017); $p<0.05$ (In et al., 2021)) and the increase in the percentage of excess weight loss (Marc-Hernández et al., 2020), with supervised, combined, resistance, endurance, and progressive exercise. There was no difference between the groups in the study, which had two intervention groups, aerobic and aerobic exercise plus strength (Hassannejad et al., 2017). Despite not having significant results, the group with combined exercise had better results than the group that did not have combined exercise, which performed aerobic exercise (Hassannejad et al., 2017).

Even with programs starting later after surgery, 12 to 24 months, the results with combined exercise were significantly better when we consider body composition, namely muscle mass. The same results were found in the other two studies, with evidence that combined exercise significantly reduces fat mass and increases muscle mass and bone mass, with a more significant reduction in waist and hip measurements (In et al., 2021; Marc-Hernández et al., 2020).

Physical function

Muscle strength was assessed in 6 of the studies using the handgrip test (Daniels et al., 2018; Hassannejad et al., 2017; Herring et al., 2017; Huck, 2015; In et al., 2021; Noack-Segovia et al., 2019) and/or one repetition maximum (1RM leg extension (Daniels et al., 2018); 1RM Chest and leg press (Huck, 2015)).

One of the studies assessed muscle quality by measuring the cross-sectional area of the right thigh muscle by magnetic resonance imaging (Daniels et al., 2018).

Regarding functional capacity, there were assessments in 4 studies, with the six-minute walk test (6MWT) (In et al., 2021), shuttle walk test (Herring et al., 2017), 12-minute walk run test (Hassannejad et al., 2017), and sit-to-stand (Hassannejad et al., 2017; Herring et al., 2017; Huck, 2015; In et al., 2021), the latter being used in three of the studies.

Physical fitness was assessed in three studies by VO_2 max (Huck, 2015; Marc-Hernández et al., 2020; Shah et al., 2011) and the Borg scale was used in two studies by (In et al., 2021; Shah et al., 2011), to measure perceived exertion.

The results of muscular strength, assessed mainly by handgrip, showed improvements in all intervention groups, but it was significant only with combined exercise ($p<0.05$) (In et al., 2021). The sit-to-stand and 1RM leg extension tests were also used, obtaining significant differences in the combined exercise also.

It is important to mention that, in the study where the investigators evaluated the cross-sectional area of the right thigh muscle through magnetic resonance imaging, they did not find any significant differences with the application of resistance training (Daniels et al., 2018).

Maximum oxygen consumption ($VO_{2\ max}$) has been an important assessment of physical fitness and in the population with obesity it is considered an important parameter to analyze morbidities associated with excess weight (Noack-Segovia et al., 2019). It has been shown to be an important parameter to assess exercise capacity but also a significant independent predictor of cardiovascular risk and overall mortality (Daniels et al., 2018).

Only 3 studies evaluated physical fitness through VO_{2max}.There were significant improvements in the intervention group, regardless of the type of exercise. There is evidence that the increase in lung function, which can occur after surgery, leads to a significant increase in $VO_{2\ max}$ and that supervised resistance training helps to improve muscle strength and functional autonomy, increasing the patient's functional capacity (Huck, 2015). An improved $VO_{2\ max}$ is mainly due to increased peak blood flow, which increases the maximum rate at which oxygen is supplied and extracted by the skeletal muscle system (Bushman, 2014; Stine et al., 2023).

Physical exercise

Physical activity was evaluated in 3 studies by IPAQ (Herring et al., 2017; In et al., 2021), in 2 studies with accelerometer (Herring et al., 2017; Shah et al., 2011), in 2 studies by self-report (Hassannejad et al., 2017; Huck, 2015), and 1 study by indirect calorimetry (Shah et al., 2011). Self-monitored feeding was only evaluated in 3 studies (Hassannejad et al., 2017; Herring et al., 2017; Shah et al., 2011) , and metabolism was calculated in one of these studies (Noack-Segovia et al., 2019).

In all studies, the practice of structured physical exercise is directly proportional to weight loss and improvement in body composition, that is, more physical exercise means better body composition. Even in the studies with no significant differences, the results were always different in the groups subject to intervention, that is, the groups with intervention obtained better results on body composition.

Significant differences regarding body composition existed only in the groups with combined exercise (p=0.039; p=0.013) (In et al., 2021; Marc-Hernández et al., 2020), since no significant improvements were observed in interventions with resistance or aerobic exercises, despite better results relative to the control group.

Combined exercise achieves an improvement in anthropometric parameters, more specifically in muscle mass, even though it was started one year after surgery (Herring et al., 2017) (p=0.034) and three years after surgery (p<0.001) (Marc-Hernández et al., 2020).

Discussion

This systematic review aims to analyze the effects of exercise on prevention of sarcopenia in patients undergoing bariatric surgery. The chosen studies focused on combined resistance and aerobic training, all demonstrating promising results in body composition improvement but with different results in terms of the skeletal muscle system and, consequently, in muscle strength and function.

Bariatric surgery often leads to significant weight loss, but it can also affect body composition, including a reduction in skeletal muscle mass (K. M. Kim et al., 2016; Vassilev et al., 2022). While decreased skeletal muscle mass may occur despite exercise, engaging in regular physical activity post-bariatric surgery can still offer significant benefits. Exercise can help individuals maintain a healthier body composition by preserving or improving muscle mass and reducing the overall loss of muscle tissue compared to those not exercising (Boppre et al., 2022).

It's important to highlight that there can be a difference between muscle condition/function and muscle morphology, especially concerning the impact of exercise after surgery (Nuijten et al., 2022). In essence, exercise may not entirely halt the changes in muscle morphology following bariatric surgery, but it can substantially enhance muscle condition and functionality, ensuring that the remaining muscle mass performs optimally and contributes to an individual's overall well-being (Castello et al., 2011; Hassannejad et al., 2017; Huck, 2015).

Combined training was analyzed in four studies, starting either shortly after surgery or three years after surgery. Significant changes in anthropometric measurements and body composition were reported in intervention groups (aerobic and combined) but without a significant difference in BMI between groups. That is, without a great variation in weight but with significant improvements in body composition, namely maintenance and even improvement in muscle mass and quality (In et al., 2021).

A previous study demonstrated a mean loss of 21% of fat-free mass (17.5%-31.3%) and 22% of lean body mass one year after surgery (Nuijten et al., 2022). Considering this, most changes occur in the first months after surgery so, the best time for developing an exercise program might be in the first weeks after surgery (Hassannejad et al., 2017).

Furthermore, a combined 12-week exercise program with three progressive phases, 50-80% intensity, aerobic, and resistance exercise, was found to significantly improve body composition, physical function, cardiovascular function, and functional capacity (Herring et al., 2017). These data suggest that combined exercise may be more effective than isolated aerobic exercise in increasing muscle mass, even when started in the weight stabilization phase. In one study, the loss of muscle mass at the end of the 12-week exercise intervention amounted to 13% of the total reduction in body mass. This number is lower than that observed in previous tests and did not harm the results of handgrip strength and functional capacity (Nuijten et al., 2022).

Some guidelines also move in this direction, recommending moderate intensity combined exercise to maintain the skeletal muscle system. Although there are still no definitive guidelines for exercise after surgery, the American College of Sports Medicine (ACSM) states that, from the moment the patient is surgically discharged from the clinic, a progressive exercise program for all individuals should follow the FITT-VP principle (frequency, intensity, time, type, volume, progression) for weight loss and maintenance, for overweight and obesity (Bushman, 2014). Also, the American Society for Metabolic and Bariatric Surgery (ASMBS) recommends, in addition to preoperative exercises, a progressive walking program, starting on the first postoperative day, which should include aerobic exercises and strength training ≥ 30 min/day (*2022 ASMBS and IFSO: Indications for Metabolic and Bariatric Surgery | American Society for Metabolic and Bariatric Surgery*, n.d.; Aminian et al., 2018).

In the study with combined exercise, the program started 37 weeks after surgery, based on previous observations that found that maximum weight loss is achieved between 12 and 24 months after surgery (Marc-Hernández et al., 2020). Likewise, other studies observed a significant weight recovery between 24 and 36 months (Blume et al., 2012), and between 24 and 48 months after surgery (C. Santos, Carvalho, et al., 2022). The investigators monitored the subjects from the 1st month after surgery and found that the patients achieved their maximum fat loss between months 7 and 13 months after surgery. From that moment on, an increase in fat mass was observed in both groups, being significantly higher 37 months after surgery (Marc-Hernández et al., 2020).

According to the results of this study, progressive combined exercise programs, started with eight minutes until fifty minutes duration per session, two to four days per week, between 50-75% one maximum repetition and 60-80% maximum heart rate, showed significant reductions in the percentage of fat mass, a trend towards total weight reduction and an increase in the percentage of excess weight lost and muscle mass, at the end of the exercise program. The monitoring of these subjects showed that, during the same period after the surgery, the weight and the percentage of fat mass continued to increase significantly in the control group, while there were significant reductions in the percentage of excess weight lost (Marc-Hernández et al., 2020).

On the other hand, resistance training is an important potentiator of muscle strength and muscle quality. However, it does not cause a significant increase in muscle mass or changes in the cross-section of the muscle (Daniels et al., 2018). In this same study, muscle quality, which is an important factor to consider after bariatric surgery, was evaluated through magnetic resonance imaging of the right thigh, namely the cross-sectional area of the right thigh muscle, with no alterations being observed. A possible explanation for the lack of an increase in the cross-sectional area of the muscle may be an inadequate substrate availability for protein synthesis due to the severe caloric restriction induced by the surgery (Hassannejad et al., 2017).

At the end of 12 weeks of aerobic exercise after bariatric surgery, weight loss, changes in BMI, and muscle strength levels were similar both in the control and intervention groups (Castello et al., 2011). These results are similar those of Shah et al., (2011) who evaluated the effect of aerobic exercise in patients after surgery. Despite the results of muscle mass being different, there are no significant differences between the groups that practice aerobic exercise and those that do not practice exercise (Shah et al., 2006, 2011). Aerobic exercise does not have better results in terms of the musculoskeletal system and consequently does not have better results in the prevention of sarcopenia.

In a more complete and ambitious study, they were able to compare two types of training. When they added resistance to the aerobic exercise program it did not have an additional effect on weight loss. Also, the experimental groups did not have significant differences in this item but found positive effects of combined exercise on improvement in muscle mass. According to these results, sarcopenia has less incidence with the practice of combined exercises. Furthermore, muscle mass was decreased in all three groups, but the control group and aerobic exercise group lost more muscle mass and strength than the combined exercise group (Hassannejad et al., 2017).

Despite not showing significant differences in muscle mass, 12 weeks of supervised resistance training improved muscle strength in addition to providing progression in flexibility and strength of prehension, but with no significant alterations (Huck, 2015). Even in studies with a longer duration, 24 weeks, when starting just one month after the surgery, the results were similar (Noack-Segovia et al., 2019). This means that the exercise time should increase, or on the other hand, it should be maintained in the long term.

These data show that a progressive combined resistance and aerobic three times a week, at least 60 minutes, during 12 to 20 weeks of exercise, can also contribute to an increase in muscle mass directly proportional to muscle strength, which, in turn, improves physical performance and consequently decreases sarcopenia levels.

Conclusion

In this systematic review, we provide a general approach to the effectiveness of physical exercise on body composition, namely on muscle mass and strength and, consequently, on the levels of sarcopenia in bariatric surgery patients.

Aerobic exercise, or aerobic exercise combined with resistance, has been found to promote greater weight loss compared to physically inactive patients. In the postoperative period, aerobic exercise has a positive impact on reducing fat mass and on the preservative effect on muscle mass of the addition of a resistance program. On the other hand, combined exercise promotes improvement of the skeletal muscle system and consequently decreases the occurrence of postoperative sarcopenia. In the future, it is important to consider that muscle condition or function refers to the actual performance and capabilities of the muscles. This includes factors like strength, endurance, flexibility, and overall functionality. Exercise, particularly combined training, can significantly impact muscle condition by improving strength, endurance, and functional capacity.

An individualized and supervised combined exercise program in the first weeks after surgery decreases weight generates a reduction in fat mass, and a tendency to increase muscle mass. Furthermore, implementing lifestyle interventions and consultations in clinical settings after bariatric surgery is crucial for ensuring long-term success and patient well-being. Overall, the key is to ensure that these interventions are accessible, tailored to individual needs, and embedded within the overall care pathway after bariatric surgery. Engaging patients in their own care and providing continuous support can significantly enhance the chances for successful weight management and improved health outcomes

CHAPTER 3 – PROTOCOL

Article 2: Protocol methodology

Effects of physical exercise in sarcopenia on patients undergoing bariatric surgery: A protocol for a randomized clinical trial

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Abstract

Severe obesity is a chronic disease and bariatric surgery is the treatment with more proven efficacy in reducing weight. After surgery, the weight loss is greatly associated with a significant reduction of skeletal muscle and bone mineral mass, with an increased risk of sarcopenia for these patients. Prophylactic programs that prevent sarcopenia in bariatric surgery patients seems to be one of the crucial points for the long-term surgical success of bariatric and metabolic surgery. This article aims to describe a protocol using supervised exercise applied after bariatric surgery on skeletal muscle mass index, body composition and strength to determine sarcopenia in bariatric patients. A RCT will be conducted with 46 patients. Baseline measures will be compared with measures after de exercise program, in five different chronologic times. Participants will be randomly allocated to: 1) combined exercise group or 2) control group. The intervention will be 16 weeks for a combined exercise, started 1 month after surgery. The present study is

expected to generate significant information about the role of exercise in patients undergoing bariatric surgery.

Citation: Santos, C. A., Cinza, A. M., Laranjeira, Â., Amaro, M., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2023). Effects of physical exercise in sarcopenia on patients undergoing bariatric surgery: A protocol for a randomized clinical trial. MethodsX, 10, 102043. https://doi.org/10.1016/j.mex.2023.102043

Subject area: Medicine and Dentistry

More specific subject area: Assessment of skeletal muscle mass index, body composition and strength to determine sarcopenia in bariatric patients

Name of your protocol: EXPOBAR

Reagents/tools: DEXA (DXA, Hologic QDR, Hologic, Inc., Bedford, MA, USA) (Biodex®, System 3 Pro, Biodex Corp., Shirley, NY, USA) Handrip, Chair, 6 minutes' walk teste circuit

Experimental design Experimental randomized controlled trial (RCT), open-label, phase III-type study with 46 patients in HD. Protocol using supervised exercise applied after bariatric surgery on skeletal muscle mass index, body composition and strength to determine sarcopenia in bariatric patients. A RCT will be conducted with 46 patients. Baseline measures will be compared with measures after de exercise program, in five different chronologic times. Participants will be randomly allocated to exercise group or control group. The intervention will be 16 weeks for a combined exercise, started 1 month after surgery.

Trial registration: The study protocol was registered in the Clinicaltrials.gov NCT05289219 (APPENDIX 10)

Ethics: Ethics approval was obtained from the Ethics Committee for Research of University of Évora and Hospital Espírito Santo de Évora (Ref. No. 21051 and HESE_CE_1917/21, APPENDIX 11).

Value of the Protocol

- This protocol is important to evaluate the effects of supervised and structured physical exercise on possible sarcopenia induced by bariatric surgery.
- There is a lack of knowledge about the effects of combined exercise on long term after bariatric surgery

- This article is important to contribute to the recommendations of the practice of exercise after bariatric surgery.

Description of protocol

Bariatric surgery is one of the treatments for severe obesity, effective on reducing weight and diseases associated with obesity. After bariatric surgery, weight loss is greatly associated with a significant reduction of skeletal muscle and bone mineral mass, which leads us to induce that after bariatric surgery, patients incur an increased risk of sarcopenia. Prophylactic programs are need for prevent sarcopenia in bariatric surgery patients and seems to be one of the crucial points for the long-term surgical success of bariatric and metabolic surgery. The aim of this randomized clinical trial is to analyze the effects of a 16-week supervised exercise intervention program on the prevention of sarcopenia, after bariatric surgery. As a secondary purpose, it is also intended to characterize metabolic risk factors, physical fitness, and quality of life in post-bariatric surgery patients.

Study design

To evaluate the effectiveness of the intervention, a randomized clinical trial, registered as EXPOBAR, will be conducted, and the SPIRIT (Standard Protocols Items: Recommendations for Interventional Trials) recommendations will be followed.

Subjects

Participants will be selected from the list for surgical intervention in the hospital.

Inclusion and Exclusion Criteria

As inclusion criteria, patients should be enrolled for bariatric surgery at the hospital, aged between 18 and 60, with a body mass index between 35 and 50Kg/m2, men and women, without contraindication to exercise, and agree to participate in the study.

We will exclude patients with problems in locomotion, previous bariatric surgery complications, and psychiatric diseases or disorders.

Sample size calculation

The sample size was calculated by the Gpower, assuming an alpha error of 0.05 and a power of 95%; a total of 46 patients will be needed to detect an effect (between-group difference) of at least 0,7 standard deviations in the outcome risk of sarcopenia (Pekař et al., 2020). Anticipating a potential 20% loss to follow-up and based on the number of follows in our center, a total of 55 patients will be recruited and will be randomized into a Control Group (CG) and Intervention Group (IG). Exercise training will begin one month after surgery, with a frequency of three times per week, up to a maximum of 55 minutes per session.

Recruitment

The invitation to participate will be made after consultation, and participants who agree to participate in the study will be delivered the free and informed consent form (APPENDIX 12) previously approved by the University and Hospital Ethics Committee.

Randomization

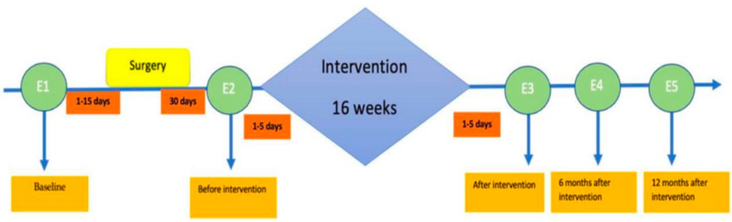
After signing the informed consent form and conducting the initial assessments, each participant will be randomly assigned to each group. All laboratory samples and data collected will be identified with an ID, safeguarding the confidentiality of the collected data.

At the end of this study, all participants of the control group will be offered the same intervention as the exercise group.

Procedures

Immediately after recruitment, all enrolled patients who agree to participate in the study will sign the informed consent form. The subjects will then proceed to the baseline data collection, intervention protocol and final assessments (figure 3.1.1).

Figure 3.1.1. Training Schedule



Weight evaluation will be done using a scale and height of a stadiometer. Based on these values, the body mass index will be calculated, and the abdominal circumference will be determined by a measuring tape.

- Metabolic risk factors will be determined by clinical analyses (blood sample) performed in the context of routine surgical evaluation, with the determination of inflammatory markers. The mean blood pressure will be evaluated by a digital sphygmomanometer. The hormonal profile will be determined through the analytical profile, as leptin and ghrelin concentrations..
- Saliva collection will be made at the moments of evaluation, for a small recipient during five minutes, which will be analyzed by the biochemistry department.
- The glycemia variation will be done through an implantable 24-hour monitoring device for 5 days.
- To evaluate body composition, the Dual-energy X-ray absorptiometry - DEXA (DXA, Hologic QDR, Hologic, Inc., Bedford, MA, USA) device will be used to measure the % fat mass, muscle mass and bone mass.
- The muscle strength of the upper limbs will be evaluated by manual pressure dynamometry (Handgrip) in both hands, with a maximum contraction of five seconds. The muscle strength of the lower limbs will be evaluated by the sit to stand test, in which participants will be instructed to stand and sit for 30 seconds, as many times as possible. The strength of lower limbs, as well as muscle fatigue, will be evaluated with an isokinetic dynamometer (Biodex®, System 3 Pro, Biodex Corp., Shirley, NY, USA) using a protocol with two series, the first of which is 3 repetitions at 60º/sec. and the second with maximo repetitions during 30 seconds at 180º/sec (Jassil, Richards, Carnemolla, Lewis, Montagut-Pino, et al., 2022).
- Cardiorespiratory fitness will be assessed using the 6-minute walk test (TC6) (Jassil, Richards, Carnemolla, Lewis, Montagut-Pino, et al., 2022).
- Sedentary Behavior and Physical Activity will be measured by accelerometer, through the feature of the application of accelerometers

(ActiGraph GT3X model, Fort Walton Beach, Florida, USA) for 5 days before the surgery and three times after the exercise program (Jassil, Richards, Carnemolla, Lewis, Montagut-Pino, et al., 2022).

- Questionnaire "Bariatric Analysis and Reporting Outcome System (BAROS) as a life quality self-report measure, validated for Portuguese, specific for bariatric surgery (A. M. Wolf et al., 2000).

Intervention description

The exercise program will cover a combination of aerobic and strength training, based on other experimental studies already developed for patients with severe obesity, but also following the Consensus on Exercise Reporting Template (CERT) (Villa-González et al., 2019).

The duration of the program is 16-weeks, 3-times a week, for up to 50 minutes per session, starting 1 month after surgery, based on the recommendations of the WHO and the ACSM, because the guidelines for patients with severe obesity undergoing bariatric surgery are not defined. Information on exercises for adults with severe obesity is limited, so the exercise programs will follow the guidelines for adults aged 18 to 65 years healthy, with chronic diseases or disabilities (Burke et al., 2021; Bushman, 2014).

In recent recommendations, those who have chronic diseases, or some type of disability should start by doing small amounts of physical activity with a gradual increase in frequency, intensity, and duration. In addition, for additional benefits should do strengthening activity involving all major muscle groups and moderate or high intensities, at least 2 days a week. As general recommendations, a combination of intensities throughout the week, 150 to 300 minutes of moderate-intensity physical activity or 75 to 150 minutes of vigorous-intensity physical activity (Petta et al., 2017).

High-intensity interval training programs typically involve short periods of high-intensity exercise followed by a short period of rest or active recovery. Interval training is a type of training, which consists of alternating between periods of moderate to high-intensity exertion and rest, with variable duration, according to the exercise performed and the objective of the person. This type of training has been shown to be more beneficial to improve abdominal fat and body weight while maintaining muscle mass., in increasing weight loss, as well as a positive effect on bone mineral density, aerobic capacity and muscle strength (Voican et al., 2018).

Exercise prescription includes the type, intensity, duration, frequency, and progression of physical activity. These five components are applicable to the development of exercise programs for persons regardless of age, functional capacity, and presence or absence of coronary heart disease risk factors. These five components of exercise prescription are reported as Frequency, Intensity, Time, and Type (FITT) with the Volume of exercise added along with the Progression component to produce the acronym FITT-VP. The training sessions (table 3.1.2) will follow an evolution subdivided by progressive phases in training (table 3.1.1). As carried out in previous studies, this strategy carried out through phases of increment of training variables allows better adaptability for this type of patients (Mechanick et al., 2013, 2020; Villa-González et al., 2019).

Each session will start with 5 minutes of warm-up and finalization with 10 minutes of a cool-down, with work of flexibility and proprioception. The maintenance of balance and postural stability may be compromised in patients with obesity, depending on the degree of obesity, although the support base provided by the position of the foot is proportional to the structural morphology of each subject. Flexibility is also gradually impaired in individuals with obesity and of course, these changes may be related to postural changes aggravated by a sedentary lifestyle and biological aging itself alongside all metabolic alterations inherent to the pathology of obesity (Scheffer & Latini, 2020).

And the warm-up and the cool-down will be developed as the component of training with the evolution by phases, both in time and in intensity. The first phase will include 20 minutes of interval training, encompassing circuit strength training. Each phase will have an increment of 10 minutes in the central block, always with a prior evaluation of the patient's response.

Table 3.1.1. Training Protocol

WEEK															
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
Phase 1 – Training resistance				Phase 2 – Training Hypertrophy						Phase 3 – Training Strength					

Evaluation

We have five evaluations, baseline (before surgery), before the program (1 month after surgery), after the program (5 months after surgery), 6 months after the program (11 months after surgery) and 12 months after the program (17 months after surgery), as show in table 3.1.2. De CG will be evaluated while the IG (figure 3.1.1).

Table 3.1.2. EXPOBAR Protocol

	Intervention Group	**Control Group**
1st Evaluation **Before Surgery**	Baseline	Baseline
2nd Evaluation **Before the Program**	1 month (post-surgery)	1 month (post-surgery)
3rd Evaluation **After the Program**	5 months (post-surgery)	5 months (post-surgery)
4th Evaluation	11 months (post-surgery) 6 months (post program)	11 months (post-surgery) 6 months (post program)
5th Evaluation	17 months (post-surgery) 12 months (post program)	17 months (post-surgery) 12 months (post program)

Discussion

EXPOBAR aims to be the first RCT in Portugal to evaluate the effects of supervised and structured physical exercise on possible sarcopenia induced by bariatric surgery. Previous studies suggest that there is a decrease in sarcopenia in the immediate period after bariatric surgery when patients have a record of physical exercise.

Interval training has proven to be the most effective in fat mass loss and in preventing muscle mass loss after bariatric surgery. Also infers an improvement in the cardiometabolic condition, with decreased risk factors.

In addition, we intend to contribute to the recommendations of the practice of exercise after bariatric surgery.

Article 3: Protocol of the randomized controlled trial

The impact of exercise on prevention of sarcopenia after bariatric surgery: The study protocol of the EXPOBAR randomized controlled trial

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Abstract

Introduction*:* Bariatric surgery is one of the treatments for severe obesity, with proven efficacy in reducing weight and diseases associated with obesity. Weight loss associated with bariatric surgery is greatly associated with a significant reduction of skeletal muscle and bone mineral mass, which leads us to induce that after bariatric surgery, patients incur an increased risk of sarcopenia. The need for prophylactic programs that prevent sarcopenia in bariatric surgery patients seems to be one of the crucial points for the long-term surgical success of bariatric and metabolic surgery. The aim of this randomized clinical trial will be to study the effects of a 16-week supervised exercise intervention program on the prevention of sarcopenia, in patients undergoing bariatric surgery. As a secondary purpose, it is also intended to characterize metabolic risk factors, physical fitness, and quality of life in post-bariatric surgery patients.

Method: A total of 45 patients on the waiting list for bariatric surgery and who have subsequently performed the surgery, will be include on EXPOBAR (*EXercise POst*

BARiatric) and randomized into 2 groups, experimental and control. The intervention starts one month after surgery, for a total of 16 weeks. Parameters of body composition, metabolic risk, quality of life, physical activity, physical fitness, and sedentary behavior will be determined. For each participant, outcomes are measured at five different time points: before the surgery, before the exercise program, after the exercise program, six and twelve months after de exercise program.

Results: This study will provide the effects of a physical exercise on sarcopenia, in patients after bariatric surgery.

Trial registration: The trial was registered at Clinicaltrials.gov NCT05289219

Keywords: exercise, bariatric surgery, fat-free mass, sarcopenia, metabolic risk factors, quality of life

Citation: Amaro Santos, C., Cinza, A. M., Laranjeira, Â., Amaro, M., Carvalho, M., Martins, S., Bravo, J., & Raimundo, A. (2022). The impact of exercise on prevention of sarcopenia after bariatric surgery: The study protocol of the EXPOBAR randomized controlled trial. *Contemporary clinical trials communications*, *31*, 101048. https://doi.org/10.1016/j.conctc.2022.101048

Introduction

The high prevalence of obesity leads to it being considered as a public health problem, with high mortality (Hämälaïnen et al., 2020). Severe obesity, categorized as a chronic disease, has associated pathological conditions, leading to other chronic diseases such as diabetes, and cardiovascular diseases, in addition to psychological disorders and social repercussions (Tavares et al., 2011).

Bariatric surgery is one of the most effective treatments for severe obesity, with proven efficacy in reducing weight and diseases associated with obesity, resulting in a short time, weight loss that can reach 60% of excess weight, as well as an improvement in comorbidities (Fried et al., 2008; Welbourn et al., 2016; Welbourn, Hopkins, et al., 2018).

Weight loss associated with bariatric surgery is greatly associated with a significant reduction of skeletal muscle and bone mineral mass, which leads to induce that after bariatric surgery, patients are at an increased risk of sarcopenia (Silva et al., 2019).

Sarcopenia is a pathological disorder characterized by generalized loss of skeletal muscle mass and function, with implications for quality of life. Sarcopenia is also associated with diabetes, metabolic syndrome, and cardiovascular diseases (Petta et al., 2017).

In fact, sarcopenia is associated whit severe obesity whit a prevalence of 2% in adults' patients in age group of 60-70 years (Cesari et al., 2009) then increases to 8% when the patients are woman (Voican et al., 2018) and to 10% in older patients (Cesari et al., 2009). Although, obesity and sarcopenia increase health risk when they co-exist (Pekař et al., 2020).

In this context, several authors suggested that reduced levels of physical activity are a predictor in the development of sarcopenia and that the combination of aerobic and strength exercises in bariatric patients can be effective, preventively and in the treatment, of sarcopenia (Minniti et al., 2022). This mechanism is important also because in the first years after bariatric surgery, de muscle mass significantly decrease and continued to drop out at two years, with a muscle mass loss represented more than 20% (Martínez et al., 2022).

The repercussions of large weight loss after bariatric surgery and the onset of sarcopenia or modification of pre-existing sarcopenia remain little documented or studied, however, the existed studies show different results. One year after surgery, the early establishment of adequate nutritional support in combination with physical activity is an important anabolic stimulus for muscle protein synthesis and prevention of muscle mass loss and the occurrence of sarcopenia (Voican et al., 2018), but two years after surgery, the loss of muscle mass may not relate to the parameters of protein metabolism or surgical technique. However, physical exercise could positively influence skeletal muscle mass in many clinical populations (*ACSM's Guidelines for Exercise Testing and Prescription*, n.d.; Mechanick et al., 2020; Villa-González et al., 2019), where we can include bariatric patients. In this point, bariatric surgery predisposes patients to sarcopenia and consequently osteoporosis, because the relationship is relevant (Bushman, 2014; Gould et al., 2014).

The guidelines recommended combined moderate-intensity exercise to maintain muscle mass. The American College of Sports Medicine (ACSM) states that from the moment the patient is surgically discharged, a program of progressive exercises for all individuals, should follow the FITT-VP principle (frequency, intensity, time, type, volume, progression) (Burke et al., 2021). Also, The American Society for Metabolic and Bariatric Surgery (ASMBS) recommends, in addition to preoperative exercises, a progressive walking program, starting on the first postoperative day, which includes aerobic exercises and strength training ≥ 30 min/day (Mechanick et al., 2020). Regarding the type of training, we have evidence that in the population with obesity, strength training and aerobic training can increase muscle strength and metabolic improvements (Herring et al., 2017).

The need for prophylactic programs that prevent sarcopenia in bariatric surgery patients is one of the crucial points for the long-term surgical success of bariatric and metabolic surgery. However, sarcopenia prevalence in the long-term after surgery remains unclear and the lack of evidence of short and long-term programs highlights the need to address their development.

Objectives

First Objectives

To analyze the effects of a 16-week supervised exercise intervention program on the prevention of sarcopenia, in patients undergoing bariatric surgery. As a secondary purpose, it is also intended to characterize metabolic risk factors, physical activity, physical fitness, and quality of life in post-bariatric surgery patients.

Secondary Objectives

1. Identify, evaluate, and synthesize evidence on the effects of physical activity and exercise on the body composition of patients undergoing bariatric surgery.
2. Synthesize evidence on the effects of physical exercise on a level of sarcopenia in patients undergoing bariatric surgery.
3. Characterize the cardiometabolic profile of patients undergoing bariatric surgery.
4. Study the validity and reliability of physical fitness tests for patients undergoing bariatric surgery.
5. Characterize inflammatory markers in obesity after bariatric surgery.
6. Understand the barriers and facilitators for physical activity practice in patients undergoing bariatric surgery.
7. Understand and characterize the hormonal profile after bariatric surgery.
8. Evaluate noninvasive biomarkers in the mechanism of obesity after bariatric surgery.

9. Understand the impact of physical exercise on the quality of life of patients undergoing bariatric surgery.

10. Evaluate the effects of the exercise program applied to patients undergoing bariatric surgery, in body composition, comorbidities, sedentary behavior, life quality, hormonal and inflammatory profile, and physical fitness.

11. Check the evaluations and changes produced before the surgery, before and after the exercise program, and 6 and 12 months after the end of the structured and monitored exercise program.

Material and methods

Study design

A randomized clinical trial, registered as EXPOBAR whit de number NCT05289219. The study will be conducted by the University and the Hospital Center for Integrated Responsibility of Bariatric Surgery and Metabolic Diseases (CRI.COM). All procedures will be management by a team member, common to the two intuitions.

Participants will be selected from the list for surgical intervention in the hospital, with criteria for performing bariatric surgery, and will be randomized into Control Group (CG) and Intervention Group (IG). Exercise training will begin one month after surgery, with a three times per week frequency, up to a maximum of 55 minutes per session (Villa-González et al., 2019). The present study protocol complies with the SPIRIT 2013 recommendations (Standard Protocol Items: Recommendations for International Trials) (Chan et al., 2013).

The invitation to participate will be made in the context of consultation and participants who agree to participate in the study will be delivered the free and informed consent form, previously approved by the University and Hospital Ethics Committee.

