Tesis Doctoral

PHYSICAL ACTIVITY IN ADULTS UNDERGOING BARIATRIC SURGERY: ROLE ON WEIGHT LOSS AND CARDIO-METABOLIC MARKERS

Alejandro Carretero Ruiz

Febrero 2022

PROGRAMA DE DOCTORADO EN CIENCIAS MÉDICAS
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A mi madre, hermano, familia, amigos y a mi pareja.

«Las vidas de las personas son un reflejo directo de las expectativas de su grupo cercano»

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CERTIFICA:

Que la Tesis Doctoral titulada "PHYSICAL ACTIVITY IN ADULTS UNDERGOING BARIATRIC SURGERY: ROLE ON WEIGHT LOSS AND CARDIO-METABOLIC MARKERS" que presenta D. Alejandro Carretero Ruiz al superior juicio del Tribunal que designe la Universidad de Almería, ha sido realizada bajo mi dirección durante los años 2017-2022, siendo expresión de la capacidad técnica e interpretativa de su autor en condiciones tan aventajadas que lo hacen merecedor del Título de Doctor por la Universidad de Almería, siempre y cuando así lo considere el citado Tribunal.

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En Almería, 20 de diciembre de 2021

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El doctorando D. Alejandro Carretero Ruiz y los directores de la tesis D. Enrique García Artero, D. Aberto Soriano Maldonado y D. Manuel Ferrer Márquez:

Garantizamos, al firmar esta Tesis Doctoral, que el trabajo ha sido realizado por el doctorando bajo la dirección de los directores de la tesis y hasta donde nuestro conocimiento alcanza, en la realización del trabajo, se han respetado los derechos de otros autores al ser citados, cuando se han utilizado sus resultados o publicaciones.

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Directores de la Tesis

Enrique García Artero | Alberto Soriano Maldonado | Manuel Ferrer Márquez

Doctorando

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CONTENTS (CONTENIDOS)

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groups.

- **Figure 15.** Forest plot of systolic blood pressure between intervention and control groups.
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- **Figure 17.** Graphic representation of the results obtained in studies II and III (systematic reviews).

ABSTRACT

Background: Obesity has become one of the biggest health problems today, due to the comorbidities associated with it and the cardiometabolic risk that it entails. Morbid / severe obesity not only affects health but also the quality of life and socioeconomic status of patients. In isolation, physical activity and bariatric surgery are effective tools to improve comorbidities associated with morbid / severe obesity and to reduce body weight, but there are few studies that combine both, which could be a possible solution to the problems faced by by severely obese patients.

Aims: -Study I: to describe physical activity levels, body composition, blood pressure, arterial stiffness and functional capacity in adults with morbid / severe obesity awaiting bariatric surgery, as well as to analyse the association of physical activity with these health indicators. **-Study II:** To analyze the evidence on the effects of exercise training after bariatric surgery in relation to weight loss. **-Study III:** To review the evidence on the effectiveness of exercise training to improve cardiometabolic risk in patients with morbid / severe obesity who are undergoing bariatric surgery.

Main findings: Patients with morbid / severe obesity awaiting bariatric surgery have elevated levels of body fat, hip and neck circumference. In addition, patients spend most of their time doing sedentary and light activities. Exercise training after bariatric surgery seems not to result in greater weight loss compared to patients receiving only normal postoperative care. On the other hand, there are improvements in VO2max / peak in relation to body weight, absolute VO2max / peak, HDL cholesterol, and resting heart rate when using exercise as a complementary therapy after bariatric surgery.

General conclusions: This thesis provides and expands the evidence of how the combination of bariatric surgery and physical exercise affects patients with morbid / severe obesity, as well as how patients get to the surgery and the amount of physical activity they perform.

RESUMEN

Antecedentes: La obesidad se ha convertido en uno de los mayores problemas para la salud hoy en día, por las comorbilidades asociadas a la misma y el riesgo cardiometabólico que esto conlleva. La obesidad mórbida / severa no afecta únicamente a la salud sino también a la calidad de vida y al nivel socioeconómico de los pacientes. De forma aislada la actividad física y la cirugía bariátrica se muestran como herramientas efectivas para mejorar las comorbilidades asociadas a la obesidad mórbida / severa y para reducir el peso corporal, pero hay limitados estudios que combinen ambos, lo que podría suponer una solución a los problemas que afrontan los pacientes que sufren obesidad severa.

Objetivos: -Artículo I: Describir los niveles de actividad física, composición corporal, presión arterial, rigidez arterial y capacidad funcional en adultos con obesidad morbida / severa en espera de cirugía bariátrica, así como analizar la asociación de PA con estos indicadores de salud. **–Artículo II:** Analizar la evidencia en relación a los efectos del ejercicio físico después de la cirugía bariátrica en relación con la pérdida de peso. -**Artículo III:** Revisar la evidencia sobre la efectividad del ejercicio físico para mejorar el riesgo cardiometabólico en pacientes con obesidad mórbida / severa que se someten a cirugía bariátrica.

Principales hallazgos: Los pacientes con obesidad mórbida / severa a la espera de ser operados de cirugía bariátrica muestran altos niveles de grasa corporal, perímetro de cadera y de cuello. Además, estos pacientes pasan la mayoría de su tiempo realizando actividades de carácter sedentario y ligero. El ejercicio físico después de la cirugía bariátrica parece no producir una pérdida de peso mayor que aquellos pacientes que reciben únicamente los cuidados post-operatorios habituales. En cambio, sí que parecen existir mejoras en el VO_{2max} / pico en relación al peso corporal, VO_{2max} / pico absoluto, colesterol HDL y frecuencia cardiaca de reposo.

Conclusión general: La presente tesis proporciona y amplía la información de cómo afecta la combinación de cirugía bariátrica y ejercicio físico a los pacientes con obesidad mórbida / severa, así como el estado en que llegan los pacientes a la cirugía, el tipo y la cantidad de actividad física que realizan.

ABBREVIATIONS (ABREVIATURAS)

6MWT - 6 minute walk test

95% CI - 95% Confidence intervals

BMI – Body mass index / Indice de masa corporal

BP – Blood pressure / Presión sanguínea

BS – Bariatric surgery / Cirugía bariátrica

DBP - Diastolic blood pressure / Presión sanguínea diastólica

ES – Effect size

FFM – Fat-free mass / Masa libre de grasa

FM – Fat mass / Masa grasa

HC – Hip circumference / Perímetro de cintura

HR – Heart rate / Frecuencia cardíaca

HRV - Heart rate variability

MO – Morbid obesity / Obesidad mórbida

MUAC - Middle-upper arm circumference / Perímetro del brazo medio-superior

MVPA - Moderate to vigorous physical activity / Actividad física moderada a vigorosa

NC – Neck circumference / Perímetro de cuello

PA – Physical activity / Actividad física

PWV- Pulse wave velocity / Velocidad de onda de pulso

RCT-Randomized controlled trial / Ensayo controlado aleatorizado

RHR – Resting heart rate / Frecuencia cardiaca de reposo

SD - Standard deviation

SMD - Standardized mean difference

RYGB - Roux-en-Y gastric bypass

SBP - Systolic blood pressure / Presión sanguínea sistólica

SO – Severe obesity / Obesidad severa

VO_{2max} - Maximum oxygen consumption / Consumo máximo de oxígeno

WC – Waist circumference / Perímetro de cadera

INTRODUCCIÓN (INTRODUCTION)

OBESITY IN TODAY'S SOCIETY

Obesity is defined as an abnormal or excessive accumulation of fat mass (FM) that can be detrimental to health [1,2]. Due to the health problems associated, obesity is currently defined as a disease itself [3]. Obesity is usually classified according to the body mass index (BMI) as a BMI≥ 30 kg/m^2, severe (or class II) obesity as a BMI ≥ 35 kg/m^2, and morbid (or class III) obesity as a BMI ≥ 40 kg/m^2 [1,2].

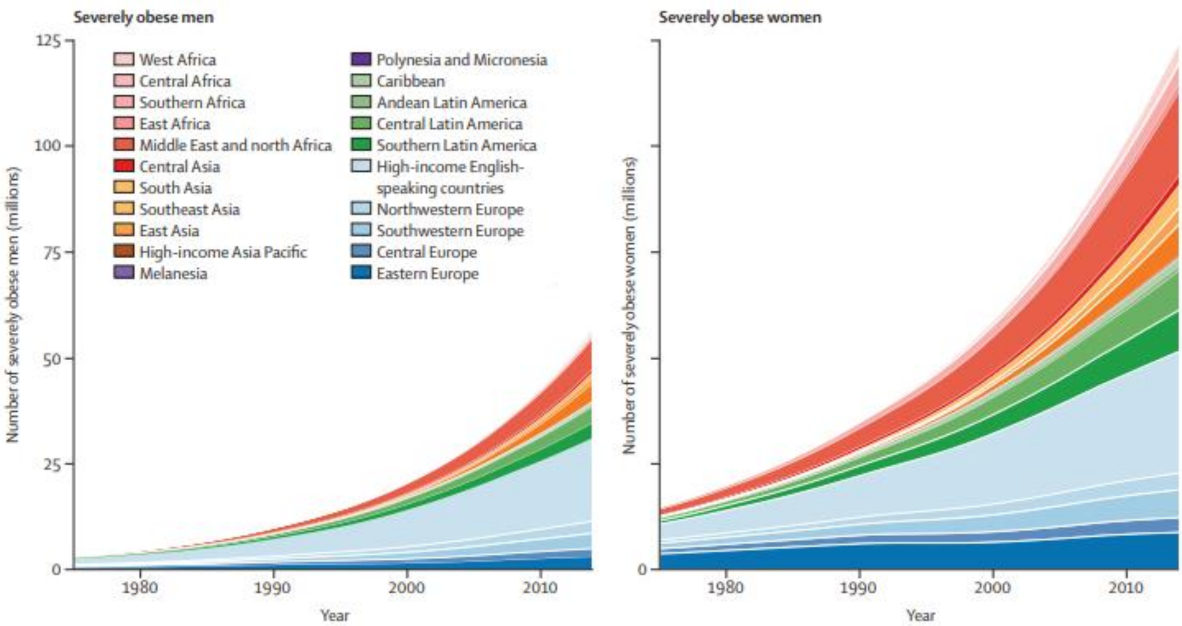


Figure 1. Trends in the prevalence of obesity and severe obesity by region.

- Source: NCD Risk Factor Collaboration [4]

Obesity is currently epidemic in nature [3], also, the trend in its prevalence is only increasing and is expected to continue in the near future. [5]. The number of people with obesity has tripled since 1975, affecting more than 650 million people worldwide in 2016. [6,7]. It has increased between 10 and 14% in most European countries in the last 10 years [8]. At the national level, in Spain the prevalence of obesity has also increased by more than 10% in the last decade [9].

In patients with obesity, healthcare cost are triggered by the greater need for medical attention, not by weight or excess FM itself but specially by the comorbidities associated with obesity. [10,11]. Morbid obesity (MO) and severe obesity (SO) mean presents a problem not only at a health level, but also at an economic level, the cost in these patients with MO / SO doubles the cost of patients with normal weight [12]. Direct medical expenses are not the only issues that suppose an extra cost, it is necessary to account in the same way those produced by receipt/purchase of drugs, loss of productivity, time in hospital and time invested by health workers, among others [13,14].

COMORBIDITIES ASSOCIATED WITH MORBID / SEVERE OBESITY

SO directly affects cardiometabolic health markers [15], causing comorbidities like hypertension [16], hyperlipidemia, type 2 diabetes, metabolic syndrome[17], respiratory problems, and sleep apnea [18], among others. In addition, the high level of adipose tissue in morbidly obese women can cause serious irregularities in menstruation, ovulation, and polycystic ovaries [19].

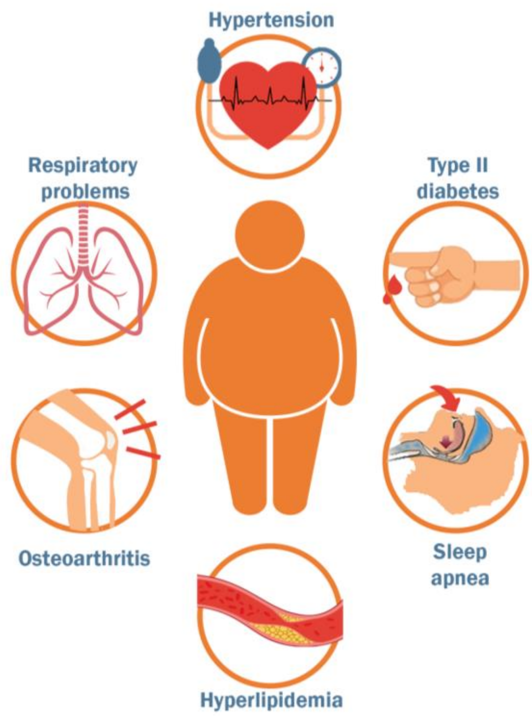


Figure 2. Graphic representation of some of the comorbidities associated with severe/morbid obesity.

Patients with obesity have a higher risk of all-cause mortality than those with a normal weight. In moderately obese patients (BMI ≥ 30 kg/m^2) the risk of death increases between 45-94% [20] compared to normal weight people, while in patients with MO (BMI ≥ 40 kg/m^2), who have a higher risk of mortality than any other obesity group [21], the risk of mortality from all-causes increases 176% [20]. This, in addition to being caused by the aforementioned comorbidities, is directly associated with the alteration of the cardiometabolic risk factors suffered by these patients, both in men and in women, highlighting that those patients who do not perform physical activity (PA) present the most adverse cardiometabolic risk profile [22]. Arterial stiffness is a marker that directly influences cardiometabolic risk and therefore it is used as a predictor of mortality [23]: patients with obesity are more likely to have high arterial stiffness [24,25], being even higher in women with MO / SO[26].

MO / SO obesity also coexists with comorbidities that limit the patient´s locomotor and functional capacity[27,28], postural control, or static-dynamic balance [29,30], such as chronic body pain associated with fibromyalgia [31,32], osteoarthritis [33,34], foot and lower back pain [35]. In addition, excess weight causes alterations in movement patterns [36].

It must be taken into account that MO / SO not only has a negative impact on health, but also on other factors that affect quality of life [37,38]. Studies have found correlations between mental illness and body weight [39]. Patients with MO have a higher number of anxiety disorders, depression [40] and social phobias [38]. Similarly, MO has a negative impact on social relationships, suffering discrimination both at work and in interpersonal relationships [41]. Furthermore, MO is associated with a lower socioeconomic status in women [42].

STRATEGIES TO MANAGE MORBID / SEVERE OBESITY AND ITS ASSOCIATED COMORBIDITIES

Weight loss significantly reduces all-cause mortality and the incidence of MO / SO-associated comorbidities [43], therefore, reducing cardiovascular risk and increasing longevity [44]. In addition, it is associated with improvements in glycemic control and reduction in the inflammatory markers associated with type II diabetes [45,46], facilitatting the remission of metabolic syndrome and hypertension [46]. Weight loss is also directly associated with improved movement patterns, reducing knee pain and improving the ability to walk [47], and increasing postural stability in people with MO [48].

Bariatric surgery (BS) is becoming the predominant treatment option for the majority of people who are clinically / severely obese and have –therefore- the highest risk of MO / SO -related mortality and comorbidity [49,50]. The most common procedures are Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy, adjustable gastric banding, and biliopancreatic diversion/duodenal switch [51,52]. BS is presented as one of the most effective strategies for weight loss and to treat comorbidities associated with SO[50,53,54]. Patients with MO / SO lose on average 12% of total body weight in the first 6 months after BS, reaching up to 45% loss of body weight during the 3 years after BS [55].

PA is a basic tool to improve health status of people with SO without BS intervention, reducing the associated comorbidities [56], directly decreasing cardiovascular risks [22] coronary heart diseases [57], asthma [58], insulin resistance, hypercholesterolemia[59], and hypertension [60]. Furthemore, exercise training decreases waist circumference (WC) [59] and reduce knee osteoarthritis pain in populations with MO [61]. Although physical training alone has not shown to be an effective strategy to increase weight loss in patients with obesity, it does play an important role in maintaining weight loss achieved by other means. [62]

The World Health Organization (WHO) recommends that adults aged 18-64 perform at least 150 minutes of moderate-intensity aerobic PA throughout the week, or at least 75 minutes of vigorous-intensity aerobic PA, or an equivalent combination of moderate- and vigorous-intensity activity (MVPA) [63]. People with MO / SO who perform a low level of PA show impaired functional capacity [64], body composition and cardiometabolic risk [65].

PHYSICAL ACTIVITY AND EXERCISE TRAINING IN BARIATRIC SURGERY PATIENTS

Patients who perform high levels of PA before BS have a better recovery after surgery, with better body composition and functional capacity [66]. Not only that, it also produces changes in lifestyle and healthy habits, which help patients to have better PA levels and better adapt to physical training after BS. [67]. It should be noted that patients with MO / SO awaiting BS do not usually comply with PA recommendations, neither in the length nor in the necessary intensity [64].

After BS there is a high probability to regain weight [68], usually 12 to 24 months later [69]. This weight gain negatively affects the functional capacity of the individual [70] and the probability of relapse of comorbidities associated with MO / SO [71], which makes it necessary to carry out lifestyle interventions (before and after [72] [73]) to prevent this from happening.

As we previously indicated, PA can directly help to maintain weight loss in patients who regain weight after BS [74]. Although PA by itself has not shown a great influence when it comes to losing body weight [62], it does when it comes to preventing weight regain and maintaining weight loss over time [75].

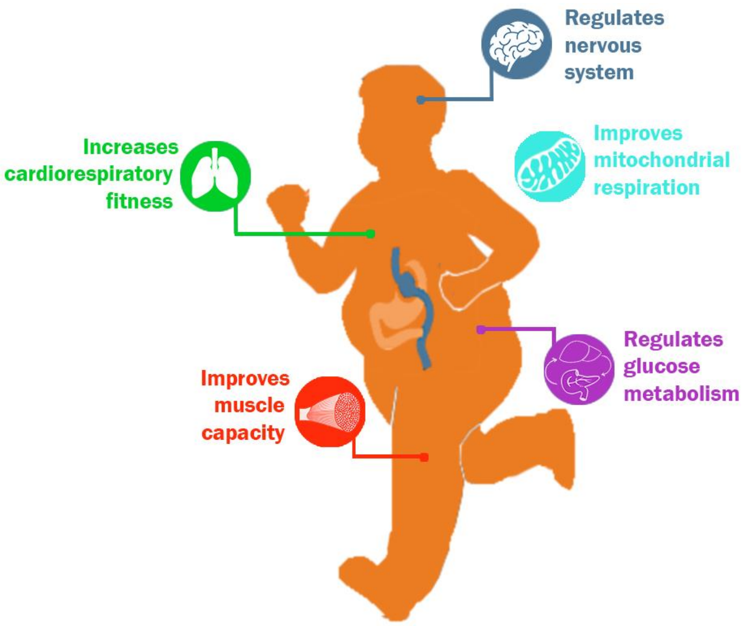


Figure 3. Graphic representation of the effects of combining BS and exercise in previous literature.

Although there are a limited number of intervention studies investigating the possibilities offered by exercise after BS, it could play a basic role and be a possible solution to the problem of MO / SO and its associated comorbidities [74,76]. Exercise training programs have been shown to be feasible, safe for BS patients [74] and produces significant improvements in cardiorespiratory fitness [77], muscle capacity [78], helping to improve mitochondrial respiration, glucose metabolism [79] and regulate autonomic nervous system dysfunction [77].

THESIS CONTRIBUTIONS

Previous studies have shown that PA levels in people with MO / SO are below the recommended amount and intensity [64]. However, there is little research on the relationship of PA with functional capacity and body composition in people with a high degree of obesity awaiting BS. **Study I** of this thesis aims to assess how patients get to BS and relate how PA affects their cardiometabolic health status.

Although there are meta-analysis prior to **study II** of this thesis that study the effect of the combination of BS and physical exercise on weight loss, none of them exclusively included studies whose intervention is solely exercise / PA, which makes it difficult to discern whether the weight loss is caused by PA or by the other components (such as nutritional, psychological or pharmacological strategies). Furthermore, no previous meta-analysis took into account the specific characteristics of each training program, which can undoubtedly influence its effect (most prevous studies, only quantified the effect of the training program and did not explore the effect size (ES) according to its characteristics).

After reviewing all the literature for **study III**, it seems necessary to clarify how exercise interventions after BS affect markers related to cardiometabolic health, given that most recent reviews have focused on the effect of the exercise program weight loss after BS or simply on the result of VO_{2max} [80].

AIMS (OBJETIVOS)

GENERAL AIM

The overall aim of this Doctoral Thesis was to assess the association of pre-BS PA with relevant obesity-related cardiometabolic markers, as well as to synthesize the evidence on the effects of post-BS exercise on weight change and cardiometabolic risk markers in patients with MO / SO undergoing BS.

SPECIFIC AIMS

Study I

I. To describe PA levels, body composition, blood pressure, arterial stiffness and functional capacity in adults with MO / SO awaiting BS, as well as to analyse the association of PA with these health indicators.

Study II

I. To analyze the evidence on the effects of exercise after BS in relation to weight loss.

II. To determine what type of exercise training could be the most appropriate for weight loss in people undergoing BS.

Study III

I. To review the evidence on the effectiveness of exercise to improve cardiometabolic risk in patients with MO / SO undergoing BS.

METHODS (MÉTODO)

The methods used to undertake the three studies comprised in this Doctoral Thesis are briefly summarized in this section.

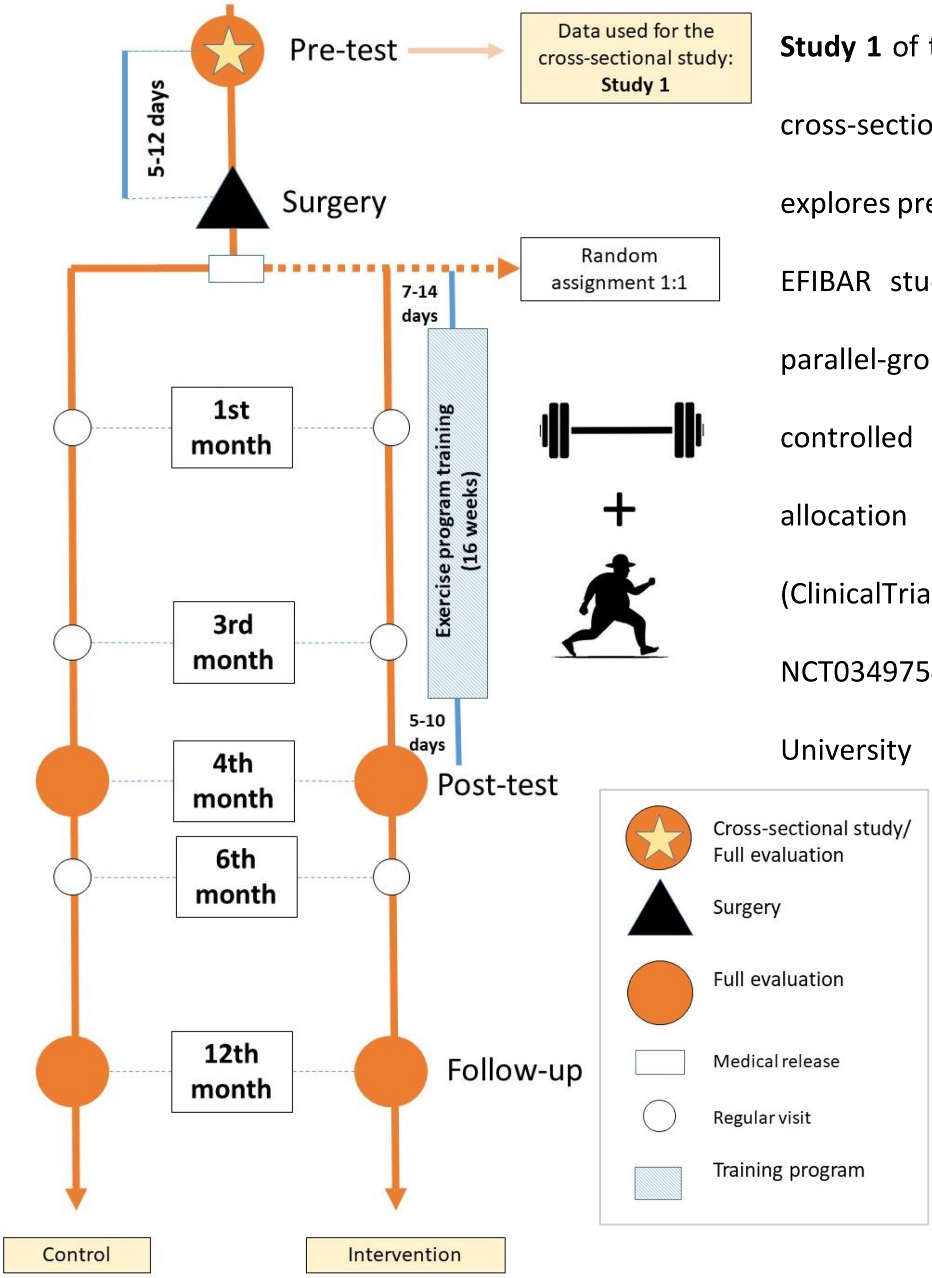


Figure 4. Diagram of the EFIBAR Project.

Study 1 of the present thesis is a cross-sectional analysis that explores pre-surgery results of the EFIBAR study. This project is a parallel-group randomized controlled trial (RCT) with an allocation ratio of 1:1 (ClinicalTrials.gov ID: NCT03497546), carried out at the University of Almería (SPORT Research Group, CTS-1024), in which patients from Torrecárdenas University Hospital and the HLA Mediterráneo Hospital were recruited (Almería, España). Participants in **study I** were evaluated from May 2018 to January 2021.

Once they are recruited to participate in EFIBAR study, patients undergo a total of 3 days of pre-surgery evaluations (**study I**). After the surgery, at medical discharge, patients are randomly allocated to the Control or Experimental group. In the case of Experimental Group, they receive 16 weeks of concurrent training (strength training and aerobic exercise combined in the same session, in that order). Once the intervention phase is finished, all participants (both at EG and CG) are re-evaluated at 4 and 12 months, as can be seen in the **figure 4**. Reduced follow-up evaluations are also present at months 3, 6 and 9 after the surgery. The EFIBAR study has been more extensively decribed in the corresponding protocol manuscript [81], and the EFIBAR training program has been adequately reported using CERT consensus [82]. All the variables and tests carried out in **study I** are summarized in **table 1,** and are developed in the methodology section of the article itself **(Annexes Study 1)**.