Sample

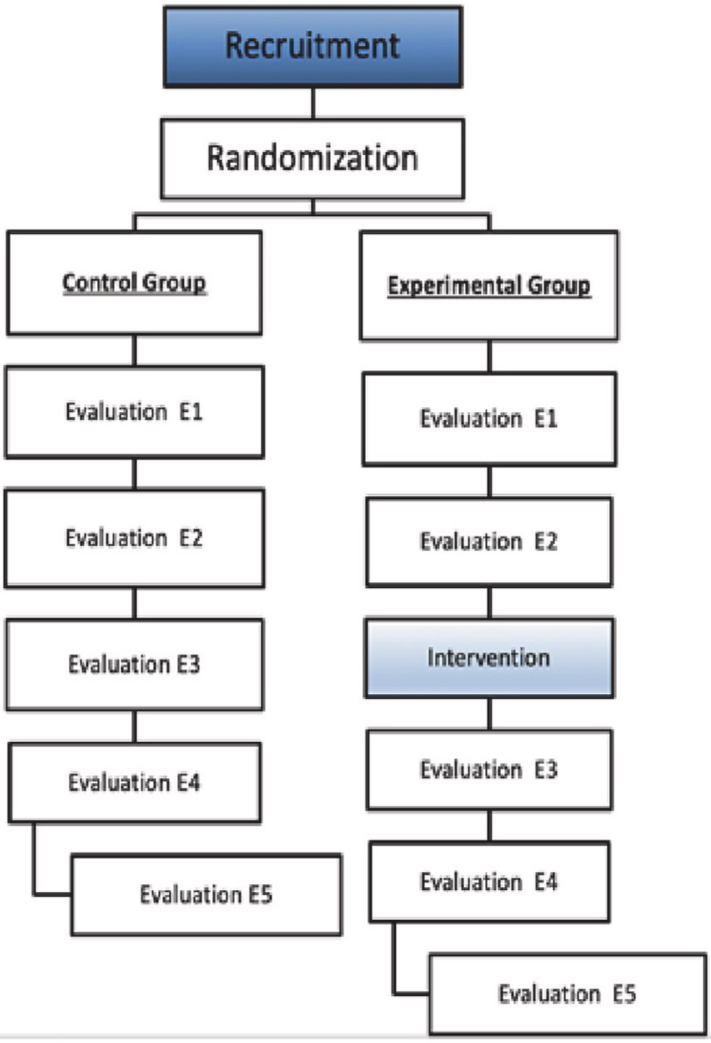
The sample size was calculated by the Gpower, assuming an alpha error of 0.05 and a power of 95%, a total of 46 patients (n = 23 patients per group) will be needed to detect an effect (between group difference) of at least 0,7 standard deviations in the outcome risk of sarcopenia (Kang, 2021). Anticipating a potential 20% lost to follow-up, and based on the number of follows in our center, a total of 55 patients will be recruited.

Randomization

Each participant will be randomly assigned to each group after signing the informed consent and conducting the initial assessments (figure 3.2.1). All laboratory samples and data collected will be identified with identification ID, safeguarding the confidentiality of the collected data.

At the end of this study, all participants of the control group will be offered the same intervention as the exercise group.

Figure 3.2.1. – Study design flow diagram



Inclusion and exclusion criteria

As inclusion criteria, patients should be enrolled for bariatric surgery at the hospital, aged between 18 years and 60 years, body mass index between 35 and 50Kg/m^2, men and woman, without contraindication to the practice of exercise and agree to participate in the study.

Will be excluded patients with problems in locomotion, with previous bariatric surgery, with bariatric surgery complications, and psychiatric diseases or disorders.

Outcomes

- Anthropometry

Weight evaluation will be done using a scale and height of a stadiometer. Based on these values, the body mass index will be calculated, and the abdominal circumference will be determined by a measuring tape.

- Metabolic risk factors

Metabolic risk factors will be determined by clinical analyses (blood sample) performed in the context of routine surgical evaluation, with the determination of inflammatory markers, like C-reactive protein, that is a relevant indicator of inflammation, likely decrease with exercise (Scheffer & Latini, 2020). The mean blood pressure will be evaluated by a digital sphygmomanometer. Through the analytical profile will be determined the hormonal profile, since leptin concentrations seem to decrease after bariatric surgery and ghrelin levels decrease after gastric sleeve and increase after gastric bypass, which assumes that the contribution of ghrelin to weight loss or metabolic benefits after bariatric surgery is not direct but influenced by several factors (Karamanakos et al., 2008).

- Harvest saliva

The study of the physiological mechanisms involved in obesity can be enriched by the evaluation of noninvasive biomarkers, such as saliva amylase. This fluid has several functions, including the perception and ingestion of food, which makes it particularly suitable for the study of obesity. In a study to assess changes in salivary amylase in women with severe obesity, to provide information on mechanisms potentially related to the development of obesity, and to evaluate whether these changes persist after weight loss, it was observed that the enzymatic activity of amylase was increased in the group not submitted to bariatric surgery and decreases in the group that performed the surgery. In this way, a saliva collection will be made at the moments of evaluation, which will be analyzed by the biochemistry department.

- Glycemia Variation

This evaluation will be done through an implantable 24-hour monitoring device for 5 days as a way of evaluating the glycemic response to exercise and food intake (Rubino et al., 2016; Schauer & Rubino, 2011; Sjöström et al., 2004).

- Physical Fitness

Body composition: To evaluate body composition, the Dual-energy X-ray absorptiometry - DEXA (DXA, Hologic QDR, Hologic, Inc., Bedford, MA, USA) device will be used to measure the % fat mass, muscle mass and bone mass (Pekař et al., 2020; Soriano-Maldonado et al., 2020).

Muscle strength: The muscle strength of the upper limbs will be evaluated by manual pressure dynamometry (Handgrip) in both hands, with a maximum contraction of five seconds. The muscle strength of the lower limbs will be evaluated by the sit to stand test, in which participants will be instructed to stand and sit for 30 seconds, as many times as possible (Soriano-Maldonado et al., 2020). The strength of lower limbs, as well as muscle fatigue, will be evaluated with an isokinetic dynamometer (Biodex®, System 3 Pro, Biodex Corp., Shirley, NY, USA) using a protocol with two series, the first of which is 3 repetitions at 60º/sec. and the second with maximo repetitions during 30 seconds at 180º/sec.

Cardiorespiratory fitness: Cardiorespiratory fitness will be assessed using the 6-minute walk test (TC6) (Soriano-Maldonado et al., 2020).

- Sedentary Behavior and Physical Activity

Accelerometer, through the feature of the application of accelerometers (ActiGraph GT3X model, Fort Walton Beach, Florida, USA) for 5 days before the surgery and after the exercise program (Jassil, Richards, Carnemolla, Lewis, Montagut-Pino, et al., 2022).

- Quality of life

Questionnaire "Bariatric Analysis and Reporting Outcome System (BAROS) as a self-report measure, validated for Portuguese, specific for bariatric surgery. This evaluation instrument was developed by the members of the NIH Consensus Conference panel in 1998 to respond to the need for a standardized method to analyze and report the results of bariatric surgery (De Queiroz et al., 2017; Soriano-Maldonado et al., 2020).

Variables

A health data questionnaire will be used to assess clinical, biochemical, and inflammatory markers, anthropometric parameters, and surgical data. Other variables to consider in this study are:

- Demographics: Gender, Age, Educational level.
- Anthropometry: weight (scale), height (stadimeter), body mass index, abdominal circumference (measuring tape).
- Body composition: DEXA (DXA, Hologic QDR, Hologic, Inc., Bedford, MA, USA)
- Clinical Data: Comorbidity and metabolic risk factors (total cholesterol, HDL, LDL, triglycerides, glucose, insulin, glycated hemoglobin, mean blood pressure, vitamin D, total proteins, PTH, iron, ferritin, hemoglobin, albumin, prealbumin, lymphocytes, alcohol intake - hepatic steatoses).
- Hormonal Profile: blood ghrelin and leptin measurement.
- Inflammatory markers: C-reactive protein glucose, insulin, and mean blood pressure.
- Saliva harvest: salivary amylase.
- Glycemia Variation: Evaluation continues through an implantable device for 5 days.
- Physical Fitness: Dynamometer, isokinetic evaluation, muscle strength performance. The muscle strength of the upper limbs will be evaluated by manual pressure dynamometry (Handgrip) and lower limbs muscle strength will be evaluated with Biodex.
- Cardiorespiratory fitness: 6-minute walk test (TC6) and sit-to-stand test for 30 seconds.
- Sedentary behavior: accelerometers for 5 days
- Quality of life: Questionary "BAROS" as a self-report measure

Intervention

The exercise program will cover a combination of aerobic and strength training, based on other experimental studies already developed for patients with severe obesity, but also following the Consensus on Exercise Reporting Template (CERT) (Soriano-Maldonado et al., 2020).

Exercise prescription includes the type, intensity, duration, frequency, and progression of physical activity. The duration of the program is 16-weeks, 3-times a week, for up to 50 minutes per session, starting 1 month after surgery, based on the recommendations of the World Health Organization (WHO) and the American College of Sports Medicine (ACSM), because the guidelines for patients with severe obesity undergoing bariatric surgery are not defined. Each session will start with 5 minutes of warm-up and finalization with 10 minutes of a cool-down, with work of flexibility and proprioception. And the warm-up and the cool-down will be developed as the component of training with the evolution by phases, both in time and in intensity. The first phase will include 20 minutes of interval training, encompassing circuit strength training. Each phase will have an increment of 10 minutes in the central block, always with a prior evaluation of the patient's response (table 3.2.1). The intensity of the exercise will be evaluated and what has been used and suggested is the Borg scale, with values in a continuous progression of the evaluation of the perceived effort of the exercise performed. And this scale allows an assessment on a scale from 0 to 20 of how rating of perceived exertion, being an evaluation of the perceived effort (Castello et al., 2011).

Two personal trainers with training in sports sciences will be responsible for the training program. Their scheduling will be considered considering the program's development. Once the study is completed, the CG will be invited to carry out the exercise program.

Table 3.2.1. - Training periodization

	F	**I**	**T**	**T**			**V**	**P**
	Frequency	Intensity	Time	Type			Volume	Progression
	Warm-up: 5min on the treadmill - 50-60% FC reserve							
Phase 1 **Week 1-4** **Resistance Training**	3x/week	- 40-59% HRR - 10-12 Borg	Time: 35/39/43 min	Strength training	3/4/5 minutes	Major muscle groups	1 set 15-20 Rep (1ª + 2ª week) 2 sets 12-15 rep (3ª + 4ª week)	Intensity Time (ITT)
				Aerobic training	7/8/9 minutes	Aerobic		
				Strength training	3/4/5 minutes	Major muscle groups		
				Aerobic training	7/8/9 minutes	Aerobic		
Phase 2 **Week 5-10** **Hypertrophy Training**	3x/week	- 60-80% HRR - 12-14 Borg	Time: 45 min	Strength training	5 minutes	Major muscle groups	2 sets 12-15 Repetitions	Intensity Time (ITT)
				Aerobic training	10 minutes	Aerobic		
				Strength training	5 minutes	Major muscle groups		
				Aerobic training	10 minutes	Aerobic		
Phase 3 **Week 11-16** **Strength Training**	3x/week	- 70-89% HRR - > 14 Borg	Time: 55 min	Strength training	8 minutes	Major muscle groups	3 sets 12-15 Repetitions	Intensity Time (ITT)
				Aerobic training	12 minutes	Aerobic		
				Strength training	8 minutes	Major muscle groups		
				Aerobic training	12 minutes	Aerobic		
	Cool-down: up to 10 min - flexibility (myofascial release, mobility, static and dynamic stretching)							

Evaluation

We have five evaluations, baseline (before surgery), before the program (1 month after surgery), after the program (5 months after surgery), 6 months after the program (11 months after surgery) and 12 months after the program (17 months after surgery), as show in figure 3.2.2 and table 3.2.2. De CG will be evaluated at the same time that the IG.

Figure 3.2.2. - Evaluation schedule

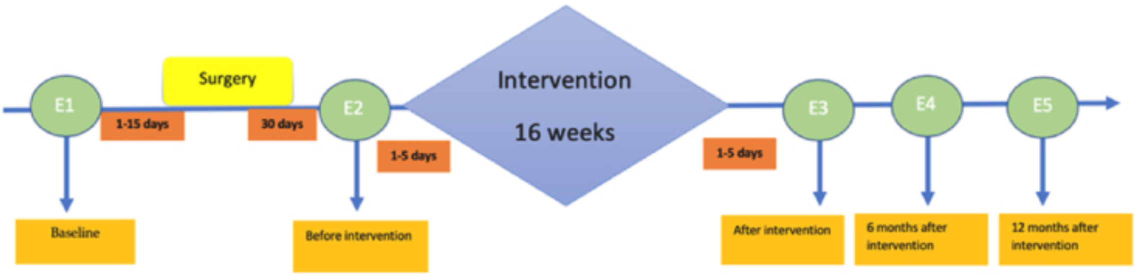


Table 3.2.2. - Evaluation schedule

	Group intervention	**Group control**
1st Evaluation **Before Surgery**	Baseline	Baseline
2nd Evaluation **Before the Program**	1 month	1 month
3rd Evaluation **After the Program**	5 months	5 months
4th Evaluation	11 months (post-surgery) 6 months (post program)	11 months (post-surgery) 6 months (post program)
5th Evaluation	17 months (post-surgery) 12 months (post program)	17 months (post-surgery) 12 months (post program)

Results

- Before surgery

- Before the intervention
- After the intervention
- Six months after the intervention
- Twelve months after the intervention

Statistical methods

Statistical software will be used to determine the parameters to be evaluated. Data normality will be assessed with the Shapiro-Wilk test and will be used an independent t-test or the chi-squared test, to examine differences between groups. To compare dependent variables, a two-way ANOVA will be used considering group (intervention group and control group) and five time points (pre and post-intervention),

Discussion

In recent recommendations, those who have chronic diseases, or some type of disability should start by doing small amounts of physical activity with a gradual increase in frequency, intensity, and duration. In addition, for additional benefits should do strengthening activity involving all major muscle groups and moderate or high intensities, at least 2 days a week. As general recommendations, a combination of intensities throughout the week, 150 to 300 minutes of moderate-intensity physical activity or 75 to 150 minutes of vigorous-intensity physical activity (Aminian et al., 2018; Burke et al., 2021).

High-intensity interval training programs typically involve short periods of high-intensity exercise followed by a short period of rest or active recovery. Interval training is a type of training, which consists of alternating between periods of moderate to high-intensity exertion and rest, with variable duration, according to the exercise performed and the objective of the person. This type of training has been shown to be more beneficial to improve abdominal fat and body weight while maintaining muscle mass., in increasing weight loss, as well as a positive effect on bone mineral density, aerobic capacity and muscle strength (Kalarchian et al., 2016).

Exercise prescription includes the type, intensity, duration, frequency, and progression of physical activity. These five components are applicable to the development of exercise programs for persons regardless of age, functional capacity, and presence or absence of coronary heart disease risk factors. These five components of exercise prescription are reported as Frequency, Intensity, Time, and Type (FITT) with the Volume of exercise added along with the Progression component to produce the acronym FITT-VP. The training sessions will follow an evolution subdivided by progressive phases in training. As carried out in previous studies, this strategy carried out through phases of increment of training variables allows better adaptability for this type of patients (Baillot et al., 2017; Jassil, Richards, Carnemolla, Lewis, Montagut-Pino, et al., 2022).

Each session will start with 5 minutes of warm-up and finalization with 10 minutes of a cool-down, with work of flexibility and proprioception. The maintenance of balance and postural stability may be compromised in patients with obesity, depending on the degree of obesity, although the support base provided by the position of the foot is proportional to the structural morphology of each subject. Flexibility is also gradually impaired in individuals with obesity and of course, these changes may be related to postural changes aggravated by a sedentary lifestyle and biological aging itself alongside all metabolic alterations inherent to the pathology of obesity.

EXPOBAR aims to be the first RCT in Portugal to evaluate the effects of supervised and structured physical exercise on possible sarcopenia induced by bariatric surgery. Previous studies suggest that there is a decrease in sarcopenia in the immediate period after bariatric surgery when patients have a record of physical exercise.

Interval training has proven to be the most effective in fat mass loss and in preventing muscle mass loss after bariatric surgery. Also infers an improvement in the cardiometabolic condition, with decreased risk factors.

In addition, we intend to contribute to the recommendations of the practice of exercise after bariatric surgery.

Article 4: Dataset

A dataset on skeletal muscle mass index, body composition and strength to determine sarcopenia in bariatric patients

Cláudia Mendes [1,2,3,4] *, Ana Margarida Cinza[1,2], Ânia Laranjeira[1,2], Margarida Amaro[1,2], Manuel Carvalho [1,2], Jorge Bravo [3,4], Sandra Martins [6,7] and Armando Raimundo [3,4]

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Abstract

Bariatric surgery is the treatment for severe obesity, with proven efficacy in reducing weight. Weight loss associated with bariatric surgery is greatly associated with a significant reduction of skeletal muscle and bone mineral mass, which leads us to induce that after bariatric surgery, patients incur an increased risk of sarcopenia. Prophylactic programs that prevent sarcopenia in bariatric surgery patients seems to be one of the crucial points for the long-term surgical success of bariatric and metabolic surgery. This article presents a initial data set of skeletal muscle mass index, body composition and strength to determine sarcopenia in bariatric patients. The data were collected in a Central Hospital and in the University. In total, is necessary to recruit 46 patients waiting for bariatric surgery, between 18 and 60 years, men, and woman, without contradiction for exercise. The patients are randomized in two groups, for exercise group and control group. The evaluation is made on five points of timeline, before the surgery, after the surgery, after de exercise program, six months, and twelve months after the exercise program.

Citation: Santos, C. A., Cinza, A. M., Laranjeira, Â., Amaro, M., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2023). A dataset on skeletal muscle mass index, body composition and strength to determine sarcopenia in bariatric patients. *Data in brief*, *46*, 108881. https://doi.org/10.1016/j.dib.2022.108881

Subject: Sport Sciences, Therapy and Medicine

Specific subject area: Assessment of skeletal muscle mass index, body composition and strength to determine sarcopenia in bariatric patients

Type of data: Table

How the data were acquired

- Anthropometry: Scale and stadiometer.
- Body composition: Dual-energy X-ray absorptiometry - DEXA (DXA, Hologic QDR Hologic USA)
- Muscle strength: Manual pressure dynamometry (Handgrip) for upper limbs. The muscle strength of the lower limbs will be evaluated by the sit to stand test. The strength of lower limbs, as well as muscle fatigue, will be evaluated with an isokinetic dynamometer (Biodex®, System 3 Pro USA)
- Cardiorespiratory fitness: the 6-minute walk test (TC6)
- Sedentary Behavior and Physical Activity: Accelerometer (ActiGraph GT3X model, Fort Walton Beach, Florida, USA) for 5 days before the surgery and after the exercise program

Data format: Raw**;** Analyzed**;** Filtered

Description of data collection

All patients are enrolled for bariatric surgery at the hospital, aged between 18 years and 60 years, body mass index between 35 and 50Kg/m^2, men and woman, without contraindication to the practice of exercise and agree to participate in the study. Exclude patients with problems in locomotion, with previous bariatric surgery, with bariatric surgery complications and, psychiatric diseases or disorders.

Data source location

- Institution: CHRC - Comprehensive Health Research Centre (Évora University)
- City/Town/Region: Évora
- Country: Portugal

Data accessibility: Tables are available with this article. The dataset is available through the following data repository.

Repository name: Mendeley Data

Data identification number: 10.17632/hmscsnprv3.1

Direct URL to data: https://data.mendeley.com/datasets/hmscsnprv3/3

Value of the data

- The data of this article are important observing functional performance, strength, power and body composition assessments, where there is a need to choose tests with similar reliability in bariatric patients.
- EXPOBAR aims to be the first RCT in Portugal to evaluate the effects of supervised and structured physical exercise on possible sarcopenia induced by bariatric surgery.
- Population-specific data of physical performance for interval training has proven to be the most effective in fat mass loss and in preventing muscle mass loss after bariatric surgery.
- Contribute to the recommendations of the practice of exercise after bariatric surgery.

Objective

To analyze the effects of a 16-week supervised exercise intervention program on the prevention of sarcopenia, in patients undergoing bariatric surgery. As a secondary purpose, it is also intended to identify, evaluate, and synthesize evidence on the effects of physical activity and exercise on the body composition of patients undergoing bariatric surgery

Data description

The present data focus on test of functional fitness and strength, power, and body composition assessments in bariatric patients. The data set comprises various parameters relevant to assess related changes in skeletal muscle mass. Those parameters have been suggested by the European Working Group in Sarcopenia for Older People (EWGSOP) (Cruz-Jentoft et al., 2010) in its initial and revised consensus statements to be used for the diagnosis and treatment of sarcopenia (Donini et al., 2022; Galata et al., 2020). Age group and sex-specific baseline characteristics of the participants including anthropometric data are provided Table 3.3.1. Table 3.3.2 show test reliability of various functional performance tests included in the senior fitness test manual, such as the 30-s chair stand test or sit-to-stand test and the six-minutes walking test (6MWT), and test reliability of laboratory-based assessments of isokinetic peak torque as well as handgrip results. Finally, Table 3.3.3 summarizes test reliability of parameters derived from DEXA analyses such as body fat percentage, muscle mass, skeletal muscle indexand bone mass.

Table 3.3.1. Anthropometric measures changes between baseline, before and after exercise program

	Evaluation 1			Evaluation 2			Evaluation 3		
	Control Group	**Intervention Group**	**p-value**	**Control Group**	**Intervention Group**	**p-value**	**Control Group**	**Intervention Group**	**p-value**
Participants [number (%)]	4 (50%)	4 (50%)		4 (50%)	4 (50%)		4 (50%)	4 (50%)	
Weight [kg]	93 ± 4,7	113,9 ± 6,4	**0,002**	83,6 ± 3,9	99 ± 2,7	**<0,001**	62,4 ± 0,5	79,3 ± 4,4	**<0,001**
BMI [kg/m²]	39,9 ± 1,4	40,7 ± 2,9	0,632	35,8 ± 1,6	35,4 ± 33,1	0,827	26,8 ± 1,6	28,4 ± 3,2	0,389
Waist [cm]	112 ± 8,7	119,5 ± 9,1	0,278	101,3 ± 10,2	104,8 ± 11,8	0,669	84 ± 10	90,3 ± 11,84	0,451

Table 3.3.2. Physical fitness measures changes between baseline, before and after exercise program

	Evaluation 1			Evaluation 2			Evaluation 3		
	Control Group	**Intervention Group**	**p-value**	**Control Group**	**Intervention Group**	**p-value**	**Control Group**	**Intervention Group**	**p-value**
30-s chair stand [rep]	13 ± 3,37	16 ± 4,24	0,310	15,3 ± 3,95	16 ± 2,94	0,771	14,8 ± 3,86	20,3 ± 4,35	0,107
6-min walk test [m]	402,4 ± 103,7	492,5 ± 94,3	0,246	390 ± 67,45	437,5 ± 118,2	0,511	362,5 ± 85,4	626,3 ± 199	0,051
Peak torque extension, 60°/s [Nm]	94,4 ± 14,9	155 ± 50,1	0,083	87,5 ± 11,30	134 ± 43,3	0,107	66 ± 3,39	133 ± 41,2	**0,018**
Peak torque flexion, 60°/s [Nm]	46,6 ± 9,98	78,8 ± 23,9	**0,047**	43,4 ± 10,32	70,6 ± 24,4	0,086	34,6 ± 7,03	79,8 ± 21,2	**0,007**
Work fatigue extension, 180°/s [Nm]	33,3 ± 22,9	30,1 ± 16,3	0,829	47,4 ± 2,1	42,4 ± 14,47	0,524	-1,8 ± 38,5	44,6 ± 7,2	0,055
Work fatigue flexion, 180°/s [Nm]	26,3 ± 18,9	35,7 ± 16,5	0,482	41,9 ± 10,2	46,5 ± 17,6	0,664	-45,1 ±140,9	48,5 ± 7,3	0,233
Handgrip strength – right [kg]	24,2 ± 2,5	37,1 ± 6,9	**0,013**	22,3 ± 2,2	37,8 ± 8,43	**0,012**	22,3 ± 1,3	37,7 ± 7,1	**0,005**
Handgrip strength – left [kg]	23,3 ± 2,37	34,4 ± 6,83	**0,022**	21,3 ± 2,6	33,5 ± 11,35	0,081	20,7 ± 3,2	32,4 ± 8,0	**0,034**

BMI – body mass index

Table 3.3.3. Body composition measures changes between baseline, before and after exercise program

	Evaluation 1			Evaluation 2			Evaluation 3		
	Control Group	**Intervention Group**	**p-value**	**Control Group**	**Intervention Group**	**p-value**	**Control Group**	**Intervention Group**	**p-value**
Body mass [kg]	48 ± 4,1	60,7 ± 10,6	0,066	41,6 ± 2,6	51,6 ± 10,8	0,121	38 ± 8	51,7 ± 11,5	0,097
Body fat [%]	45,2 ± 3,7	45,2 ± 7	0,990	45,1 ± 3,2	44,1 ± 10,4	0,860	32,8 ± 9,3	32,3 ± 12,1	0,942
Skeletal muscle mass [Kg]	50,1 ± 4,5	63,3 ± 11,0	0,069	43,8 ± 2,9	54,2 ± 11,3	0,124	42,7 ± 3,5	21,6 ± 2,6	0,113
Skeletal muscle index [kg/m²]	20,5 ± 0,7	21,6 ± 2,6	0,479	17,8 ± 0,9	18,3 ± 3	0,765	16,2 ± 2,8	18,3 ± 2,9	0,339
Bone mineral density [g/cm^2]	1,2 ± 0,2	1,1 ± 0,1	0,507	1,2 ± 0,1	1,6 ± 0,1	0,795	1,2 ± 0,1	0,5 ± 1,3	0,353

Methods

This is a randomized controlled trial registered in clinicaltrials.gov NCT05289219.

Outcomes

Anthropometry: Weight evaluation will be done using a scale and height of a stadiometer. Based on these values, the body mass index will be calculated, and the abdominal circumference will be determined by a measuring tape (Pekař et al., 2020).

Body composition: To evaluate body composition, the Dual-energy X-ray absorptiometry - DEXA (DXA, Hologic QDR, Hologic, Inc., Bedford, MA, USA) device will be used to measure the % fat mass, muscle mass and bone mass.

Muscle strength: The muscle strength of the upper limbs will be evaluated by manual pressure dynamometry (Handgrip) (In et al., 2021) in both hands, with a maximum contraction of five seconds. The muscle strength of the lower limbs will be evaluated by the sit to stand test, in which participants will be instructed to stand and sit for 30 seconds, as many times as possible. The strength of lower limbs, as well as muscle fatigue, will be evaluated with an isokinetic dynamometer (Biodex®, System 3 Pro, Biodex Corp., Shirley, NY, USA) using a protocol with two series, the first of which is 3 repetitions at 60º/sec. and the second with maximo repetitions during 30 seconds at 180º/sec (Soriano-Maldonado et al., 2020).

Cardiorespiratory fitness: Cardiorespiratory fitness will be assessed using the 6-minute walk test (TC6) (Herring et al., 2017).

Sedentary Behavior and Physical Activity: Accelerometer, through the feature of the application of accelerometers (ActiGraph GT3X model, Fort Walton Beach, Florida, USA) for 5 days before the surgery and after the exercise program (Jassil, Richards, Carnemolla, Lewis, Montagut-Pino, et al., 2022).

Intervention

The exercise program will cover a combination of aerobic and strength training, based on other experimental studies already developed with patients with obesity, but also following the Consensus on Exercise Reporting Template (CERT) (Villa-González et al., 2019).

Exercise prescription includes the type, intensity, duration, frequency, and progression of physical activity. The duration of the program is 16-weeks, 3-times a week, for up to 50 minutes per session, starting 1 month after surgery, based on the recommendations of the The World Health Organization (WHO) and the American College of Sports Medicine (ACSM) (Burke et al., 2021), because the guidelines for patients with obesity undergoing bariatric surgery are not defined. Each session will start with 5 minutes of warm-up and finalization with 10 minutes of a cool-down, with work of flexibility and proprioception. And the warm-up and the cool-down will be developed as the component of training with the evolution by phases, both in time and in intensity. The first phase will include 20 minutes of interval training, encompassing circuit strength training. Each phase will have an increment of 10 minutes in the central block, always with a prior evaluation of the patient’s response. The intensity of the exercise will be evaluated and what has been used and suggested is the Borg scale, with values in a continuous progression of the evaluation of the perceived effort of the exercise performed. And this scale allows an assessment on a scale from 0 to 20 of how rating of perceived exertion, being an evaluation of the perceived effort (Castello et al., 2011).

Those responsible for the training program will be two personal training with training in sports sciences, whose scheduling will be carried out considering the development of the program. Once de study is completed, the CG will be invited to carry out the exercise program.

Evaluation

We have five evaluations, baseline (before surgery), before the program (1 month after surgery), after the program (5 months after surgery), 6 months after the program (11 months after surgery) and 12 months after the program (17 months after surgery). De CG will be evaluated while the IG.

Results

1. Before surgery
2. Before the intervention
3. After the intervention
4. Six months after the intervention
5. Twelve months after the intervention

Statistical methods

Statistical software will be used to determine the parameters to be evaluated. Data normality will be assessed with the Shapiro-Wilk test and will be used an independent t-test or the chi-squared test, to examine differences between groups. To compare dependent variables, a two-way ANOVA will be used considering group (intervention group and control group) and five time points (pre- and post-intervention).

CHAPTER 4 – EXPERIMENTAL STUDY´S

Article 5 – Experimental Trial - **Impact of bariatric surgery on sarcopenia related parameters and diagnosis – Preliminary results of EXPOBAR RCT – uncontrolled before and after study**

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Abstract

Introduction: Obesity affects over 650 million individuals worldwide and it is a major public health problem. Bariatric surgery is the most effective treatment for severe obesity, resulting in significant weight reduction and improvement in obesity-related conditions. However, the weight loss achieved through bariatric surgery often correlates with a notable decrease in skeletal muscle. This correlation suggests an elevated risk of sarcopenia among patients after surgery. The aim of this study was to evaluate the effects of obesity and bariatric surgery on sarcopenia-related indicators and diagnosis before and after surgery.

Methods: A total of 17 bariatric surgery patients were included in this prospective study. The parameters to diagnose sarcopenia were determined for each participant, based on EWGSOP2 and EASO/ESPEN consensuses. All evaluations were performed on the five moments of this study: before surgery and at 1, 6, 12 and 18 months after surgery.

Results: In this study, 88.2% of the subjects were female, the mean BMI was 42.9 kg/m² and the mean weight was 105.9 kg. After surgery, the mean weight consistently decreased, with all differences from baseline being statistically significant ($p<0.001$). When using the SARC-F questionnaire for screening, the risk of sarcopenia increased post-surgery, and decreased at 12 months, declining to zero at 18 months. Muscle strength decreased significantly ($p=0.002$) at the 1 month after surgery assessment, with slight variations thereafter, none statistically significant. Muscle mass was normal before surgery but decreased significantly post-surgery ($p<0.001$). When applying the ESPEN/EASO consensus cut-off criteria for sarcopenic obesity, 35.3% of the patients met the criteria preoperatively. After surgery, the results increased to 70.6% in the first month but decreased afterward to 41.2% at 6 months.

Discussion: This study evaluated the impact of bariatric surgery on sarcopenia and sarcopenic obesity, for a duration of up to 18 months after surgery, using the EWGSOP2 and ESPEN/EASO consensuses criteria. Bariatric surgery, the most effective treatment for severe obesity, often results in muscle mass loss alongside fat loss. Handgrip strength, a key sarcopenia indicator, showed a significant early post-surgery decline, whereas the weight-dependent sit-to-stand test did not. This suggests weight loss impacts different muscle function tests variably. Muscle mass decreased continuously after surgery. However, other indicators had mixed results. Applying ESPEN/EASO guidelines, the study found a temporary post-surgery increase in sarcopenic obesity, peaking at one month and returning to pre-surgery levels by six months. However, different criteria led to different results.

Conclusion: The results indicate a clear deleterious impact of bariatric surgery on muscle strength and mass, the most important indicators of sarcopenia. Also, the impact occurs very early after surgery, indicating that the appropriate timeframe to try to prevent this effect may be the prehabilitation period followed by the post-surgery timeframe.

Keywords: bariatric surgery; fat-free mass; sarcopenia; sarcopenic obesity; skeletal muscle mass; muscle mass

Citation: Mendes, C., Carvalho, M., Bravo, J., Martins, S., & Raimundo, A. (2024). Impact of Bariatric Surgery on Sarcopenia Related Parameters and Diagnosis—The Preliminary Results of EXPOBAR Study. Healthcare. https://doi.org/10.20944/preprints202407.1018.v1

Introduction

Obesity is a multifactorial disease and a significant public health issue as it is closely linked to higher mortality rates and numerous comorbidities (Engin, 2017; Sardinha et al., 2012). Bariatric surgery has emerged as the most treatment for severe obesity and is known for its ability to reduce weight and associated diseases (Andolfi & Fisichella, 2018). Surgical management has the highest evidence-based approach to achieve sustained weight loss and improve associated medical conditions. However, it is important to note that bariatric surgery-induced weight loss can also lead to a significant decrease in skeletal muscle mass, eventually increasing the risk of sarcopenia (Matos et al., 2020).

Sarcopenia is a clinical condition characterized by a significant loss of muscle mass and strength, that is generally studied in older adults patients (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019; Ruthes et al., 2022). However, it also appears to be present in patients with obesity, conditioned not by age but by metabolic, physical and lifestyle changes (Donini et al., 2022). Muscle tissue plays a critical role in overall health, and its loss is linked to various adverse outcomes. Recognizing the importance of sarcopenia, several international study groups have recently published consensuses on its definition and diagnosis (Batsis et al., 2014).

As suggested in the European Working Group on Sarcopenia in Older People (EWGSOP2), sarcopenia is a muscle disease that may occur at any age. Sarcopenia is common in older age but may also occur earlier in life (Cruz-Jentoft et al., 2010). The group identified the need to update its initial definition and the new EWGSOP2 consensus focuses on low muscle strength as a key for diagnosing sarcopenia, as well as muscle quantity and quality to confirm the diagnosis (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019). The EWGSOP2 introduces a novel algorithm for identifying sarcopenia. Unlike the traditional method, which relies on a diminished skeletal muscle mass (SMM) alongside a decreased walking speed or muscle strength decline, this algorithm adopts the Find-Assess-Confirm-Severity (F-A-C-S) approach. Muscle strength is evaluated after screening yields positive results or clinical suspicion arises. If muscle weakness is detected, sarcopenia is suspected, and muscle mass is addressed. SMM, appendicular skeletal muscle mass (ASMM), and index

(ASMMI) are assessed, and any observed decrease confirms the presence of sarcopenia. Furthermore, severe sarcopenia is identified by a decline in physical performance, such as gait speed (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, & Zamboni, 2019; Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019; Ramirez et al., 2022).