Table 1. Summary of the methodology used in the cross-sectional analysis (study I)

Study	Design/ Project	Participants	Outcomes	Methodology	Instruments
I.Association of physical activity with blood pressure, arterial stiffness, body composition and functional capacity in patients awaiting bariatric surgery: baseline results from the EFIBAR Study	Cross-sectional analysis / EIBAR project (RCT)	68 adults (47 women, 21 men) evaluated 5-12 days before BS, recruited at the Torrecárdenas University Hospital and the HLA Mediterráneo Hospital (Almería, España). - Age: 42.4 ± 9.6 - Weight: 129. 7 ± 22.5 kg	Body composition (anthropometric measurements and bio-impedance analysis)	• NC, MUAC, HC y WC • % FM, FM, FFM, weight and BMI	• Anthropometric tape measure • Inbody 270 bioelectrical impedance device
			Functional capacity	• Grip strength • 30-second chair stand test. • Back scratch test. • Maximal stress test following Bruce's protocol.	• Digital dynamometer T.K.K. 540 • Treadmill
			BP and arterial stiffness	• SBP and DBP • PWV	• Mobil-O-Graph® oscillometry-based pulse analysis system
			PA	• Time per day spent in sedentary activities, and activity of light, moderate and vigorous intensity • Steps per day	• Triaxial accelerometer GT3X + Actigraph

Data are presented as mean ± standard deviation (SD).

BS: Bariatric surgery; BP: Blood pressure (mmHg); DBP: Dyastolic blood pressure (mmHg); FM: Fat mass (both % and kg); FFM: Fat-free mass (kg); HC: Hip circumference (cm); MUAC: Middle-upper arm circumference (cm); NC: Neck circumference (cm); PA: Physical activity; PWV: Pulse wave velocity; RCT: randomized controlled trial; SBP: Systolic blood pressure; WC: Waist circumference

Study II is a systematic review and meta-analysis of controlled experimental studies (both randomized or non-randomized) investigating weight loss in patients undergoing BS combined with postoperative PA. A summary of the methodology used is shown in **table 3,** and is also fully explained in the article itself. The search strategy was performed using the databases MEDLINE, EMBASE, Scopus, Cochrane and Web of Science, with a deadline of May 23, 2019, and using these key words and conectors:

- (“Bariatric Surgery” OR “stapling stomach” OR “weight loss surgery” OR “obesity surgery” OR “weight reduction surgery” OR “Biliopancreatic Diversion” OR “Duodenal switch” OR “laparoscopic band” OR “lap band” OR “gastric band” OR “gastric banding” OR “Gastric Bypass” OR “Gastroplasty” OR “gastric sleeve” OR “sleeve gastrectomy” OR “gastric bypass surgery” OR “gastric bypass” OR “Roux-en-Y Gastric Bypass” OR “Maestro Rechargeable System” OR “gastric balloon” OR “gastric bubble” OR “ballobes balloon” OR “Greenville gastric bypass”) AND (“physical exercise” OR “Physical Therapy” OR “physical activity” OR “physical education” OR “physical training” OR exercise OR fitness OR sport OR “Exercise Movement” OR “exercise program” OR “Complementary Therapies” OR “physiotherapy” OR “physio therapy” OR “therapeutic exercise” OR “Occupational Therapy” OR “Exercise therapy”) AND (“body mass index change” OR “weight maintenance” OR “weight loss” OR “weight regain” OR obesity OR overweight)

Similarly, **study III** is a systematic review and meta-analysis of experimental controlled studies (again, randomized and non-randomized), but in this case including only studies analysing the effect of combining BS and PA post-surgery on cardiometabolic risk markers. **Table 3** shows a summary of the methodology used and all variables included, and is also fully explained in the article itself **(Annexes Studies II and III)**. The search strategy was performed using the databases MEDLINE, EMBASE, Scopus, Cochrane, and

Web of Science with a deadline of December 6, 2020, and using the key words and conectors indicated in **table 2.**

Table 2. Search strategy (study III)

Surgery Mode		Risk Factors		Exercise
(“Bariatric Surgery” OR “stapling stomach” OR “weight loss surgery” OR “obesity surgery” OR “weight reduction surgery” OR “Biliopancreatic Diversion” OR “Duodenal switch” OR "laparoscopic band" OR “lap band” OR “gastric band” OR “gastric banding” OR “Gastric Bypass” OR “Gastroplasty” OR “gastric sleeve” OR “sleeve gastrectomy” OR “gastric bypass surgery” OR “gastric bypass” OR “Roux-en-Y Gastric Bypass” OR “Maestro Rechargeable System” OR “gastric balloon” OR “gastric bubble” OR “ballobes balloon” OR “Greenville gastric bypass”)	AND	(“Risk factors” OR “biomarkers”) **OR** (“glycemic control” OR “metabolic outcomes” OR “diabetes” OR “diabetes mellitus” OR “type II Diabetes” OR “peptide c” OR “glycemia” OR “glucose” OR “hemoglobin level” OR “glycated hemoglobin” OR “hba1c” OR “insulin resistance” OR “fasting insulin” OR “fasting glucose”) **OR** (“Hypertension” OR “heart rate” OR “arterial hypertension” OR “blood pressure” OR “endothelial function” OR “hypertensive” OR “systolic blood pressure” OR “diastolic blood pressure” OR “diastolic” OR “systolic” OR “blood”) **OR** (“Hyperlipidemia” OR “ lipids” OR “lipoproteins” OR “dyslipidemia” OR “high cholesterol” OR “high density lipoprotein” OR “low density lipoproteins” OR “cholesterol” OR “HDL” OR “LDL” OR “blood markers” OR “triglycerides” OR “cardiometabolic risk” OR “cardiovascular diseases”) **OR** (“Inflammation” OR “Interleukin 6” OR “IL-6” OR “C-reactive protein” OR “CRP” OR “alfa1-acid glycoprotein” OR “AGP” OR “adipokines” OR “adiponectin” OR “cytokines”)	AND	(“physical exercise” OR “Physical Therapy” OR “physical activity” OR “physical education” OR “physical training” OR exercise OR fitness OR sport OR “Exercise Movement” OR “exercise program” OR “Complementary Therapies” OR “physiotherapy” OR “manual therapy” OR “therapeutic exercise” OR “Occupational Therapy” OR “Exercise therapy” OR “Physical Fitness” OR “Resistance Training” OR “rehabilitation”)

Table 3. Summary of the methodology used in the systematic reviews (studies II and III).

Study	**Design**	**Search Strategy**	**Inclusion Criteria**	**Exclusion Criteria**	**Quantitative Outcomes**
II.Effects of exercise training on weight loss in patients who have undergone bariatric surgery: a systematic review and meta-analysis of controlled trials.	Systematic review and meta-analysis	The systematic search was carried out using the databases MEDLINE, EMBASE, Scopus, Cochrane, and Web of Science, Deadline May 23, 2019	Randomized and non-randomized controlled trials analysing the effect of post-surgery PA on weight loss in BS patients	a. Articles not written in English or Spanish b. Studies that do not report change in body weight c. Studies in which the PA intervention is performed before BS d. Studies not performed in humans e. Articles with participants under 18 years of age f. Studies that combine PA with another type of intervention (medication, nutrition, among others) g. Studies retracted h. Duplicate studies i. Non-selectable publications, such as reviews, guidelines, interviews, comments, or case studies	• Loss of body weight
III.Impact of exercise training after bariatric surgery on cardiometabolic risk factors: a systematic review and meta-analysis of controlled trials	Systematic review and meta-analysis	The systematic search was carried out using the databases MEDLINE, EMBASE, Scopus, Cochrane, y Web of Science Deadline December 6, 2020	a. Randomized and non-randomized controlled trials b. PA-based intervention in patients undergoing BS c. Written in Spanish or English d. Measuring at least one outcome related to cardiometabolic risk (VO_2max or peak, BP, HR, lipid profile, glucose, insulin, or markers of inflammation)	a. Articles not written in English or Spanish b. Studies that do not report at least one of the selected outcomes (VO_2max or peak, BP, HR, lipid profile, glucose, insulin, or markers of inflammation) c. Studies in which the PA intervention is performed before BS d. Animal studies	• VO_2máx or peak absolute • VO_2máx or peak relative to body weight • HDL Cholesterol • RHR • DBP • SBP

			e. Articles with participants under 18 years of age f. Studies that combine PA with other types of intervention, such as medications, nutrition, lifestyle, etc g. Studies retracted h. Duplicate studies i. Non-selectable publications, such as reviews, guidelines, interviews, comments, or case studies	

BP: Blood pressure; BS: Bariatric surgery; DBP: Diastolic blood pressure; HR: Heart rate; PA: Physical activity; RHR: Rest heart rate; SBP: Systolic blood pressure.

STATISTICAL ANALYSIS

Analyses conducted for study I

The different data collected in this study is shown as frequency and percentage, or mean and standard deviation (SD). Both parametric and non-parametric tests were performed. To verify normality in the distribution the Kolmogorov-Smirnov test was used, while one-way ANOVA test was used to determine homogeneity of variance. T test for independent samples was used to compare men and women means in data with normal distribution, and the Mann-Whitney U test for variables with non-parametric distribution. In addition, to analyze correlation between variables, P-Pearson was used for variables with parametric distribution and Spearman's rank correlation for variables with non-parametric distribution. Statistical analyses were performed using the SPSS V.23.0 statistical software package (IBM SPSS Statistics, Chicago, IL, USA), and statistical significance was determined at $p < 0.05$.

Analyses conducted for study II

The software used to perform the statistical analyses of the meta-analysis was StataSE V.14.0. The analysis variable (the result) was the weight loss at the end of the treatment in each of the groups, the quantification of the effect was calculated through the standardized mean difference (SMD) and through the unbiased Hedges estimator [83]. Weightings and SDs were extracted for each study and group before and at the end of the treatment. In the case of not having the SD values, these were imputed as the average value of each group [84]. On the other hand, the differences of the weight means and the SD of the difference for each of the articles were calculated; for the latter, a correlation of 0.59 was considered between the values before and after starting the treatment [85]. A positive SMD value indicated greater weight loss in the intervention group compared to the control group. The DerSimonian-Laird random effects method was used and the 95% confidence intervals were calculated (95% CI) [86]. As a test to evaluate heterogeneity, we estimated the I^2 statistic [87] - values of 0% indicated non-heterogeneity whereas values of 25%, 50% and 75% were interpreted as having a low, moderate and high level of heterogeneity, respectively. In addition, the Q statistic and its P value were calculated.

The publication bias was evaluated by the funnel plot and the Egger test was obtained. To complete the statistical analysis, certain details were contemplated: I) when two or more studies obtained the data from the same database, only the main study was taken into account; II) those papers with two intervention groups were analyzed as two individual studies; III) pre-operative body weight data were collected using the baseline and post-intervention data from the evaluation performed immediately after the surgery. Subgroups analyses were carried out considering the following characteristics of the training intervention protocols: I) the type of PA intervention; II) the start of the intervention after the surgery; III) the duration of the intervention; IV) the type of exercise; and V) the total exercise time per week.

Meta regressions with random effects were employed using the aggregate level data to know the effect of the intervention and the heterogeneity in relation to: I) the average age of the participants, II) the time per session, and III) the length of the intervention.

Finally, a sensitivity analysis was conducted by performing the calculations again, without each of the studies, to know the robustness of that particular study.

Analyses conducted for study II

The comprehensive MetaAnalysis 2.0 software was used to perform the main statistical analysis as well as the sensitivity analysis. The outcomes were HDL, systolic blood pressure (SBP) and diastolic blood pressure (DBP), resting heart rate (RHR), fasting glucose, absolute VO_{2max}, and VO_2max relative to weight. The size effect, which quantifies the degree to which the sample results diverge from the expectations specified in the null hypothesis [88], was calculated using the SMD and the Hedge´s g estimator [83]. Furthermore, sizes effect were expressed as the weighted mean difference between control and intervention group when the results of the evaluations were performed with the same units of measurement and the evaluation tests were similar, such as VO_{2max} / VO_{2peak} relative to weight, RHR, SBP and DBP. Random-effects meta-analysis using the DerSimonian-Laird method was used and the 95% CI were calculated [86]. The direction of the effects in the funnel plot was positive when it favored the intervention group and negative when it favored the control group.

Two-sided P<.05 were calculated as the significance level. In addition, The Q-value and the I^2 statistic were used to assess heterogeneity between the studies included in the different forest plots [87,89]. A I^2 value of 0-40% indicates non-important heterogeneity, 30-60% moderate heterogeneity, 50-90% substantial heterogeneity, and 75-100 % considerable heterogeneity [90].

When performing the statistical analyses and extracting the data from each study, the following criteria were applied: I) if two or more studies used an identical intervention taken from the same database to achieve an outcome, only the data from the main study were used; and II) outcome data were collected using the pre- and post-intervention evaluations (i.e., before and after the PA program). Only in the absence of a pre-intervention assessment were the pre-surgery data used as a proxy. Sensitivity analyses were conducted by removing each study one by one to observe possible variations. Funnel plots and the Egger test were performed to check for the presence of publication bias [91], $P \leq 0.1$ was used as the Egger test significance level [92]. Meta-regressions and subgroup analyses could not be performed because there were not enough studies (at least 10 studies for meta-regressions and 4 for subgroup analyses).

RESULTS (RESULTADOS)

The results of each study that make up and derive this doctoral thesis are presented below.