In this context, sarcopenia may have a complex relationship with obesity. Despite the importance of understanding the consequences of substantial weight loss after bariatric surgery and the development of sarcopenia, there is limited documentation and research on this topic. Existing studies also present varying results, emphasizing the need for further investigation.

To answer these limitations, the European Association for the Study of Obesity (EASO) and the European Society for Clinical Nutrition and Metabolism (ESPEN) developed a consensus for evaluating sarcopenia in patients with obesity. This document is similar to the EWGSOP2 but introduces also obesity diagnosis tools, like weight, BMI and waist circumference.

Sarcopenic obesity is a complex clinical condition that presents a unique challenge due to the combination of obesity and sarcopenia. As a result, individuals with sarcopenic obesity face a higher risk for metabolic diseases, functional impairment, and other adverse clinical outcomes compared to those with either condition alone (Donini et al., 2022; Tsigos et al., 2011). However, if eating disorders and excess fat mass can have negative consequences on muscle mass and its function, on the other hand, patients with obesity may have needed to develop previously more muscle mass to be able to carry out their activities of daily living, such as simply walking (Martínez et al., 2022), further confounding the interpretation of the post-surgical data.

Moreover, screening and diagnostic procedures for sarcopenic obesity need to be practical, affordable, and time-efficient, with a focus on assessing altered skeletal muscle functional parameters and body composition. Staging of sarcopenic obesity based on the presence of complications related to altered body composition and muscle function may be essential for guiding treatment and follow-up (Batsis et al., 2014; Donini et al., 2022; Prado et al., 2008).

Studies evaluating sarcopenia after bariatric surgery are limited and consider mainly compromised muscle mass. In this study, we prospectively evaluated the impact of bariatric surgery on sarcopenia-related parameters over 18 months after surgery in patients undergoing the procedure. Specifically, the study aims to assess changes in muscle strength, muscle mass, and the prevalence of sarcopenic obesity at various time points before and after surgery. We hypothesize that while bariatric surgery will result in significant weight loss, it will also lead to a concomitant reduction in muscle mass and strength, thereby increasing the risk of sarcopenia shortly after surgery. Additionally, we aim to determine whether these changes persist or diminish over an 18-month follow-up period. The significance of this study lies in its potential to inform clinical practice and improve the management of patients undergoing bariatric surgery, possibly influencing guidelines and recommendations for post-bariatric surgery monitoring and rehabilitation programs.

Methods

Study Design

This prospective study of patients undergoing bariatric surgery was conducted at a single surgical center: the Center for Integrated Responsibility for Bariatric Surgery and Metabolic Diseases (CRI.COM) at a Portuguese Hospital (ULSAC). The entire protocol has been previously described (Amaro Santos et al., 2023).

The invitation to participate was made in the context of an outpatient appointment, and participants who agreed to participate in the study were delivered the free and informed consent form previously approved by the University and Hospital Ethics Committee (HESE_CE_1917/21).

As inclusion criteria, patients should be enrolled for bariatric surgery at the hospital, both men and women, aged between 18 and 65, with a Body Mass Index (BMI) of more than 35 kg/m^2, with medical-associated morbidities, who agree to participate in the study. Patients with previous bariatric surgery were excluded. Participants were recruited during outpatient appointments, where the study was explained, and they were invited to participate. Screening included a detailed medical history and physical examination to ensure eligibility. All patients underwent bariatric and metabolic surgery between December 2021 and December 2022.

During the study period, all patients were followed using standard follow-up by bariatric surgeons, nutritionists, psychologists and nurses.

Perioperative management

The multidisciplinary team evaluated and performed the surgery in all patients according to a standard protocol. The surgical procedure was a Roux-en-Y Gastric Bypass (RYGB). After surgery, the participants received similar support from the different team specialists, with standard follow-up appointments and consultations.

Outcomes Definition and Data Collection

According to the study plan, all parameters were evaluated at the five moments before surgery and at 1, 6, 12, and 18 months after surgery.

Weight evaluation was measured using a scale. The patients were without shoes or heavy clothing. Height was determined by a manual stadiometer. BMI was calculated ($weight/height^2$), and the abdominal circumference was determined by a measuring tape (Devonshire-Gill, 2018; Norton, 2018). To evaluate body composition, the Dual-energy X-ray absorptiometry - DEXA (DXA, Hologic QDR, Hologic, Inc., Bedford, MA, USA) was used (Pekař et al., 2020).

For screening, both the EWGSOP2 and the ESPEN/EASO consensuses recommend the use of the SARC-F questionnaire (FIND) in clinical practice (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, & Zamboni, 2019; Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019; Ramirez et al., 2022).

The SARC-F is a self-reported questionnaire with five questions: Strength (S), Assistance walking (A), Rising from a chair (R), Climbing stairs (C), and Falls (F). Each answer is rated on a scale of 0 to 2, ranging from "not at all" to "very difficult." A total score is calculated out of 10. The recommended cutoff value for positive screening for sarcopenia is ≥4 points (Malmstrom & Morley, 2013; “SARC-F; Screening Tool for Sarcopenia,” 2019; Woo et al., 2014).

All participants completed the SARC-F scale at the five moments.

In both documents, the first diagnostic criteria (ASSESS) for sarcopenia are low muscle strength. In our study, muscle strength was determined by two tests: the handgrip strength test and the five-times-to-stand test.

The handgrip strength test was conducted using manual pressure dynamometry for measuring grip strength (Jamar®) to evaluate muscle strength of the upper limbs.

Participants were instructed to stand with their elbows fully relaxed and straight. Each hand was tested twice, and the maximum grip strength value obtained was recorded as the muscle strength test value (Cooper et al., 2022; Roberts et al., 2011). The dynamometer was calibrated before each testing session to ensure accuracy, and all tests were administered by trained personnel to minimize inter-rater variability.

The sit-to-stand test evaluated the muscle strength of the lower limbs, in which participants were instructed to stand and sit for 30 seconds as many times as possible (25). The timed chair stand test is a variation that counts how many times a patient can rise and sit on the chair over a 30-second interval (Beaudart et al., 2016; Cesari et al., 2009). Because the chair stand test evaluates both strength and endurance, it offers a reliable yet practical measure of strength.

The cut-off used for handgrip strength was set <27 kg for males and <16 kg for females (Dodds et al., 2014) and >15s for five rises on the chair rise test (5-times sit-to-stand) (Cesari et al., 2009).

Confirmation of sarcopenia (*CONFIRM*) based on muscle quantity or mass can be reported by appendicular skeletal muscle mass (ASMM) using dual-energy X-ray absorptiometry-DEXA. DEXA has been chosen because it is a common method for measuring skeletal muscle mass (Ramirez et al., 2022). SMM refers to the amount of muscle that is attached to the skeleton and helps in systemic movement and posture maintenance, whereas ASMM is the sum of muscle mass of the four limbs (Studenski et al., 2014).

To estimate ASMMI, it was used the sum of the muscle mass of the upper and lower extremities (muscle mass of arms [kg] + muscle mass of legs [kg]) dividing for height squared (m^2) (ASMMI= ASMM/height^2) (Gould et al., 2014). The ASMMI value has been used to assess sarcopenia in different populations, but there is still an ongoing debate about the preferred parameter to represent muscle mass (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019). As suggested by ESPEN/EASO consensus, in the present study we also considered the values of ASMM/weight for male (cut-off < 28.27%) and female patients (cut-off <23.47%) were considerate (Donini et al., 2022).

The severity (SEVERITY) of sarcopenia using the 400-m walk test to assess walking ability and endurance and the staging level by the presence of at least one complication attributable to sarcopenic obesity. Participants were asked to complete 20 laps of 20 meters each as fast as possible and were allowed up to two rest stops during the test (Baroudi et al., 2020; Vestergaard et al., 2009). Low physical performance was considered when the test was not completed or when it took more than 6 minutes to complete (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019).

Algorithm to diagnose Sarcopenia and Sarcopenic Obesity - F-A-C-S

According to EWGSOP2, sarcopenia diagnosis is based on low muscle strength combined with decreased muscle mass (male grip strength < 27 kg, ASMM < 20 kg, ASMMI < 7.0 kg/m^2; female grip strength < 16 kg, ASMM < 15 kg, ASMMI < 5.7 kg/m^2,) (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019). Sarcopenia is considered severe when low physical performance is identified (400m walk test ≥ 6min) (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019). For Sarcopenic Obesity (ESPEN/EASO) all previous cut-off values were considered, adding the ESPEN/EASO consensus parameters BMI (BMI > 30 kg/m^2), waist circumference (WC) (WC ≥ 102 cm for male and ≥ 88 cm for Female) and ASMM/weight (ASMM/Weight < 28.27% for Male and < 23.47% for Female) (Donini et al., 2022).

Statistical methods

Statistical software was performed with the SPSS version 27.0 (IBM SPSS Inc., Chicago, IL, USA) to determine the parameters and outcomes. Categorical variables are expressed as frequencies and percentages, and continuous variables are expressed as mean and standard deviation. Data normality was assessed using the Shapiro-Wilk test. For group comparisons, we employed independent t-tests for normally distributed continuous variables and Mann-Whitney U tests for non-normally distributed variables. Repeated measures ANOVA was used to evaluate changes over time within the same group, with post-hoc tests conducted using Bonferroni correction to adjust for multiple comparisons.

For categorical variables, Chi-square tests were used to compare proportions between groups, with Fisher's exact test applied when expected frequencies were low. Statistically significant results were considered for p-values ≤ 0.05.

Results

Weight

A total of 17 participants (88.2% female) were enrolled in this study with a mean age of 46.9 (± 11.4) years, a mean BMI of 42.9 (± 5.14) kg/m^2, a mean weight of 105.9 (± 17.5) kg and a mean waist circumference of 123 (± 12) cm (Table 4.1.1).

Table 4.1.1. Baseline characteristics of participants.

Variables (*Mean ± SE)	Total (n=17)
Age (years)	50 ± 11.0
Sex (female/male) %	88.2/11.8
Body weight (kg)	106 ± 17.5
BMI (kg/m^2)	42.6 ± 5.00
Waist circumference (cm)	123 ± 12.0
Handgrip (Kg)	20.4 ± 6.44
Sit-to-stand test (s)	12.6 ± 3.55
Fat mass (Kg)	46.3 ± 15.11
Body fat (%)	47.1 ± 3.90
Lean mass (Kg)	53.46 ± 10.48
ASMM (Kg)	21.92 ± 5.13
ASMM/Weight (%)	20.6 ± 2.36
ASMMI (Kg/m^2)	8.79 ± 1.57
ASMM/BMI	0.514 ± 0.096
400-m walk test (min)	7.61 ± 2.81

BMI: Body Mass Index, SMM: Skeletal Muscle Mass, ASMM: Appendicular Skeletal Muscle Mass, ASMMI: Appendicular Skeletal Muscle Mass Index.

After surgery and throughout the study period, the mean weight decreased and was always significantly lower than the baseline, namely 91.8Kg at 1-month post-surgery ($p<0.001$), 75.4Kg at 6 months ($p<0.001$), 69.9Kg at 12 months ($p<0.001$) and 70.8Kg at 18 months ($p<0.001$). The comparison between the weight observed at each assessment point and the preoperative weight (baseline) was always statistically significant.

When the several assessment moments were compared sequentially, the differences between the baseline weight and the weight at 1 month, the weight at 1 month and the weight at 6 months, and the difference between 6 and 12 months all showed a decrease with statistical significance (p<0.001). On the other hand, between 12 months and 18 months, weight remained practically stable, with no statistically significant difference (Table 4.1.2). BMI and waist circumference assessments showed similar evolutions.

Table 4.1.2. Comparative analysis of sarcopenia algorithm parameters before surgery and 1,6,12 and 18 months after surgery.

	Before Surgery	**After Surgery**										
	Baseline - E0	***1month - E1***		***6month - E2***			***12month - E3***			***18month - E4***		
Variables (*Mean ± SE)			***E1*E0 p-value***		*E2*E0 p-value*	*E2*E1 p-value*		*E3*E0 p-value*	*E3*E2 p-value*		*E4*E0 p-value*	*E4*E3 p-value*
Anthropometry												
Body weight (kg)	105.9 ± 17.5	91.8 ± 14.7	**< 0.001**	75.4 ± 14.70	**< 0.001**	**< 0.001**	69.9± 12.1	**< 0.001**	**< 0.001**	70.8 ± 12	**< 0.001**	0.438
Total weight loss (%)	NA	NA	NA	13.1 ± 4.32	NA	NA	29 ± 4.58	NA	**<0.009**	32.5 ± 9.76	NA	0.251
BMI (kg/m²)	42.6 ± 5	37 ± 4.53	**< 0.001**	30.2 ± 4.17	**< 0.001**	**< 0.001**	28.2 ± 4.34	**< 0.001**	**0.008**	28.7 ± 4.93	**< 0.001**	0.313
Waist circumference (cm)	123 ± 12	110 ± 11.4	**< 0.001**	97.2 ± 12.8	**< 0.001**	**< 0.001**	94.2 ± 12.2	**< 0.001**	**0.016**	93.6 ± 11	**< 0.001**	0.575
Physical function and strength												
Handgrip (Kg)	20.4 ± 6.44	18.1 ± 6.44	**0.002**	16.8 ± 5.25	**0.002**	0.358	17.7 ± 5.11	**0,016**	0.257	17.3 ± 5.44	**0.005**	0.479
Sit-to-stand (STS) (n)	12.6 ± 3.55	12.8 ± 3.33	0.415	13.2 ± 2.88	0.105	0.120	13.1 ± 2.45	0.073	0.956	12.8 ± 2.70	0.259	0.157
Body composition												
Fat mass (Kg)	46.34 ± 15.1	44.47 ± 9.97	**0.003**	37.42 ± 7.92	**0.003**	**< 0.001**	34.19± 6.99	**0.002**	**< 0.001**	30.45 ± 11.6	**< 0.001**	0.098
Body fat (%)	47.1 ± 3.90	45.5 ± 4.99	**0.023**	40.6 ± 7.26	**< 0.001**	**< 0.001**	37.4 ± 6.34	**< 0.001**	**< 0.001**	37 ± 7.71	**< 0.001**	0.711
Lean mass (Kg)	53.45 ± 10.48	48.01 ± 9.47	**< 0.001**	44.65 ± 9.54	**< 0.001**	**< 0.001**	39.98 ± 5.08	**< 0.001**	**< 0.001**	37.14 ± 4.6	**< 0.001**	**< 0.001**
ASMM (Kg)	21.92 ± 5.13	19.72 ± 4.79	**< 0.001**	17.53 ± 4.11	**< 0.001**	**< 0.001**	15.90 ± 4.06	**< 0.001**	**< 0.001**	14.40 ± 4.32	**< 0.001**	**< 0.001**
ASMMI (Kg/m²)	8.79 ± 1.57	7.91 ± 1.48	**< 0.001**	7.03 ± 1.22	**< 0.001**	**< 0.001**	6.39 ± 1.28	**< 0.001**	**< 0.001**	5.79 ± 1.45	**< 0.001**	**< 0.001**
ASMM/Weight (Kg/kg)	20.6 ± 2.36	21.4 ± 2.18	**0.039**	23.3 ± 3.13	**< 0.001**	**< 0.001**	21.1 ± 3.12	0.328	**< 0.001**	20.5 ± 5.65	0.517	0.538
ASMM/BMI	0.514 ± 0.10	0.535 ± 0.12	**0.034**	0.580 ± 0.11	**< 0.001**	**< 0.001**	0.496 ± 0.19	**0.003**	0.515	0.570 ± 0.14	0.535	**0.002**
Physical performance												
400-m walk test (min)	7.61 ± 2.81	8.79 ± 3.40	**0.016**	8.74 ± 3.05	**0.005**	0.890	9.58 ± 3.58	**< 0.001**	**0.019**	10.1 ± 4.12	**< 0.001**	0.134

BMI: Body Mass Index, SMM: Skeletal Muscle Mass, ASMM: Appendicular Skeletal Muscle Mass, ASMMI: Appendicular Skeletal Muscle Mass Index, 400-m: 400 meters.

Screening

The application of the SARC-F questionnaire before and after surgery showed an increase in the SARC-F result between the preoperative and postoperative assessments.

This increase may reflect an increase in the risk of developing sarcopenia during the peri-operative period and may be a result of the surgical intervention.

Applying the EWGSOP2 sarcopenia screening criteria (SARC-F), 70.6% of patients had a positive screening at the preoperative assessment. During the post-operative period the number of positive screenings was 88.2%, 70.6%, 58.8% and 0% at 1 month, 6, 12 and 18 months respectively. Only the result at 18 months showed a statistically significant difference compared to baseline (Table 4.1.3).

Table 4.1.3. Algorithm to Diagnose Sarcopenia – EWGSOP2

F-A-C-S	Before Surgery	After Surgery			
	Baseline - E0	*1month - E1*	*6month - E2*	*12month - E3*	*24month - E4*
***FIND CASES -** Screening* **SARC-F**	70.6%	88.2%	70.6%	58.8%	**0%***
***ASSESS -** Skeletal muscle strength* **HANDGRIP**	35.3%	**70.6%***	**64.7%***	52.9%	52.9%
***CONFIRM -** Skeletal muscle quantity* **ASMMI**	0%	0%	**11.8%***	**29.4%***	**52.9%***
DIAGNOSIS - assess^confirm	0%	0%	**11.8%***	**29.4%***	**52.9%***
***SEVERITY -** Physical Performance* **400-m WALK TEST**	58.8%	70.6%	76.5%	**82.4%***	**94.1%***

*McNemar test; p-value<0,050 significant result relative to E0.

ASMMI: Appendicular Skeletal Muscle Mass Index.

Using the ESPEN/EASO screening criteria for sarcopenic obesity (assessed using also BMI, waist circumference and the SARC-F questionnaire), the result was positive at the preoperative assessment in 70.6% of patients. This percentage was 88.2% in the first month after surgery, but the difference was not statistically significant. After the first month, the screening was considered positive in a decreasing percentage of patients (35.3% at 6 and 12 months and 0% at 18 months) and these differences were considered significant (Table 4.1.4).

Table 4.1.4. Algorithm to Diagnose Sarcopenia – EASO and ESPEN

DIAGNOSE PROCEDURES	Before Surgery	After Surgery			
	Baseline – E0	*1month - E1*	*6month - E2*	*12month - E3*	*24month - E4*

SCREENING ***1.*** High BMI	100%	100%	35.3%	35.3%	41.2%
SCREENING ***2.*** High Waist circumference	100%	100%	82.4%	58.8%	58.8%
SCREENING ***3.*** SARC-F	70.6%	88.2%	70.6%	58.8%	0%
SCREENING ***1^2^3***	70.6%	88.2%	**35.3%***	**35.3%***	**0%***
DIAGNOSIS ***1.*** Altered skeletal muscle functional - Handgrip	35.3%	**70.6%***	**64.7%***	52.9%	52.9%
DIAGNOSIS ***2.*** Altered body composition - ASMM/Weight	94.1%	88.2%	70.6%	88.2%	94.1%
DIAGNOSIS ***1^2***	35.3%	**70.6%***	41.2%	52.9%	52.9%
STAGING – *STAGE I: No complications*	0	0	0	0	0
STAGING – *STAGE II: Whit complications*	100%	100%	100%	100%	100%

*McNemar test; p-value<0,050 significant result relative to E0.

ASMMI: Appendicular Skeletal Muscle Mass Index.

Muscle strength

The handgrip assessments at 1 month, 6 months, 12 months and 18 months were 18.1 Kg, 16.8 Kg, 17.7 Kg and 17.3 Kg respectively. All these results were lower than the handgrip assessed before surgery (20.4 kg), showing a statistically significant difference. When comparing handgrip strength between consecutive assessment times, there was a reduction between the baseline value and the 1st post-operative month (20.4Kg *versus* 17.8Kg) with a statistically significant difference. Subsequent comparisons, between the first month and six months (17.8Kg *versus* 16.8Kg), between six months and 12 months (16.8Kg *versus* 17.7Kg) and between 12 months and 18 months (17.7Kg *versus* 17.3Kg), showed only slight variations without statistical significance.

The Sit-to-stand test showed results at 1 month, 6 months, 12 months and 18 months of 12.8 (n), 13.2 (n), 13.1 (n) and 12.8 (n) respectively. None of these evaluation moments showed a statistically significant difference when compared to the preoperative (baseline) value of 12.6.

The cut-offs to classify as normal or abnormal the results of the handgrip strength by the EWGSOP2 and the ESPEN/EASO consensus are the same. When we use these criteria were used for the handgrip test evolution before and after surgery, 35.3% of the patients already met the criterion for compromised muscle strength before surgery. At 1-month post-surgery, 70.6% met the criterion and at 6 months 64.7%. These differences with the baseline were statistically significant. At 12 and 18 months, 52.9% of patients were positive, and these differences from baseline were not significant.

Muscle mass

The ASMM parameter showed decreasing post-operative results: 19.72kg, 17.53kg, 15.90kg and 14.40kg, respectively. The difference when compared with the preoperative baseline result (21.92kg) was always statistically significant ($p<0.001$). The sequential comparison between assessment moments throughout the postoperative period, between the 1st month and 6 months (19.73Kg *versus* 17.53Kg), between 6 and 12 months (17.53Kg *versus* 15.90Kg) and between 12 and 18 months (15.90Kg *versus* 14.40Kg) always showed a statistically significant decrease.

The ASMMI (Kg/m^2) also showed a constant decrease from the baseline result (8.79) to 7.91, 7.03, 6.39 and 5.79 respectively at one month, 6, 12 and 18 months after surgery. All differences were statistically significant ($p<0.001$).

ASSM/weight (Kg/Kg) increased significantly between the preoperative assessment (20.6%) and the assessments carried out at 1 month ($p=0.039$) and 6 months ($p<0.001$) after surgery (21.4% and 23.3%). On the other hand, the assessments carried out at 12 and 18 months (21.1% and 20.5%) showed no significant difference when compared to the baseline assessment. In terms of progress, there was a significant difference between the preoperative assessment and the first month (20.6% versus 21.4%) and between the first month and six months (21.4% versus 23.3%). Between six and 12 months there was also a significant difference, but in the opposite direction (23.3 Kg/Kg versus 21.1%). There was no difference between 12 and 18 months (21.1% versus 20.5%).

Applying the EWGSOP2 suggested cut-off for ASSMI (Kg/m^2), all patients had a normal index at baseline and one month after surgery. After that evaluation, 11.8%, 29.4% and 52.9% of patients had an abnormal index at 6, 12 and 18 months respectively, and this difference was statistically significant.

When the ESPEN/EASO recommended cut-off for ASMM/weight (Kg/Kg) was applied at the different evaluation moments, we found out that 94.1% of patients had already an abnormal result at baseline. This number was 88.2%, 70.6%, 88.2% and 94.1% at one month, 6, 12 and 18 months respectively.

Severity

The results of the 400-m walk test showed an increase in test time in all assessments 8.79min, 8.74min, 9.58min and 10.1min respectively at the first month, 6 months, 12 months and 18 months, when compared to the baseline value (7.61min).

Over time, there was a significant increase ($p=0.016$) in the test value between the preoperative assessment and the first month (7.61min *versus* 8.79min) and stability between the first month and six months (8.79min *versus* 8.74min). Again, a significant difference between six and twelve months ($p=0.019$) (8.74min *versus* 9.58min) and stable between 12 and 18 months (9.58min *versus* 10.1min).

Sarcopenia diagnosis

Applying the two cumulative EWGSOP2 criteria for diagnosing sarcopenia (criteria 1: reduced strength assessed by handgrip test and criteria 2 reduced muscle mass measured by decreased ASMM/height^2) and its proposed cut-offs, allow to be found that at baseline 35% of the patients had probable sarcopenia but no patients met both criteria for achieving a diagnosis. At one month after surgery the result was the same. Beyond that moment, 11.8%, 29.4% and 52.9% of the patients met both criteria to attain a diagnosis of sarcopenia.

When we applied the two ESPEN/EASO cut-offs for diagnosing sarcopenia associated with obesity, both of muscle function (handgrip) and body composition (ASSM/weight), in a cumulative way, led to a result of 35.3% of patients already with sarcopenia at baseline. After surgery, the patients that met the same criteria for sarcopenia were 70.6%, 41.2%, 52.9% and 52.9% at 1 month, 6, 12 and 18 months respectively. This increase, when compared to the baseline, was only statistically significant up to 6 months ($p<0.05$).

Discussion

This study provides valuable insights into the impact of bariatric surgery on sarcopenia and sarcopenic obesity over an 18-month period, utilizing EWGSOP2 and ESPEN/EASO consensus criteria. The findings indicate significant weight loss post-surgery, accompanied by reductions in muscle mass and strength, particularly evident in the early post-operative period. Notably, handgrip strength declined significantly one month after surgery, while other muscle function tests, such as the sit-to-stand test, did not show significant deterioration. The prevalence of sarcopenic obesity increased immediately post-surgery, peaking at one month and returning to pre-surgery levels by six months.

Bariatric surgery is currently the most effective type of treatment for moderate and severe obesity. On the other hand, the weight loss caused by bariatric surgery represents not only fat mass loss but is often accompanied by muscle mass loss. Addressing this subject is not an easy task due to the different muscle function and body composition study methods and the absence of a clear consensus on the preferred tools and cut-offs to be used to establish a diagnosis of sarcopenic obesity. Also, different surgical procedures and other variables may impact on muscle mass and function differently.

In this study, were used the assessment tools recommended by both the EWGSOP2 group and the EASO/ESPEN consensus, including muscle function and mass assessments, with a focus on the handgrip test as a surrogate for muscle function and ASMM, ASMM/weight, ASMMI and ASMM/height^2 to represent muscle mass. This data allowed to evaluate the patients according to the algorithms proposed by both those consensuses. The decision to perform multiple assessments, before and after surgery to better elucidate this complex relationship between weight, adiposity, muscle mass, and muscle function after bariatric surgery.

Considering the specific bariatric surgery results on weight management, there was, as expected, a reduction in the patient´s median weight, BMI, and waist circumference up to the first year of follow-up, with no relevant change at 18 months. Besides reducing weight and adiposity, the eventual loss of muscle mass and muscle function is a concern in bariatric surgery. This effect may be an undesired side-effect of surgery.

Screening

Using the cut-offs for positive results, screening for sarcopenic obesity was already positive in most patients before surgery. When we apply the EWGSOP2 criteria were used, the number of patients at risk for this condition decreases only 18 months after surgery, but when the ESPEN/EASO criteria was applied, the decrease is already present 6 months after surgery. This result shows that patients who are candidates for bariatric surgery already have a significant risk for sarcopenic obesity before surgery and that bariatric surgery may take some time to decrease that risk as evaluated by the screening tool.

Muscle strength

Muscle strength, one of the key aspects of sarcopenia, was assessed by different tests, but with a special focus on handgrip strength. This test is recommended both by the EWGSOP2 (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019) and the ESPEN/EASO consensus (Donini et al., 2022). Previously, the FNIH recommendations also stated that grip strength was the preferred method to assess muscle strength (using a cut-off of 26 Kg for males and 16 Kg for females) (Studenski et al., 2014).

The sit-to-stand test did not show identical results. There was no difference when the results before or after surgery were compared, or even during follow-up. It is interesting to note that the test in which muscle strength is analyzed without interference from the patient's weight, the handgrip, was the test that showed a clear and significant change, while the test that is dependent on weight did not. It can be argued that, in the specific context of patients with obesity who have undergone surgery and whose weight has decreased significantly between each two assessments, this reduction in weight could have interfered with the results of the 5-times sit-to-stand test since decreasing body weight also decreases the muscular effort assessed in this test. On the other hand, weight loss is not expected to interfere with the handgrip muscle strength test, so the best test to show sarcopenia in this context is the handgrip.

The impact of bariatric surgery on the handgrip test has been debated. A recent meta-analysis by Jung et al. (Jung et al., 2023)concerning muscle strength after bariatric surgery could not show a muscle strength loss when all the data was pooled. Nevertheless, the aggregated number of subjects was not very large (n=301), and the authors stated that their analysis had several limitations, namely that the studies were heterogeneous and represented only specific populations. Also, the timing of the assessments after surgery was heterogeneous with most studies being performed only after 6 months of the surgical procedure. In none of those studies' strength was assessed one month after surgery as in the current study. Other variables that are probably relevant are gender and the surgical procedure chosen for each patient because these factors may also impact weight and muscle loss.

Nevertheless, even if the global pooled data did not indicate, some of the included studies in the meta-analysis showed a clear absolute decrease in muscle strength decrease.

Alba et al., showed a significant decrease from preoperative values (p= 0.001). The mean 12-month change in absolute strength showed a decline of 2.6 kg, with all the decline occurring in the first 6 postoperative months. Oppert et al., also showed a 21 Kg muscle strength decrease (Bellicha et al., 2021), and Cole et al., showed a 2.8 Kg decline (Cole et al., 2017). It is worth mentioning that these three studies were the only ones included in the meta-analysis where the only surgical procedure used was the RYGB.

Stegen et al., in 2010, already showed a 7% or 18% reduction in handgrip strength in RYGP patients (Stegen et al., 2011). Another study, not included in the meta-analysis, by Crispim Carvalho et al., where the great majority of patients were RYGP patients (16/21), also showed a significant decrease in handgrip strength at one-year follow-up (Crispim Carvalho et al., 2023). Another study published in 2019 also showed a reduction from 34.18 Kg to 31.91Kg in handgrip strength 6 months after surgery (Noack-Segovia et al., 2019), even though it is unclear what surgical procedure was performed.

In the present study, contrary to the overall result of the meta-analysis, the handgrip test did show a clear decrease in strength as early as one month after surgery, with no further changes or deterioration afterwards and up to 18 months.

If we look closely into the data of the meta-analysis by Jung et al., (Jung et al., 2023), only three papers included, like in this study, exclusively RYGP patients. These three papers (Alba et al., 2019; Battista et al., 2021; Cole et al., 2017; Oppert et al., 2018) all showed the same result: a decrease in handgrip strength, that was also found by other papers (Crispim Carvalho et al., 2023; Noack-Segovia et al., 2019; Stegen et al., 2011) also in RYGP patients showed the same results as ours.

Gender also seems to be a factor in muscle strength loss. Jung et al. performed a sub-group analysis of the pooled data in their meta-analysis based on the percentage of men below or above 30%. They concluded that in the studies where over 70% of women were present, handgrip strength was reduced by 1.5 Kg. This is in accordance with the current results, where 80% of the patients were women, and we found a reduction in muscle strength was.

The results show that the decline in muscle function in RYGP patients after surgery is clear. It also appears very early in the postoperative period, at the one-month evaluation. It can be speculated that the first assessments performed in other studies, after 6 months, may not capture this early effect.

The relationship between post-bariatric surgery status and the strength assessed by the handgrip test is not yet clear. The differences in results of several studies may result from different patient selection and methodology. Attention must be given to the type of surgical procedure, gender, and the time elicited after surgery.

Muscle mass

Muscle mass loss is one of the critical components of sarcopenia and of sarcopenic obesity. Bariatric surgery causes significant weight loss. This is dependent mainly on fat mass loss, but muscle mass loss is also present. In this setting, muscle mass loss can be present before surgery and be caused or aggravated by surgery, resulting in a new onset sarcopenic obesity or worsening of a previous condition.

Nujten et al. performed a meta-analysis studying lean body mass, skeletal muscle mass, and fat-free mass losses after bariatric surgery. They concluded that there is a clear loss of muscle mass – 8.13Kg LBM - one year after surgery (Nuijten et al., 2022). They also studied the impact of different procedures and found that the gastric band had a lesser impact, but the other procedures (RYGP, Sleeve, BPD) all had similar outcomes.

Han Na Jung et al. performed a Systematic Review and Meta-analysis of muscle strength and muscle mass after bariatric surgery. They found a decrease in lean mass in all studies except for two. The pooled data showed a reduction of 7.4 Kg in this parameter. Rodrigues studied Skeletal muscle mass in three groups of bariatric patients, divided according to BMI levels. In all groups, there was a loss of SMM between 5.8 and 6.8 Kg one year after surgery (Rodrigues et al., 2024).

There is debate about which parameter should be used to define sarcopenic obesity. In this study, ASMM, ASMMI and ASMM/weight over 18 months were studied. These parameters were chosen because they are recommended by the EWGSOP2 consensus (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, & Zamboni, 2019; Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019) or by the ESPEN/EASO consensus (Donini et al., 2022). Another option would have been to assess ALM/BMI, previously proposed by the FNIH Sarcopenia Project (Studenski et al., 2014).

In the current study, the loss of muscle mass was somewhat more profound than in other investigations. This decrease was in line with the decrease in total body weight. Nevertheless, ASMM/weight, a parameter less dependent on weight and recommended by ESPEN/EASO guidelines as a representation of muscle mass in bariatric patients, did not show any decrease.

Other authors found similar results. Alba et al., observed a decline of 14% in lean mass and of 16% on ALM 12 months after surgery (Alba et al., 2019). Pekar et al. (Pekař et al., 2020) found a decrease in ALMI from 9.7 to 7.7 Kg/m^2 18 months after surgery. Vassilev et al., found a decrease in lean body mass from 63.38 to 58.87 Kg 24 weeks after surgery. With MRI, those authors observed a decrease in skeletal muscle index from 52.65 to 42.48 cm^2/m^2 in the same time span (Vassilev et al., 2022). Using BIA, Martinez el al., found a decrease in fat-free mass from 66.47 Kg to 55.48 Kg 24 months after surgery.

Severity

The test used to determine severity, the 400-m walk, showed contradictory results in patients of the present study. However, we must remember that this context corresponds to bariatric surgery patients. In this treatment, there is a significant weight loss between the time of the preoperative assessment and the time of the postoperative assessment. This marked weight loss achieved with bariatric surgery could compromise the reliability of the 400m-walk physical performance test since performance in this test will depend not only on the quantity and quality of skeletal muscle but also on the physical effort required for walking. This effort in these patients after surgery may be facilitated due to the weight loss achieved.

Sarcopenia diagnosis

The consensus from EWGSOP2 and ESPEN/EASO aim to define Sarcopenia and Sarcopenic Obesity (Donini et al., 2022). They advance a set of tests that can be chosen to determine the presence of this condition and suggest cut-offs to get a clear diagnosis. This will be essential to facilitate research on the predisposing factors, consequences, prevention and treatment of this condition.

However, presently few studies have yet been published using both these consensuses as it was made in the present research, where handgrip strength was used to assess muscle function and ASMM, ASMMI and ASMM/weight for body composition. As cut-offs, were chosen 27 kg for males and 16 kg for females for handgrip strength; < 7.0 kg/m^2 for males and < 5.7 kg/m^2 for females for ASMMI; and 28.27% for males, and 23.47% for females for ASMM/weight.

According to these results, one-third of the patients already presented sarcopenic obesity before surgery when the complete ESPEN/EASO criteria was used but the result was 0% when the EWGSOP2 criteria was applied.

After surgery, there were clear differences in the results of the function and muscle mass tests over time. However, when applying the cut-offs for the diagnosis pathway only one month after surgery, there was also a clear difference in diagnosis when using the different consensuses. In fact, using EWGSOP2, the percentage of patients that met diagnostic criteria increased from 6 months onwards, affecting half the patients 18 months after surgery. However, when the ESPEN/EASO criteria were used, the percentage of patients classified as sarcopenic obesity increased one month after surgery (from 35.3% to 70.6%) when one-third of the patients develop new-onset. Afterwards, from 6 to 18 months, this percentage was not different from baseline.

Future research should focus on larger, multicenter studies to confirm these findings and examine the long-term effects of bariatric surgery on sarcopenia and sarcopenic obesity. Investigating the efficacy of targeted interventions, such as resistance training programs and nutritional support, in preventing muscle loss post-surgery is also essential. Moreover, studies exploring the underlying mechanisms of muscle loss and recovery in bariatric patients will help develop more effective strategies for maintaining muscle health. Understanding the role of different bariatric procedures and patient characteristics in influencing these outcomes will further refine post-operative care protocols.

One limitation of this study is its small sample size of 17 patients, which may affect the generalizability and statistical power of the findings. The limited sample size might have restricted our ability to detect smaller yet clinically significant differences. Additionally, most participants were female, which may not fully represent the broader bariatric surgery population. Future studies with larger, more diverse samples are needed to validate these findings and explore potential gender differences in the impact of bariatric surgery on muscle mass and strength. Despite these limitations, our study provides important preliminary insights into the changes in muscle function and mass post-surgery.

Conclusion

A short-term consequence of obesity surgery, specifically in the post-operative period, may be an increase in sarcopenia. This is shown by a clear decrease in muscle function when assessed by the handgrip test. On the other hand, this effect does not appear in tests whose performance is influenced by the patient's weight: the 5-times sit-to-stand

and the 400m walk tests results did not suffer any deterioration. One possible interpretation is that, in these tests, the effects of the reduction in muscle mass and strength are masked by the reduction in the degree of physical demand of these three tests caused by the reduction in body weight resulting from the surgery.

Also, muscle quantity, as measured by ASMM or ASMMI, decreased continuously after surgery. However, when ASMM is adjusted by weight or BMI the results are equivocal. This could probably be a result of a lack of a clear understanding of the relative influence of surgery and of weight loss itself on muscle mass.

When both muscle strength and muscle mass criteria and cut-offs are used in a cumulative way, and according to both consensuses, antagonistic results were observed. This may be a consequence of the present lack of a clear-cut definition of sarcopenia, despite the different studies, reviews and other papers that have been published on this subject. Nevertheless, the present results seem to indicate a significant deleterious impact of bariatric surgery on muscle strength and mass, the most important indicators of sarcopenia. This is very clear in the handgrip test, ASMM and ASSMI. Considering the relevance of muscle strength and muscle mass for health and well-being, it could be considered that these indicators should be preferred for sarcopenic obesity diagnosis. Also, the impact seems to occur very early after surgery, which may indicate that the appropriate timeframe to try to prevent this effect may be the prehabilitation period followed by the post-surgery timeframe.

Article 6 – Randomized Controlled Trial - **Effect of a 16-week Combined Supervised Exercise Program after Bariatric Surgery on Sarcopenia Parameters Based on FNIH, EWGSOP2, and EASO/ESPEN Criteria – The results of the EXPOBAR randomized trial program**

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Abstract

Introduction: Bariatric surgery is a recognized treatment option for severe obesity, and its effectiveness in reducing weight and controlling obesity-related conditions has been demonstrated. However, it can also lead to decreased skeletal muscle mass and strength, increasing the risk of sarcopenia after surgery. This randomized clinical trial studied the effects of a 16-week supervised combined exercise program on sarcopenia in bariatric surgery patients.

Methods: Thirty-seven surgery candidates participated in the EXPOBAR (EXercise POst BARiatric) program and were randomized into experimental or control groups. The intervention lasted 16 weeks, starting one month after surgery, and included a supervised combined aerobic and resistance exercise intervention. The outcomes, including body composition and physical fitness parameters, were assessed at four time points. All participants underwent gastric bypass surgery (RYGB).

Results: The EXPOBAR trial revealed significant and meaningful effects of the exercise intervention on anthropometric indices, such as weight ($p=0.039$) and waist circumference ($p=0.010$). The EXPOBAR trial also showed that after bariatric surgery, there was a clear decrease in muscle mass, and this loss continued through the duration of follow-up, despite the exercise protocol. The most substantial improvements were observed in physical function and strength metrics ($p=0.005$ and $p<0.001$, respectively), along with a reduction in fat mass ($p=0.006$), indicating the intervention's effectiveness in enhancing both physical fitness and body composition.

Discussion: Current findings indicate that following an initial decrease due to bariatric surgery, a combined exercise intervention significantly improves functional physical capacity and strength. The exercise program in this study effectively reversed the surgery-induced loss in function and strength, reducing the number of patients at risk of sarcopenia. Physical and functional capacity are crucial noninvasive indicators for diagnosing muscle quality and sarcopenia.

Conclusion: Long-term management of sarcopenia and sarcopenic obesity in bariatric surgery patients requires frequent monitoring of body composition and muscle function. This approach is essential for tracking progress and optimizing treatment strategies over time. This study highlights the importance of integrating structured exercise programs into after bariatric surgery care to mitigate the risk of sarcopenia. Future options include nutritional protein supplementation and changes in the exercise protocol.

Trial registration: The trial was registered at Clinicaltrials.gov (NCT05289219).

Keywords: exercise, bariatric surgery, fat-free mass, sarcopenia, skeletal muscle mass

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Introduction

Obesity is a significant public health issue because it is closely linked to increased mortality and morbidity rates. It is a chronic illness and is related to other chronic conditions, such as metabolic syndrome, diabetes, cardiovascular disease, psychological disorders and social problems (Tan et al., 2022).

Surgical treatment is considered the most effective management tool for morbid obesity and is known for its ability to induce substantial weight loss (60% or more excess weight) and improve associated obesity complications. However, the weight loss achieved after bariatric surgery is not only due to fat reduction but also due to a significant loss of lean tissue, accounting for up to 25% of the overall body mass reduction (Batsis et al., 2014; Donini et al., 2022; Tsigos et al., 2011). This reduction in lean tissue mass, especially muscle mass, poses a challenge because it can decrease both resting and activity-related energy expenditure.

Healing after major surgical procedures can cause a significant increase in the body's need for protein. However, in the initial months following bariatric surgery, there is typically a significant decrease in food intake. This can result in temporary protein deficiency, especially after surgical interventions, which can affect the body's ability to absorb nutrients. This deficiency usually resolves once the patient's metabolism adjusts to the changes caused by surgery and food intake become sufficient and consistent according to needs (Blume et al., 2012; Kessler et al., 2020; Mechanick et al., 2013).

The muscle requires energy to function properly, so a decrease in muscle mass can decrease both resting and activity-related energy expenditure. As a result, patients who have obesity and sarcopenia before surgery are less likely to lose weight and are more prone to regain weight than are those who have a healthy skeletal muscle system (Wei et al., 2023). After surgery, the combination of muscle tissue loss, temporary protein deficiency and surgical trauma can contribute to or worsen preexisting conditions of sarcopenia (Shrestha et al., 2022).

Furthermore, if muscle weakness occurs or worsens after surgery, weight loss may slow or stop altogether, increasing the likelihood of obesity relapse. Additionally, sarcopenia increases the risk of metabolic complications and can ultimately compromise life expectancy, even if weight loss is achieved (Minniti et al., 2022).

For bariatric patients with severe obesity, muscle weakness can give rise to notable clinical complications following surgery. Preoperative sarcopenia has been shown to be a reliable indicator of complications and mortality during major abdominal surgery. Additionally, older individuals face an increased risk of cardiovascular events in the perioperative period. It is worth noting that the age of patients seeking metabolic/bariatric surgery may increase, leading to a greater number of individuals older than 60 years undergoing the procedure, which is when sarcopenia becomes a clinically significant issue (C. Liu et al., 2023). Therefore, it is crucial to carefully consider the occurrence of complications in patients with obesity with sarcopenia who undergo significant surgical bariatric procedures (Xu et al., 2019).

The prevalence of sarcopenia in patients with obesity ranges from 10 to 50%, with wide variation likely the result of the absence of a standardized clinical approach to evaluate sarcopenia in both qualitative and quantitative terms.

The European Working Group on Sarcopenia in Older People (EWGSOP) established a structured approach to identify, evaluate, and address issues related to sarcopenia in 2010. In 2019, they published a consensus based on the presence of low lean mass and low muscle strength, the EWGSOP2. This document uses the Find-Assess-Confirm-Severity (F-A-C-S) algorithm, which is utilized in various fields, including medicine, psychology and risk management, among others (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, & Zamboni, 2019; Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019).

Furthermore, in 2014, the Foundation of the National Institutes of Health (FNIH) published a standardized diagnostic approach with the Sarcopenia Project, which suggested adjusting the criteria to account for differences in body mass index (BMI) (Studenski et al., 2014).

More recently, in 2022, the EASO and ESPEN recommended introducing weight adjustment, particularly for individuals with obesity who are at risk of developing sarcopenia (Donini et al., 2022), considering that sarcopenia and muscle mass loss are significant concerns for individuals undergoing bariatric surgery.

BMI is a crucial criterion for selecting patients for obesity surgery and an indicator used to assess an individual's body composition and overall health status (EP Williams, 2015). When defining sarcopenia parameters after bariatric surgery, BMI plays a significant role and reflects changes in body composition, particularly muscle mass and fat mass, which can impact a person's health following surgery. BMI is a widely used metric for assessing obesity and has also been suggested to be a valuable tool for defining sarcopenic obesity in this population (Beaudart et al., 2016).

Given that few studies have assessed sarcopenia and sarcopenic obesity after bariatric surgery, additional experimental studies are needed so that clear criteria can be defined regarding useful tools and procedures to prevent and treat sarcopenic obesity after bariatric surgery.

Several guidelines suggest a combination of moderate-intensity exercise to maintain muscle mass. The American College of Sports Medicine (ACSM) recommends a progressive exercise program for all individuals following the FITT-VP principle, which includes frequency, intensity, time, type, volume, and progression (*ACSM's Guidelines for Exercise Testing and Prescription*, n.d.; Bushman, 2014). Similarly, the American Society for Metabolic and Bariatric Surgery (ASMBS) advocates starting a progressive walking program on the first day after surgery, incorporating aerobic exercises and strength training for at least 30 minutes daily (*2022 ASMBS and IFSO: Indications for Metabolic and Bariatric Surgery | American Society for Metabolic and Bariatric Surgery*, n.d.; Aminian et al., 2018).

Regular and targeted exercise programs are fundamental for managing sarcopenia and sarcopenic obesity. Resistance training has been proven effective at promoting muscle strength, enhancing function and improving body composition by reducing excess adiposity (Burke et al., 2021; Huck, 2015; Oppert et al., 2018).

Both strength training and aerobic training have been shown to improve strength and metabolism in patients with obesity. However, the long-term incidence of sarcopenia after surgery remains unclear, underscoring the need for research on both short-term and long-term exercise programs.

Objectives

The main objective was to analyze the long-term effects of a 16-week supervised combined exercise program on sarcopenia incidence, sarcopenic obesity, and sarcopenia parameters in patients undergoing RYGP.

Methods

Study design

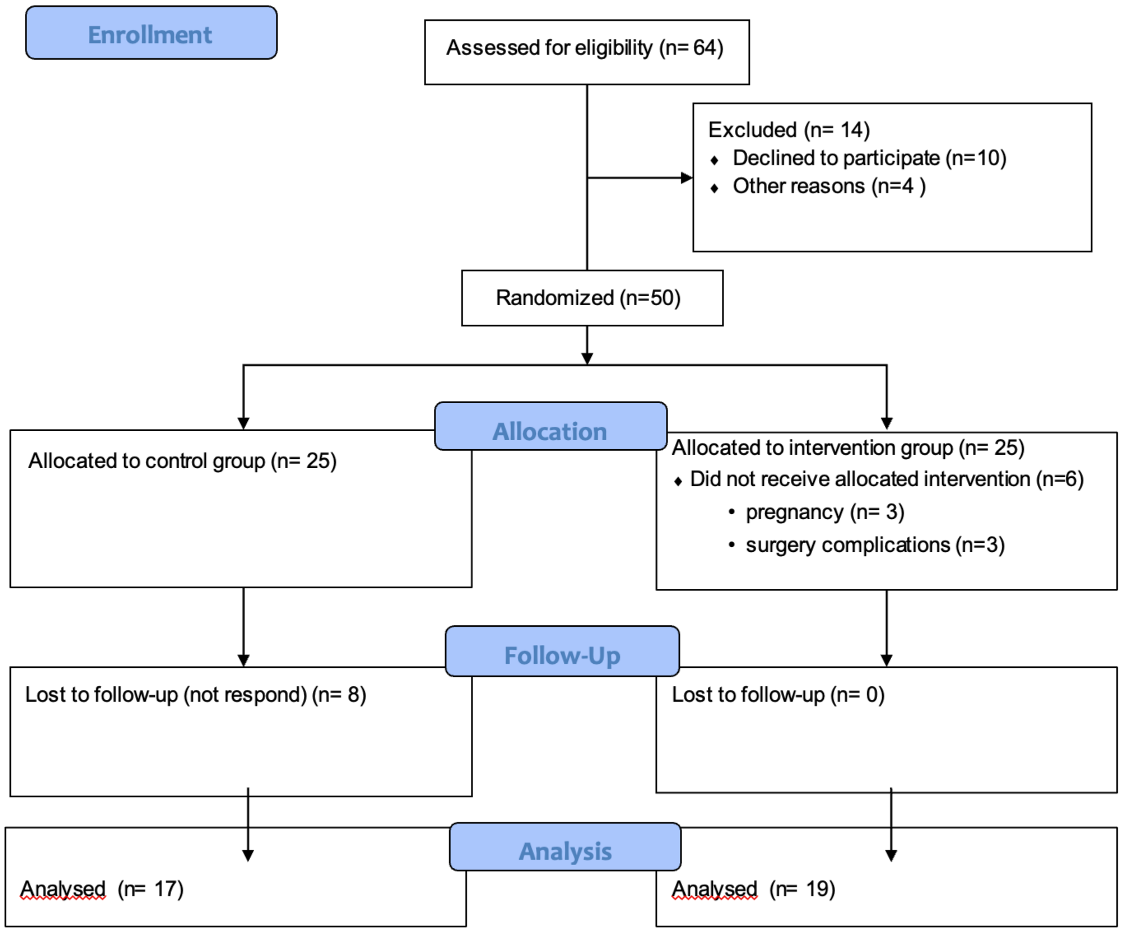
This randomized controlled study (NCT05289219) was developed at a single health institution, the Center for Integrated Responsibility of Bariatric Surgery and Metabolic Diseases (CRI. COM), performed at a Portugal Hospital (ULSAC) and at the University (ESDH-CHRC). The protocol has been previously described (Amaro Santos et al., 2023).

Recruitment took place between December 2021 and December 2023 from among candidates who met the diagnostic criteria for bariatric surgery. A team member of the two institutions managed all the procedures.

A bariatric surgeon and a sports specialist nurse contacted the patients and randomized them into the control group (CG) and intervention group (IG). The invitation to participate was made in the context of the outpatient office, and participants who agreed to participate in the study were given the free and informed consent form previously approved by both the University and Hospital Ethics Committee (HESE_CE_1917/21).

Exercise training began one month after surgery, with a frequency of three times per week, up to a maximum of 55 minutes per session, for 16 weeks. The study included four evaluations over a 17-month period. All assessments were conducted by researchers who were blinded to the study's objectives and the participants' group allocation to minimize potential biases and ensure the integrity of the data collected. This study protocol complied with the CONSORT 2010 recommendations (figure 4.2.1).

Figure 4.2.1. Consort flow Diagram



Eligibility criteria

The inclusion criteria for patients were as follows: were candidates for bariatric surgery, aged between 18 and 60 years, had a BMI between 35 and 50 kg/m2, were men and women, had no contraindications to exercise and agreed to participate voluntarily in the study. The BMI range was chosen to target individuals with moderate to severe obesity. Patients with other previous bariatric surgical interventions or bariatric surgery complications were excluded from the study.

Sample Size and Randomization

This was a prospective study, and the sample size was calculated by the G*power (Faul et al., 2007). A total of 17 participants were included in each group to enable the detection of a moderate estimated effect size (between-group differences) of at least 0.99

standard deviations in the outcome risk of sarcopenia(Pekař et al., 2020). Two-way independent sample t tests were performed with an alpha error of α=0.05 and a power of 1-β=0.80.

Patients proposed for bariatric surgery (gastric bypass-RYGB) were randomly assigned at the time of proposal by a systematic random process to usual care (CG) or usual care plus an exercise program (IG).

Outcomes

After surgery, all outcomes were assessed before and after the exercise program. The first assessments were performed before the training program, and the remaining three were performed at different moments after the exercise program.

- *Anthropometry and body composition*

Weight was measured with a digital scale (Tanita MC 780-P MA), and height was determined by a manual stadiometer. This assessment was made before breakfast and at least six hours after eating, without shoes or wearing light clothes. Waist circumference was determined using a measuring tape, and BMI was calculated (weight/height^2)(Devonshire-Gill, 2018; Norton, 2018). Dual-energy X-ray absorptiometry (DEXA) (DXA, Hologic QDR, Hologic, Inc., Bedford, MA, USA) was used to estimate body composition (fat mass and skeletal muscle mass) (Pekař et al., 2020).

- *Sarcopenia screening – FIND*

In clinical practice, the EWGSOP2 and EASO/ESPEN both recommend the use of the SARC-F for sarcopenia screening (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, & Zamboni, 2019; Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019; Ramirez et al., 2022). All participants completed this tool at the four time points.

This tool consists of five questions: strength (S), assistance walking (A), rising from a chair (R), climbing stairs (C), and falling (F). A total score is calculated out of 10 for each question, ranging from "not at all" to "very difficult". The recommended cutoff value for predicting sarcopenia is $\geq$4 points. Low values indicate no risk of sarcopenia

(Malmstrom & Morley, 2013; "SARC-F; Screening Tool for Sarcopenia," 2019; Woo et al., 2014).

- *Sarcopenia Diagnosis – ASSESS*

Skeletal muscle strength:

Sarcopenia is primarily diagnosed by searching for weak muscles. To assess evidence of sarcopenia, the EWGSOP2 recommends the use of grip strength or a chair stand measure with specific cutoff points for each test.

The handgrip strength test was performed using manual pressure dynamometry (Jamar®) to assess the muscle strength of the upper limbs. The participants were told to stand with their elbows straight and completely relaxed. The muscle strength test value was determined by recording the greatest grip strength value obtained after two trials with each hand (Cooper et al., 2022; Roberts et al., 2011).

The sit-to-stand test, which requires participants to alternate between standing and sitting for thirty seconds as often as they could, was used to assess the muscle strength of the lower limbs (Soriano-Maldonado et al., 2020). The chair stand test provides a trustworthy and useful way to measure strength because it assesses both endurance and strength (Beaudart et al., 2016; Cesari et al., 2009).

A handgrip strength of less than 27 kg for men and less than 16 kg for women (Dodds et al., 2014) or >15 s for five rises on the chair rise test (5-times sit-to-stand) were the chosen cut-offs. The timed chair stand test is a variation that counts how many times a patient can rise and sit in the chair over a 30-second interval (Cesari et al., 2009).

- *Sarcopenia confirmation – CONFIRM*

Skeletal muscle mass:

Different methods can be used to report skeletal muscle mass, such as dual-energy X-ray absorptiometry (DEXA), bioelectrical impedance analysis (BIA) or muscle cross-sectional area (MRI) analysis. Given that DEXA is a widely used technique for determining skeletal muscle mass, it was chosen for all four assessments (Ramirez et al., 2022).

Appendicular skeletal muscle mass (ASM) was determined as the total skeletal muscle mass of the four limbs. This muscle mass is attached to the skeleton and plays a fundamental role in systemic movement and posture maintenance (Studenski et al., 2014).

The upper and lower extremity muscle masses (arm + leg muscle mass [kg]) were summed and divided by height (meters) squared (m2) to calculate the skeletal muscle index (ASMMI) or the Baumgartner index (ASMMI= ASM/height^2) (Gould et al., 2014; T. N. Kim et al., 2017). Sarcopenia assessment results vary among groups, but the ASMMI score is the most widely considered variable (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019).

As recommended by the EWGSOP2, the following ASMM and ASSMI cutoff values were used in the present study: ASSM<20 kg and ASSMI < 7.0 kg/m2 for males and ASSM <15 kg and ASSMI < 5.5 kg/m2 for females (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, & Zamboni, 2019). As such, we propose the use of the Baumgartner index as the cutoff for ASMM/weight < 28.27% for males and < 23.47% for females. The FNIH uses another ratio, which is considered ASMM/BMI < 0.789 for males and < 0.512 for females.

Sarcopenia Severity Level - SEVERITY

Physical Performance:

Once the diagnosis of sarcopenia was established, the severity was assessed using the 400-meter walk test, which assesses walking endurance and ability. During the test, participants were allowed to take up two rest breaks and were required to perform 20 laps of 20 meters each as quickly as possible (Baroudi et al., 2020; Vestergaard et al., 2009). When the test was not finished or took longer than six minutes to complete, the participants were classified as having low physical performance (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019).

The algorithm for diagnosing sarcopenia and sarcopenic obesity

Sarcopenia according to the EWGSOP2 criteria: Based on low muscle strength, low muscle mass and low physical performance (male grip strength < 27 kg, ASMM < 20 kg, ASMMI < 7.0 kg/m2, and 400 m walk test ≥ 6 min; female grip strength < 16 kg, ASMM < 15 kg, ASMMI < 5.7 kg/m2, and 400 m walk test ≥ 6 min), sarcopenia was diagnosed and classified according to severity (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019).

Sarcopenic obesity according to EASO/ESPEN and FNIH: The parameters BMI, waist circumference (WC), and ASMM score based on weight and BMI (BMI > 30 kg/m2, WC ≥ 102 cm for males and ≥ 88 cm for females; ASMM/weight < 28.27% for males and < 23.47% for females; and ASMM/BMI < 0.789 for males and < 0.512 for females) were added to the EWGSOP2 variables (Donini et al., 2022; Studenski et al., 2014).

Intervention

The exercise combined aerobic and strength training in the same session in a progressive combined training program. The exercise prescriptions included information about frequency, intensity, time, type, volume, and progression (FITT-VP) (Bushman, 2014).

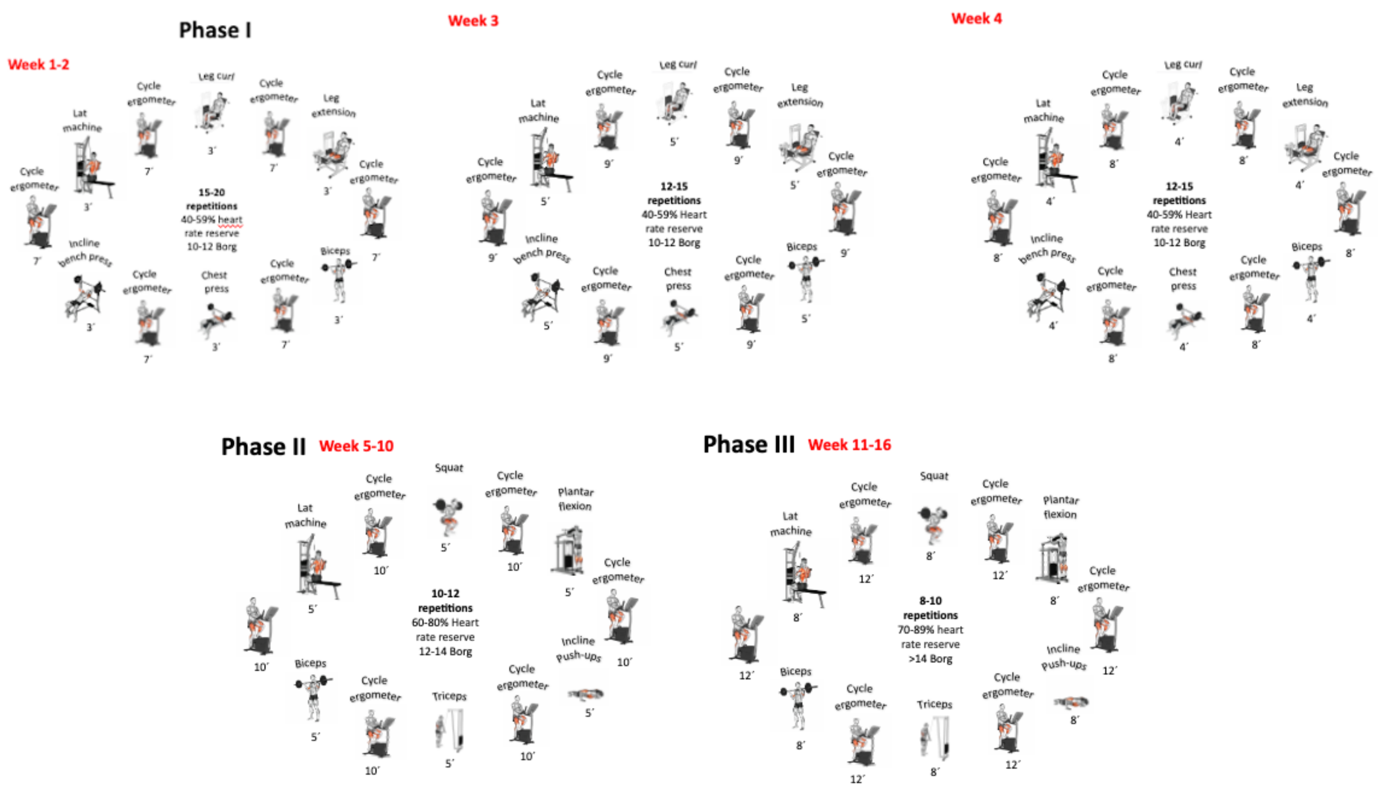
Based on the recommendations of the World Health Organization (WHO) (Hämälaïnen et al., 2020) and the ACSM (Bushman, 2014), the duration of the program was 16 weeks, with a frequency of three times a week, for up to 55 minutes per session and starting one month after surgery. Each session started with a 5-minute warm-up and finalized with a 10-minute cool-down, with stretching and flexible work.

Patients assigned to the IG engaged in a combined exercise training program lasting for 16 weeks. Each exercise session included the following components: (a) a 5-minute specific warm-up; (b) phase 1 – resistance training (weeks 1-4); (c) phase 2 – hypertrophy training (weeks 5-10); (d) phase 3 – strength training (weeks 11-16); and a 10-minute cool-down for flexibility (myofascial release, mobility, static and dynamic stretching). The detailed combined exercise programmed is presented in Figure 4.2.2.

The first phase included 20 minutes of interval training, encompassing circuit strength training. Each posterior phase has an increment of 10 minutes in the central block, always with an interval assessment of the patient’s adaptive response, based on heart rate reserve and the Borg scale (Castello et al., 2011).

Three personal trainers with training in sports sciences assessed physical fitness and prescribed and accompanied the training sessions. All training sessions took place in a fitness facility three times per week on nonconsecutive days from 7 to 10 a.m. The patients participated in the sessions in small groups (1-3) and were educated and motivated to exercise regularly.

Figure 4.2.2. FITT-VP exercise for individuals after bariatric surgery



Statistical methods

The statistical analysis was performed with SPSS version 27.0 (IBM SPSS, Inc., Chicago, IL, USA) to determine the outcomes. To assess whether the incidence of risk and diagnosis of sarcopenia were dependent on exercise, the chi-square test was used, and a type I error probability of 0.05 was used for all the inferential analyses. Categorical variables are expressed as frequencies and percentages, and continuous variables are expressed as the mean and standard deviation. The percentages were compared using the chi-square test or Fisher's exact test. Data normality was assessed with the Shapiro–Wilk test, and group differences were examined with an independent t test or a Mann–Whitney test. To compare dependent variables, two-way ANOVA with sphericity and homogeneity tests, Spearman correlation, and logistic regression analyses were performed considering the intervention group and control group and the four sequential assessments (one pre- and three post-intervention programs).

Results

A total of 36 patients participated in this study. The mean age was 46.9 (± 11.4) years, and the mean BMI was 42.9 (± 5.14) kg/m^2. All patients were previously sedentary before surgery. Of the study participants, 15 patients (33.3%) had T2DM, 13 (28.8%) had arterial hypertension, 19 (42%) had dyslipidemia, 10 (22.2%) had hypothyroidism, and 17 (37.8%) had obstructive sleep syndrome apnea (OSA).

The participants were randomly assigned to the IG or CG. At baseline, no significant differences were observed between the groups (p>0.05), except for weight, which was greater in the IG (103±14.5 V, 91.8±14.7; p=0.025), as presented in Table 4.2.1.

Table 4.2.1. Patient baseline characteristics in the intervention and control groups

Variables (Mean ± SD)	Intervention Group n=19	Control Group n=17	*p value*
Age (years)	43.68 ± 11.00	50.53 ± 10.97	0.071
Anthropometry			
Weight (kg)	103 ± 14.5	91.8 ± 14.7	**0.025**
BMI (kg/m^2)	37.8 ± 5.38	37 ± 4.53	0.639
Waist circumference (cm)	112 ± 9.68	110 ± 11.4	0.459
Body Composition			
Fat mass (kg)	44.26 ± 12.16	44.47 ± 9.97	0.957
Body fat (%)	44.2 ± 6.46	45.5 ± 4.99	0.489
Total SMM mass (kg)	52.09 ± 9.05	48.01 ± 9.47	0.195
ASMM (kg)	22.29 ± 3.92	19.72 ± 4.79	0.086
ASMMI (kg)/m^2)	8.09 ± 1.03	7.92 ± 1.47	0.672
ASMM/Weight (%)	21.7 ± 3.44	21.4 ± 3.18	0.795
ASMM/BMI	0.601 ± 0.14	0.535 ± 0.12	0.130
Physical function and strength			
Handgrip (kg)	22.4 ± 10.6	18.1 ± 6.44	0.154
30s Sit-to-stand test (n)	14.2 ± 2.35	12.8 ± 3.33	0.138
400-m walk test (min)	7.24 ± 2.26	8.79 ± 3.40	0.113

BMI: body mass index, SMM: skeletal muscle mass, ASMM: appendicular skeletal muscle mass, ASMMI: appendicular skeletal muscle mass index.

To determine the prevalence of sarcopenia and sarcopenic obesity, three algorithms were used to assess the parameters of these diseases (Table 4.2.2).