STUDY I. ASSOCIATION OF PHYSICAL ACTIVITY WITH BLOOD PRESSURE, ARTERIAL STIFFNESS, BODY COMPOSITION AND FUNCTIONAL CAPACITY IN PATIENTS AWAITING BARIATRIC SURGERY: BASELINE RESULTS FROM THE EFIBAR STUDY (Annexes. Study I)

Out of 70 participants who completed pre-surgery examinations, 2 were excluded due to not meeting the accelerometer wear-time criterion. Thus, a total of 68 patients (47 women, 69%) were included in this analysis (**figure 7**). Descriptive characteristics of the study participants are shown in **Table 2**. Mean age was 42.4 ± 9.6 years, with an average weight of 129.7 ± 22.5 kg, a BMI of 47.4 ± 7.1 kg/m^2, fat free mass (FFM) of 64.0 ± 12.8 kg, and percentage body fat of 50.8 ± 5.3 %. The average neck circumference (NC) was 42.4 ± 6.1 cm and WC 126.7 ± 15.9 cm. Significant differences between men and women were observed in all parameters except in age, SBP, BMI, fat mass (kg), middle-upper arm circumference (MUAC) and hip circumference (HC).

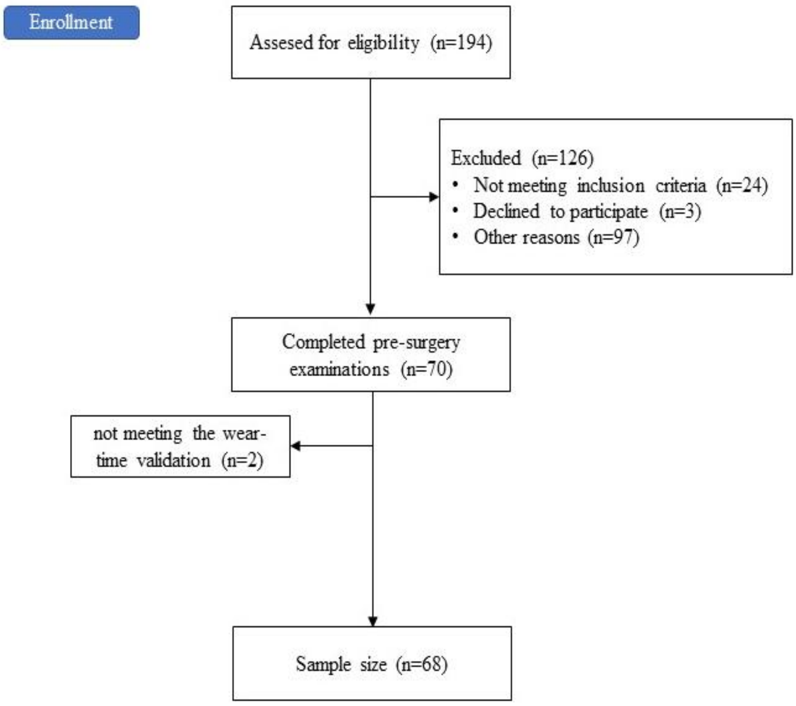


Figure 5. Enrollment flow-chart (study I)

Average scores for functional capacity tests were as follows: the back scratch test -13.8 ± 8.3 cm; chair stand test 10.7 ± 2.8 repetitions in 30 seconds; hand grip test 34.8 ± 10.3 kg; and estimated METs in the maximal treadmill test 6.1 ± 2.3. Significant differences were observed between men and women in the back scratch test, hand grip and estimated METS.

Table 4. Basic characteristics, body composition and blood pressure (study I).

	Total (n=68)	Men (n=21)	Women (n=47)	*p*
Age	42.4 (9.6)	44.7 (10.4)	41.4 (9.2)	0.19
		Body composition		
Height (cm)	165.8 (9.1)	175.3 (6.4)	161.5 (6.6)	**< 0.01**
Weight (Kg)	129.7 (22.5)	147.8 (21.0)	121.2 (17.8)	**< 0.01**
BMI (Kg/m²)	47.4 (7.1)	48.8 (8.8)	46.7 (6.1)	0.28
Fat mass (Kg)	66 (13.9)	68.8 (18.4)	64.7 (11.1)	0.27
Fat mass (%)	50.8 (5.3)	46.2 (6.6)	53.1 (2.3)	**< 0.01**
FFM (kg)	64 (12.8)	78.3 (7.4)	56.9 (7.9)	**< 0.01**
		Blood pressure and arterial stiffness		
SBP (mmHg)	131.4 (16.1)	136.5 (15.7)	128.9 (15.8)	0.08
DBP (mmHg)	83.4 (10.3)	87.6 (11.3)	81.3 (9.1)	**0.02**
PWV (m/s)	6.7 (1.0)	7.1 (0.9)	6.5 (1.0)	**0.04**
		Circumferences		
NC (cm)	42.4 (6.1)	49.3 (3.9)	39.4 (4)	**< 0.01**
MUAC (cm)	41.6 (4.8)	42.0 (2.3)	41.5 (5.5)	0.76
WC (cm)	126.7 (15.9)	138.9 (14)	121.8 (13.6)	**< 0.01**
HC (cm)	140.3 (15.4)	140.0 (16.0)	140.4 (15.3)	0.91
		Functional capacity		
Back Scratch (cm)	-13.8 (8.3)	-23.0 (11.5)	-13.8 (8.3)	**< 0.01**
30sec-chair Stand (reps)	10.7 (2.8)	11.2 (2.4)	10.5 (2.9)	0.4
Hand Grip (kg)	34.8 (10.3)	47.3 (7.2)	29 (5.1)	**< 0.01**
Maximal treadmill test				
Total time (min)	5.1 (2.3)	4.9 (1.9)	5.3 (2.3)	0.49
HR max	160.8 (14.4)	156.8 (18.3)	161.8 (11.7)	0.21
Borg scale	7.1 (1.1)	7 (1.1)	7.2 (1.1)	0.64
Estimated METS	6.1 (2.3)	5.5 (2.2)	6.9 (2.4)	0.2
		Physical activity levels		
Sedentary (%)	65.8 (12.5)	64.9 (14.4)	66.2 (10.1)	0.71
Light (%)	29.7 (10.6)	30.0 (12.0)	29.6 (10.1)	0.88
Moderate (%)	4.4 (2.8)	5.0 (3.2)	4.1 (2.5)	0.22
Vigorous (%)	0.1 (0.4)	0.1 (0.1)	0.2 (0.4)	0.39
Total MVPA (min/day)	45.7 (29.1)	49.2 (34.3)	44.2 (26.8)	0.52
Steps per day	5518 (2512)	5760 (3019)	5408 (2277)	0.61

Data are shown as mean (SD).

BMI: Body Mass Index; FFM: fat-free mass; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PWV: Pulse wave velocity; NC: Neck circumference; MUAC: Mid-upper arm circumference; WC: Waist circumference; HC: Hip circumference; HR: Heart rate; MVPA: Moderate to vigorous physical activity.

75.4% of the participants met the recommendations of 150 min/wk of MVPA. Furthermore, no significant differences were observed between men and women in any PA parameter, as seen in Table 4. The average time in sedentary activities per day was 687.0 ± 226.1 min (65.8 ± 12.5 %), in light activities 300.1 ± 107.6 min (29.7 ± 10.6 %), in moderate activities 44.3 ± 27.5 min (4.4 ± 2.8 %), and in vigorous activities 1.4 ± 3.5 min (0.1 ± 0.4 %). Women performed on average 5407.9 ± 2276.7 steps per day, while men performed 5760.3 ± 3019.3 steps.

Table 5. Correlations of physical activity with functional capacity.

Physical activity	Back Scratch (cm)	Hand Grip (Kg)	Chair Stand (reps/30seg)	Total time (min)	HR max	Borg scale	METS
Sedentary (%)	r: -0.15	r: 0.03	r: 0.09	r: -0.25	r: 0.02	r: -0.50 **	r: 0.00
Light (%)	r: 0.13	r: 0.00	r: -0.12	r: 0.01	r: -0.02	r: -0.51	r: -0.40
Moderate (%)	r: 0.17	r: 0.12	r: 0.02	r: 0.07	r: 0.04	r: 0.39 *	r: 0.14
Total MVPA/day	r: 0.15	r: 0.11	r: 0.04	r: 0.08	r: 0.04	r: 0.40	r: 0.19
Steps per day	r: 0.07	r: 0.15	r: 0.05	r: 0.14	r: -0.01	r: 0.42 *	r: 0.23

* p < 0.05; ** p < 0.01; MVPA: moderate-to-vigorous physical activity; HR: heart rate.

Table 5 shows correlations between PA and functional capacity. More time spent in sedentary activities was correlated with a lower perceived effort (Borg scale) during the maximal treadmill test (r: -0.5; *p*: 0.009). On the other hand, those participants who performed more steps per day perceived a greater effort (Borg scale) during the treadmill test (r: 0.42; *p*: 0.04), the same occurs with patients who perform a more moderate PA (r: 0.39; *p*: 0.04). Correlation analysis between PA and body composition are presented in **table 6**, with none of them achieving statistical significance.

Correlation analysis of PA with body circumferences, blood pressure and arterial stiffness is shown in **table 7**. A significant positive correlation was observed between the MUAC and time spent in sedentary activities (R: 0.31; *p*: 0.01). Negative significant correlations were between MUAC and number of steps per day MUAC (R: -0.29; *p*: 0.02), furthermore between MUAC and light PA (R: -0.34; *p*: <0.01).

Table 6. Correlations of physical activity with body composition.

Physical activity	BMI (Kg/m^2)	Fat mass (%)	FFM (kg)
Sedentary (%)	r: 0.03	r: -0.4	r: 0.03
Light (%)	r: -0.08	r: 0.09	r: -0.1
Moderate (%)	r: -0.03	r: -0.19	r: 0.11
Total MVPA/day	r: -0.02	r: -0.01	r: 0.086
Steps per day	r: 0.08	r: -0.08	r: 0.07

None of the correlations were significant.

BMI: body mass index; FFM: fat-free mass.

Table 7. Correlation analysis of physical activity with body circumferences, blood pressure and arterial stiffness.

Physical activity	NC	MUAC	WC	HC	SBP (mmHg)	DBP (mmHg)	PWV (m/s)
Sedentary (%)	r: 0.14	r: 0.31 **	r: 0.08	r: -0.04	r: -0.06	r: -0.16	r: -0.08
Light (%)	r: -0.15	r: -0.34 **	r: -0.08	r: 0.05	r: 0.14	r: 0.16	r: 0.14
Moderate (%)	r: -0.02	r: -0.10	r: -0.03	r: -0.01	r: -0.2	r: 0.14	r: -0.12
Total MVPA/day	r: -0.07	r: -0.05	r: -0.50	r: -0.03	r: -0.21	r: 0.13	r: -0.13
Steps per day	r: -0.19	r: -0.29*	r: -0.14	r: -0.09	r: -0.09	r: 0.07	r: 0.01

* p < 0.05; ** p < 0.01

MUAC: mid-upper arm circumference; WC: Waist circumference; HC: Hip circumference; NC: Neck circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PWV: Pulse wave velocity

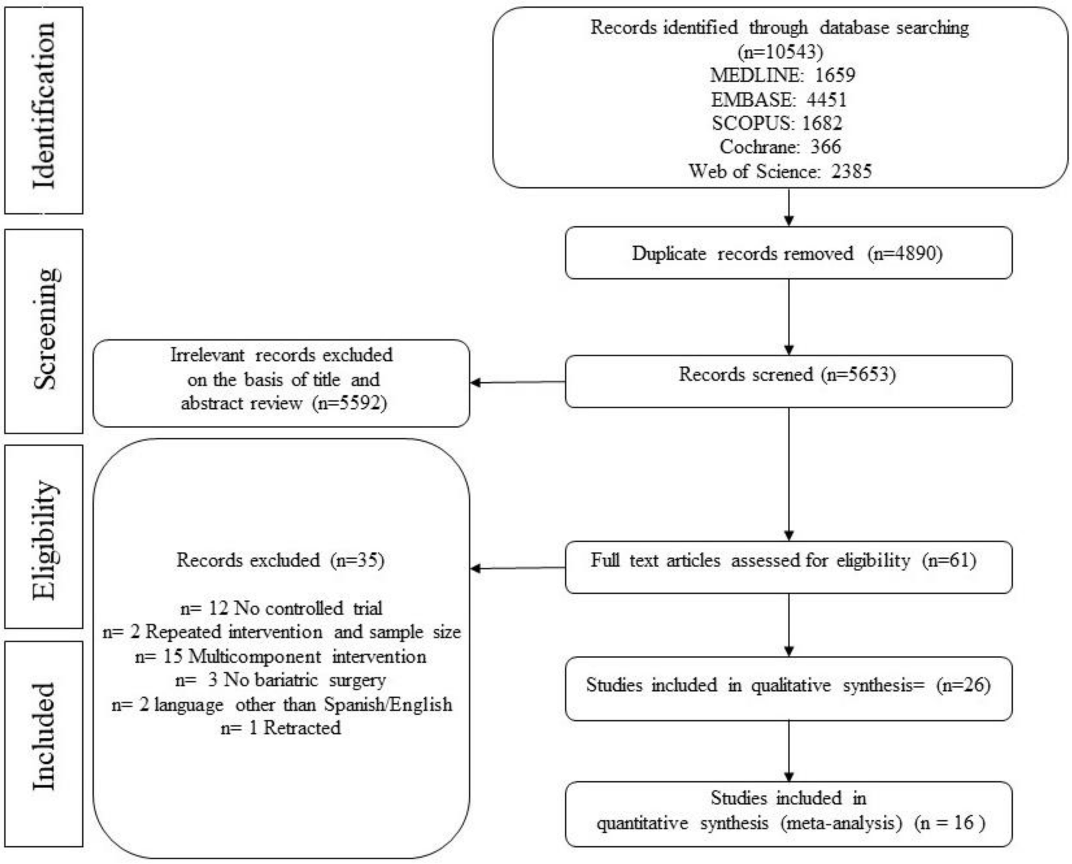
STUDY II. EFFECTS OF EXERCISE TRAINING ON WEIGHT LOSS IN PATIENTS WHO HAVE UNDERGONE BARIATRIC SURGERY: A SYSTEMATIC REVIEW AND META-ANALYSIS OF CONTROLLED TRIALS (Annexes Study II)

Systematic review

Of the 10543 studies obtained in the search, 26 documents were finally selected (**Figure 6**). These were carried out in different countries - 10 from the United States, 6 from Brazil, 2 from Iran, 4 from Denmark and 1 from Belgium, Sweden, Italy and the United Kingdom, respectively. All the studies included were experimental, most of them with an RCT design (21) while 5 were non-RCTs. All 26 studies were published between 2011 and 2018 (**Annexes Study II. Table 1**).