Table 4.2.2 Main outcomes of the EXPOBAR trial

Variables (Mean ± SE)		*Before Exercise*	*After Exercise*			Global Group Effect		Intervention effect *Moment*Group*							
Moment		Baseline T0	4-month T1	6-month T2	12-month T3	*p value*	*Effect size (η²)*	*T0* vs *T1*		*T1* vs *T2*		*T2* vs *T3*		*T0* vs *T3*	
	Group							*p value*	*Effect size (η²)*	*p value*	*Effect size (η²)*	*p value*	*Effect size (η²)*	*p value*	*Effect size (η²)*
Anthropometry															
Weight (kg)	**IG**	103.2 ± 14.5	83.1 ± 10.9 [a]	75 ± 9.2 [b]	74 ± 9.9 [c e]	**0.039**	0.078[#]	0.137	0.064[#]	0.280	0.034[#]	0.191	0.050	**0.048**	0.111[#]
	CG	91.8 ± 14.7	75.4 ± 14.7 [a]	69.9 ± 12.1 [b]	70.8 ± 12.0 [c e]										
BMI (kg/m²)	**IG**	37.8 ± 5.40	30.4 ± 4.43 [a]	27.5 ± 4.01 [b]	27.1 ± 3.8 [c e]	0.142	0.052[+]	0.531	0.012[+]	0.307	0.031[+]	0.112	0.072[#]	0.106	0.075[#]
	CG	37 ± 4.53	30.2 ± 4.17 [a]	28.2 ± 4.34	28.7 ± 4.93 [c e]										
Waist circumference (cm)	**IG**	112.2 ± 9.68	97.2 ± 8.4 [a]	90.5 ± 8.49 [b]	88.2 ± 8.8 [e]	**0.010**	**0.105***	0.316	0.030[+]	**0.027**	0.136[*]	0.292	0.033[+]	**0.023**	0.143*
	CG	109.5 ± 11.4	97.2 ± 12.8 [a]	94.2 ± 12.2	93.6 ± 11 [e]										
Total Weight Loss (%)	**IG**	12.8 ± 2.72	29.5 ± 5.92 [a]	36.1 ± 7.5 [b]	37 ± 8.08 [c e]	0.161	0.049[+]	0.675	0.005[+]	0.336	0.027[+]	0.111	0.073[+]	0.106	**0.075[#]**
	CG	13.1 ± 4.32	29 ± 4.58 [a]	33.8 ± 7.17 [b]	32.5 ± 9.76 [c e]										
Body Composition															
Fat mass (kg)	**IG**	44.26±12.16	27.66±13.55 [a]	25.22 ± 9.14	23.37 ± 9.45 [e]	**0.006**	**0.114***	**0.001**	**0.272***	0.744	0.003[+]	0.521	0.012[+]	0.052	0.107[#]
	CG	44.47 ± 9.97	34.42±7.92 [a]	34.19 ± 6.99	30.45 ± 12.6 [e]										
Body fat (%)	**IG**	44.2 ± 6.42	36.6 ± 2.29 [a]	31.9 ± 7.96 [b]	30.4 ± 6.22 [c e]	**0.044**	0.076[#]	0.095	0.080[#]	0.200	0.048[#]	0.650	0.006[+]	**0.010**	**0.180***
	CG	45.5 ± 4.99	40.6 ± 7.26 [a]	37.4 ± 6.34 [b]	37 ± 7.71 [e]										
Total SMM mass (kg)	**IG**	52.10 ± 9.04	45.43 ± 13.2 [a]	44.53 ± 9.59	37.1±12.7 [c d e]	0.138	0.052[+]	0.169	0.055[+]	0.133	0.065[#]	**0.003**	**0.233***	0.219	0.044[+]
	CG	48.01 ± 9.47	44.65±9.54 [a]	39.99±5.08 [b]	37.14 ± 5.06 [c e]										
ASMM (kg)	**IG**	22.29 ± 3.92	20.45 ± 3.71 [a]	18.94±4.14 [b]	17.02±3.8 [c d e]	0.705	0.014[+]	0.386	0.022[+]	0.817	0.002[+]	0.766	0.003[+]	0.362	0.024[+]
	CG	19.72 ± 4.79	17.53±4.11 [a]	15.91±4.06 [b]	13.86 ± 4.31 [c d e]										
ASMMI (kg)/m²)	**IG**	8.09 ± 1.03	7.43 ± 0.99 [a]	6.85 ± 1,20 [b]	6.17 ±1.05 [c d e]	0.186	0.046[+]	0.163	0.056[+]	0.718	0.004[+]	0.395	0.021[+]	0.078	0.088[#]
	CG	7.92 ± 1.48	7.03 ± 1.22 [a]	6.39 ± 1.28 [b]	6.17 ± 1.05 [c d e]										
ASMM/Weight (%)	**IG**	21.7 ± 3.44	24.08 ± 4.35 [a]	25.3 ± 4.68	22.9±3.39 [d]	**0.030**	0.084[#]	0.129	0.066[#]	0.237	0.041[#]	0.476	0.015[+]	**0.014**	**0.164***
	CG	21.4 ± 3.18	23.3 ± 3.13 [a]	22.8 ± 3.71	19.8 ± 5.82 [c d]										
ASMM/BMI	**IG**	0.601± 0.14	0.687 ± 0.17 [a]	0.701 ± 0.18	0.635±0.1 [d]	**0.041**	0.077[#]	0.063	0.098[#]	0.286	0.033[+]	0.781	0.002[+]	**0.020**	**0.150***
	CG	0.535 ± 0.12	0.580±0.11	0.570±0.14	0.496 ± 0.19 [c d]										
Physical function and strength															
Handgrip (kg)	**IG**	22.4 ± 10.62	24.8 ± 8.44	26.9 ± 7.51	27.4 ± 7.21	**0.005**	**0.120***	**0.025**	**0.140***	0.288	0.033[+]	0.590	0.009[+]	**0.014**	**0.166***
	CG	18.1 ± 6.44	16.8 ± 5.25	17.7 ± 5.11	17.3 ± 5.44 [e]										
Sit-to-stand test (s)	**IG**	14.2 ± 2.35	15.9 ± 3.3 [a]	16.5 ± 2.17	16.8 ± 2.41 [e]	**<0.001**	**0.162***	**0.040**	**0.118***	0.323	0.029[+]	0.073	0.092[#]	**<0.001**	**0.319***
	CG	12.8 ± 3.33	13.2 ± 2.88	13.1 ± 2.45	12.8 ± 2.70										
400-m walk test (m)	**IG**	7.24 ± 2.26	6.05 ± 1.86 [a]	5.82 ± 1.58	5.57 ± 1.19 [e]	**<0.001**	**0.303***	**0.021**	**0.146***	**0.007**	**0.193***	**0.033**	**0.126***	**<0.001**	**0.424***
	CG	8.79 ± 3.40	8.74 ± 3.05	9.58 ± 3.58 [c]	10.14 ± 4.1 [c d]										

BMI: body mass index, SMM: skeletal muscle mass, ASMM: appendicular skeletal muscle mass, ASMMI: appendicular skeletal muscle mass index.

ANOVA was used to assess the global group effect at all time points. The post hoc test revealed results within each group; a p value <0.05 indicated statistical significance.

[a]- T0 vs T1 post hoc test, Bonferroni significance; [b]- T1 vs T2 post hoc test, Bonferroni significance; [c]- T1 vs T3 post hoc test, Bonferroni significance; [d]- T2 vs T3 post hoc test, Bonferroni significance;

[e]- T0 vs T3 post hoc test, Bonferroni correction, significant.

[+] Small effect size (0.01-0.06); [#] Medium effect size (0.06-0.14); * Large effect size (>0.14)

The EXPOBAR trial showed that the intervention had significant and meaningful effects on several anthropometric measures, body composition parameters, physical function and strength outcomes. While several variables, such as BMI and ASMM score, had nonsignificant global group effects ($p=0.142$, $p=0.705$), they still had significant effects at 4, 6 and 12 months according to the post hoc test ($p<0.05$). However, muscle mass decreased continuously after surgery in both groups despite the exercise protocol used in the intervention group.

The most substantial improvements were observed in physical function and strength metrics, suggesting that the intervention was effective at enhancing physical fitness, with a significant group effect ($p<0.001$) and large effect size ($\eta^2=0.303$). Additionally, handgrip strength and lower body strength had significant group effects ($p=0.005$ and $p<0.001$, respectively) and large effect sizes ($\eta^2=0.120$ and $\eta^2=0.162$). There were notable and meaningful increases in the measured outcomes over all interval periods, and these increases were substantial enough to have practical benefits or applications (table 5.2.2).

The latest and most important guidelines about this subject were used. The EWGSOP2 group consensus used the FACS sequence assessment, while the EASO/ESPEN and FNIH algorithms were based on weight and BMI criteria (Table 4.2.3).

Table 4.2.3 Logistic regression analysis of the ability of different *algorithms to diagnose sarcopenia – EASO, EWGSOP2, FNIH*

	Intervention Group				**Control Group**				***Intervention effect* vs *baseline***		
Major risk and severity (%)	***Pre-Exercise***	***After Exercise***			***Pre-Exercise***	***After Exercise***			*p value*		
	Baseline T0	**4-month T1**	**6-month T2**	**12-month T3**	**Baseline T0**	**4-month T1**	**6-month T2**	**12-month T3**	*4-month*	*6-month*	*12-month*
EASO											
SCREENING - High BMI	100%	31.6%	31.6%	26.3%	100%	35.3%	35.3%	41.2%	0.892	0.629	0.280
SCREENING - High Waist circumference	100%	73.7%	42.1%	10.5%	100%	82.4%	58.8%	58.8%	0.995	0.293	0.113
SCREENING - SARC-F	84.2%	5.3%	10.5%	0%	88.2%	70.6%	58.8%	0%	**< 0.001**	**0.005**	1.000
DIAGNOSIS – Altered functional skeletal muscle	47.4%	15.8%	5.3%	10.5%	70.6%	64.7%	52.9%	52.9%	**0.005**	**0.008**	**0.011**
DIAGNOSIS – Altered body composition	89.5%	42.1%	52.6%	84.2%	88.2%	70.6%	88.2%	94.1%	0.179	0.464	0.728
STAGING – STAGE II: With complications	100%	15.8%	5.3%	10.5%	100%	100%	100%	100%	**0.034**	**0.002**	**< 0.001**
EWGSOP2											
SCREENING - SARC-F	84.2%	5.3%	10.5%	0%	88.2%	70.6%	58.8%	0%	**< 0.001**	**0.005**	1.000
ASSESS - Skeletal muscle strength	47.4%	15.8%	5.3%	10.5%	70.6%	64.7%	52.9%	52.9%	**0.005**	**0.008**	**0.011**
CONFIRM - Skeletal muscle mass	0%	0%	15.8%	47.4%	0%	11.8%	29.4%	52.9%	0.077	0.325	0.294
SEVERITY - Physical performance	73,7%	42.1%	31.6%	21.1%	70.6%	76.5%	82.4%	94.1%	**0.034**	**0.002**	**< 0.001**
FNIH											
SKELETAL MUSCLE STRENGTH	47.4%	15.8%	5.3%	10.5%	70.6%	64.7%	52.9%	52.9%	**0.005**	**0.008**	**0.011**
SKELETAL MUSCLE MASS	47.4%	21.1%	15.8%	26.3%	64.7%	23.5%	47.1%	76.5%	0.858	**0.050**	**0.004**

BMI: Body mass index

The intervention effect was reported to the baseline. A p value <0.05 was considered to indicate statistical significance.

The first step in all the algorithms is screening. The FACS uses the SARC-F questionnaire to determine risk. The EASO and ESPEN use both BMI and waist circumference. Before the exercise program, all patients met these two last criteria as positive criteria. Immediately after the exercise program, the patients presented different screening results (IG 5.3% *versus* CG 70.6%, $p<0.001$), with a decreased risk in the IG after the exercise intervention. The same result was obtained at six months (10.5% for the IG *versus* 58.8% for the CG; p=0.005).

According to the results of assessing, confirming, and diagnosing sarcopenia, there was a decrease after the exercise intervention in the IG (47.4% to 15.8%) and a small difference in the CG (70.6% to 64.7%). This difference was significant after the exercise program (p=0.005), at 6 months (p=0.008) and 12 months (p=0.011). To confirm the diagnosis, three different indices and cut-offs were used to assess muscle mass.

The ASMMI did not significantly differ between the groups. When the EASO/ESPEN criteria were applied based on weight, the results were similar. Different results were found for the FNIH criteria, which did not significantly improve after the exercise intervention (IG 21.1% *versus* CG 23.5%) but did improve long-term after exercise at 6 (IG 15.8% *versus* CG 41.7%) and 12 months (IG 26.3% *versus* CG 76.5%).

The severity of sarcopenia was significantly different immediately after and long after the exercise program (p=0.034, p=0.002, $p<0.001$).

To perform a more detailed analysis of the results associated with physical exercise and its temporal impact on the risk and incidence of sarcopenia, a logistic regression was carried out to analyze the causal relationship in addition to the associations already described. There was a greater number of participants at risk of sarcopenia in the CG than in the IG (5.3% *versus* 70.6%, respectively; $p<0.001$). This effect was maintained at 6 months (p=0.005) but not at 12 months ($p>0.05$).

Regarding sarcopenia screening and diagnosis, 64.7% of the CGs had a positive assessment for subsequent diagnosis of sarcopenia after exercise (p=0.005). In comparison, only 15.8% of the IG had the same positive assessment, highlighting the decrease in upper limb skeletal muscle strength in the CG. This relationship was maintained at 6 and 12 months (p=0.008, p=0.011). According to the results of the inferential statistical analysis, after exercise, there was a significant probability of confirming the diagnosis and changing the assessment of the level of sarcopenia between the IG and CG (p=0.002).

There were no significant differences in the EASO or EWGSOP2 score, but when the FNIH consensus was used (ASMM/BMI), the differences in the confirmation of sarcopenia were statistically significant at 6 months (p=0.05) and 12 months (p=0.004).

Discussion

The EXPOBAR trial is the first randomized controlled trial in Portugal to evaluate the effects of supervised and structured physical exercise programs on the risk and diagnosis of sarcopenia induced by bariatric surgery using the tools and cut-offs recommended by current consensuses.

Conflicting findings have been reported in several studies and papers regarding the impact of weight loss on sarcopenia and muscle weakness. The clinical and biological effects of metabolic/bariatric surgery on sarcopenia and muscle weakness are still not fully understood.

The current findings revealed a significant increase in the risk of sarcopenia within the first month after surgery, highlighting the need to implement exercise programs to preserve muscle mass and function. This can occur during bariatric surgery, particularly because of the very marked initial weight loss (Cadena-Obando et al., 2020). These alterations make it increasingly important to assess the risk of sarcopenia in patients undergoing bariatric surgery. The intense weight loss that occurs in the first few months can lead to an increase in falls and fractures (Bentham et al., 2017; van de Laar et al., 2018) due to changes in proprioception (Cibulková et al., 2022) and the metabolic impact associated with bariatric surgery and obesity. These changes are closely associated with frailty and instability, especially among older adults people. However, sarcopenia has implications for more than older adults people (Montano-Loza et al., 2014; Prado et al., 2008).

The present data show that the risk of initial sarcopenia is important and that the risk of sarcopenia can be clinically assessed and managed with early intervention. Based on the evidence, if a patient is at risk of sarcopenia and has been diagnosed with sarcopenia, treatment measures for the disease should be taken (Beaudart et al., 2016). The first treatment option for sarcopenic obesity is to combine nutritional and exercise goals with the aim of reducing adipose tissue but also enhancing and preserving muscle mass and function (Prado et al., 2024). Due to the significantly increased risk observed in the first month after surgery, prehabilitation and early interventions after surgery should probably be implemented.

Different screening tools, strength tests and skeletal muscle mass indices have been proposed for assessing sarcopenia. These indices consider adjustment factors such as height squared, weight or BMI. By using these indices, healthcare professionals can better evaluate and diagnose sarcopenia (Galata et al., 2020). In this study, these indices were used to diagnose sarcopenia and sarcopenic obesity, revealing that while some body composition metrics did not show significant group effects, the improvements in muscle function and strength underscore the importance of using objective diagnostic criteria.

The intervention group experienced significant improvements in muscle function and physical performance, which emphasizes the potential of structured exercise programs to counteract the negative impacts of body composition on individuals associated with obesity, sarcopenia and bariatric surgery (Minniti et al., 2022).

Bariatric surgery has an impact on adipose tissue, but in the first few months, it also has a relevant effect on muscle mass (Coen et al., 2018; In et al., 2021; Villa-González et al., 2019). This highlights the importance of introducing combined exercise (aerobic and strength training), as was the case in the present study, where an important impact of exercise on muscle quality and consequently a reduction in the risk of worsening and developing sarcopenia was found.

The ACSM recommends resistance exercise to improve the function of the musculoskeletal system (Bushman, 2014). Combined with aerobic training, it can potentially improve cardiorespiratory promotion of anabolic muscle adaptation and consequently improve muscle quality and quantity (Bellicha et al., 2021; Castello et al., 2011; Konopka & Harber, 2014). There was a difference in the evolution of these diagnostic criteria among the patients who practiced combined physical exercise, as reported in the last systematic review (Bellicha et al., 2021), but this difference was not statistically significant.

Body composition metrics, BMI and the ASMMI score did not significantly affect the participants in this study, raising questions about the overall effectiveness of the intervention. These include the intervention duration, the baseline fitness levels of participants, and potential differences in adherence to the intervention protocols. BMI, a general measure of body fat based on weight and height, and the ASMMI score, which specifically measures muscle mass in the limbs, did not significantly change. This could be due to several factors. These parameters might not have been sensitive enough to detect differences between the two groups because of the strong confounding effects caused by the surgical procedure.

These findings underline an important point regarding the FITT-VP principle recommended by the ACSM (Burke et al., 2021; Stine et al., 2023). The lack of differences in the results shows that adjusting at least one of the exercise parameters, namely, frequency or intensity, may be necessary to obtain better results. This can be done in accordance with the ASMBS guidelines by increasing the training frequency.

Nevertheless, the results showed that combined exercise significantly improved functional physical capacity and strength after an initial decline after bariatric surgery. In other words, exercise was able to reverse the functional and strength loss that was the result of the surgical procedure, with a reduction in the number of patients at risk of a diagnosis of sarcopenia after bariatric surgery. This finding aligns with previous research (Alba et al., 2019) indicating that weight loss can improve physical performance by reducing mechanical factors and improving mobility and walking time, although it was observed that there was a decrease in strength assessed by handgrip strength in the first year after bariatric surgery.

The study's long-term effects, particularly at 6 and 12 months, underscore the sustainability of improvements in muscle function and physical performance. At the 6-month mark, improvements in muscle function were evident, demonstrating that the initial gains were not short-lived. By 12 months, participants continued to exhibit enhanced physical performance, indicating that these benefits can be sustained with consistent exercise. These findings emphasize the critical importance of continuous exercise for maintaining and building upon the benefits observed. These sustained improvements suggest that regular exercise is essential not only for achieving initial gains but also for preserving and enhancing muscle function and physical performance over time.

However, there was muscle mass loss in both groups, and this loss continued throughout the study duration, despite the exercise protocol used in the intervention group.

In the present study, when the complete diagnostic criteria defined by EASO/ESPEN and EWGSOP2 were used, no significant differences were found in either index, which may indicate that it might be essential to use the muscle strength criterion, which is probably the most important and decisive criterion for diagnosing sarcopenia in patients undergoing bariatric surgery.

The fundamental component and first step in defining the diagnosis of sarcopenia is muscle function. In a clinical context, the sarcopenia diagnostic index associated with weight is an essential parameter that significantly affects the outcome after long-term exercise, as is the case with the adjustment for BMI suggested by the FNIH (Studenski et al., 2014).

Changes in sarcopenia parameters, such as physical function, are associated with changes in muscle mass and overall body weight, suggesting that BMI is a valuable parameter for adjusting the risk of sarcopenia. Physical and functional capacity are important indicators for diagnosing muscle quality, and they are noninvasive indicators. In studies involving individuals with other medical conditions and healthy individuals, it was already observed that muscle quality measured by the handgrip test is a more reliable indicator than the quantity of the muscle itself (Bohannon, 2015, 2019; Celis-Morales et al., 2018; Huerta Ojeda et al., 2021).

Sarcopenia is a particularly concerning problem in the context of bariatric surgery because it can impair physical function, increase the risk of frailty, and negatively impact overall health outcomes. Sarcopenia is a complex and multifactorial condition that is influenced by a variety of factors, including age, physical activity, nutritional status, and underlying medical conditions. Accurately defining sarcopenia parameters in after bariatric surgery patients is therefore crucial for the effective management and prevention of this condition.

Muscle strength, a variable not impacted by weight loss, might be a more useful indicator of sarcopenia in bariatric patients, whereas muscle mass is heavily influenced and confounded by weight loss.

Conclusion

Sarcopenia, characterized by a loss of muscle mass and function, is a growing concern in various populations, including those undergoing bariatric surgery. This study demonstrated significant improvements in the risk of sarcopenia, muscle quality, and functional capacity following a 16-week supervised combined exercise program, although the changes in muscle quantity were not statistically significant. These findings highlight the importance of incorporating exercise interventions, as recommended by the

ACSM and the ASMBS, with an emphasis on increasing the frequency and intensity of training to effectively combat sarcopenia.

Long-term management of sarcopenia requires regular monitoring of both body composition and muscle function. Assessments of strength, skeletal muscle mass and functional status, along with periodic monitoring of body fat composition, are essential for tracking progress and optimizing treatment strategies over time. By going beyond BMI and addressing other parameters, such as physical function, healthcare providers can more accurately identify potential sarcopenia development after bariatric surgery, allowing appropriate intervention design.

Individualized care plans that consider the unique needs and circumstances of patients are crucial for achieving positive clinical outcomes. Preventive combined exercise programs are particularly important for patients undergoing bariatric surgery, as they can significantly improve strength and metabolic health, thereby enhancing long-term surgical outcomes.

Further research and clinical trials are warranted to refine and expand the current approaches available for managing sarcopenic obesity. Such efforts should aim to improve the quality of life and clinical outcomes for individuals affected by this complex condition, ensuring that interventions are both effective and sustainable over the long term.

Article 7 – Randomized Controlled Trial - **The impact of a structured physical exercise program after bariatric surgery (RYGB) on PROMs - health-related quality of life (SarQoL) - in patients with preoperative obesity and sarcopenia**

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Abstract

Introduction: Sarcopenia, a condition characterized by a decrease in muscle mass and strength, is very common in patients with obesity and can be aggravated by bariatric surgery, potentially compromising the clinical results of surgery. There is increasing interest in patient-reported outcome measures (PROMs) to assess results in other health variables that may be especially important for individual patients. The role of exercise in enhancing health-related quality of life (HRQoL) after surgery remains underexplored. This study investigated the impact of exercise on HRQoL in bariatric sarcopenic patients via the Sarcopenia Quality of Life (SarQoL) questionnaire. **Method**: Candidates for surgery took part in the EXPOBAR program and were randomized into experimental and control groups. The intervention lasted 16 weeks, starting one month after surgery, and

included combined aerobic and resistance exercise. Outcomes, including body composition and physical fitness parameters, were measured before and after the intervention. All participants underwent gastric bypass surgery (RYGB).
Results: The baseline characteristics of the participants were not significantly different between the two groups. All patients met the criteria for moderate/severe obesity and the EASO/ESPEN criteria for sarcopenia, namely, reduced muscle strength assessed by grip strength and reduced muscle mass assessed by the ASMM score/weight. After completing the study protocol, patients in both groups had increased HRQoL, but the increase was significantly greater in the intervention group than in the control group.
Conclusion: Our findings suggest that exercise plays a crucial role in improving both physical and psychological well-being in post-bariatric patients, highlighting the need to integrate structured exercise programs in post-surgery care. This study was prospectively registered at Clinicaltrials.gov (NCT05289219).
Keywords: PROMs; exercise; bariatric surgery; quality of life; sarcopenia; SarQoL; patient-centered care.

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Introduction

Obesity is a global health crisis associated with numerous comorbidities, such as diabetes, cardiovascular diseases, and musculoskeletal disorders (Morabia & Abel, 2006; Sardinha et al., 2012; H. Yuan et al., 2024). Bariatric surgery is a widely recognized treatment for severe obesity, resulting in significant weight loss and a reduction in obesity-related health risks (Raoof et al., 2015; Schauer & Rubino, 2011). Despite these benefits, many patients continue to struggle with impaired quality of life due to residual or new health issues after surgery (Raoof et al., 2015).

Health-related quality of life (HRQoL) is a comprehensive measure of the overall well-being of individuals, encompassing physical, psychological, and social domains (Brazil et al., 2021; Coulman et al., 2017; Griauzde et al., 2018). HRQoL is particularly significant in clinical and public health settings, as it reflects the impact of health status, healthcare interventions and patient-reported outcomes (C. Santos, Carvalho, et al., 2022). For bariatric patients, improving HRQoL is as important as achieving weight loss. Given the overlapping health challenges, the Sarcopenia Quality of Life (SarQoL®) questionnaire, which is specifically designed to assess quality of life in individuals with sarcopenia, needs to be adapted to evaluate HRQoL in individuals with obesity (Beaudart et al., 2017).

Sarcopenia, a progressive and generalized loss of skeletal muscle mass and strength, is a significant public health concern, especially among the older adults population, and has significantly impacted physical performance in bariatric patients (Cruz-Jentoft et al., 2010). It is associated with adverse outcomes such as physical disability, poor quality of life, and increased mortality. The condition not only impairs physical function but also affects psychological well-being, leading to a diminished HRQoL. Early detection is critical for proper management, making it essential to have criteria that can be routinely used in clinical practice. The European Working Group on Sarcopenia in Older People (EWGSOP) proposed an updated diagnostic pathway known as the EWGSOP2 criteria (Donini et al., 2022). Although initially developed for older adults, these criteria can also be relevant for bariatric patients, who often face similar muscle deterioration challenges (Ramirez et al., 2022).

Recent data indicate that the prevalence of sarcopenia in the general population is approximately 11%, with a range from 3.2% to 26.3% (Endalifer & Diress, 2020; Wei et al., 2023). This condition is particularly concerning because of its negative impact on quality of life, increased complication rates, and additional pressure on health systems (Ethgen et al., 2017). Concurrently, the prevalence of obesity remains high, and sarcopenia commonly coexists with obesity, creating a complex clinical entity known as sarcopenic obesity (SO) (Donini et al., 2022; Tsigos et al., 2011). This condition triggers pathophysiological mechanisms, including insulin resistance, systemic inflammation, and oxidative stress. Sarcopenia and obesity mutually exacerbate each other, leading to a compounded negative effect on muscle mass and strength and increasing the risk of comorbidities such as type 2 diabetes, osteoporosis, cognitive impairment, and all-cause mortality (Crispim Carvalho et al., 2023).

Despite the EWGSOP's concern over sarcopenic obesity, specific diagnostic pathways for SO were not immediately established, resulting in different diagnostic approaches in research (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, & Zamboni, 2019). However, the European Society for Clinical Nutrition and Metabolism (ESPEN) and the European Association for the Study of Obesity (EASO) have recently published the first screening and diagnostic criteria with specific cutoff values for SO (Donini et al., 2022). This instrument aims to facilitate early diagnosis and establish the clinical importance of SO and its functional implications and impact on patients' quality of life. Individuals with sarcopenic obesity generally have a poorer quality of life than those with obesity alone. Previous studies comparing the quality of life in individuals with SO versus those with sarcopenia alone have shown mixed results. Some studies indicate no significant differences or even better quality of life in people with SO (Batsis et al., 2014; R. H. Liu & Irwin, 2017). These studies, however, used different diagnostic criteria than those recently established by ESPEN/EASO, highlighting the need for further research using new diagnostic standards (Donini et al., 2022).

Evaluating the quality of life of bariatric patients with sarcopenic obesity should employ a specific tool, such as the SarQoL instrument. This tool has demonstrated good structural and psychometric properties across various cultural versions. The SarQoL questionnaire is a disease-specific instrument designed to evaluate HRQoL in individuals with sarcopenia. It covers various domains, including physical and mental health, daily activities, and social functioning, providing a comprehensive assessment of the impact of sarcopenia on quality of life (Beaudart et al., 2016a, 2017).

The primary objective of this study was to assess the eventual impact of a structured exercise program on the HRQoL of individuals with sarcopenia after bariatric surgery, as evaluated by the SarQoL questionnaire. By determining the effectiveness of exercise interventions, this research aims to provide evidence-based recommendations for improving the quality of life in this population.

Methods

Study Design

This randomized controlled trial (RCT) included patients with sarcopenia obesity who underwent gastric bypass (RYGB). The study was conducted over a period of six months at a Portuguese hospital.

The invitation to participate was made in the context of the preoperative evaluation, and participants who agreed to participate in the study were given the free and informed consent form previously approved by the University and Hospital Ethics Committee (HESE_CE_1917/21) (supplementary material).

The participants were randomly assigned to either the intervention group (IG), which received a structured exercise program, or the control group (CG), which received standard care without additional exercise intervention. Exercise training began one month after surgery and was conducted three times per week for 16 weeks, for a maximum of 55 minutes per session.

Eligibility criteria

Patients were enrolled for bariatric surgery at the hospital; were diagnosed with sarcopenia on the basis of the European Association for the Study of Obesity/European Society for Clinical Nutrition and Metabolism (EASO/ESPEN) criteria, which include low muscle mass and low muscle strength without contraindications to exercise; and agreed to participate in the study. Patients who reported problems with locomotion, other previous bariatric surgery, or bariatric surgery complications were excluded.

Sample size and randomization

A total of 35 participants were enrolled in the study, with 19 in the IG and 16 in the CG. Patients proposed for bariatric surgery (gastric bypass-RYGB) were randomly assigned at the time of proposal by a systematic random process to usual care (CG) or usual care with an exercise program (IG).

Intervention

The program lasted 16 weeks, three times a week, for up to 55 minutes per session, starting one month after surgery. Each session started with 5 minutes of warm-up and ended with 10 minutes of cool-down (Bushman, 2014). The intervention was a progressive combined exercise program based on the FITT-VP (frequency, type, intensity, time, type, duration, volume, and progression) prescription (Burke et al., 2021; Bushman, 2014).

Intervention Group: The intervention group participated in a structured exercise program designed to improve muscle strength, endurance, and overall physical function.

A certified exercise physiologist supervised each session to ensure proper technique and safety. The program included:

- Resistance training: weeks 1--4
- Hypertrophy training: weeks 5--10
- Strength training: weeks 11--16

Control Group: Participants in the control group received standard care, including regular health check-ups and nutritional counseling, but did not participate in any additional structured exercise program.

Outcomes

Anthropometry and body composition

Weight was measured with a scale with the patients wearing no shoes or heavy clothing. Height was determined by a manual stadiometer. BMI was calculated (weight/height^2), and the abdominal circumference was determined with a measuring tape (Devonshire-Gill, 2018; Norton, 2018). To evaluate body composition, we used dual-energy X-ray absorptiometry (DEXA) (DXA, Hologic QDR, Hologic, Inc., Bedford, MA, USA) (Pekař et al., 2020).

Muscle strength

To evaluate the muscle strength of the upper limbs, a handgrip strength test was conducted via manual pressure dynamometry (handgrip). The participants were instructed to stand with their elbows fully relaxed and straight. Each hand was tested twice, and the maximum grip strength value obtained was recorded as the muscle strength test value (Cooper et al., 2022; Roberts et al., 2011).

The muscle strength of the lower limbs was evaluated via the sit-to-stand test, in which participants were instructed to stand and sit for 30 s as many times as possible (Soriano-Maldonado et al., 2020). The timed chair stand test is a variation that counts how many times a patient can rise and sit in the chair over a 30-second interval (Beaudart et al., 2016; Cesari et al., 2009). Because the chair stand test evaluates both strength and endurance, it offers a reliable yet practical measure of strength but may be confounded by changes in weight after surgery.

Muscle mass

Muscle quantity or mass is evaluated by dual-energy X-ray absorptiometry (DEXA) because it is a common method for measuring skeletal muscle mass (Ramirez et al., 2022). To calculate appendicular skeletal muscle mass (ASMM), we used the sum of the muscle masses of the upper and lower limbs (muscle mass of the arms [kg] + muscle mass of the legs [kg]) (Studenski et al., 2014).

ASMM was divided by weight (meters) to diagnose sarcopenia (ASMM/weight) (Donini et al., 2022; Gould et al., 2014). The ASMM score has been used to assess sarcopenic obesity (C. Liu et al., 2023).

Health-related quality of life - SarQoL

The primary outcome measure was the SarQoL questionnaire, a validated tool. The primary outcome measure was the SarQoL questionnaire, a validated tool specifically designed to assess the quality of life of individuals with sarcopenia (Beaudart et al., 2017; Geerinck et al., 2021). The SarQoL questionnaire is a self-administered tool developed in 2013 that aims to assess quality of life specifically related to sarcopenia; it comprises 55 items condensed into 22 questions, which are rated on a 4-point Likert scale organized into seven domains of quality of life. Scores range from 0 to 100, with higher scores indicating better quality of life (Beaudart et al., 2017).

These domains include the following: 1. Physical and Mental Health: This domain assesses the overall physical and mental well-being of individuals with sarcopenia. It includes questions related to physical symptoms, emotional well-being, and overall satisfaction with health. 2. Locomotion: This domain focuses on an individual's ability to move and perform daily activities. It includes questions about mobility, balance, and the ability to perform tasks such as walking, climbing stairs, and getting in and out of chairs. 3. Body composition: This domain examines an individual's body composition, including muscle mass and body fat percentage. 4. Functionality: This domain assesses an individual's ability to perform basic functional tasks, such as dressing, bathing, and toileting. 5. Activities of Daily Living: This domain evaluates an individual's ability to perform activities that are essential for daily living, such as eating, grooming, and managing medications. 6. Leisure Activities: This domain focuses on an individual's engagement in leisure activities and hobbies. It includes questions about participation in recreational activities, hobbies, social interactions, and overall satisfaction with leisure time. 7. Fears: This domain assesses the individual's fears and concerns related to sarcopenia, such as fear of falling or fear of losing independence (Beaudart et al., 2016).

Physical Performance

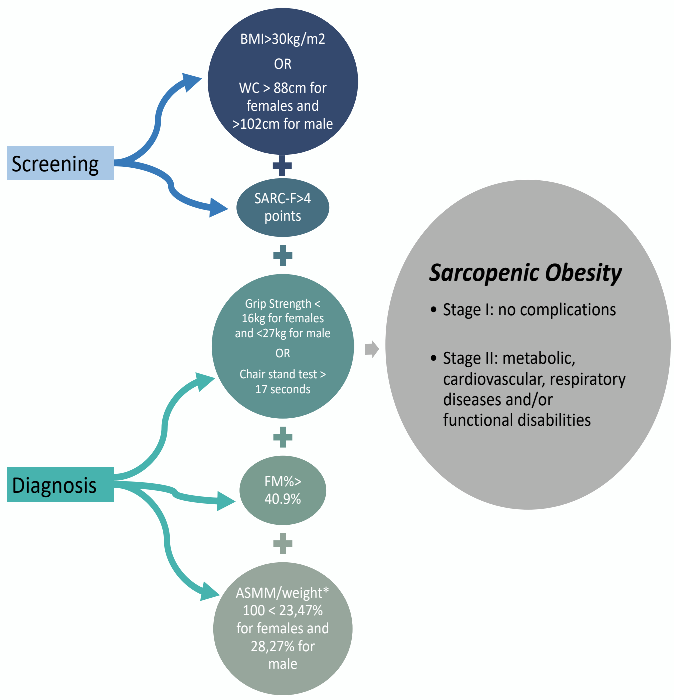
The 400-m walk test was used to measure walking ability and endurance. The participants were asked to complete 20 laps of 20 meters each as fast as possible and were allowed up to two rest stops during the test (Baroudi et al., 2020; Vestergaard et al., 2009). Low physical performance was considered when the test was not completed or when it took more than 6 minutes to complete (Cruz-Jentoft, Bahat, Bauer, Boirie, Bruyère, Cederholm, Cooper, Landi, Rolland, Sayer, Schneider, Sieber, Topinkova, Vandewoude, Visser, Zamboni, et al., 2019).

Diagnosis of Sarcopenia Obesity

Sarcopenia is diagnosed and considered severe when a high BMI or waist circumference combined with low muscle mass, low muscle strength and low physical performance are identified (Figure 4.3.1).