The internationally accepted criteria to undergo BS are a BMI ≥ 40 kg / m^2 or a BMI ≥ 35 kg / m^2 if comorbidities are present that put the patient's health at risk. Most of the selected studies included any type of surgical technique, apart from 9 of them which included only laparoscopic surgery with RYGB, and 1 study on the sleeve gastrectomy technique. The sample size of the studies varied between 12 and 120 subjects, most of them including participants of both sexes, except for 5 studies which only used women.

Figure 6. Literature search Preferred Reporting Items for Systematic Reviews and Meta-Analyses consort diagram (study II).



The PA interventions carried out were supervised in 12 of the studies, programmed in 4, while 8 were mixed interventions, combining programmed and supervised. Only 1 study used a counseling intervention type. Aerobic exercise alone was used in 11 studies, resistance exercise alone in 2 of them, whereas a combination of both was used in 10 studies, and other alternative types of exercise in 3 studies. The reviewed studies used exercise durations between 20 and 85 min per session. The maximum length of the intervention was 40 weeks and the shortest was 1 week. The start of the intervention varied between 5 days and 24 months after surgery.

Risk of bias

Regarding the risk of bias, as can be seen in **tables 8** and **9**, from the 24 studies analyzed, 10 of them show a high risk of bias (38.5%), 6 show a moderate risk of bias (23.1%) and the other 10 (38.5%) show a low risk of bias. Analyzing the sections considered in both assessment tools individually, we can observe that all non-RCTs (n=5, 100%) present deficiencies (i.e., scored as weak) in the blinding domain study, while in the case of RCTs, 38.1% (n=8) and 14.3% (n=3) show detection bias and performance bias, respectively. Among the non-RCT studies, deficiencies in the selection bias and the design of the study were present in 40% of the studies (n=2) compared to 5.3% (n=1) showing selection bias amongst the RCTs

Table 8. The Cochrane Collaboration's tool for assessing the risk of bias in randomized trials.

RCTs	Selection Bias	Performance Bias	Detection bias	Attrition bias	Reporting bias	Other bias	Risk of bias
Carnero et al 2017 [93]	Strong	Strong	Strong	Moderate	Strong	Strong	Low
Casali et al 2011 [94]	Moderate	Moderate	Weak	Moderate	Moderate	Strong	Moderate
Castello et al 2011 77	Moderate	Weak	Weak	Moderate	Moderate	Strong	High
Castello-Simoes et al 2013 [95]	Moderate	Weak	Weak	Moderate	Moderate	Strong	High
Coen et al 2015 [96]	Strong	Moderate	Strong	Strong	Strong	Strong	Low
Coen et al 2015 (2) [79]	Strong	Moderate	Strong	Strong	Strong	Strong	Low
Coleman et al 2017 [97]	Strong	Moderate	Moderate	Weak	Moderate	Strong	Moderate
Creel et al 2016 [98]	Strong	Weak	Moderate	Weak	Moderate	Strong	High
Daniels et al 2018 [99]	Strong	Strong	Strong	Moderate	Strong	Strong	Low
Hassannejad et al 2017 [100]	Strong	Moderate	Weak	Strong	Strong	Strong	Moderate
Herring et al 2017 [101]	Strong	Moderate	Weak	Strong	Strong	Strong	Moderate
López et al 2017 [102]	Strong	Strong	Moderate	Moderate	Strong	Strong	Low
Mundbjerg et al 2018 [103]	Strong	Strong	Moderate	Strong	Strong	Strong	Low
Mundbjerg et al 2018 (2)[65]	Strong	Strong	Moderate	Strong	Strong	Strong	Low
Oliveira et al 2016 [104]	Moderate	Moderate	Weak	Weak	Weak	Moderate	High
Rojhani et al 2016 [105]	Moderate	Moderate	Weak	Weak	Moderate	Moderate	High
Shah et al, 2011 [106]	Strong	Moderate	Moderate	Moderate	Weak	Strong	Moderate
Stolberg et al 2018 [107]	Strong	Strong	Moderate	Strong	Strong	Strong	Low
Stolberg et al 2018 (2) [108]	Strong	Strong	Moderate	Strong	Strong	Strong	Low
Wiklund et al 2015 [109]	Weak	Moderate	Weak	Weak	Weak	Strong	High
Woodlief et al 2015 [110]	Strong	Moderate	Strong	Strong	Strong	Strong	Low

RCTs: Randomized controlled trials.

Table 9. The Quality assessment tool for quantitative studies.

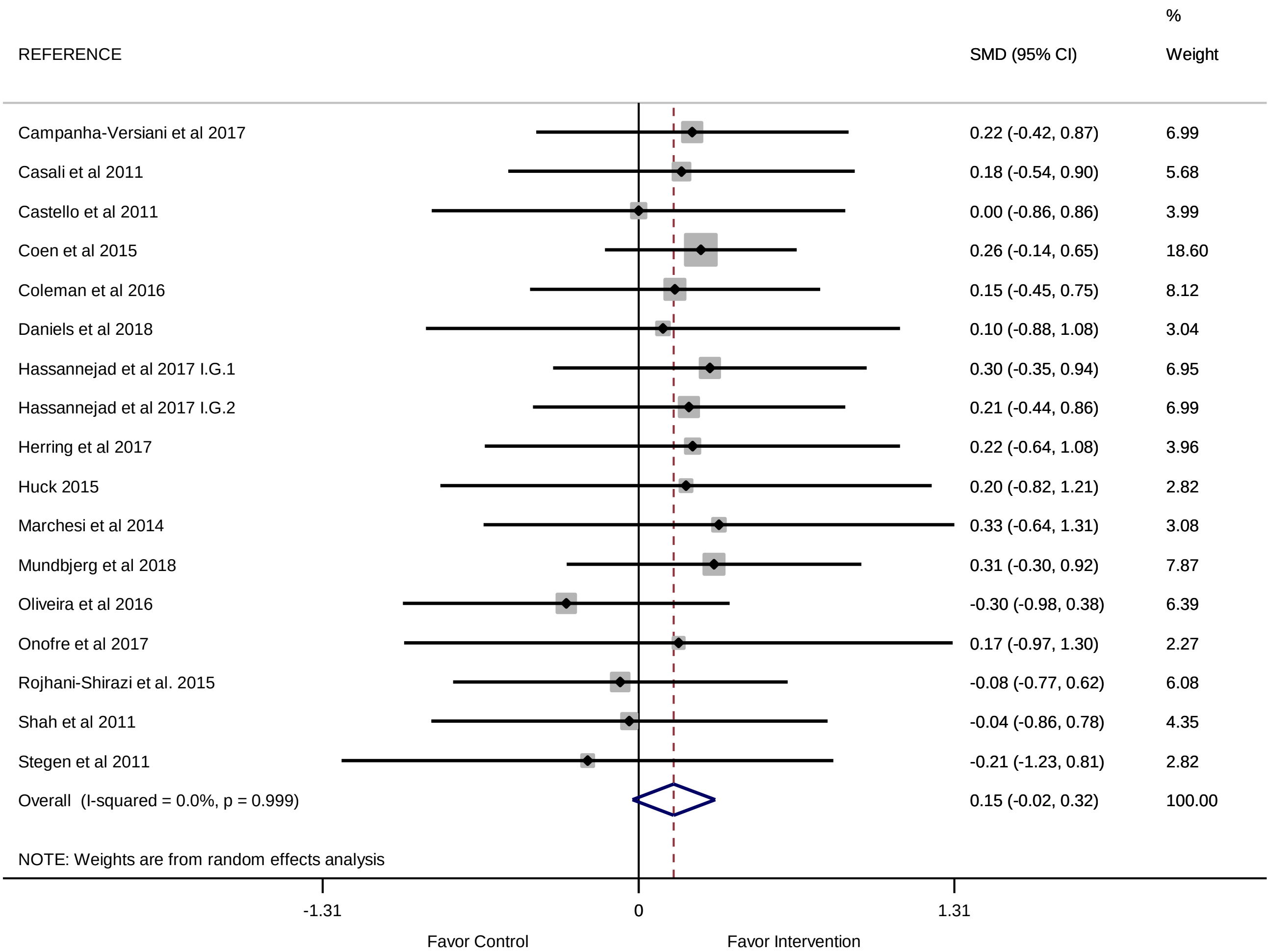
Non-RCTs	Selection bias	Study design	Confounders	Blinding	Data collection	Withdrawals/ drop-outs	Risk of bias
Campanha-Versiani et al 2017 [111]	Weak	Moderate	Strong	Weak	Strong	Strong	High
Huck et al 2015 [112]	Moderate	Moderate	Moderate	Weak	Strong	Strong	Moderate
Marchesi et al 2015 [113]	Moderate	Weak	Strong	Weak	Strong	Moderate	High
Onofre et al 2017 [114]	Weak	Moderate	Moderate	Weak	Strong	Strong	High
Stegen et al 2011 [78]	Moderate	Weak	Strong	Weak	Strong	Strong	High

Non- RCTs: Non-randomized controlled trials.

Meta-analyses

The pooled SMD estimate did not show a greater significant weight loss in favor of the intervention (exercise) group, with a small ES and no significant differences (SMD=0.15; 95% CI= -0.02, 0.32; p=0.094), as well as low heterogeneity (I^2= 0%; p = 0.999) **(Figure 7)**.

Figure 7. Forest plot of the weight loss standardized mean difference between the control group and the intervention group.



SMD: Standardized Mean Difference; CI: Confidence Interval.

Subgroup analyses

When considering the specific characteristics of the PA intervention (i.e., type of intervention, start of the intervention after surgery, duration, type of exercise and total time per week), none of the subgroups analyses showed a significant difference in favor of the control group or the intervention group, with heterogeneity being very low in all cases (I^2= 0.0%) **(Table 10)**.

Table 10. Stratified analysis according to the characteristics of the exercise program.

	Control group vs. Intervention group				
Subgroups analysis	**Number of studies**	**Pooled SMD (95%CI)**	**I^2**	**X^2**	**P**
		Type of intervention			
Physical activity programmed	3	0.153 (-0.229, 0.535)	0.0	0.63	0.434
Physical activity supervised	9	0.101 (-0.160, 0.363)	0.0	2.53	0.447
Physical activity programmed/supervised	4	**0.202 (-0.091, 0.495)**	**0.0**	**0.50**	**0.176**
		Start of intervention after the surgery			
≤ 3 months	11	0.123 (-0.081, 0.328)	0.0	3.21	0.238
> 3 months	5	**0.199 (-0.128, 0.526)**	**0.0**	**0.55**	**0.234**
		Duration of the intervention			
≤ 16 weeks	12	0.064 (-0.166, 0.294)	0.0	2.64	0.587
> 16 weeks	5	**0.248 (-0.008, 0.504)**	**0.0**	**0.18**	**0.057**
		Type of exercise			
Aerobic training	5	**0.209 (-0.073, 0.490)**	**0.0**	**0.77**	**0.146**
Resistance training	2	0.147 (-0.559, 0.853)	0.0	0.02	0.683
Aerobic/resistance combination	7	0.189 (-0.085, 0.463)	0.0	0.79	0.176
Alternative training	3	-0.075 (-0.476, 0.327)	0.0	0.90	0.715
		Time of exercise			
≤ 150 min/week	4	**0.165 (-0.110, 0.441)**	**0.0**	**2.24**	**0.240**
> 150 min/week	13	0.134 (-0.084, 0.352)	0.0	1.64	0.228

SMD: Standardized Mean Difference; CI: Confidence Interval.

Note 1: Positive SMD values indicate a higher score in outcomes favoring the intervention group.

Note 2: Results in bold, are those that show a higher SMD

Meta regressions

The meta-regression analyses showed no heterogeneity based on the participants' mean age (p=0.902), nor on the length of the intervention (p=0.377) or the time devoted to each exercise session (p=0.807) **(Table 11)**.

Table 11. Meta-regression of weight loss with mean age, length of intervention and time per session.