The first diagnostic criterion for sarcopenia is low muscle strength. Low muscle strength was defined as a handgrip strength of <27 kg for males and <16 kg for females (Dodds et al., 2014) and >17 s for the chair stand test (Cesari et al., 2009; Donini et al., 2022; Tsigos et al., 2011).

Figure 4.3.1. Algorithm based on the ESPEN-EASO criteria for sarcopenic obesity - adapted from (Donini et al., 2022)



Data collection

Data were collected at baseline and post-intervention by the same team, consisting of one specialist nurse, a surgeon, and an exercise physiologist. The participants completed the SarQoL questionnaire and underwent physical performance and muscle strength assessments at each time point.

Statistical methods

Data analysis was performed via Jamovi (version 1.6). Descriptive statistics were used to summarize the baseline characteristics. Categorical variables are expressed as frequencies and percentages, and continuous variables are expressed as the means and standard deviations. Data normality was assessed with the Shapiro–Wilk test and an independent t test or Mann–Whitney test to examine group differences. Differences between the intervention and control groups were assessed via independent t tests for continuous variables and chi-square tests for categorical variables. Reliability was analyzed according to internal consistency and considered acceptable when Cronbach's alpha was ≥ 0.7. Changes in SarQoL scores and secondary outcomes were analyzed via repeated-measures ANOVA. Correlation analyses explored the relationships between changes in SarQoL scores and physical performance measures. Statistical significance was set at $p < 0.05$.

Results

The baseline characteristics of the participants are presented in Table 4.3.1. The mean age of the participants was 46.9 years, with no significant difference between the intervention and control groups ($p = 0.071$). The sex distribution was 77.1% female and 22.9% male. Baseline SarQoL scores, physical function, muscle mass, and muscle strength were comparable between the two groups, indicating successful randomization.

Table 4.3.1. Baseline characteristics of the participants

Variables (Mean ± SE)	**Intervention Group n=19**	**Control Group n=16**	***p value***
Age (years)	43.7 ± 11.02	50.8 ± 11.29	0.071
Weight (kg)	118.3 ± 15.08	106.4 ± 17.99	**0.041**
BMI (kg/m^2)	43.2 ± 5.37	42.8 ± 5.05	0.825
Waist circumference (cm)	125.2 ± 10.27	123.5 ± 11.97	0.662
Body fat (%)	46.5 ± 5.92	47.6 ± 3.48	0.503
Total SMM mass (kg)	59.56 ± 8.67	53.46 ± 10.48	0.065
ASMM (kg)	24.86 ± 3.97	21.82 ± 5.28	0.061
ASMM/Weight (%)	21.1 ± 2.95	20.4 ± 2.30	0.442
BMC (g)	2.58 ± 0.39	2.32 ± 0.42	0.081
BMD (g/cm^2)	1.21 ± 0.16	1.14 ± 0.12	0.173
Total Body *T score*	0.55 ± 1.36	0.43 ± 1.47	0.812
Total Body *Z score*	0.41 ± 1.23	0.58 ± 1.07	0.647
Handgrip (kg)	28.02 ± 10.11	20.05 ± 6.48	**0.010**
30s Sit-to-stand test (n)	14.68 ± 2.95	12.25 ± 3.38	**0.029**
400-m walk test (min)	6.55 ± 2.85	7.49 ± 2.85	0.340
SarQoL overall score	70.1 ± 12.83	69.4 ± 10.60	0.861
SarQoL D1 Physical and mental health	83.1 ± 14.41	81.7 ± 13.78	0.769

SarQoL D2 Locomotion	70.3 ± 14.09	75.8 ± 11.71	0.227
SarQoL D3 Body composition	84.6 ± 10.90	83.3 ± 10.93	0.721
SarQoL D4 Functionality	75.2 ± 12.56	72.1 ± 11.91	0.471
SarQoL D5 Activities of Daily Living	61.0 ± 16.89	66.5 ± 18.21	0.361
SarQoL D6 Leisure activities	89.9 ± 19.56	94.5 ± 7.86	0.383
SarQoL D7 Fears	79.7 ± 9.22	77.1 ± 8.67	0.408

BMI: body mass index, SMM: skeletal muscle mass, ASMM: appendicular skeletal muscle mass, BMC: Bone mineral content, BMD: Bone mineral density

The primary outcome measure was the change in the SarQoL score from baseline to post-intervention. Reliability was analyzed according to internal consistency, and Cronbach's alpha was considered excellent (0.946). Compared with the control group, the intervention group presented significant improvements in SarQoL scores ($p < 0.001$) ($p=0.103$). The mean increase in the SarQoL score for the intervention group was 13.2 points, whereas the control group had a mean increase of 5.4 points. The group differences were significant, with a large effect size ($p=0.038$; $\eta 2=0.125$) (Table 4.3.2).

Table 4.3.2. Changes in SarQoL Scores

Time Point	Intervention Group	*p value*	Control Group	*p value*	*Group effect*	
Baseline	70.1 ± 12.8	< 0.001	69.4 ± 10.6	0.103	p value	0.038
Post-Intervention	83.3 ± 8.65		74.8 ± 8.71		Effect size	0.125

The comparative analysis of the changes after the exercise program (Table 4.3.3) revealed that participants in the intervention group demonstrated significant improvements in physical performance, as measured by the sit-to-stand and 400-m walk tests. The mean sit-to-stand score increased by 1.68 points in the IG compared with 0.41 points in the CG ($p=0.014$), and the 400-m walk test score increased by -1.18 points in the IG versus -0.04 points in the CG ($p=0.014$).

Handgrip strength improved significantly in the intervention group, with a mean increase of 2.39 kg, whereas the control group showed a mean increase of 1.29 kg ($p=0.012$).

The SarQoL questionnaire has different metric properties for all the items assessed. The overall SarQoL score significantly differed after the exercise program (p=0.038) (Figure 4.3.2) but also differed in two domains: domain 2—locomotion (p=0.094, η2=0.189) and domain 5—activities of daily living (p=0.005, η2=0.125), with a large effect size in both.

Figure 4.3.2. SarQol evolution

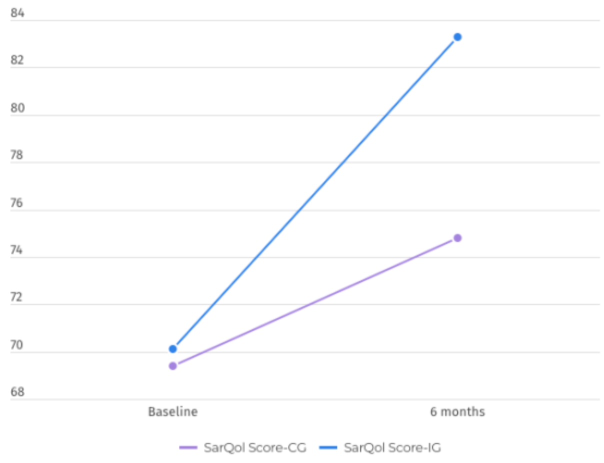


Table 4.3.3. Comparative analysis of variation after the exercise program

Variables (*Mean ± SE)	IG	CG	*Group Effect*	
			p value	*Cohen Effect size*
SarQoL overall score	13.2 ± 4.1	5.4 ± 1.9	**0.038**	0.125
SarQoL D1 Physical and mental health	-0.1 ± 2.2	-6.7 ± 1.1	0.238	0.042
SarQoL D2 Locomotion	16.0 ± 4.1	6.7 ± 1.2	**0.043**	0.094
SarQoL D3 Body composition	-3.0 ± 1.2	-10.3 ± 2.8	0.233	0.043
SarQoL D4 Functionality	12.8 ± 0.6	9,7 ± 0.4	0.455	0.017
SarQoL D5 Activities of Daily Living	17.4 ± 4.1	-0.7 ± 6.0	**0.009**	0.189
SarQoL D6 Leisure activities	-26.0 ± 6.3	-36.3 ± 14.1	0.177	0.055
SarQoL D7 Fears	18.3 ± 4.54	15.1 ± 1.43	0.319	0.030
Weight (kg)	-20.1 ± 9.18	-16.4 ± 4.36	0.198	-0.446
BMI (kg/m^2)	-7.33 ± 3.28	-6,73 ± 2.20	0.681	-0.141
Waist circumference (cm)	-14.9 ± 5.99	-12.3 ± 9.44	0.345	-0.325
Total Weight Loss (%)	16.7± 6.36	15.9 ± 5.08	0.841	0.069
Body fat (%)	-7.55 ± 4.22	-4.94 ± 4.90	0.126	-0.533
Total SMM mass (kg)	-4.97 ± 3.90	-3.36 ± 2.80	0.196	-0.448
ASMM (kg)	-18.3 ± 12.7	-21.9 ± 11.6	0.296	0.360

ASMM/Weight (%)	1.19± 2.46	-1.69 ± 4.10	0.141	0.512
Handgrip (kg)	2.39 ± 5.23	-1.29 ± 4.01	**0.012**	0.902
30s Sit-to-stand test (n)	1.68 ± 2.06	0.41 ± 1.42	**0.040**	-0.877
400-m walk test (min)	-1.18 ± 1.56	-0.04 ± 1.24	**0.014**	0.724

BMI: body mass index, SMM: skeletal muscle mass, ASMM: appendicular skeletal muscle mass

Discussion

This study aimed to explore the impact of exercise on HRQoL in bariatric patients via the SarQoL questionnaire.

Bariatric surgery, a significant intervention for treating severe obesity, aims not only to reduce weight but also to enhance overall quality of life (Sjöström, 2013). The effectiveness of bariatric surgery extends beyond physical health improvements to encompass psychological and social dimensions (Kolotkin & Andersen, 2017). Patient-reported outcome measures (PROMs), particularly HRQoL metrics, are essential tools for assessing these dimensions (Raoof et al., 2015). PROMs are instruments used to capture patients' perspectives on their health status, treatment efficacy, and overall well-being. These self-reported measures provide invaluable insights that complement clinical evaluations. HRQoL specifically focuses on aspects of quality of life directly related to health conditions and treatments, including physical functioning, mental health, and social interactions (Coulman et al., 2017).

HRQoL measures capture improvements in physical health, which include increased mobility, reduced pain, and increased energy levels. Patients often report significant gains in their ability to perform daily activities and exercise, which are critical positive indicators of surgery (Budin et al., 2024).

HRQoL is a comprehensive measure of the overall well-being of individuals, encompassing physical, psychological, and social domains. For bariatric patients, improving HRQoL is as important as achieving weight loss (Engel et al., 2005).

The results of this study indicate that a structured exercise program significantly improves HRQoL in bariatric patients diagnosed with sarcopenia, as measured by the SarQoL questionnaire (Beaudart et al., 2017). Compared with the control group, the intervention group experienced a substantial improvement in SarQoL scores, highlighting the positive impact of regular physical activity on various dimensions of quality of life, including physical and mental health, functionality, and social engagement.

These findings are consistent with previous research demonstrating the benefits of exercise in older adults and those with chronic health conditions. Exercise has been shown to enhance muscle strength, physical performance, and overall well-being, likely contributing to the observed HRQoL improvements (Steffl et al., 2017).

Several mechanisms may explain the beneficial effects of exercise on HRQoL in sarcopenic bariatric patients. First, resistance training increases muscle mass and strength, which are critical for maintaining physical function and reducing the risk of disability. Improved muscle function enables individuals to perform daily activities more efficiently and with less fatigue, leading to increased independence and quality of life (Nelson et al., 2007).

Second, aerobic exercise improves cardiovascular fitness and endurance, which can reduce the sensation of fatigue and improve overall energy levels (Newman et al., 2006). This increase in physical capacity may also enhance participation in social and recreational activities, contributing to better mental health and social well-being (Sjöström et al., 2004).

Third, flexibility and balance exercises help prevent falls and related injuries, which are common concerns in older adults with sarcopenia. By reducing the risk of falls, these exercises contribute to a greater sense of security and confidence in daily activities (Shumway-Cook et al., 1997).

Finally, regular exercise is associated with various psychological benefits, including reduced symptoms of depression and anxiety, improved mood, and better stress management. These mental health improvements likely play a significant role in the overall increase in HRQoL observed in the intervention group (Harper et al., 1998; Kubik et al., 2013).

Obesity is frequently associated with psychological issues, including depression, anxiety, and low self-esteem (Brazil et al., 2021). After surgery, many patients experience improvements in these areas, which are effectively captured through HRQL metrics. By evaluating changes in mental health status, PROMs help in understanding the psychological benefits of bariatric surgery, such as increased self-confidence, better body image, and reduced depression symptoms (Coulman et al., 2013; Mendes, Carvalho, Martins, et al., 2024).

The social implications of obesity, such as social stigma and isolation, can be profound. HRQL assessments after bariatric surgery often reveal improvements in social interactions and relationships (Tolvanen et al., 2021). Patients may experience increased social participation, better interpersonal relationships, and improved overall life satisfaction. These improvements are crucial for obtaining a holistic understanding of the impact of surgery on patients' lives (D. Wolf et al., 2008). PROMs provide an evaluation of bariatric surgery outcomes. By capturing the subjective experiences of patients, healthcare providers can tailor follow-up care and interventions to address specific needs and concerns. This personalized approach ensures that the treatment is not only clinically effective but also aligns with the patient's quality of life goals (Camolas et al., 2017).

The use of PROMs in post-surgery evaluations allows for long-term monitoring of patients' well-being. Regular HRQL assessments can help identify emerging issues or declining trends in health-related quality of life, prompting timely interventions (Coulman et al., 2016, 2020). Continuous monitoring supports sustained improvements and helps in managing any complications or psychosocial challenges that may arise. PROMs, particularly those measuring HRQL, are indispensable in evaluating the comprehensive outcomes of bariatric surgery. They provide critical insights into the physical, psychological, and social improvements experienced by patients, facilitating a holistic understanding of the impact of surgery (Mendes, Carvalho, Martins, et al., 2024). By integrating PROMs into post-surgical care, healthcare providers can enhance personalized care, ensure long-term support, and ultimately improve the overall success of bariatric interventions.

Conclusion

In conclusion, this study demonstrated that a structured exercise program significantly improved health-related quality of life in bariatric patients diagnosed with sarcopenia, as evaluated by the SarQoL questionnaire. These findings underscore the importance of incorporating regular physical activity into the management of sarcopenia to increase overall well-being and quality of life. Healthcare providers should prioritize the promotion and integration of exercise programs for sarcopenic populations to address this growing public health concern effectively.

The findings of this study have significant implications for clinical practice and public health policy. Given the substantial improvements in HRQoL observed with exercise interventions, healthcare providers should consider incorporating structured exercise programs into standard care for bariatric patients with sarcopenia. Exercise regimens should be tailored to individual capabilities and preferences, ensuring safety and adherence.

The healthcare system should support the development and implementation of community-based exercise programs for bariatric patients and individuals with sarcopenia. Providing accessible and affordable exercise options can help improve the overall quality of life in this population and reduce healthcare costs associated with sarcopenia-related complications. Additionally, research should examine the cost-effectiveness of exercise interventions in improving HRQoL and reducing healthcare utilization in sarcopenic populations, providing further evidence to support the widespread implementation of exercise programs.

Article 8 – Randomized Controlled Trial - **Interplay of physical exercise with leptin and ghrelin alterations after Roux-en-Y-gastric bypass in patients with sarcopenic obesity**

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Abstract

Introduction: Leptin and ghrelin are two hormones that play a role in weight homeostasis. Leptin, produced primarily by adipocytes and dependent on body fat mass, suppresses appetite and increases energy expenditure. Conversely, ghrelin is the "hunger hormone", it stimulates appetite and promotes fat storage. Bariatric surgery significantly alters the levels and activity of these hormones, contributing to weight loss and metabolic improvements. Clarifying the interplay between bariatric surgery, weight loss, physical exercise, leptin, and ghrelin is essential for developing comprehensive strategies for optimizing long-term outcomes for candidates for bariatric surgery, especially for sarcopenic patients.

Methods: This was a randomized controlled study with two groups (n=22). The patients in both groups have obesity and sarcopenia. A Roux-en-Y-gastric bypass (RYGB) procedure was performed in all patients. The intervention group participated in a structured exercise program three times per week beginning one month after surgery and lasting 16 weeks. Patient assessment was performed before surgery (baseline) and after completion of the exercise program. The control group received the usual standard of care and was assessed similarly.

Results: After surgery, weight, BMI and lean mass decreased significantly in both groups from baseline to the second assessment. Leptin was not significantly different from baseline to the second assessment in the physical exercise group but was significantly lower in the control group (p=0.05). Ghrelin increased over time in both groups, but the differences were not significant. When we associated leptin (the dependent variable) with weight (the independent variable), we found that lower weight was associated with lower leptin levels. A similar relationship was also observed between leptin and sarcopenia parameters (muscle strength and mass), as well as with bone health parameters (bone mineral density and t-score). Higher ghrelin levels were significantly associated with higher t-scores and z-score (p<0.05).

Conclusion: Exercise has been shown to significantly affect leptin and ghrelin levels after bariatric surgery. By incorporating regular physical activity into their lifestyles, bariatric patients can optimize their weight loss outcomes and improve their overall health. After the physical exercise protocol, patients in the intervention group revealed more established leptin levels, which may indicate a protected pattern concerning decreased leptin levels. An unfavorable profile was evidenced, according to which greater weight loss, sarcopenia, and osteoporosis were associated with lower leptin levels.

Keywords: exercise, bariatric surgery, leptin, ghrelin, sarcopenia, sarcopenic obesity

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Introduction

Obesity has become a significant public health challenge worldwide, with its prevalence rising steadily over the past few decades. The World Health Organization highlights obesity as a global health concern, affecting millions of individuals struggling to maintain a healthy weight (Bentham et al., 2017; Hämälaïnen et al., 2020).

Bariatric surgery is the most effective therapeutic approach for achieving significant and sustained weight loss in individuals with severe obesity. The surgical procedure facilitates weight loss and induces profound metabolic changes that improve or resolve obesity-associated conditions (Welbourn, Hollyman, et al., 2018).

The prevalence of sarcopenia conditions in patients with obesity varies between 10% and 50% (S. Yuan & Larsson, 2023). Post-bariatric surgery, patients with sarcopenic obesity face significant clinical challenges. Preoperative sarcopenia has been proven to be a good predictor of perioperative complications and death after major abdominal surgeries, and in older people the risk of cardiovascular events in the perioperative period increases (Ethgen et al., 2017; Prado et al., 2008).

Despite the undeniable benefits of bariatric surgery, understanding the underlying mechanisms that contribute to its success remains an active research area. The impact of this process on the complex hormonal regulation of appetite and metabolism is not fully understood. Hormonal alterations after surgery are of particular interest (Ionut et al., 2013; Rios et al., 2021).

Two such hormones, leptin and ghrelin, may play crucial roles in regulating energy appetite balance and body weight, and their levels can be significantly altered following bariatric surgery (Rios et al., 2021). Leptin, produced by adipose tissue, acts on the hypothalamus to suppress appetite and increase energy expenditure (Dorling et al., 2019). However, following bariatric surgery, significant weight loss often leads to decreased leptin levels, which can have profound implications for appetite regulation and metabolic function. This can lead to increased hunger and decreased energy expenditure, making it challenging to maintain weight loss (Matei et al., 2023).

Ghrelin, which is predominantly secreted by the stomach, has the opposite effect, stimulating appetite and promoting food intake. Alterations in leptin and ghrelin levels have been observed in individuals with obesity and after bariatric surgery, highlighting their importance in the physiological response to weight loss interventions (Matei et al., 2023; Serna-Gutiérrez et al., 2021).

Regular exercise is known to improve cardiovascular health, enhance metabolic function, and promote psychological well-being (Coleman et al., 2017; Kubik et al., 2013). In the context of bariatric surgery, exercise is recommended as a complementary intervention to maximize weight loss, maintain muscle mass and improve overall health outcomes. The interplay between exercise and hormonal changes after surgery, particularly concerning leptin and ghrelin, is an area that has garnered increasing scientific interest (Balaguera-Cortes et al., 2011).

Several studies have demonstrated the positive impact of exercise on hormone regulation after bariatric surgery (Ekici et al., 2023). Regular exercise could play an important role enhance leptin sensitivity, improving appetite control and metabolic function, also after bariatric surgery, contributing for the promotion of long-term weight maintenance (Matei et al., 2023). In some studies, exercise has been found to decrease ghrelin secretion and suppress appetite, leading to better control over food intake. By incorporating regular exercise into their routine, individuals who have undergone bariatric surgery could eventually better manage their ghrelin levels and reduce cravings for high-calorie foods (Thackray & Stensel, 2023).

Therefore, exercise has been shown to increase leptin sensitivity, decrease ghrelin secretion, and improve overall metabolic function (Bellicha et al., 2021). By engaging in regular exercise routines that include both aerobic and resistance training components, individuals may enhance their hormonal balance after surgery and increase sustainable weight loss efforts (Cornejo-Pareja et al., 2019).

However, the specific impact of exercise on leptin and ghrelin levels in individuals after bariatric surgery remains an area of active research. Understanding how exercise influences these hormonal changes can provide valuable insights into optimizing weight loss outcomes and preventing weight regain in bariatric patients.

Several mechanisms have been proposed to explain the potential effects of exercise on leptin and ghrelin regulation (Casimiro et al., 2019). Exercise-induced changes in body composition, such as increased muscle mass and reduced fat mass, may alter leptin sensitivity and secretion. Additionally, acute and chronic exercise modulate appetite-regulating hormones, including ghrelin, in both lean and patients with obesity. These physiological adaptations may contribute to the success of exercise interventions in promoting weight loss and long-term weight maintenance after bariatric surgery (Greenway, 2015).

The present study explored the effects of a regular exercise program on leptin and ghrelin levels in patients with sarcopenic obesity following bariatric surgery.

Methods

Study design

This study is part of the EXPOBAR protocol, NCT05289219 (Amaro Santos et al., 2023), which is ongoing in a single center for metabolic and bariatric surgery in Portugal (Amaro Santos et al., 2023; C. A. Santos et al., 2023).

Patients were randomized into a control group (CG) or an intervention group (IG) by either a bariatric surgeon or a sports specialist nurse. The data were collected from the hospital's electronic patient records.

The participants who agreed to participate in the study red and confirmed the free and informed consent form, which had been previously approved by the University and Hospital Ethics Committee (HESE_CE_1917/21).

Exercise training began one month after surgery, with a frequency of three times per week, up to a maximum of 55 minutes per session, for 16 weeks. This study included two evaluations, before surgery and after exercise training.

Eligibility criteria

The eligibility criteria included a body mass index (BMI) ≥40 kg/m^2 or BMI ≥35 kg/m^2 with at least one obesity-related comorbidity, age between 18 years and 60 years, a diagnosis of sarcopenic obesity based on the EASO/ESPEN criteria, no contraindication to exercise practice, and agreed to participate in the study. The exclusion criteria were patients with problems in locomotion, other previous bariatric surgery, and RYGB complications during surgery.

Sample size and randomization

This study is a secondary analysis of the registered randomized controlled trial NCT05289219 at Clinicaltrials.gov (Amaro Santos et al., 2023). Simple randomization with a random allocation rule was used to assign patients to the treatment groups to ensure equal group sizes at the end of the trial. Sequence generation was based on a random-number table.

Intervention

As a progressive combined exercise program, involves both aerobic and strength training. The exercise prescription was based on the FITT-VP principles (frequency, type, intensity, time, type, duration, volume, and progression) for people with obesity (*ACSM's Guidelines for Exercise Testing and Prescription*, n.d.; Burke et al., 2021; Bushman, 2014).

The goal of the program was to be completed in 16 weeks, three times a week, for 55 minutes per session, starting a month after surgery, in accordance with recommendations from the World Health Organization (WHO) (5) and the American College of Sports Medicine (ACSM) (Burke et al., 2021).

The participants in the IG completed the 16-week exercise training program. Each session was composed of 5 minutes of specific warm-up on a treadmill (a); (b) resistance training (weeks 1-4); (c) hypertrophy training (weeks 5-10); (d) strength training (weeks 11-16); and a 10-minute flexibility cool-down (myofascial release, mobility, static stretching, and dynamic stretching).

Interval training and circuit strength training methods were included in the first phase. The phases in the central block were increased by 10 minutes, followed by an assessment of the patient's response. To assess the perceived effort of the exercise performed, heart rate reserve and the Borg scale values were recorded, following a continuous progression (Castello et al., 2011).

Outcomes

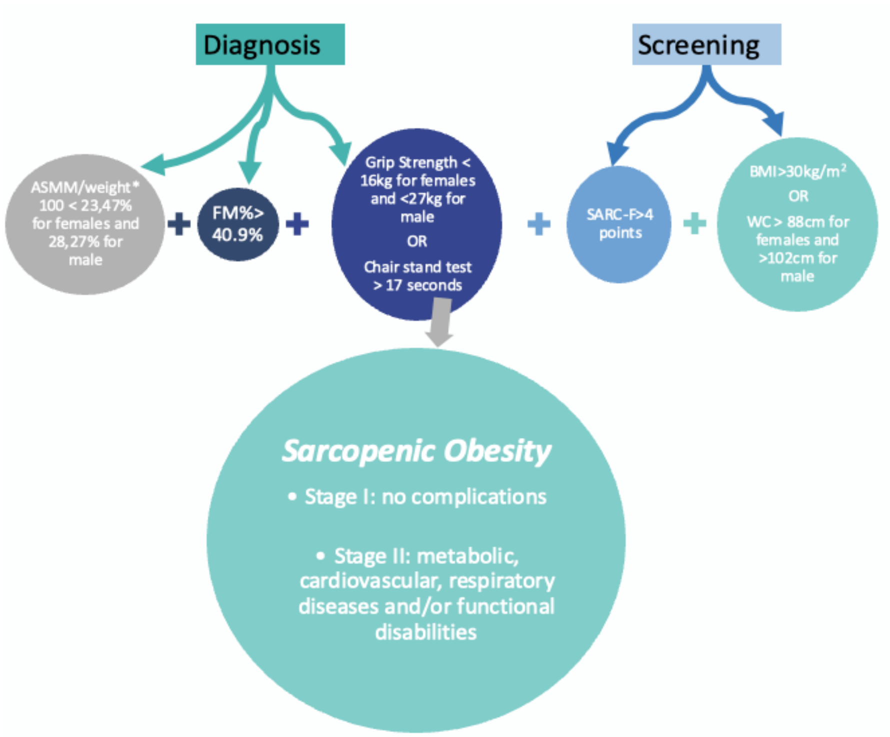
The details of the intervention have been described previously (Amaro Santos et al., 2023). Two assessment moments were performed, the first before surgery and the second after the exercise program. The CG participants were instructed to maintain their current activities. Data collection was carried out in two stages: baseline assessment and after 16 weeks of intervention.

Anthropometry and body composition: Weight (kg) and height (cm) were measured to calculate BMI (kg/m^2). Body composition was assessed via dual-energy X-ray absorptiometry (DEXA) (DXA, Hologic QDR, Hologic, Inc., Bedford, MA, USA). During this procedure, the participants were asked to fast and without metal items or adornments. It was also calculated the total weight loss percentage (%TWL) based on the initial weight and actual weight.

Perioperative blood samples - Leptin and ghrelin: Blood sampling was performed before surgery and after the exercise program completion. The fasting blood samples were collected and processed immediately according to the hospital protocol. The results were assessed one week later at the hospital database.

Sarcopenia: Sarcopenic obesity was defined as a high BMI or waist circumference combined with low muscle mass and low muscle strength (Figure 4.4.1) (Cesari et al., 2009; Donini et al., 2022; Tsigos et al., 2011).

Figure 4.4.1. Algorithm of Sarcopenic Obesity Diagnostic (Donini et al., 2022)



Statistical methods

Statistical analysis was conducted via JAMOVI version 2.3.19. Descriptive statistics was expressed as the mean ± standard deviation (SD) for parametric data and as the median ± standard deviation (SD). Data normality was assessed with the Shapiro–Wilk test and an independent t-test to examine group differences. The relative results were compared via the chi-square test or Fisher's exact test. Two-way ANOVA was used to compare the dependent variables, considering group and two-time points before and after the exercise program. Cohen's effect size was also calculated for the interaction of treatments. Relevance was interpreted as small (*d* = 0.2), medium (*d* = 0.5), or large (*d* = 0.8) (Cohen, 2013). Linear and logistic regression analyses were performed to analyze… Significance level was set at $p<0.05$.

Results

A total of 22 patients with sarcopenic obesity were randomized: 12 were assigned to the IG, and 10 were assigned to the CG. All patients in the IG completed the intended intervention. The baseline characteristics of the sample are summarized in Table 5.4.1. The baseline characteristics of both groups were similar, although there was a trend toward a difference towards weight in the IG (p=0.067).

Table 4.4.1. Baseline characteristics

Parameter (Mean ± SD)	**Intervention Group n=12**	**Control Group n=10**	***p value***
Sex (% female)	75%	90%	0.388
Age (years)	44.08 ± 13.2	50.4 ± 11.1	0.240
Weight (kg)	117.1 ± 15.8	103.6 ± 16.9	0.067
BMI (kg/m^2)	43.1 ± 5.17	41.8 ± 3.40	0.388
Leptin (ng/mL)	54.6 ± 29.75	50.9 ± 28.47	0.355
Ghrelin (pg/mL)	811 ± 762.72	1261 ± 1424	0.773

BMI: Body mass index

Significant weight loss was observed in both groups (Table 4.4.2). The intervention group experienced a smaller effect size for weight reduction (*d*=0.425).

Physical function, as evaluated by a handgrip dynamometer, decreased significantly in the CG. In the IG, the difference was not significant. For this sarcopenic parameter, the impact of exercise intervention was significant (*p*=0.050; *d*=0.500). Similar results were obtained for BMC, with a significant impact and large effect size of the exercise (*p*=0.004; *d*=0.733).

4.4.2. Main outcomes

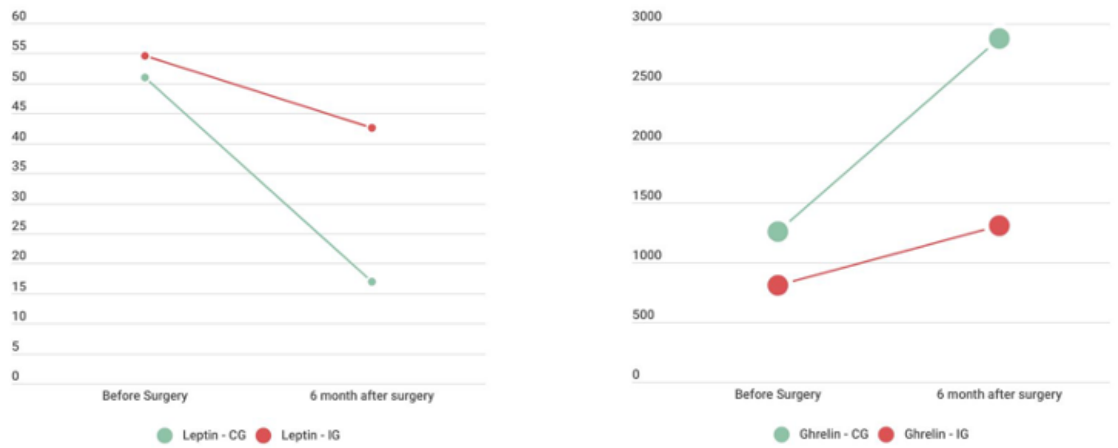
	Baseline		***6 months***		***Sig.***	***d***
	CG	***IG***	***CG***	***IG***		
Weight (kg)	103.55 ± 16.86	117.08 ± 15.79	**73.5 ± 13.2**[a]	**83.0±12.4**[a]	*p= 0.099*	*0.425*
BMI (kg/m²)	41.8 ± 3.40	43.10 ± 5.17	**29.4 ± 2.62**[a]	**30.6 ± 4.37**[a]	*p= 0.821*	*0.067*
Leptin (ng/mL)	50.9 ± 28.47	54.6 ± 29.75	**17.0 ± 18.0**[a]	42.5 ± 44.1	***p= 0.050***	***0.013***
Ghrelin (pg/mL)	1261 ± 1424	811 ± 762.72	2870 ± 2230	1311 ± 968	*p= 0.175*	*0.067*
Body fat (%)	46.60 ± 3.23	46.7 ± 6.47	**39.5 ± 5.91**[a]	**37.2 ± 8.02**[a]	*p= 0.107*	*0.417*
Handgrip (kg)	20.60 ± 7.18	25.5 ± 6.87	**16.4 ± 5.79**[a]	22.2 ± 7.09	***p= 0.050***	***0.500***
Lean mass (kg)	53.45 ± 12.48	58.19 ± 8.02	**45.23 ± 11.47**[a]	**43.38 ± 9.07**[a]	*p= 0.456*	*0.200*
BMC (kg)	2.33 ± 0.44	2.50 ± 0.37	**1.96 ± 0.17**[a]	2.42 ± 0.37	***p= 0.004***	***0.733***
BMD (g/cm2)	1.14 ± 0.13	1.21 ± 0.17	1.10 ± 0.08	1.16 ± 0.12	*p= 0.276*	*0.283*
Total Body T score	0.43 ± 1.51	0.54 ± 1.51	-0.07 ± 0.68	0.76 ± 1.23	*p= 0.306*	*0.267*
Total Body Z score	0.55 ± 1.14	0.49 ± 1.22	0.15 ± 0.46	0.49 ± 1.23	*p= 0.842*	*0.058*

BMI: Body mass index; BMD: Bone mineral density; BMC: Bone mineral content

[a] Post hoc significance between evaluations, p<0.001; *d*= Cohen effect size; *sig*= group effect

After RYGB, ghrelin levels increased, but the difference from baseline reached significance in 6 months. The results in fasting ghrelin concentrations are different between groups but not significant at the final time point. Fasting leptin levels decreased significantly at six months in the CG but not in the IG, which is a potential indicator of exercise benefits. This difference was statistically significant between the two groups (Figure 4.4.2).