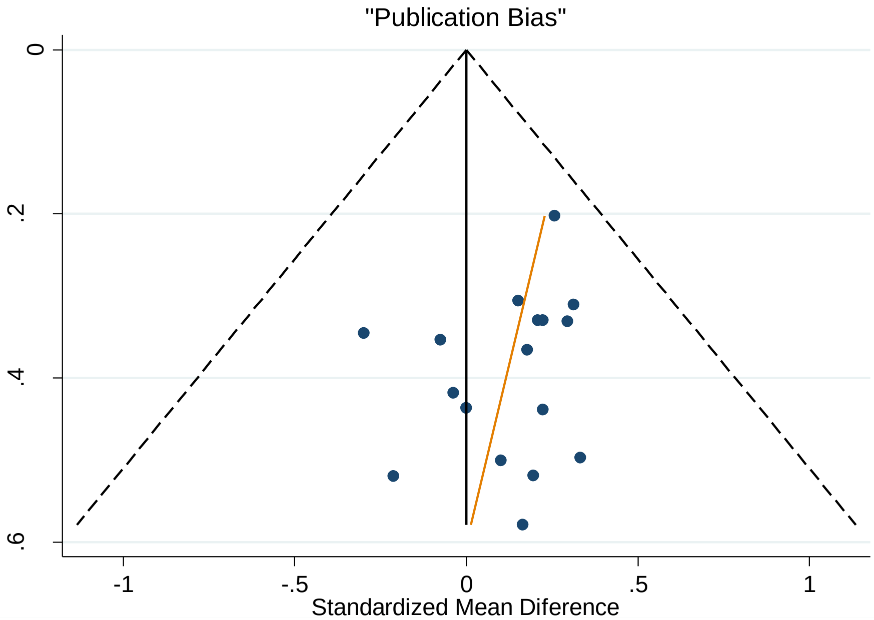
	Mean age			Length of intervention			Time per session		
	I^2	*β (95% CI)*	*p*	I^2	*β (95% CI)*	*p*	I^2	*β (95% CI)*	*P*
SMD Weight Loss	0%	-0.002 (-0.042, 0.037)	0.902	0%	0.006 (-0.008, 0.002)	0.377	0%	-0.001 (-0.013, 0.01)	0.807

CI: Confidence Interval. SMD: Standardized Mean Difference.

Sensitivity analysis and publication bias

Once the impact of each study was verified in the final result, eliminating each study individually, no changes were observed in the overall results. As seen in the funnel plot **(Figure 8)** and once the Egger test was performed, there was no evidence of significant publication bias risk (p=0.208).

Figure 8. Funnel plot with Egger test.

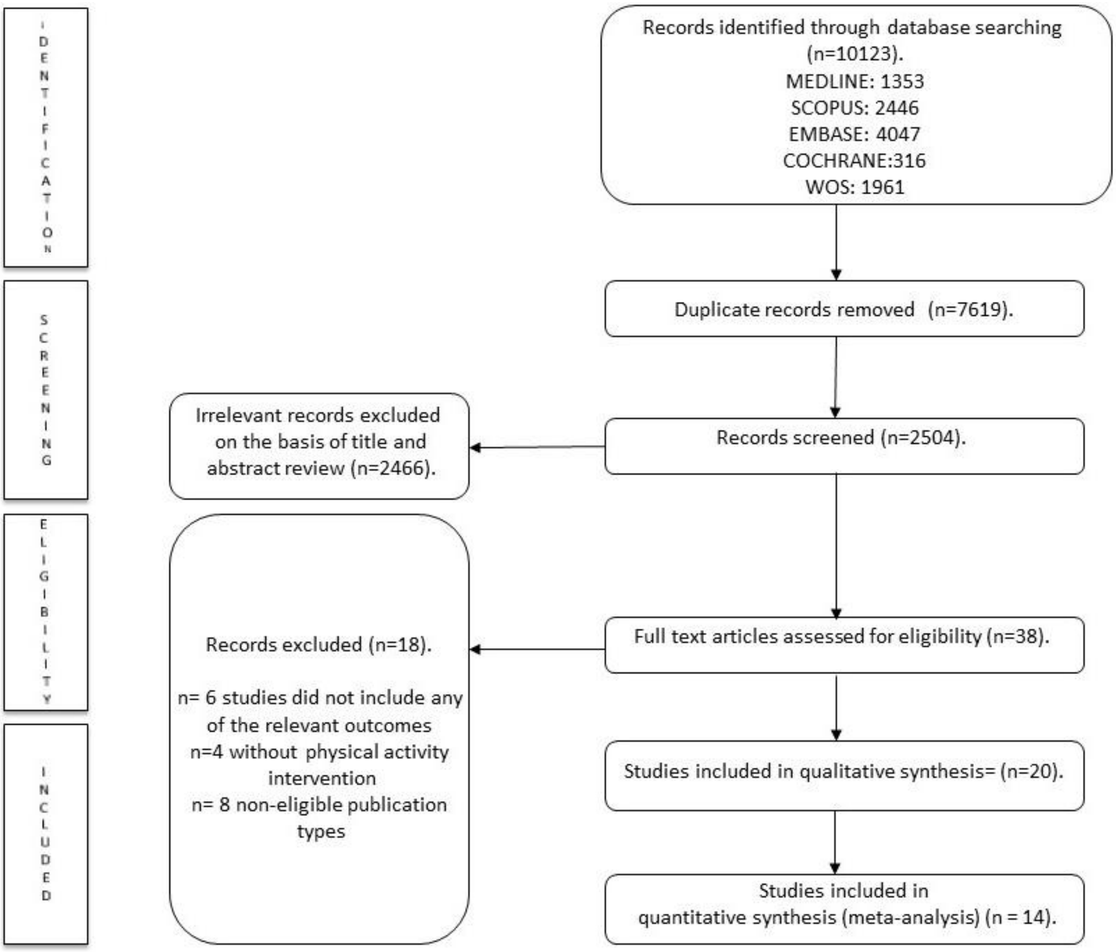


STUDY III. IMPACT OF EXERCISE TRAINING AFTER BARIATRIC SURGERY ON CARDIOMETABOLIC RISK FACTORS: A SYSTEMATIC REVIEW AND META-ANALYSIS OF CONTROLLED TRIALS (Annexes Study III)

Systematic review

Out of a total of 10,123 articles obtained in the search, 2,466 were eliminated once all the titles and abstracts were reviewed, and 20 articles were included after meeting all the selection criteria **(Figure 9)**. All the included studies had an experimental design with the participants of the intervention group performing an exercise program after the BS, 16 of them being RCTs and four non-randomized (non-RCTs). Finally, 14 of them could be used for the meta-analysis.

Figure 9. Literature search Preferred Reporting Items for Systematic Reviews and Meta-Analyses consort diagram (study III).



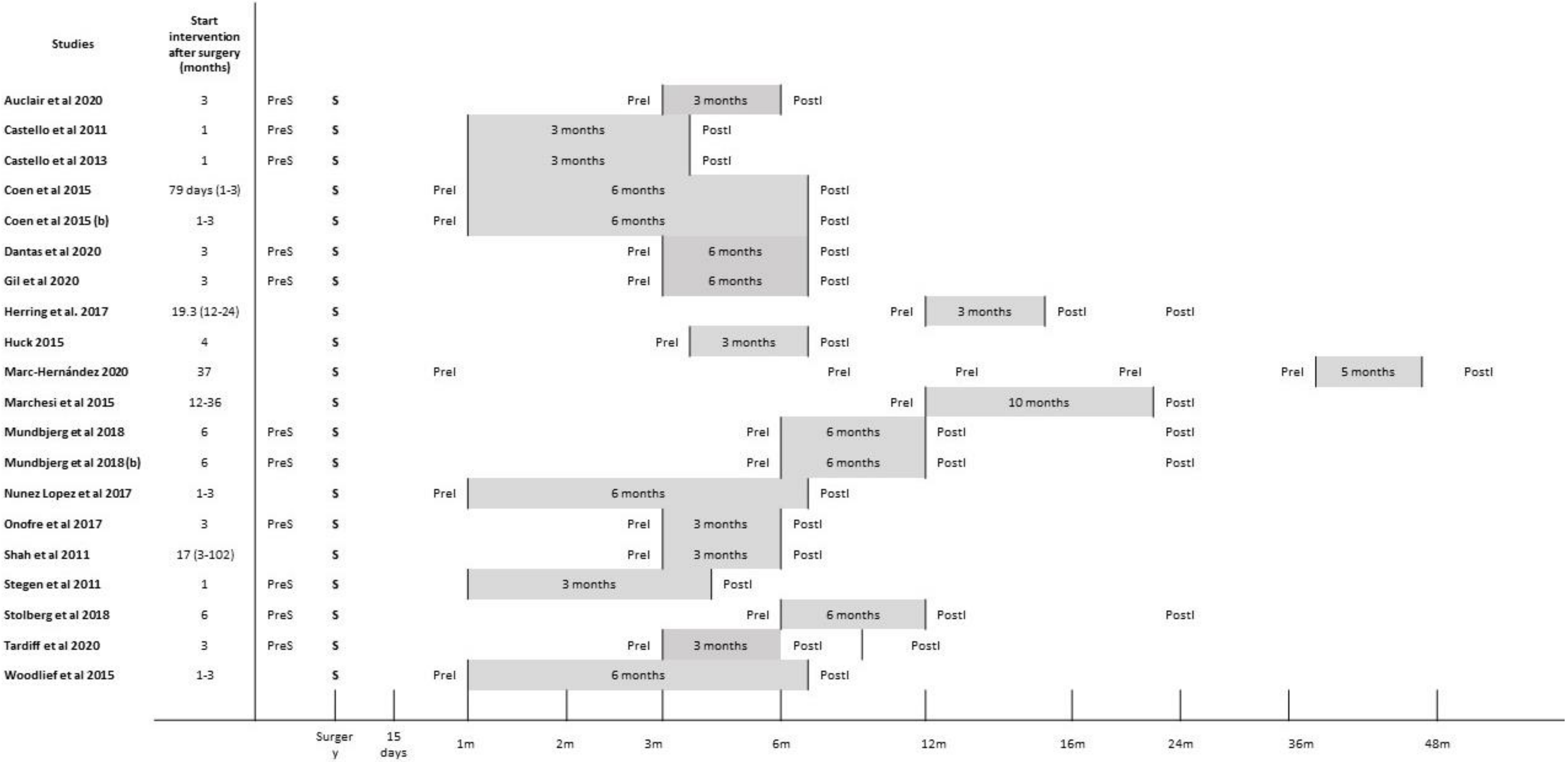
All the studies were published between 2011 and 2020 and were conducted in different countries: six in the USA, five in Brazil, three in Denmark, two in Canada, one in Belgium, one in Italy, and one in Spain and one in the United Kingdom **(Annexes study III. Table 2)**. A wide variety of BS techniques were performed: 16 (80%) studies used gastric bypass, four (20%) sleeve gastrectomy, two (20%) gastric band and two (20%) biliopancreatic diversion with duodenal switch (BPD/DS). Of these studies, 14 (70%) used one single type of surgery, five (25%) used two different types, and one (5%) study used any type of BS.

All the articles included in this review (n=20) provided at least one outcome related to cardiometabolic risk: HDL were reported in 9 studies (45%); fasting insulin, VO_{2max} or VO_{2peak} in ml / min and LDL in 8 studies (40%); total cholesterol, triglycerides, fasting glucose, SBP, and DBP in 7 of the studies (35%); VO_{2max} or VO_{2peak} in ml / min / kg in 6 (30%); VO_{2max} or VO_{2peak} in ml / min / FFM in 5 studies (25%); HR_{max} or peak and RHR in 3 studies (15%); $HR_{reserve}$, mean HR from heart rate variability (HRV) and mean HR from 6 minute walk test (6MWT) in 2 studies (10%); insulin sensitivity, SBP_{max}, DBP_{max} and VO_2 relative to the muscle mass of the middle thigh in one study (5%).

Participants' characteristics

The study samples ranged from 15 to 134 patients and among the 20 articles it comprises a total of 942 participants (88% women), with a mean age of 42.6±4 years old. Most of them (12 studies, 60%) included participants of both sexes, although in 8 studies (40%), only women participated.

Figure 10. Temporalization of the interventions carried out in each study.



S= surgery; PreS= pre-surgery examination; PreI= pre-intervention examination; PostI= post-intervention examination; m= months
Grey color = Physical activity intervention;

Intervention characteristics

As described in **figure 10**, the exercise programs started between one and 102 months after surgery. The most frequent intervention durations were 6 months used in nine studies [79,96,102,103,110,115–119] and 3 months in other nine interventions [77,78,95,101,106,112,114,116,120], except for two studies in which the intervention lasted 5 months [121] or 10 months [113].

The characteristics of the physical exercise interventions are summarized in **annexes study III. table 2**. Eight of the studies conducted an endurance training[77,79,95,96,102,106,110,113]. Endurance training was done in different ways. Two studies with the same protocol did incremental treadmill training in which they did 5 min of stretching and diaphragmatic breathing, 5 min of treadmill warm up, 4 steps of 10 minutes, the 1st at 50%, the 2nd at 60% and the 3rd - 4th at 70% of the HR_{peak} and 10 minutes of stretching and diaphragmatic breathing again, 3 days per week always by a physiotherapist [77,95]. Four studies carried out the same intervention, 3 to 5 days a week (of which at least one must be supervised), training on a treadmill or bicycle between 60-70% HR_{max}. Participants progressed over 3 months to a minimum of 120 min/week of exercise, they were encouraged to get at least 30 minutes of exercise a day [79,96,102,110]. Marchesi et al [113] conducted a training program with 3 supervised hours per week in the first three weeks and 1 additional self-managed hour from the third to the sixth week; the intensity was increased, the first 3 months alternation of slow walking 55-65% and fast walking 65-75% HR_{max} then 3 intermediate months running 55-65% and fast walking 65-85% HR_{max} and the last 4 months 70 min of continuous running at 70-90% HR_{max} interweaving short stretches of slow walking between 60-70% HR_{max}.