Figure 4.4.2. Leptin and Ghrelin evaluation after surgery and post-proposed exercise program



Associations between leptin and ghrelin levels and clinical variables related to sarcopenic obesity parameters were examined via multivariable linear regression. We found that weight (r=0.475; p=0.009), BMI (r=0.625; p=0.022), bone mineral density (r=0.709; p=0.011), muscle mass and strength (r=0.689; p=0.014), and *t scores* (r=0.510; p=0.045) were positively associated with leptin levels. The *t score* (CG: r=0.578, p=0.040; IG: r=0.640, p=0.012) and *z score* (CG: r=0.673, p=0.016; IG: r=0.628, p=0.014) were positively correlated with ghrelin levels (Table 4.4.3).

Table 4.4.3. Analysis between variables and leptin and ghrelin levels after exercise

	Leptin (ng/mL)				***Ghrelin (pg/mL)***			
	CG		***IG***		***CG***		***IG***	
	r	***p value***	***r***	***p value***	***r***	***p value***	***r***	***p value***
Age (years)	-0.384	0.921	-0.369	0.903	-0.088	0.622	-0.059	0.579
%TWL (%)	-0.518	0.937	0.194	0.273	0.353	0.159	0.314	0.160
Weight (kg)	**0.475**	**0.009**	0.102	0.376	0.356	0.156	-0.145	0.673
BMI (kg/m²)	**0.625**	**0.022**	0.051	0.431	0.137	0.353	-0.167	0.716
Body fat (%)	0.359	0.154	0.225	0.241	0.230	0.205	0.040	0.245
Handgrip (kg)	**0.689**	**0.014**	-0.068	0.658	0.027	0.470	-0.097	0.618
Lean mass (kg)	**0.718**	**0.010**	-0.316	0.841	**0.502**	**0.028**	-0.151	0.680
BMC (g)	0.144	0.304	-0.094	0.561	0.348	0.162	-0.084	0.612
BMD (g/cm2)	**0.709**	**0.011**	-0.008	0.510	0.341	0.167	0.208	0.258
Total Body T score	0.171	0.319	**0.510**	**0.045**	**0.578**	**0.040**	**0.640**	**0.012**
Total Body Z score	0.197	0.293	0.283	0.186	**0.673**	**0.016**	**0.628**	**0.014**

BMI: Body mass index; BMD: Bone mineral density; BMC: Bone mineral content; TWL: Total weight loss.

r: Pearson coefficient; Significance defined as p<0.05

Discussion

This study aimed to explore the impact of exercise on the regulation of leptin and ghrelin in sarcopenic obesity individuals who have recently undergone bariatric surgery. Our results show that exercise directly influences leptin sensitivity and can contribute to stabilizing ghrelin levels, suggesting a promising complementary approach to optimizing post-operative outcomes.

We anticipate that this study's findings provide novel insights into how exercise modulates leptin and ghrelin levels in patients who have undergone bariatric surgery. Specifically, we expect improvements in leptin sensitivity and reduced ghrelin levels due to exercise interventions (Matei et al., 2023). These hormonal changes likely enhance appetite control, increase energy expenditure, and improve weight loss maintenance (van de Laar et al., 2018).

Previous studies have already shown that the significant weight loss induced by bariatric surgery results in a reduction in leptin levels, an expected effect due to the decrease in fat mass, the main producer of this hormone (Mendes, 2023; Mendes, Carvalho, Bravo, et al., 2024; Mohammadi et al., 2024). This reduction is expected and correlates with weight loss. However, the role of exercise in modulating leptin levels after bariatric surgery has different interpretations (Rios et al., 2021). In this study, leptin levels decreased significantly in the CG. In the IG, it was firmly established that weight loss positively improves leptin sensitivity, and that exercise plays a crucial role in regulating this mechanism. The stabilization of leptin levels in the intervention group suggests that exercise plays a protective role, preventing abrupt drops in leptin, which could make it difficult to maintain weight loss and affect appetite control in the long term. Min et al. revealed that 2 years after bariatric surgery, greater weight loss was associated with a greater reduction in leptin, but there was no effect on adiponectin levels after 4 years of follow-up (de Assis & Murawska-Ciałowicz, 2023; Min et al., 2020).

However, several studies have demonstrated that exercise can influence leptin levels independent of weight loss (de Assis & Murawska-Ciałowicz, 2023; Min et al., 2020). Exercise is known to improve leptin sensitivity, which can be diminished in individuals with obesity due to leptin resistance. This improvement in leptin sensitivity means that the body can respond more effectively to hormones, potentially enhancing appetite regulation and energy balance. The results of this research help elucidate how exercise impacts leptin levels and sensitivity in post-bariatric surgery patients, which is essential for developing comprehensive postoperative care strategies that optimize long-term weight loss and metabolic health.

Unlike leptin, ghrelin levels increase before meals and decrease afterward, reflecting its role in meal initiation (Kojima et al., 1999; Mohammadi et al., 2024). Bariatric surgery, particularly procedures that involve significant anatomical changes to the stomach, such as sleeve gastrectomy and RYGB, drastically alters ghrelin production.

The impact of RYGB on ghrelin concentrations has been widely studied, with controversial results (Kojima et al., 1999). Some groups report a significant decrease in ghrelin levels after RYGBP (Frühbeck, Diez-Caballero, et al., 2004; Frühbeck, Rotellar, et al., 2004; Kojima et al., 1999). These low levels of ghrelin after RYGB could determine increased satiety and reduced food intake, helping to explain the long-term effects this surgery has on patients with severe obesity. However, other studies have not reported changes in ghrelin after RYGB, suggesting that it is unlikely to contribute to suppressing food intake in the postoperative stage (Karamanakos et al., 2008; Kruljac et al., 2016). In accordance with the results of this study, some studies have reported higher ghrelin concentrations after RYGBP than before surgery (Alamuddin et al., 2017; Tsouristakis et al., 2019).

In addition, the association between higher ghrelin levels and higher BMD and T and Z scores in our study raises important questions about the role of this hormone in preserving bone health after bariatric surgery. The existing literature shows controversial results regarding changes in ghrelin levels after bariatric surgery, with some studies reporting a decrease in levels and others, like ours, showing an increase. This variability can be explained by methodological differences between studies, including the type of surgery, the length of follow-up and the characteristics of the population studied.

Physical exercise, especially resistance training and combined aerobics, has been shown to have important effects on hormone regulation, which included profound effects on ghrelin levels. Acute bouts of exercise generally reduce ghrelin concentrations, which may help suppress appetite postexercise. In our study, the intervention group showed an attenuation in the increase in ghrelin compared to the control group. Although the increase in ghrelin is expected due to the body's adaptation to weight loss, the fact that the intervention group showed a less pronounced increase suggests that exercise can modulate ghrelin secretion and help control appetite. Regular exercise may, therefore, play an important role in preventing weight regain after surgery, contributing to appetite control and improving satiety in the long term (Dorling et al., 2019; Ouerghi et al., 2021). Regular exercise training, however, has a more nuanced adaptation concerning ghrelin regulation (Ouerghi et al., 2021), which can vary depending on the intensity and duration of the exercise regimen. Investigating how different types and intensities of exercise influence ghrelin levels in the context of bariatric surgery is crucial for understanding the hormonal adaptations that support weight loss and maintenance.

The leptin produced in adipocytes seems to be related to sarcopenic obesity, as it can reduce the capacity of myocytes for protein synthesis (Malin et al., 2020); however, the evidence concerning muscle strength is inconsistent (Gunton & Girgis, 2018). In this study, the results revealed that a decrease in leptin was associated with a reduction in muscle strength, which may suggest that patients who have already been diagnosed with obesity-related sarcopenia and who, after bariatric surgery, have a more significant decrease in muscle strength have a greater decrease in leptin levels and, consequently, satiety levels, which may prone them to weight gain in the long term.

The effects of leptin on bone mass and the regulation of bone metabolism are also unclear (Matos et al., 2020; Zhang et al., 2023). Current results indicate that a greater decrease in leptin levels is associated with a significant reduction in bone mineral content, although this effect was less pronounced in the exercise group. This demonstrates the protective effect of exercise, with minimal impact on the t score and z score. This allows us to corroborate the results reported by Mohammadi et al. that leptin can be an important biomarker for diagnosing osteoporosis (Mohammadi et al., 2024).

The protective effects of exercise observed in our results also extend to preserving muscle strength and lean mass. The association between decreased leptin and reduced muscle strength in the control group suggests that excessive loss of leptin may be related to loss of muscle mass, particularly in sarcopenic patients. These findings reinforce the importance of including a post-surgical exercise program to prevent muscle deterioration and maintain physical functionality. Similarly, the preservation of bone mineral density in the intervention group indicates that physical exercise may be a protective factor against osteoporosis in patients undergoing bariatric surgery, as suggested in other studies.

Finally, our results offer a promising insight into the role of exercise in hormonal modulation after bariatric surgery. The positive impact of exercise on leptin and ghrelin optimizes weight loss. It can improve patients' quality of life by helping to control appetite, maintain muscle mass and preserve bone health. These findings reinforce the need to routinely include structured exercise programs in the postoperative care of bariatric patients, especially those with sarcopenic obesity.

This study has limitations, such as the small sample size and the limited follow-up time. Future studies should involve a larger sample size and a longer intervention period to assess the sustainable effects of exercise on hormone levels and their correlation with weight loss maintenance and long-term metabolic health. In addition, exploring different types and intensities of exercise may provide additional insights into the best approach to optimizing post-surgical hormone regulation.

Conclusion

Bariatric surgery represents a powerful tool in the fight against obesity, offering significant and sustained weight loss for individuals with severe obesity. However, the success of this intervention depends on a comprehensive approach that includes lifestyle modifications such as exercise. The hormonal adaptations induced by exercise, particularly leptin and ghrelin may be critical to understanding and optimizing postoperative outcomes.

Exercise has been shown to have a significant effect on leptin and ghrelin levels after bariatric surgery. By incorporating regular physical activity into their lifestyle, bariatric patients can optimize their weight loss outcomes and improve their overall health. Further research is needed to fully understand the mechanisms by which exercise influences hormone regulation post-surgery, but current evidence suggests that physical exercise could be a key to long-term success in bariatric patients.

Article 9 – Randomized Controlled Trial - **The impact of bariatric surgery and exercise on Systemic Immune Inflammation Index in patients with sarcopenia obesity**

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Abstract

Introduction: Obesity's contribution to inflammation is an influential factor in the progression of obesity-associated medical issues. Metabolic and bariatric surgery has been proven effective in obtaining weight loss and remission of associated conditions. The Systemic Immune Inflammation Index (SII) was developed to offer more comprehensive data on inflammation and is presented as a prognostic indicator regarding many adverse conditions. The present study aimed to investigate the association between SII and bariatric surgery in patients with sarcopenic obesity and evaluate the eventual impact of exercise on SII.

Methods: All participants were sarcopenic patients with obesity, underwent bariatric surgery - RYGP - and were randomized to participate in a structured physical exercise or to control group. The assessments were performed following standardized procedures, with the data evaluated during routine clinic follow-up at preoperative and 20-weeks postoperative after the exercise program. **Results:** At baseline, before surgery, patients in both groups had similar anthropometrics, body composition, muscle strength variables and percentage of comorbidities. SII was also similar in both groups. To better understand

the association of SII with the different variables, a Pearson correlation test was performed at baseline using SII. There was an inverse association of SII with BMC, handgrip strength and ASMM at baseline, which was maintained 5 months after surgery. At the end of the study, the combined results of the two groups showed that weight, BMI, % of body fat, muscle mass and muscle strength, the 30s sit-to-stand test and bone mineral density all decreased significantly as expected, along with the SII. also decreased significantly. The intervention group showed higher ASMM, handgrip strength, 30s Sit-to-stand test and 400-m walk test and bone mineral density when compared with the control group. However, SII showed no difference between both groups ($p>0.05$).

Discussion: The results of the current research show a positive impact of bariatric surgery on weight and associated conditions control and a negative impact on muscle mass and function. SII responded very favorably to surgery with or without exercise, with a clear decrease in its score. Higher SII is associated with lower muscle mass and function, and this may be a reflex of the compromise that obesity causes on health, in this case, increasing systemic inflammation and decreasing muscle mass and function. The role of physical exercise in the management of surgical bariatric patients is still not clear. After surgery, the patients in the physical exercise program group had better results in muscle mass and function when compared to the patients in the control group (without exercise). However, there were no differences in SII score between the two groups, which may be interpreted as a lack of positive effect of physical exercise *per se* in the short-term on the systemic inflammatory condition present in obesity.

Keywords: Bariatric surgery, Obesity, Systemic immune-inflammation index, Inflammation, sarcopenia obesity

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Introduction

The World Health Organization (WHO) defines obesity as abnormal or excessive fat accumulation that poses a risk to health (*WHO | World Health Organization*, n.d.). Obesity not only causes serious economic costs but also increases the risk of several medical conditions, such as hypertension, diabetes, and obstructive sleep apnea (Hämälaïnen et al., 2020). This chronic inflammation contributes to the progression of various diseases. The association between obesity and chronic low-grade inflammation, known as meta inflammation, is well-documented. Consequently, there is a growing interest in developing strategies to preventing the onset and progression of obesity-related diseases (Morabia & Abel, 2006).

Metabolic and bariatric surgery provide long-term effectiveness in weight loss and yielded satisfactory results in the remission of comorbid diseases that are associated with cardiovascular risk and obesity (Peluso & Vanek, 2007; C. Santos, Carvalho, et al., 2022; Shah et al., 2006). The American Society of Metabolic and Bariatric Surgery (ASMBS) and the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) recommend MBS in individuals with a body mass index (BMI) >35 kg/m2, regardless of the presence and severity of comorbidities (*2022 ASMBS and IFSO: Indications for Metabolic and Bariatric Surgery | American Society for Metabolic and Bariatric Surgery*, n.d.; Aminian et al., 2018).

The Systemic Immune-Inflammation Index (SII), a novel measure for inflammation, was created by Hu et al. in 2014 (Hu et al., n.d.) and is a multi-marker index that provides a comprehensive assessment of the systemic immune-inflammatory response in the human body (Sun et al., 2024). This index is a combination of independent white blood cells and platelets and is believed to reflect the interaction between thrombocytosis, inflammation, and immunity (J. Zhao et al., 2023) predicts poor prognosis for various medical conditions and patient recurrence and survival post-surgeries (Sun et al., 2024). Studies show that the SII objectively reflects inflammation-immunity balance in malignant tumor patients (Crusz & Balkwill, 2015; H. Zhao et al., 2021) and is a prognostic indicator (Guthrie et al., 2013). Elevated SII levels have been associated with worse prognoses for several medical conditions and higher mortality in patients with cancer and cardiovascular disease (Ye et al., 2023). Some studies have suggested that SII serves as a marker of chronic inflammation (Yang et al., 2024).

Sarcopenia, the age-related loss of skeletal muscle mass and function, has emerged as a significant public health concern in our aging global population (Cruz-Jentoft et al., 2010). This progressive condition not only impacts physical performance and quality of life but also increases the risk of adverse health outcomes, including falls, fractures, and mortality (Minniti et al., 2022). As researchers strive to understand the complex pathophysiology of sarcopenia, attention has been increasingly focused on the role of chronic low-grade inflammation, often referred to as inflammation, in its development and progression (Dalle et al., 2017).

While initially developed and validated in oncology settings, the potential utility of SII in age-related conditions like sarcopenia is now being explored. The relationship between inflammation and sarcopenia is multifaceted, involving complex interactions between pro-inflammatory cytokines, oxidative stress, and muscle protein metabolism (Antuña et al., 2022). Chronic inflammation has been implicated in promoting muscle catabolism, impairing muscle protein synthesis, and interfering with muscle regeneration processes. Given these connections, the SII may offer valuable insights into the inflammatory status of individuals at risk for or already experiencing sarcopenia (Xie & Wu, 2024).

The complex interplay between physical activity and the immune system has also been a subject of increasing interest in recent years. As researchers continue to unravel the multifaceted effects of exercise on human health, attention has turned to various biomarkers that may provide insights into the body's inflammatory and immune responses to physical exertion (Matei et al., 2023). Initially developed in the context of cancer prognosis, the SII has since been explored in various other health conditions, including cardiovascular diseases and metabolic disorders. However, its potential role in exercise physiology and sports medicine remains relatively unexplored.

Exercise is known to induce acute and chronic changes in the immune system, with effects varying based on its intensity, duration, and type of physical activity (Scheffer & Latini, 2020). Understanding these changes through easily accessible biomarkers like the SII could provide valuable insights into exercise-induced inflammation, recovery processes, and potential long-term health implications of different exercise regimens (Kurowski et al., 2022).

In the present study, the purpose was to investigate the impact of bariatric surgery in the Systemic Immune Inflammation Index in Sarcopenic Obesity patients and study the impact of exercise on the SII.

Methods

Study Design and Data Collection

This study is part of the EXPOBAR protocol, performed at a single center of Bariatric and Metabolic Surgery, involving the Hospital (ULSAC) and the University (ESDH-CHRC). The study was previously described and registered with the document number NCT05289219. The complete protocol has been described previously (C. Amaro Santos et al., 2023).

The indication for surgery was based on the indications recommended by the ASMBS and IFSO. All surgical procedures were performed laparoscopically by the same surgeon. A bariatric surgeon and a sports specialist nurse randomly assigned patients to the Control Group (CG) and Intervention Group (IG).

A sports specialist nurse carried out the two evaluations before the surgery and after the exercise program had been completed. Data was obtained from the hospital's electronic database and collected in two stages: baseline evaluation and after completing the proposed exercise program.

Eligibility criteria

The eligibility criteria were BMI ≥40 kg/m^2 or BMI ≥35 kg/m^2 with at least one comorbidity associated with sarcopenic obesity, age between 18 years and 60 years, with no without contraindication to exercise practice, candidates for bariatric surgery that agreed to participate in the study. The exclusion criteria were patients with problems in locomotion, previous bariatric surgery, and bariatric surgery complications.

Intervention

The exercise program was designed to be a progressive combination of aerobic and strength training. It includes specific recommendations for the frequency, type, intensity, time, duration, volume, and progression (FITT-VP) (Bushman, 2014). The program aimed to be completed over 16 weeks, with sessions scheduled three times a week for 55 minutes each, beginning one month after the surgery, in line with the guidelines from the World Health Organization (WHO) (Hämälaïnen et al., 2020) and the American College of Sports Medicine (ACSM) (Burke et al., 2021).

Data Collection

The sociodemographic characteristics, perioperative comorbidities (diabetes, hypertension, dyslipidemia, OSAS, fibromyalgia, osteoporosis, DRGE, depression), blood tests and body composition were assessed. The data was retrieved from the hospital's electronic database. DEXA, handgrip test, 400-m walk test and 30s Sit-to-stand test, were evaluated in the Exercise and Health laboratory of the School of Health and Human Development of the University of Évora.

Primary Outcome

The primary aim of this study was to investigate the association between Systemic Immune Inflammation Index and bariatric surgery in sarcopenic patients.

Secondary Outcome

The secondary outcome of the present study was to evaluate the impact of exercise on SII after bariatric surgery.

Variables

Anthropometry and body composition: Anthropometric measurements of weight (in kilograms) and height (in centimeters) were taken, and the BMI was calculated. The participants' body composition was assessed using Dual-energy X-ray absorptiometry (DEXA or DXA) with the Hologic QDR system from Hologic, Inc., based in Bedford, MA, USA. During the DEXA procedure, participants were required to fast and abstain from wearing any metal items or jewelry. Additionally, the study analyzed the total weight loss percentage (%TWL) by comparing participants' initial and end of the study weights.

Preoperative blood tests: Preoperative blood tests were collected to analyze markers associated with obesity. These blood tests were performed both before surgery and after the exercise program. According to the hospital's protocol, the first sample was taken in the week of preparation for surgery, and the second was obtained after the end of the exercise program.

Systemic Immune Inflammation Index – SII: Platelet (PLT) count, neutrophil (NEU) count and lymphocyte (LYN) count (expressed as $\times 10^3$ cells/µl) were measured by hematology analyzers and validated by a pathologist. The following formula was utilized to calculate SII= (PLT count × NEU count)/LYN count (Xie & Wu, 2024).

Sarcopenic obesity: Sarcopenic Obesity according to European Association for the Study of Obesity/ European Society for Clinical Nutrition and Metabolism (EASO/ESPEN) and Foundation for the National Institutes of Health (FNIH) use the consensus statement parameters of BMI, waist circumference (WC), and Appendicular Skeletal Muscle Mass (ASMM) based on weight and BMI (BMI > 30 kg/m2, WC ≥ 102 cm for males and ≥ 88 cm for females, and ASMM/Weight < 28.27% for males and < 23.47% for females, ASMM/BMI < 0.789 for males and < 0.512 for females) were added to the preceding values for Sarcopenic Obesity (Donini et al., 2022; Studenski et al., 2014).

Statistical analysis

Parameters and outcomes were determined by statistical analysis using the computer software JAMOVI version 2.3.19. In descriptive statistics, mean ± standard deviation (SD) was used for parametric data, while median ± standard deviation (SD) was used for non-parametric data. Data normality was checked using the Shapiro-Wilk test, and group variances were examined with an independent t-test. Percentages were compared using the Chi-square test or the exact Fisher test. Dependent variables were compared using a two-way ANOVA and logistic regression analyses, considering group and two-time points before and after the exercise program.

Results

A total of 35 patients were enrolled in this study. All patients met criteria for sarcopenic obesity ads received a RYGP. The preoperatory weight of patients was 113 ± 17.3 kg, mean age was 46.9 ± 11.5 years and mean BMI was 43 ± 5.2. Diabetes was present in 17.1% of the patients, Dyslipidemia in 25.7%, and Hypertension was present in 68.6% of the participants. Baseline characteristics and clinical data of the participants are given in Table 4.5.1.

Table 4.5.1. Sample baseline characteristics before surgery

Variables (Mean ± SE)	**Total n=35**	**IG n=19**	**CG n=16**	***p-value***
Age (years)	46.9 ± 11.5	43.7 ± 11.02	50.8 ± 11.29	0.071
Weight (Kg)	113 ± 17.3	118.3 ± 15.08	106.4 ± 17.99	0.041
BMI (kg/m^2)	43.0 ± 5.16	43.2 ± 5.37	42.8 ± 5.05	0.825
Waist circumference (cm)	124 ± 10.9	125.2 ± 10.27	123.5 ± 11.97	0.662
Body fat (%)	47.0 ± 4.92	46.5 ± 5.92	47.6 ± 3.48	0.503
Total SMM mass (Kg)	56.7 ± 10.06	59.56 ± 8.67	53.46 ± 10.48	0.065
ASMM (Kg)	23.5 ± 4.79	24.86 ± 3.97	21.82 ± 5.28	0.061
ASMM/Weight (%)	20.8 ± 2.66	21.1 ± 2.95	20.4 ± 2.30	0.442

BMC (g)	2.47 ± 0.42	2.58 ± 0.39	2.32 ± 0.42	0.081
BMD (g/cm^2)	1.18 ± 0.15	1.21 ± 0.16	1.14 ± 0.12	0.173
Total Body *T-score*	0.50 ± 1.39	0.55 ± 1.36	0.43 ± 1.47	0.812
Total Body *Z-score*	0.49 ± 1.15	0.41 ± 1.23	0.58 ± 1.07	0.647
Handgrip (Kg)	25.6 ± 9.42	28.02 ± 10.11	20.05 ± 6.48	0.010
30s Sit-to-stand test (n)	13.6 ± 3.34	14.68 ± 2.95	12.25 ± 3.38	0.029
400-m walk test (min)	6.98 ± 2.85	6.55 ± 2.85	7.49 ± 2.85	0.340
SII	504 ± 240	455 ± 136	563 ± 318	0.189
Glycemia (mg/dl)	99.3 ± 17.8	101 ± 22.3	97.6 ± 10.7	0.601
HbA1c (%)	4.83 ± 2.44	5.05 ± 2.58	4.56 ± 2.31	0.561
LDL (mg/dl)	174 ± 36.1	173 ± 40.2	175 ± 31.7	0.820
Triglycerides (mg/dl)	137 ± 56	132 ± 56.6	143.9 ± 56.4	0.524
HDL (mg/dl)	45.5 ± 15.5	46.4 ± 15.7	44.4 ± 15.7	0.820

BMI: Body Mass Index, SMM: Skeletal Muscle Mass, ASMM: Appendicular Skeletal Muscle Mass, ASMMI: Appendicular Skeletal Muscle Mass Index, HbA1c: Glycated Haemoglobin, SII: Systemic immune-inflamatory index, LDL: Colesterol, HDL: Colesterol

The changes in the inflammatory indicators over time were examined in all patients, before surgery and at the end of the study (table 4.5.2). A statistically significant decrease and large effect size was detected for anthropometric, body composition and osteoporosis parameters (p<0.001; d>0.8), but also in physical strength evaluated by handgrip (p<0.001; d=0.75) and sit-to-stand test (p=0.011; d=0.46). Overall, the 400-m walk test did not show differences after surgery, but the group who performed exercise had significant improvements (p=0.002) when compared with the control group. Several obesity-associated diseases significantly improved, such as Diabetes (glycemia) and Dyslipidemia (LDL and triglycerides) parameters (p=0.004; p=0.026), but HbA1c did not have significant differences after surgery in any group.

A statistically significant decrease was detected in SII at the end of the study compared to the preoperative values (p=0.024) with no differences between the exercise and control groups (p=0.462). The IG also significantly improved muscle mass (p=0.034), bone mineral content (p<0.001), and physical function (p=0.002) when compared with CG (table 4.5.3)

Table 4.5.2. Comparative analysis

Variables (Mean ± SE)	*Surgery Effect*			
	Before Surgery	*After Surgery*		
	Total sample n=35	Total sample n=35	*p-value*	*Effect size (d)*
Weight (Kg)	112.8 ± 17.3	80.0 ± 13.3	<0.001	3.96
BMI (kg/m²)	42.0 ± 5.16	29.5 ± 4.27	<0.001	4.32
Waist circumference (cm)	124.4 ± 10.9	97.5 ± 10.6	<0.001	2.93
Body fat (%)	47.0 ± 4.92	38.6 ± 7.37	<0.001	1.63
Total SMM mass (Kg)	56.69 ± 10.1	46.01 ± 9.33	<0.001	2.80
ASMM (Kg)	23.47 ± 4.80	19.10 ± 4.18	<0.001	3.18
ASMM/Weight (%)	20.8 ± 2.66	24.0 ± 3.88	<0.001	-1.37
BMC (g)	2.47 ±0.42	2.26 ± 0.41	<0.001	0.83
BMD (g/cm²)	1.18 ± 0.15	1.12 ± 0.12	<0.001	0.61
Total Body *T-score*	0.50 ± 1.39	0.27 ± 1.13	0.175	0.23
Total Body *Z-score*	0.49 ± 1.15	0.32 ± 0.87	0.126	0.27
Handgrip (Kg)	23.5 ± 9.42	21.1 ± 18.4	<0.001	0.75
30s Sit-to-stand test (n)	13.6 ± 3.34	14.5 ± 3.36	0.011	0.46
400-m walk test (min)	6.98 ± 2.85	7.30 ± 2.85	0.359	-0.16
Total Protein (g/dl)	6.55 ± 1.72	6.21 ± 2.00	0.339	0.16
Albumin (g/dl)	3.83 ± 1.02	3.64 ± 1.19	0.339	0.16
SII	504 ± 240	411 ± 191	0.024	0.401
Glycemia (mg/dl)	99.3 ± 17.8	89.4 ± 10.5	0.004	0.52
HbA1c (%)	4.83 ± 2.44	4.15 ± 2.63	0.201	0.22
LDL (mg/dl)	173.8 ± 36.1	157.8 ± 47.6	0.026	0.393
Triglycerides (mg/dl)	137.2 ± 56	107.6 ± 45.6	0.002	0.577
HDL (mg/dl)	45.5 ± 15.5	44.5 ± 16.5	0.731	0.059

BMI: Body Mass Index, BMC: Body mineral content, BMD: Body mineral density, SMM: Skeletal Muscle Mass, ASMM: Appendicular Skeletal Muscle Mass, ASMMI: Appendicular Skeletal Muscle Mass Index, HbA1c: Hemoglobin Glycate, SII: Systemic immune-inflammatory index, LDL: Cholesterol, HDL: Cholesterol

d=Choen effect size; small=0.2-0.49, medium=0.5-0.79, large>0.8.

Table 4.5.3. Variation analysis after exercise

Variables (Mean ± SE)	*Surgery + Exercise Effect* IG n=19	CG n=16	*p-value*	*Effect size (d)*
Weight (Kg)	-20.1 ± 9.18	-16.9 ± 4.05	0.198	0.902
BMI (kg/m^2)	-7.33 ± 3.28	-6,93 ± 2.10	0.681	-0.14
Waist circumference (cm)	-14.9 ± 5.99	-12.4 ± 9.44	0.345	-0.32
Total Weight Loss (%)	16.7± 6.36	16.3 ± 4.93	0.841	0.07
Body fat (%)	-7.55 ± 4.22	-5.09 ± 5.02	0.002	-1.13
Total SMM mass (Kg)	-4.97 ± 3.90	-3.41 ± 2.89	0.196	-0.45
ASMM (Kg)	-18.3 ± 12.7	-22.7 ± 11.4	0.034	3.18
ASMM/Weight (%)	3.07 ± 2.66	1.89 ± 1.78	0.141	0.51
BMC (g)	0.12 ± 0.01	0.05 ± 0.03	<0.001	0.83
BMD (g/cm^2)	0.06 ± 0.02	1.09 ± 0.07	0.114	0.61
Total Body *T-score*	0.03 ± 0.22	-0.32 ± 0.23	0.069	0.23
Total Body *Z-score*	0.01 ± 0.11	0.39 ± 0.32	0.451	0.27
Handgrip (Kg)	2.39 ± 5.23	-1.74 ± 3.66	0.002	0.75
30s Sit-to-stand test (n)	1.68 ± 2.06	0.38 ± 1.45	0.002	0.46
400-m walk test (min)	-1.18 ± 1.56	0.06 ± 1.21	0.002	-0.16
SII	-163 ± 56	-126 ± 115	0.462	0.401
Glycemia (mg/dl)	-12.9 ± 14.6	-7.7 ± 3.5	0.436	0.52
HbA1c (%)	-0.58 ± 0.06	-0.79 ± 0.66	0.441	0.22
LDL (mg/dl)	-0.11 ± 0.64	-22 ± 21.7	0.556	0.393
Triglycerides (mg/dl)	-0.27 ± 0.05	-0.45 ± 0.03	0.292	0.577
HDL (mg/dl)	-1.2 ± 0.22	-0.1 ± 0.05	0.957	0.059

BMI: Body Mass Index, BMC: Body mineral content, BMD: Body mineral density, SMM: Skeletal Muscle Mass, ASMM: Appendicular Skeletal Muscle Mass, ASMMI: Appendicular Skeletal Muscle Mass Index, HbA1c: Hemoglobin Glycate, SII: Systemic immune-inflammatory index, LDL: Cholesterol, HDL: Cholesterol

d=Choen effect size; small=0.2-0.49, medium=0.5-0.79, large>0.8.

The remission rates of various conditions (Diabetes, Hypertension, Dyslipidemia, and OASA) 5 months after surgery, comparing the intervention group (IG) with the control group (CG), are present in Table 4.5.4. It also examines the effects of surgery and surgery + exercise on these conditions.

Table 4.5.4. Associated obesity disease remission

Variables	*Remission 5-months after surgery*						*Surgery Effect*	*Surgery +Exercise Effect*
	Before Surgery			*After Surgery*				
	IG n=19	CG n=16	*p-value*	IG n=19	CG n=16	*p-value*	*p-value*	*p-value*
Diabetes	5.7%	11,4%	0.271	2.9%	2.9%	0.904	0.046	0.317
Hypertension	34.3%	34.3%	0.467	5.7%	8.6%	0.503	<0.001	0.002
Dyslipidemia	5.7%	20%	0.025	0%	8.6%	0.050	0.014	0.163
OASA	5.7%	20%	0.025	0%	8.6%	0.050	0.014	0.163

OASA: obstructive sleep apnea

Table 5.5.5 presents data on the relationship between the SII and various body composition and physical function measures at baseline (E0) and after 5 months (E1). The columns provide information on each variable's correlation coefficient (r2), p-value, and 95% confidence interval (CI).

A significant negative correlation between SII and BMC ($\boldsymbol{r^2}$=−0.373; p=0.027; CI: -0.628; -0.045) and with *t-score* ($\boldsymbol{r^2}$=−0.447; p=0.007; CI: -0.679; -0.133) at baseline. Five months after RYGB the negative correlation is with handgrip ($\boldsymbol{r^2}$=−0.367; p=0.030; CI: -0.039; -0.624), ASMM ($\boldsymbol{r^2}$=−0.397; p=0.018; CI: -0.645; -0.074) and ASMM/Weight ($\boldsymbol{r^2}$=−0.557; p<0.001; CI: -0.751; -0.274), the EASO/ESPEN parameter to diagnose sarcopenia.

Table 4.5.5. Linear regression analysis based on SII

Variables	***Systemic immune-inflammatory index - SII***					
	Before Surgery			*After Surgery + Exercise*		
	r^2	*p-value*	*CI 95%*	r^2	*p-value*	*CI 95%*
BMC (g)	-0.373	0.027	- 0.628; -0.045	-0.278	0.106	-0.559; 0.061
Body fat (%)	0.072	0.680	-0.664; -0.107	0.232	0.179	-0.109; 0.525
Handgrip (Kg)	-0.322	0.060	-0.591; 0.013	-0.367	0.030	-0.039; -0.624
ASMM (Kg)	-0.313	0.067	-0.585; 0.023	-0.397	0.018	-0.645; -0.074
ASMM/Weight (%)	-0.251	0.147	-0.539; 0.090	-0.557	<0.001	-0.751; -0.274
Total Body *T-score*	-0.447	0.007	-0.679; -0.133	-0.254	0.140	-0.542; 0.086

Discussion

This study evaluated the effects of Roux-en-Y gastric bypass (RYGB) surgery and subsequent exercise interventions on SII in a cohort of 35 patients diagnosed with sarcopenic obesity.