Nine studies conducted a resistance plus endurance training [78,101,103,114–121]. Three of them performed the same protocol [103,117,118], two weekly sessions of 40 minutes, always supervised by a physiotherapist which consisted of 10 minutes of bicycle training, 10 minutes of upper resistance training and 15 of endurance training; the subjects could choose stair climbing, treadmill, or rowing. The training programme was divide in three phases. Phase 1: endurance training at 50% of VO_{2max} and resistance at 60% 1 RM (20 repetitions); Phase 2: endurance training at 50-70% of VO_{2max} and resistance at 65% 1 RM (15 repetitions); Phase 3: endurance training at 70% of VO_{2max} and resistance at 75% 1 RM (10 repetitions). Onofre et al [114] did 3 weekly sessions of one hour, divided into 5 minutes of warm-up, 30 minutes of resistance training on a treadmill; periods of 40-60% HRR interspersed with periods of 85-90% HRR, 20 minutes of upper and lower limb resistance training at 60-80% of 1 RM, and 5 minutes of stretching. Marc-Hernández et al [121] proposes sessions between 35 and 50 minutes supervised by graduates in sports science, in addition, volume and intensity progressively increases in blocks as shown in table 2. Herring et al [101] and Stegen et al [78] effectuated 2 weekly supervised sessions. Stegen et al [78] divided sessions in 10 minutes of cardiovascular warm up, 25 minutes of resistance training at 60 % RM, 30 minutes of endurance (10 min cycling, 10 min walking, 10 min stepping) at 64 -77% HR_{max}. Finally 4 studies [115,116,119,120] carried out 3 weekly sessions that began 3 months after surgery, Gil et al[119] and Dantas et al[120] divided the sessions into a 5-minute warm-up, 30 to 60 minutes (10-minute progression every 4 weeks) of treadmill training at a 50% difference between the ventilatory threshold and the respiratory compensation point, and 3 sets of 8-12 reps of strength training on major muscle groups with 60 seconds rest. On the other hand, Auclair et al[116] and Tardif et al[115] performed 60-minute sessions divided into 5-minute warm-up, 35-minute resistance training at 60-75% $HR_{reserve}$, and 25-minute strength training (3 sets of 10-12 reps).

One study performs resistance training only [112]. They performed 2 weekly sessions the first 6 weeks and 3 weekly sessions the last 3 weeks. Each session consisted of 5 minutes of cardio warm-up, 45 minutes of resistance training, and 5 minutes of stretching. The resistance training had an initial intensity of 60% of the estimated 1 RM and was gradually increased to 75%, performing between 8 and 12 repetitions of the main muscle groups.

Quality assessment

As shown in **table 12**, the methodological quality was classified as good in 65% of cases (thirteen studies), fair in 25% (five studies), and poor in 10% (two studies). All the studies showed deficiencies (or no information) in the type of intervention performed, in the fields of blinding therapist / trainers and in blinding subjects. Due to the intervention being physical exercise, it is not possible to blind the patients or therapists/trainers. In addition, 55% of the studies (n = 11) had shortcomings (or no information) in the blinding of the evaluators/assessors. The remaining quality items on the PEDro scale were generally achieved.

Table 12. PEDRo scale to measure the quality of the studies.

	Eligibility Criteria	Random allocation	Concealed Allocation	Similarity groups' baseline	Blinding Subjects	Blinding therapist/trainers	Blinding assessors	Measured more than 85% of subjects	Intention to treat	Between groups statistical	Point measure	Score
Auclair et al 2020	1	1	1	1	0	0	1	1	1	1	1	8/10
Castello et al 2011	1	1	1	1	0	0	0	0	0	1	1	5/10
Castello et al 2013	1	1	1	1	0	0	0	0	0	1	1	5/10
Coen et al 2015	1	1	1	1	0	0	1	0	1	1	1	7/10
Coen et al 2015 (b)	1	1	1	1	0	0	1	1	1	1	1	8/10
Dantas et al 2020	1	1	1	1	0	0	1	1	1	1	1	9/10
Gil et al 2020	1	1	1	0	0	0	1	1	1	1	1	8/10
Herring et al 2017	1	1	1	1	0	0	0	1	1	1	1	7/10
Huck 2015	1	0	0	1	0	0	1	1	0	1	1	5/10
Marc-Hernández 2020	1	1	1	1	0	0	1	1	0	1	1	8/10
Marchesi et al 2015	1	0	0	1	0	0	0	0	0	1	1	3/10
Mundberj et al 2018	1	1	1	1	0	0	0	1	1	1	1	7/10
Mundberj et al 2018 (b)	1	1	1	1	0	0	0	1	1	1	1	7/10
Nunez Lopez et al 2017	1	1	1	1	0	0	1	1	1	1	1	8/10
Onofre et al 2017	1	0	0	1	0	0	0	1	1	1	1	4/10
Shah et al 2011	1	1	0	1	0	0	0	0	1	1	1	5/10
Stegen et al 2011	1	0	0	1	0	0	0	0	0	1	1	3/10
Stolberg et al 2018	1	1	1	1	0	0	0	1	1	1	1	7/10
Tardiff et al 2020	1	1	1	1	0	0	0	1	1	1	1	8/10
Woodlief et al 2015	1	1	1	1	0	0	1	0	1	1	1	7/10

1= reported; 0= not reported.

Outcomes

Cardiorespiratory fitness and heart rate

Cardiorespiratory fitness was examined in twelve of the twenty trials. Four studies reported it as absolute VO_{2peak} [78,79,114,116,121], three as absolute VO_{2max} [102,103,110], three as VO_{2peak} relative to body weight [78,114,116,121], three as VO_{2peak} relative to FFM [78,79,102], three as VO_{2max} relative to body weight[106,112,113], Woodlife et al [110] reported it as VO_{2pmax} relative to FFM and, Auclair et al[116] as $VO_{2\ indexed}$ to the muscle mass of the middle thigh. Of these, ten measured cardiorespiratory fitness using a gas analyzer or indirect calorimetry [78,102,106,110,113–116,121], and two by indirect formulas after a submaximal stress test [112,117].

Exercise in patients undergoing BS show an increase in the absolute cardiorespiratory fitness (VO_{2max} or VO_{2peak}) with significant changes in six trials [79,102,110,115,117,121]. Although Onofre et al [114] and Stegen et al [78] show no significant changes. Similarly, positive changes are reported in cardiorespiratory fitness in relation to body weight (VO_{2max}/BW or VO_{2peak}/BW) in six studies [78,106,113–115,121]. All the studies that measure cardiorespiratory fitness in relation to fat-free mass (VO_{2max} / FFM or VO_{2peak} / FFM) show a significant improvement [102,110], except Stegen et al [78], who showed no changes in the intervention group.

Heart rate (HR) was measured in different ways in eight of the seventeen studies [77,78,95,101,103,112–114,119]. Five of them measured RHR [101,103,112,113,119]. Three of the tests evaluate the mean HR during the 6MWT test [77,78,95]. Castello et al [77] reported it as mean HR during the HRV test, Onofre et al [114] and Gil et al[119] reported maximum HR in a cardiopulmonary exercise testing until physical exhaustion. Only Gil et al[119] reported the

$HR_{reserve}$.

None of the articles indicate significant variations in RHR [101,103,112,113], with the exception of Gil et al [119], with the same happening in the trial evaluating HR_{max} [114]. In contrast, there is a significant decrease in mean HR during 6MWT of the intervention group in two of the studies [78,95], but the same does not happen in Castello et al [77], who do not report any significant difference. During the HRV measurement, Castello et al [77] showed a significant decrease in mean HR in the intervention group.

Blood pressure

Blood pressure (BP) was measured in eight of the sixteen trials [77,96,101,103,106,112,114,116,121], all reported data for both SBP and DBP. In all the studies, they took a rest period of 5 to 10 minutes prior to taking the BP, except Auclair et al[116] and Onofre et al [114], who did it during the stress test, and Castello et al [77], who took the measurements during the 6MWT test.

Interventions showed positive results decreasing the SBP in three of the studies [77,101,110], whereas in the other five studies [103,106,112,114,121], no significant effects were found in the intervention group. The same occurs with DBP, there are two trials that report a significant decrease in it [77,101] and six that do not report significant changes [96,103,106,112,114,121].

Lipid profile

Eight of the twenty studies included in this systematic review provided results related to the lipid profile [96,102,103,106,113,115,120,121] All of them, except Shah et al[106], reported the total cholesterol [96,102,103,113,115,120,121], seven the HDL and the triglycerides [96,102,103,106,113,115,120,121], and six the LDL [96,102,103,106,113,115,120,121] . All blood tests were performed with at least 10 hours of fasting.

Six of the studies that measure total cholesterol do not show significant changes in patients undergoing BS who perform physical exercise after the operation [96,102,103,113,115,120], only Marc-Hernández et al [121] shows a significant decrease in it. Four articles indicate a positive effect on the reduction of triglycerides in the blood [96,102,106,120], while three other studies indicate that there are no significant changes[103,113,115] All studies, except Marchesi et al [113] and Shah et al[106], report a significant increase in HDL in the intervention group [96,102,103,115,120]. None of the studies found significant results in LDL in the intervention group [96,102,103,106,115], except Dantas et al [120].

Glucose and Insulin concentrations

Among the twenty trials included in the systematic review, eight report fasting glucose [79,96,102,103,106,113,120,121] and five report fasting insulin [79,96,102,103,106,120]. In all cases the blood tests or analyses were performed after at least 10 hours of fasting.

There is agreement in all the studies that measure fasting insulin[79,96,102,103], since all show a significant reduction in the group that performed physical exercise, except Shah et al [106] and Dantas et al[120]. On the other hand, in fasting glucose only Coen et al (2) [79] and Marc-Hernández et al[121] report significant changes indicating that there is a reduction in blood glucose in the intervention group.

Meta-analyses

The meta-analyses revealed a large size effect and a significant difference regarding VO_2max / peak in relation to body weight in favor of the experimental groups (ES= 0.673; 95% CI= 0.287, 1.060; p=0.001) **(Figure 11)** (Mean Difference=1.250 ml/kg/min; 95% CI=

0.480, 2.019; p=0.001). Significant differences and sizes effect were also observed regarding VO_2max / peak (ES= 0.317; 95% CI= 0.065, 0.569; p=0.014) **(Figure 12)**, HDL (ES= 0.22; 95% CI= 0.009, 0.430; p=0.041) **(Figure 13)** and RHR (ES= -0.438; 95% CI= -0.753, -0.022; p=0.007) **(Figure 14)** (Mean Difference= -3.925 BPM; 95% CI= -6.536, -1.313; p=0.003), in favor of the experimental groups.

On the other hand, no significant differences were observed in either SBP (ES= -0.157; 95% CI= -0.399, 0.084; p=0.202) **(Figure 15)** (Mean Difference= -2.646 mmHg; 95% CI= -7.321, -1.109; p=0.267) or DBP (ES= -0.117; 95% CI= -0.446, 0.212; p=0.485) **(Figure 16)** (Mean Difference= -1.405 mmHg; 95% CI= -5.559, 2.749; p=0.507).

Figure 11. Forest plot of VO2max-VO2peak in relation to body weight between intervention and control groups.

Study name	Statistics for each study						
	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Huck 2015	0,471	0,495	0,245	-0,499	1,440	0,952	0,341
Marchesi et al 2015	1,516	0,491	0,241	0,554	2,478	3,088	0,002
Onofre et al 2017	1,280	0,594	0,352	0,117	2,443	2,156	0,031
Shah et al 2011	0,691	0,363	0,132	-0,021	1,403	1,903	0,057
Stegen et al 2011	0,014	0,487	0,237	-0,940	0,969	0,029	0,977
Auclair et al 2020	0,475	0,280	0,078	-0,073	1,023	1,700	0,089
	0,673	0,197	0,039	0,287	1,060	3,413	0,001

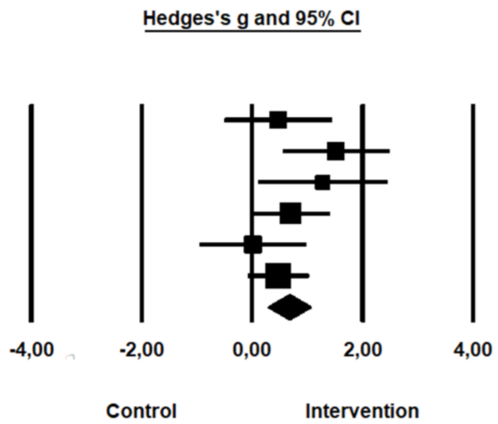


Figure 12. Forest plot of vo2max-VO2peak between intervention and control groups.

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Coen et al 2015 (b)	0,297	0,199	0,039	-0,093	0,686	1,493	0,135
Mundberj et al 2018 (b)	0,263	0,257	0,066	-0,240	0,766	1,024	0,306
Onofre et al 2017	1,468	0,611	0,374	0,269	2,666	2,401	0,016
Stegen et al 2011	0,108	0,488	0,238	-0,847	1,064	0,222	0,824
Auclair et al 2020	0,251	0,277	0,077	-0,292	0,794	0,907	0,364
	0,317	0,129	0,017	0,065	0,569	2,465	0,014

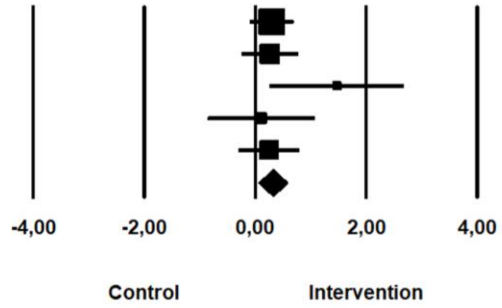


Figure 13. Forest plot of HDL cholesterol between intervention and control groups.