The SSI can assess inflammatory conditions. This index includes neutrophils, lymphocytes, and platelet count in a blood sample. It is a simple, efficient, and low-cost test. Other studies have shown that it has a predictor value in tumors, cardiovascular disease, hepatic steatosis, osteoporosis (Zhang et al., 2023), diabetes, and other conditions. Higher levels of SSI are associated with worse prognosis and increasing mortality (Yücel et al., 2022).

Our baseline characteristics reveal a population with severe obesity, sarcopenic obesity and a high prevalence of related comorbidities, setting the stage for the assessment of the potential benefits of RYGB surgery. Preoperatively, higher SII is associated with lower muscle mass and function, and this may be a reflex of the compromise that obesity causes on health, in this case, simultaneously increasing systemic inflammation and affecting muscle mass and function.

After surgery, our results show a favorable impact of bariatric surgery on weight and associated conditions control and a negative impact on muscle mass and function. SII responds very favorably to surgery with or without exercise, with a clear decrease in its score.

The study shows significant improvements in anthropometric and body composition parameters after surgery. The reductions in weight, BMI, and body fat percentage were statistically significant with large effect sizes. These findings are consistent with the expected outcomes of bariatric surgery, which typically results in substantial weight loss and improved body composition (Felsenreich et al., 2016; Gloy et al., 2013).

Lin Shi et al, studied the relationship between SSI and muscle mass. They concluded that the increased SII levels were associated with an increased risk of low muscle mass in a large population. This association is present in the patients in our study before surgery. All have sarcopenic obesity with low muscle mass assessed by ASMM/weight, and the mean SII is high. However, after surgery, there is a decrease in SII but also in muscle mass. If we extrapolate the results from Lin we should have the inverse result, but we can reason that the bariatric surgery influence on weight loss and muscle mass loss is greater than the protective effect that can result from decreasing SII (Shi et al., 2023).

There were significant improvements in Diabetes (glycemia) and Dyslipidemia (LDL and triglycerides) postoperatively. However, HbA1c levels did not show significant differences. The remission rates for Diabetes, Hypertension, Dyslipidemia, and OSAS also improved significantly post-surgery, highlighting the surgery's efficacy in managing obesity-related diseases (Courcoulas et al., 2014; C. Santos, Carvalho, et al., 2022; Shah et al., 2006). However, there were no differences between the intervention and the control groups.

Nevertheless, the role of physical exercise in the management of surgical bariatric patients is still not clear. Physical strength, measured by handgrip and sit-to-stand tests, improved postoperatively in the intervention group but not in the control group, and the difference at the end of the study was significant. This indicates that, while RYGB surgery alone may not improve strength, combining it with exercise leads to better functional outcomes. After surgery the patients in the physical exercise program group had better results in muscle mass and strength when compared to the patients in the control group (without exercise).

The SII significantly decreased when measured five months after surgery, suggesting reduced systemic inflammation. The lack of significant differences in the exercise group compared to the control group could imply that surgery plays an import role in reducing inflammation than exercise (Shi et al., 2023; J. Zhao et al., 2023). However, after surgery with exercise, the group that exercised improved have better results, and linear regression shows that more significant reductions in inflammation are associated with better results in muscle mass (ASMM and ASMM/weight) and strength, highlighting the interconnectedness of the inflammatory status and physical health in sarcopenic obesity.

However, there were no significative differences in SII score between the two groups, which may be interpreted as a lack of positive effect of physical exercise on the systemic inflammatory condition in obesity.

Conclusion

This study underscores the multifaceted benefits of RYGB surgery in patients with sarcopenic obesity. RYGB showed effects that were considered positive on inflammatory markers obtained from routine blood tests. Significant improvements were observed in weight, body composition, comorbidities, and inflammatory markers. The addition of exercise further enhanced physical function. The correlations between SII and various health metrics suggest that reducing systemic inflammation through surgery could play a critical role in improving muscle mass and especially physical strength. These findings support the integrated approach of combining surgical and exercise interventions to optimize health outcomes in patients with sarcopenic obesity.

CHAPTER 5 – DISCUSSION

This study investigates the impact of a combined exercise program on the prevention of sarcopenia in patients undergoing bariatric surgery.

Obesity, a chronic disease affecting millions globally and bariatric surgery is a proven treatment for severe obesity, enabling patients to lose excess weight and improve overall health conditions. However, rapid weight loss after surgery often leads to significant reductions in skeletal muscle mass and strength, increasing the risk of sarcopenia (Pinto et al., 2017; Sardinha et al., 2012).

Sarcopenia, traditionally associated with aging, is also prevalent among post-bariatric surgery patients due to substantial muscle mass loss during rapid weight reduction. This loss can negatively impact physical function, increasing the risk of frailty and long-term metabolic dysfunction. This thesis investigates how structured combined exercise can prevent sarcopenia in these patients, offering potential interventions to maintain muscle health post-surgery (Endalifer & Diress, 2020; Wei et al., 2023).

A systematic review conducted as part of the thesis analyzes eight randomized trials assessing the impact of exercise on sarcopenia prevention. It concludes that combined aerobic and resistance exercise interventions significantly improves body composition, muscle mass, and overall physical performance. Notably, combined exercise programs initiated shortly after surgery (within the first few months) showed the best outcomes in preserving muscle quality. In a comprehensive study, researchers compared two types of training programs and they found that adding resistance to the aerobic exercise regimen did not lead to any additional weight loss. Although the experimental groups showed no significant differences in weight loss, they did observe positive effects of combined exercise on muscle mass improvement. These findings suggest that combined exercises are associated with a lower incidence of sarcopenia. While muscle mass decreased in all three groups, the control group and the aerobic exercise group experienced greater losses in muscle mass and strength compared to the combined exercise group (Hassannejad et al., 2017).

The impact of bariatric surgery on the handgrip test has been debated. A recent meta-analysis concerning muscle strength after bariatric surgery could not show a muscle strength loss when all the data was pooled, but in none of those studies' strength was assessed one month after surgery as in the current study. Other variables that are probably relevant are gender and the surgical procedure chosen for each patient because these factors may also impact weight and muscle loss (Jung et al., 2023).

Nevertheless, even if the global pooled data did not indicate, some of the included studies in the meta-analysis showed a clear absolute decrease in muscle strength. Alba et al. (2019), showed a significant decrease from preoperative values. The mean 12-month change in absolute strength showed a decline of 2.6 Kg, with the entire decline occurring in the first 6 postoperative months. Oppert et al., also showed a 21 Kg muscle strength decrease (Bellicha et al., 2021), and Cole et al., showed a 2.8 Kg decline (Cole et al., 2017). It is worth mentioning that these three studies were the only ones included in the meta-analysis where the only surgical procedure used was the RYGB.

The EXPOBAR trial is a randomized clinical study aimed at assessing the effect of a 16-week supervised exercise program on muscle mass and physical function in post-bariatric patients. Participants were divided into control and intervention groups, with the latter engaging in a combined aerobic and resistance exercise program, starting one-month post-surgery. The results of the randomized clinical trials revealed that the intervention program induced significant improvements in several parameters, such as muscle strength, body composition and quality of life. The loss of skeletal muscle mass was reduced in the groups that underwent supervised physical exercise, while bone mass also showed better results.

This study reveals that a combined physical exercise program, that starts early after bariatric surgery, is an effective intervention for preventing sarcopenia and improving patients' quality of life. Controlled clinical trials performed within this research work show that exercise promotes significant gains in muscle strength, muscle mass, and bone health, alongside with significant improvements in inflammatory indices, highlighting physical exercise as an essential strategy for improving long-term surgical outcomes.

The intervention group showed a significant improvement in physical function and strength, measured by handgrip strength and lower body strength tests. Although there was a continuous decline in muscle mass in both groups, participants in the exercise group retained greater muscle function. This supports the effectiveness of a structured exercise programs in mitigating the adverse effects on body composition of obesity, sarcopenia, and bariatric surgery (Minniti et al., 2022). While bariatric surgery primarily affects adipose tissue, it also significantly influences muscle mass in the initial months post-surgery (Coen et al., 2018; Coen & Goodpaster, 2016; Villa-González et al., 2019).

This underscores the need for incorporating a combination of aerobic and strength training, as demonstrated in this research, which revealed that exercise positively impacted muscle quality and reduced the risk of sarcopenia progression.

The EXPOBAR trial also reports significant improvements in health-related HRQoL in the exercise group, measured through the SarQoL questionnaire, which assesses physical and psychological well-being in sarcopenic patients. This is the first study to evaluate the quality of life in patients with sarcopenic obesity with a specific questionnaire for sarcopenia.

These findings are consistent with previous research demonstrating the benefits of exercise in older adults and in those with chronic health conditions. Exercise has been shown to enhance muscle strength, physical performance, and overall well-being, likely contributing to the observed HRQoL improvements (Steffl et al., 2017).

The social implications of obesity, including stigma and isolation, can be significant. HRQL assessments following bariatric surgery often show improvements in social interactions and relationships (Tolvanen et al., 2021, 2022). Patients frequently experience enhanced social participation, stronger interpersonal connections, and greater overall life satisfaction. These enhancements are vital for understanding the full impact of surgery on patients' lives. Patient-reported outcome measures (PROMs) offer a way to evaluate the results of bariatric surgery. By capturing patients' subjective experiences, healthcare providers can tailor follow-up care and interventions to meet specific needs and concerns. This personalized approach ensures that treatment is not only clinically effective but also aligned with the patient's quality of life goals (Bentham et al., 2017; Camolas et al., 2017).

Using PROMs in post-surgery evaluations facilitates long-term monitoring of patients' well-being. Regular HRQL assessments can help detect emerging issues or declining trends in health-related quality of life, allowing for timely interventions (Coulman et al., 2017, 2020). Continuous monitoring supports sustained improvements and assists in managing any complications or psychosocial challenges that may arise. PROMs, particularly those assessing HRQL, are essential for evaluating the comprehensive outcomes of bariatric surgery. They provide valuable insights into the physical, psychological, and social improvements experienced by patients, helping to create a holistic understanding of the surgery's impact.

By incorporating PROMs into post-surgical care, healthcare providers can enhance personalized support, ensure long-term follow-up, and ultimately improve the overall success of bariatric interventions.

This study also explores the effect of exercise on systematic inflammation and metabolic biomarkers such as leptin and ghrelin, hormones critical in regulating appetite and energy balance post-surgery. The structured exercise program positively influenced these markers, reducing systemic inflammation and improving appetite regulation. Moreover, improvements in SII were noted, suggesting that exercise reduces inflammatory responses, a key contributor to sarcopenic conditions. The current research also reveals a significant reduction in the systemic inflammatory index, particularly in the intervention group, indicating a relationship between systemic inflammation, weight loss and gains in muscle strength.

The results corroborate previous studies that indicate the essential role of physical exercise in patients undergoing bariatric surgery to maintain muscle mass and physical function (Boppre et al., 2022; Hassannejad et al., 2017; Marc-Hernández et al., 2020). The reduction in inflammation and improvements in bone health reinforce that bariatric surgery combined with exercise is more effective than surgery alone (Casimiro et al., 2019; Matos et al., 2020; Zhang et al., 2023).

However, unlike other studies that suggest a significant loss of strength postsurgery, this study showed that early intervention (as early one month after surgery) can attenuate this loss and promote functional recovery.

Bariatric surgery, particularly RYGB, promotes rapid weight loss by restricting calorie intake and reducing nutrient absorption, impacting not just fat mass but muscle mass as well. This study shows that weight loss associated with bariatric surgery is greatly associated with a significant reduction of skeletal muscle and bone mineral mass, highlighting the muscle deterioration that follows surgery. The muscle depletion increases the risk of sarcopenia, emphasizing the need for prophylactic measures such as combined exercise programs. Exercise is a key intervention for maintaining muscle mass and function.

According to this investigation, a combined aerobic and resistance exercise program seems to be one of the most effective approaches for mitigating sarcopenia in post-bariatric surgery patients. Such interventions can not only prevent muscle loss but also improve overall physical fitness, as seen in the EXPOBAR trial's significant improvements in muscle strength and functional capacity.

The broader implication of these findings is that exercise should be a standard recommendation for bariatric patients, not just for weight loss but also for muscle preservation and metabolic health. By integrating structured exercise into postoperative care, healthcare providers can improve long-term outcomes and quality of life for bariatric patients.

The current thesis provides strong evidence supporting the integration of combined aerobic and resistance exercise programs in post-bariatric surgery care. These programs significantly improve muscle strength, physical function, and quality of life, reduce systemic inflammation and help to regulate hormonal imbalances, helping to mitigate the risk of sarcopenia. The findings from the EXPOBAR trial demonstrate that structured physical activity is a crucial component of postoperative recovery and long-term health in bariatric patients.

Conclusion

The EXPOBAR trial revealed that a combined physical exercise program, starting 1-month after bariatric surgery, is an effective intervention to prevent sarcopenia and to improve patients' quality of life. Controlled clinical trials performed within the current research show that exercise promotes significant gains in muscle strength, muscle mass, and bone health, while significantly improving inflammatory indices, highlighting exercise as an essential strategy for improving long-term surgical outcomes.

The results corroborate previous studies that indicate the essential role of physical exercise in patients undergoing bariatric surgery in order to maintain muscle mass and physical function. The reduction in inflammation and improvements in bone health reinforce the concept that bariatric surgery combined with exercise is more effective than surgery alone.

The impact of the exercise program intervention suggests the need to implement combined exercise programs as part of the clinical guidelines for the postoperative follow-up of patients undergoing bariatric surgery. The early introduction of such programs may not only prevent sarcopenia but also improve long-term quality of life by reducing metabolic and inflammatory risk factors.

The relatively small sample limits generalising the results. In addition, the follow-up time, although significant (up to 18 months), could be extended to observe the long-term effects and possible relapses in terms of muscle mass and inflammation parameters. Adherence to the exercise program may also vary among patients, which could influence the results obtained.

However, by addressing an important gap in the literature on the impact of sarcopenia after bariatric surgery, this thesis contributes with new evidence on the relevance of structured physical exercise to maintain and optimize muscle and metabolic function in these patients.

Practical implications/suggestions for future work

Future studies should investigate the long-term impact of combined exercise programs on sarcopenia prevention and explore additional interventions such as nutritional supplementation to further mitigate muscle loss. Additionally, the role of personalized exercise programs in reducing the risk of sarcopenia across diverse populations should be examined.

Future research could, also, explore the combination of different types of exercise manipulating training variables and their influence on preserving muscle mass and improving metabolic health in post bariatric surgery patients.

Another area that needs further research is the analysis of the interaction between nutritional intervention and exercise, as well as an evaluation of long-term hormonal results in patients with sarcopenic obesity.

Although the study shows promising results, generalising data is limited by the sample size and length of follow-up. Future research should focus on larger cohorts and greater long-term follow-up to assess the sustainability of the benefits of physical exercise and its interaction with other factors, such as nutritional and hormonal interventions.

In addition, exploring different types of exercise and their combinations may provide a more solid basis for optimizing preventive and therapeutic interventions for bariatric patients.

Despite promising results, this thesis highlights the challenges of implementing exercise program interventions in bariatric patients. Factors such as low baseline physical fitness, lack of motivation, and psychological barriers pose obstacles to sustained participation in exercise programs. The study suggests tailoring exercise prescriptions based on patient-specific needs, including their fitness levels and comorbidities, to enhance adherence and outcomes.

This research has contributed to the advancement of knowledge on the management of sarcopenia in patients undergoing bariatric surgery, demonstrating that combined physical exercise is a crucial intervention for improving muscle health and quality of life. These results can guide future interventions and contribute to the development of clinical guidelines to improve postsurgical outcomes and ensure a more complete and sustainable recovery after bariatric surgery.

Limitations and implications

Despite the methodological rigor adopted in this study, it is important to acknowledge several limitations that may influence the interpretation of the results and their implications for clinical practice and future research.

One of the main limitations of this study is the relatively small sample size. A larger number of participants would have provided greater statistical power and enhanced the generalizability of the findings. The limited sample size may have affected the ability to detect significant differences across some variables and limited the feasibility of more robust multivariate analyses.

Another challenge was the control of adherence to the intervention, particularly regarding the implementation of the physical activity protocol or other postoperative recommendations. The lack of close monitoring of adherence may have introduced variability in the outcomes, potentially compromising the accurate assessment of the intervention's impact.

Additionally, the analyses were not adjusted for potential confounding factors, such as age, sex, preoperative physical activity levels, nutritional status, or comorbidities. The absence of such adjustments may have led to overestimation or underestimation of some observed effects.

The randomization process took place before bariatric surgery, which may have influenced the outcomes, considering that participants' clinical and psychological status can change substantially during the perioperative period, thereby affecting their response to the intervention and overall engagement with the study.

It is also important to note that clinical guidelines are continuously evolving, especially regarding the definition, diagnosis, and management of sarcopenia and sarcopenic obesity. Therefore, some of the criteria used in this study, although valid at the time of data collection, may not fully reflect the most recent recommendations, limiting the comparability and clinical relevance of the findings in light of emerging evidence.

These limitations do not invalidate the findings but do require a cautious and contextualized interpretation. The results should be seen as preliminary and hypothesis-generating rather than definitive. Future research should consider larger sample sizes, more effective adherence monitoring strategies, and statistical methods that better handle missing data, such as multiple imputation.

Moreover, future studies would benefit from adjusting for relevant confounders and continuously aligning methodological decisions with updated clinical guidelines to ensure the relevance, rigor, and applicability of their conclusions in evolving clinical contexts.

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APPENDIX'S

Appendix 1

SPCO | Sociedade Portuguesa de Cirurgia da Obesidade e Doenças Metabólicas

OBESIDADE · CIRURGIAS AO VIVO · CASOS CLÍNICOS

XII CONGRESSO

DE CIRURGIA DE OBESIDADE E DOENÇAS METABÓLICAS

19-20 DE SETEMBRO DE 2024 | HOTEL MONTEBELO EM ÍLHAVO

CERTIFICADO

Certifica-se que o resumo:

Impact of bariatric surgery on sarcopenia related parameters and diagnosis – The preliminary results of EXPOBAR study

Foi aceite como **Comunicação Oral**
no **XII Congresso de Cirurgia de Obesidade e Doenças Metabólicas,** que decorreu entre os dias 19 e 20 de setembro de 2024 no Hotel Montebelo Vista Alegres em Ílhavo.

Autores: Cláudia Mendes[1,2]; Manuel Carvalho[1]; Armando Raimundo[2,3]; Jorge Bravo[2,3]; Sandra Martins[4]

1 - ULSAC; 2 - CHRC; 3 - UE; 4 - universidade europeia

23-09-2024

Dr. Mário Nora
PRESIDENTE SPCO

Appendix 2

SPCO | Sociedade Portuguesa de Cirurgia da Obesidade e Doenças Metabólicas

OBESIDADE · CIRURGIAS AO VIVO · CASOS CLÍNICOS

XII CONGRESSO DE CIRURGIA DE OBESIDADE E DOENÇAS METABÓLICAS

19-20 DE SETEMBRO DE 2024 | HOTEL MONTEBELO EM ÍLHAVO

CERTIFICADO

Certifica-se que o resumo:

The interplay of weight loss, physical exercise and leptin and ghrelin changes after Roux-en-Y-Gastric Bypass in patients with sarcopenic obesity

Foi aceite como **Comunicação Oral** no **XII Congresso de Cirurgia de Obesidade e Doenças Metabólicas,** que decorreu entre os dias 19 e 20 de setembro de 2024 no Hotel Montebelo Vista Alegres em Ílhavo.

Autores: Cláudia Mendes[1,2]; Manuel Carvalho[1]; Armando Raimundo[2,3]; Jorge Bravo[2,3]; Sandra Martins[4]

1 - ULSAC; 2 - CHRC; 3 - UE; 4 - universidade europeia

23-09-2024

Dr. Mário Nora
PRESIDENTE SPCO

Appendix 3

SPCO | Sociedade Portuguesa de Cirurgia da Obesidade e Doenças Metabólicas

OBESIDADE · CIRURGIAS AO VIVO · CASOS CLÍNICOS

XII CONGRESSO
DE CIRURGIA DE OBESIDADE E DOENÇAS METABÓLICAS

19-20 DE SETEMBRO DE 2024 | HOTEL MONTEBELO EM ÍLHAVO

CERTIFICADO

Certifica-se que o resumo:

Effect of a 16-week Combined Supervised Exercise Program after bariatric surgery on Sarcopenia parameters based on FNIH, EWGSOP2, EASO/ESPEN criteria

Foi aceite como **Comunicação Oral**
no **XII Congresso de Cirurgia de Obesidade e Doenças Metabólicas,** que decorreu entre os dias 19 e 20 de setembro de 2024 no Hotel Montebelo Vista Alegres em Ílhavo.

Autores: Claudia Mendes[1,2]; Manuel Carvalho[1]; Armando Raimundo[2,3]; Jorge Bravo[2,3]; Sandra Martins[4]

1 - ULSAC; 2 - CHRC; 3 - UE; 4 - universidade europeia

23-09-2024

Dr. Mário Nora
PRESIDENTE SPCO

Appendix 4


Effects of physical exercise in sarcopenia on patients undergoing bariatric surgery: A protocol for a randomized clinical trial and preliminary results
Cláudia Amaro Santos[1,2,3] Manuel Carvalho[1,2] Sandra Martins[4] Armando Raimundo[3]
[1]Hospital Espírito Santo de Évora, EPE
[2]CRI.COM - Bariatric Integrated Surgical Responsibility and Metabolic Diseases Center
[3]CHRC - Comprehensive Health Research Centre
[4]Faculty of Social Sciences and Technology, European University
[5]Departamento de Desporto e Saúde, Escola de Saúde e Desenvolvimento Humano, Universidade de Évora
SOCIEDADE PORTUGUESA DE CIRURGIA MINIMAMENTE INVASIVA
CHRC
COMPREHENSIVE HEALTH RESEARCH CENTRE
UNIVERSIDADE DE ÉVORA
CRI.com

Appendix 5

SPCO | Sociedade Portuguesa de Cirurgia da Obesidade e Doenças Metabólicas

OBESIDADE · CIRURGIAS AO VIVO · CASOS CLÍNICOS

XII CONGRESSO DE CIRURGIA DE OBESIDADE E DOENÇAS METABÓLICAS

19-20 DE SETEMBRO DE 2024 | HOTEL MONTEBELO EM ÍLHAVO

CERTIFICADO

Certifica-se que o resumo:

The impact of exercise after bariatric surgery on Systemic Immune Inflammation Index and sarcopenia obesity

Foi aceite como **E-poster com apresentação** no **XII Congresso de Cirurgia de Obesidade e Doenças Metabólicas,** que decorreu entre os dias 19 e 20 de setembro de 2024 no Hotel Montebelo Vista Alegres em Ílhavo.

Autores: Armando Raimundo[2,3]; Jorge Bravo[2,3]; Sandra Martins[4]; Cláudia Mendes[1]; Manuel Carvalho[1]

1 - ULSAC; 2 - CHRC; 3 - UE; 4 - Universidade europeia

23-09-2024

Dr. Mário Nora
PRESIDENTE SPCO

Appendix 6

EACCME
European Accreditation Council for Continuing Medical Education

CERTIFICATE

XXVII IFSO WORLD CONGRESS 2024

Melbourne, Australia
3 September 2024 - 6 September 2024

Cláudia Mendes

Effects of a randomized 16-week training program in sarcopenia on patients undergone gastric bypass - EXPOBAR results

Ahmad Aly
Congress President

Each medical specialist should claim only those credits that he/she actually spent in the educational activity.

The EACCME® is an institution of the European Union of Medical Specialists (UEMS), www.uems.eu. Through an agreement between the European Union of Medical Specialists and the American Medical Association, physicians may convert EACCME® credits to an equivalent number of AMA PRA Category 1 Credits™. Information on the process to convert EACCME® credits to AMA credits can be found at www.ama-assn.org/education/earn-credit-participation-international-activities.

Live educational activities occurring outside of Canada, recognised by the UEMS-EACCME® for ECMEC® credits are deemed to be Accredited Group Learning Activities (Section 1) as defined by the Maintenance of Certification Program of the Royal College of Physicians and Surgeons of Canada.

IFSO

Appendix 7

2nd INTERNATIONAL MEETING OF THE

PORTUGUESE SOCIETY OF PHYSIOLOGY

11th and 12th | November 2022

Escola Superior de Tecnologia da Saúde do Politécnico de Coimbra

SPFisiologia portuguese physiological society

CERTIFICATE

This certifies that the Poster

The impact of exercise on prevention of sarcopenia after bariatric surgery: The Study Protocol of the EXPOBAR Randomized Controlled Trial

Cláudia Amaro Dos Santos[1]

1 - CHRC

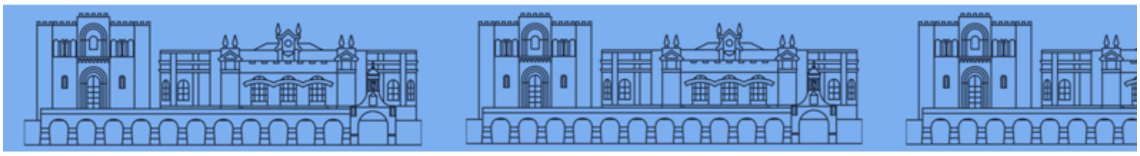
was presented at the

2nd International Meeting of the Portuguese Society of Physiology,

on November 11 and 12, 2022 at ESTeSC – Coimbra.

Prof. Luis Monteiro Rodrigues

President of SPFIS



Appendix 8

CHRC COMPREHENSIVE HEALTH RESEARCH CENTRE

3rd Annual Summit

3rd - 4th November 2022

CERTIFICATE

This is to certify that **Cláudia Amaro dos Santos** presented a Poster entitled **Effects of a randomized 16-week training program in sarcopenia on patients undergone gastric bypass - EXPOBAR protocol and primary results** at the **3rd Comprehensive Health Research Centre Annual Summit**, held on November 3rd & 4th 2022 at the NOVA Medical School. The work presented is authored by Cláudia Amaro dos Santos, Manuel Carvalho, Sandra Martins & Armando Raimundo.

Helena Canhão, MD, PhD
CHRC Coordinator

Hosted by UNIVERSIDADE DE ÉVORA

Appendix 9

NIHR | National Institute for Health Research

PROSPERO
International prospective register of systematic reviews

Citation

Claudia Amaro dos Santos, Armando Raimundo, Sandra Martins, Manuel Carvalho. Effects of exercise on sarcopenia in patients undergoing bariatric surgery. PROSPERO 2022 CRD42022324642 Available from: https://www.crd.york.ac.uk/prospero/display_record.php?ID=CRD42022324642

Review question

Is physical exercise associated with less loss of muscle mass, better QoL and improved metabolic risk factors in patients undergoing bariatric surgery?

Searches [1 change]

MEDLINE via PubMed, SPORTDiscus and Cochrane Library. English-language articles reporting on primary research published in the last 10 years

Types of study to be included

RCT, Experimental Studys, Observational Studys

Condition or domain being studied

Bariatric surgery is a treatment for severe obesity with associated pathologies, with proven evidence in its benefits. Treating overweight allows a better and even reversal of pathologies associated with obesity. In this context, physical exercise is important in the weight loss process, however, and especially in bariatric surgery, the characteristics of physical activity are not consensual, as well as the effect of programs and physical exercise in this population. Currently there are no specific recommendations for obese people undergoing bariatric surgery, whether pre-surgery or post-surgery, and the recommendations that exist include only guidelines for obesity in general. Weight loss associated with bariatric surgery is greatly associated with a significant reduction in skeletal muscle and bone mineral mass, which leads us to induce that after bariatric surgery, patients incur an increased risk of sarcopenia. The need for prophylactic programs that prevent sarcopenia in bariatric surgery patients seems to be one of the crucial points for framing the long-term surgical success of bariatric and metabolic surgery.

Participants/population

Adult patients in the Bariatric surgery program

Intervention(s), exposure(s)

Exercise Programs after Bariatric Surgery

Comparator(s)/control

Usual Care

Context [1 change]

English-language articles reporting on primary research published in the last 10 years

Main outcome(s) [1 change]

Any quantitative measure describing on the exercise training, body composition, anthropometry, exercise, life quality, metabolic risk factors, strength, physical fitness

Measures of effect

Anthropometry

Quality of life

Appendix 10

ClinicalTrials.gov PRS
Protocol Registration and Results System

ClinicalTrials.gov Protocol Registration and Results System (PRS) Receipt
Release Date: March 12, 2022

ClinicalTrials.gov ID: NCT05289219

Study Identification

Unique Protocol ID:	21051
Brief Title:	Effects of Physical Exercise on Sarcopenia After Bariatric Surgery (EXPOBAR)
Official Title:	Effects of Physical Exercise on Sarcopenia After Bariatric Surgery: Protocol of a Randomized Controlled Study
Secondary IDs:	

Study Status

Record Verification:	March 2022
Overall Status:	Recruiting
Study Start:	September 1, 2021 [Actual]
Primary Completion:	December 2022 [Anticipated]
Study Completion:	December 2023 [Anticipated]

Sponsor/Collaborators

Sponsor:	University of Évora
Responsible Party:	Principal Investigator Investigator: Cláudia Mendes [cdossantos] Official Title: Principal Investigator Affiliation: University of Évora
Collaborators:	University of Évora

Oversight

U.S. FDA-regulated Drug:	No
U.S. FDA-regulated Device:	No
U.S. FDA IND/IDE:	No
Human Subjects Review:	Board Status: Approved Approval Number: 21059 Board Name: Comissão de Ética Board Affiliation: Universidade de Évora Phone: 968575053 Email: cmendes@hevora.min-saude.pt Address:

Appendix 11

Documento 2 1 0 5 1

Comissão de Ética da Universidade de Évora

A Comissão de Ética da Universidade de Évora informa que, com base nas apreciações favoráveis dos seus membros, deliberou dar

Parecer Positivo

para a realização do Projeto: "*Efeitos do exercício físico na sarcopenia pós cirurgia bariátrica: um estudo controlado e randomizado.*", pela doutoranda **Cláudia Sofia Orvalho Mendes Amaro dos Santos** sob a supervisão do Prof. Doutor Armando Manuel de Mendonça Raimundo (responsável académico).

Universidade de Évora, 14 de outubro de 2021

A Presidente da Comissão de Ética

(Prof.ª Doutora Margarida I. Almeida Amoedo)

Hospital do Espírito Santo E.P.E. Évora

COMISSÃO DE ÉTICA

Hospital do Espírito Santo de Évora, EPE (HESE, EPE)

Título do Projeto: Efeitos do exercício físico na sarcopenia após cirurgia bariátrica: Protocolo de um estudo controlado aleatório

Nome: Cláudia Sofia Orvalho Mendes Amaro dos Santos

Instituição: Universidade de Évora

Enquadramento Académico: Doutoramento em Motricidade Humana

Tipo de Estudo: ensaio clínico aleatório

Com base nos documentos apresentados

- Estão definidos os critérios de inclusão __Sim___

- São apresentados os Instrumentos de recolha de dados ___Sim__

- Está garantida a confidencialidade dos dados recolhidos __Sim___

- Está garantida a participação livre, voluntária e informada, dos participantes __Sim__

AUTORIZAMOS

ATA N.º 48, em 15/12/21

O Conselho de Administração

Maria Filomena Mendes
Presidente

Francisco Chalaça
Vogal

Luís Cavaco
Vogal

Maria Elisa Brissos
Enfermeira Diretora

Isabel Pita
Directora Clínica

Parecer da Comissão de Ética do HESE, EPE:

Favorável __X__

Condicional ___

NOTAS:

Data: 02/12/2021

Dr. Rui Rosado
(Presidente da Comissão de Ética)

Telefone: 266 740 100 | Fax: 266 701 821
geral@hevora.min-saude.pt | www.hevora.min-saude.pt
Hospital do Espírito Santo de Évora E.P.E. | Largo Senhor da Pobreza, s/n - 7000-811 Évora
Entidade Pública Empresarial | Matriculada na Conservatória do Registo Comercial de Évora
sob o n.0 508 085 888 NIPC/NIF: 508 085 888 | Capital Estatutário: 40.280.000,00 euros

Appendix 12

CONSENTIMENTO INFORMADO, LIVRE E ESCLARECIDO

Designação do Estudo: Efeitos do exercício físico na sarcopenia pós cirurgia bariátrica: um estudo controlado e randomizado

Paciente

Eu, abaixo-assinado, (nome completo do doente) -- --, compreendi a explicação que me foi fornecida, acerca da minha participação na investigação que se tenciona realizar, bem como do estudo em que serei incluído(a).

- Foi-me explicado, que a investigadora terá acesso aos dados clínicos e bioquímicos, bem como aos dados recolhidos em todos os momentos de avaliação do estudo, com garantia do anonimato.

- Todos os dados serão protegidos em base de dados pessoal da investigadora, com garantia do anonimato e privacidade dos participantes.

- Foi-me dada oportunidade de fazer as perguntas que julguei necessárias e de todas obtive resposta satisfatória.

- Tomei conhecimento de que, de acordo com as recomendações da Declaração de Helsínquia, a informação ou explicação que me foi prestada mostrou os objetivos e os métodos, com explicação dos benefícios previstos, os riscos potenciais e o eventual desconforto. Além disso, foi-me garantido que tenho o direito de recusar a todo o tempo a minha participação no estudo, sendo todos os dados eliminados, sem que isso possa ter como efeito qualquer prejuízo pessoal. Por isso, consinto a minha inclusão no estudo, proposto pela investigadora.

Declaro ter compreendido os objetivos do estudo, ter-me sido dada oportunidade de fazer todas as perguntas sobre o assunto e para todas elas ter obtido resposta esclarecedora, ter-me sido garantido que não haverá prejuízo para os meus direitos assistenciais se eu recusar esta solicitação, e ter-me sido dado tempo suficiente para refletir sobre esta proposta.

☐ *Autorizo* ☐ *Não Autorizo* ***(assinalar a opção)*** *a participação no estudo, bem como os procedimentos diretamente relacionados que sejam necessários no meu próprio interesse e justificados por razões clínicas fundamentadas.*

Hospital do Espírito Santo de Évora E.P.E, ___/___/_____
Nome: ____
Assinatura: ____