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Castello et al 2011	-0,644	0,354	0,125	-1,338	0,050	-1,819	0,069
Herring et al 2017	-0,546	0,402	0,162	-1,334	0,242	-1,359	0,174
Huck 2015	-0,326	0,491	0,241	-1,288	0,635	-0,665	0,506
Marchesi et al 2015	-0,855	0,449	0,202	-1,735	0,025	-1,904	0,057
Mundberj et al 2018	-0,181	0,256	0,066	-0,683	0,321	-0,707	0,480
	-0,438	0,161	0,026	-0,753	-0,122	-2,718	0,007

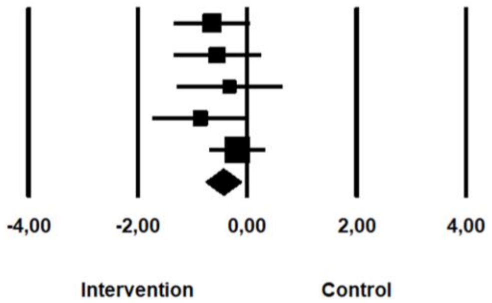


Figure 14. Forest plot of resting heart rate between intervention and control groups.

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Coen et al 2015 (a)	-0,038	0,176	0,031	-0,383	0,306	-0,217	0,828
Dantas et al 2020	0,404	0,253	0,064	-0,093	0,901	1,594	0,111
Marchesi et al 2015	0,383	0,433	0,187	-0,465	1,230	0,885	0,376
Mundberj et al 2018 (b)	0,398	0,258	0,067	-0,108	0,904	1,543	0,123
Shah et al 2011	0,243	0,354	0,126	-0,452	0,937	0,685	0,493
Tardif et al 2020	0,384	0,307	0,095	-0,218	0,987	1,250	0,211
	0,220	0,107	0,012	0,009	0,430	2,048	0,041

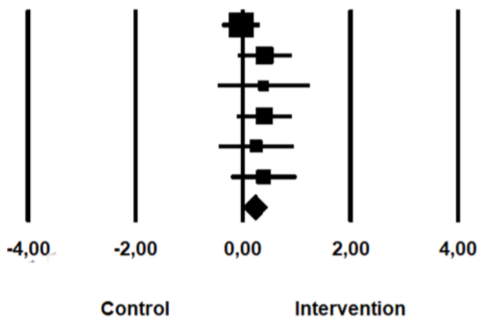


Figure 15. Forest plot of systolic blood pressure between intervention and control groups.

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Coen et al 2015 (a)	-0,146	0,176	0,031	-0,491	0,199	-0,832	0,406
Herring et al 2017	-0,536	0,402	0,161	-1,324	0,251	-1,335	0,182
Huck 2015	0,550	0,497	0,247	-0,425	1,524	1,105	0,269
Mundberj et al 2018	-0,135	0,256	0,065	-0,636	0,366	-0,529	0,597
Shah et al 2011	-0,308	0,355	0,126	-1,004	0,388	-0,868	0,385
	-0,157	0,123	0,015	-0,399	0,084	-1,275	0,202

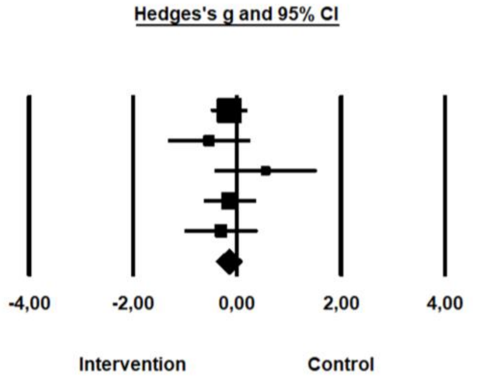
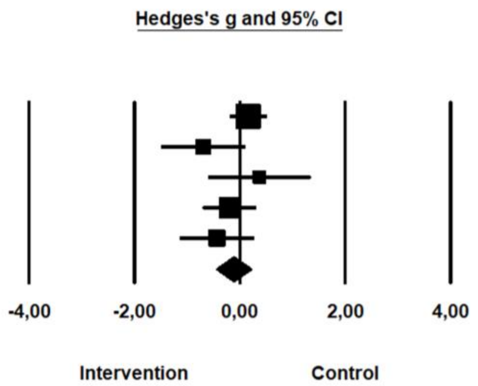


Figure 16. Forest plot of diastolic blood pressure between intervention and control groups.

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Coen et al 2015 (a)	0,157	0,176	0,031	-0,188	0,502	0,892	0,372
Herring et al 2017	-0,696	0,407	0,165	-1,493	0,101	-1,711	0,087
Huck 2015	0,372	0,492	0,242	-0,592	1,336	0,757	0,449
Mundberj et al 2018	-0,192	0,256	0,066	-0,694	0,310	-0,749	0,454
Shah et al 2011	-0,433	0,357	0,127	-1,133	0,266	-1,214	0,225
	-0,117	0,168	0,028	-0,446	0,212	-0,698	0,485



Heterogeneity

From the six meta-analyses performed, four of them showed non-significant heterogeneity: VO_2max / peak in relation to body weight (I^2=22.8%; p=0.26) (**Figure 11**), VO_2max / peak (I^2=0%; p=0.43) (**Figure 12**), HDL (I^2=0%; p=0.61) (**Figure 13**), SBP (I^2=0%; p=0.54) (**Figure 14**), and RHR (I^2 = 0%; p = 0.66) (**Figure 15**). In contrast, a significant heterogeneity was observed regarding DBP (I^2=34%; p=0.19) (**Figure 16**).

Sensitivity analysis

Once each study was individually removed and each ES was re-calculated, no changes in ES, effect direction or p-values were observed compared to those obtained in the original forest plots. The largest change was observed in the HDL when eliminating the

Coen et al. study [96] (original p=0.042; re-calculated p=0.006).

Publication bias

In all the funnel plots performed, a symmetrical study distribution was observed, leaving all the studies within the limits of the funnel plot. In all cases, the Egger's statistics were not significant.

Table 13. Summary of the main findings of each article.

	Main findings
Study I	• Patients awaiting BS are at high cardiometabolic risk due to FM, HC, and NC well above normal values. • These patients spend most of their time performing sedentary or light-intensity activities. These high levels of sedentarism activity are associated with a higher value in MUAC • Most of the patients (75.4%) comply with the recommendations of 150 min / week of MVPA, but no direct relationship has been found between the amount of MVPA and body composition or functional capacity.
Study II	• Performing an exercise program after BS does not seem to cause a greater weight loss compared to the usual care normally received after the surgery. • None of the analyzed characteristics of the PA intervention programs (duration of the intervention, when the intervention begins after the surgery, type of intervention, type of PA, exercise time) shows greater weight loss in those patients who engaged in PA after BS.
Study III	• Those patients who perform a PA program after BS show significant improvements in VO_2max / peak in relation to body weight, VO_2max / peak absolute, HDL, and RHR. • DBP and SBP does not seem to be affected by performing a PA program after BS.

BS: Bariatric surgery; DBP: Diastolic blood pressure; FM: fat mass; HC: Hip circumference; MUAC: Middle-upper arm circumference; MVPA: Moderate to vigorous physical activity; NC: Neck circumference; PA: Physical activity; SBP: Systolic blood pressure; WC: Waist circunference.

GENERAL DISCUSSION (DISCUSIÓN GENERAL)

Each of the articles included this Doctoral Thesis helps to improve the understanding of how BS and PA can be combined for the treatment of patients with MO / SO. More specifically, **study I** provides information on how patients get to the BS in terms of body composition, BP, arterial stiffness and functional capacity. **Study II** reviews, analyses and summarizes the scientific evidence on how a PA program after BS may affect weight loss. And finally, similarly to the previous one, **study III** describes how a PA program performed after BS may affect certain markers of cardiometabolic risk. **Table 4** shows the summary of the findings from each of the studies.

MAIN FINDINGS OF THIS THESIS COMPARED TO THE RESULTS OF PREVIOUS STUDIES

In **study I** patients who are about to undergo BS present large dimensions of neck circumference (NC), well above normal values. These results are similar to those observed in the study of Serafin et al. [122] in these patients before following a carbohydrate-restricted diet. As in the study of Rioux et al. [64] patients awaiting BS analyzed in this Doctoral Thesis spend most of their time doing sedentary or light-intensity activities. In addition, as in **study I**, Rioux et al. did not find any relationship between sedentary time and patients' performance in functional capacity evaluations (grip strength, 30-second chair-stand test, back scratch and treadmill stress test). Rioux et al. [64] reported, however, a positive relationship between time spent in vigorous activities and performance in the standing test, which is not observed in our data, maybe due to the fact that our patients barely performed vigorous PA (0.1±0.4% time/day). At the cardiovascular level, our patients showed normal levels of BP, both diastolic blood pressure (DBP) and systolic blood pressure (SBP), as well as regarding arterial stiffness (pulse wave velocity), which is in accordance with previous studies [123,124].

Regarding **study II**, previous systematic reviews [125–127] and meta-analysis [80] obtained some results different to ours. They conclude that interventions combining BS and PA lead to greater weight los compared to only BS [80]. On the contrary, our results reflect that the difference in weight loss between both groups did not reach statistical significance (ES = 0.15; p =0.094), what we consider could be due to a number of reasons:

1- Previous systematic reviews and meta-analyzes included some studies in which the intervention was multicomponent (i.e., not only PA was performed after BS, but also dietary, medical or psychological intervention).
2- The way to carry out the meta-analysis was also different, because in **study II** we used standardized means difference while Bellicha et al [80] used a difference of means.
3- Our article **(study II)** is more recent and, therefore, include new studies in the meta-analysis exploring weight loss after BS plus PA.

Study III shows a significant increase in VO_{2max} / $_{peak}$ absolute (ES=0.317; p=0.014) and also relative to body weight (ES=0.673; p=0.001), between patients who performed PA after BS and those who only received usual care. Similar results obtained by Silva et al. [128] and Bellicha et al. [80] in previous meta-analyses. For the rest of the findings obtained in this study (decreased RHR, increased HDL concentrations, and no change in DBP or SBP), no previous meta-analyzes have been found that analyze these study variables in this population. However, there are other studies that do so in other populations, confirming that regular PA produces an increase in HDL concentrations in people with obesity who are not have undergone BS [129] as well as in people with normal weight [130].

REASONS AND CONSEQUENCES OF THE FINDINGS

Participants in **study I** presented very high levels of FM (50.8 ± 5.3%), which is directly related to foot pain due to mechanical stress [131] and high cardiometabolic risk, especially in those with abdominal fat accumulation [132], as it is the case of these patients awaiting BS average waist circumference (WC) 138.9 ± 14 cm in men, 121.8 ± 13.6 cm in women), well above the cut-off points established to define abdominal obesity (102 cm for men and 88 cm for women) [133]. Similarly, these patients also presented an average neck circumference (NC), 49.3 ± 3.9 cm in men, 39.6 ± 9.0 cm in women) clearly higher than recommended upper limit of 37 cm in men and 34 cm in women [134]. "Neck obesity" has been directly related to hyperuricemia [135], cardiometabolic risk factors [136,137] and metabolic syndrome [138].

As we previously indicated, participants in **study I** showed high levels of sedentary time (65.8±12.5%) and light activity (29.7±10.6%), which is likely related to the excess body weight and fat, and linked to increased risk of death from cardiovascular disease, metabolic syndrome, and all-cause mortality [139]. Furthermore, according to our results, this PA pattern could also be associated with a higher arm circumference (MUAC), which is associated with a greater risk of cardiometabolic disorders [140].

Regarding the functional capacity of our patients awaiting BS, it is somehow surprising that those who spend more time in sedentary and light activities also report a lower perceived exertion (Borg scale) during the maximum treadmill test. We hypothesize that this perhaps occured because maybe many of the patients were not able to reach maximum intensity in the treadmill test, due to mobility problems, an increase in BP, or due to the subjectivity of the scale itself, as it occurs in other populations of sedentary patients with little exercise experience, who tend to answer with little consistency [141].

As indicated **study II,** the combination of BS with PA does not seem to produce a greater weight loss compared to BS *per se*. Furthermore, according to the subgroup analyses we performed, none of the selected PA programs' characteristics (duration of the intervention, initiation of the intervention after BS, type of intervention, type of PA, time of exercise) was associated with a significant difference in weight loss (ES = 0.15; p =0.094). This could probably be due to:

1- The design of most of the PA programs used in the reviewed studies is quite deficient, they were not apparently conceived by experts in PA and sports sciences. Which translates into inadequate doses of PA (volumes and intensities of training that do not increase as patients improve), in addition to insufficient and / or poorly described frequency and duration of training.
2- Most of the training programs have not been reported, or registered, through consensual protocols that facilitate their subsequent reproducibility -and therefore require in detail explanation-, such as the CERT consensus [142].

3- Only the studies by Coen et al. [96] and Mundbjerg et al. [117] had an adequate sample size to reach a solid conclusion.

4- Many studies did not control for -or even did not report- important variables such as PA performed outside the training program, nutritional habits, sleep or other factors that may influence weight loss.

From the results of the **study II**, and based on other studies, we could hypothesize that to optimize weight loss in patients undergoing BS it is necessary to accompany physical training with changes in eating habits, caloric reduction or nutritional education, as occurs in people with obesity and overweight not undergoing BS [62,143].

As a result of some of the reviewed studies included in our **studies II** and **III**, we strongly believe that it is necessary to carry out new RCTs in which physical training adapts to the most appropriate paradigms for this type of population and is adequately informed, in order to design specific PA guidelines in people who have undergone BS [74]. In patients with SO/MO undergoing BS, these could be some effective strategies to increase weight loss and to improve functional capacity:

- Concurrent training [144], which combines strength and aerobic exercise in the same session.
- At least 150 min / week of MVPA, because it seems to provoke improvements at the cardiorespiratory, skeletal muscle and neuromotor level [145].
- Training programs of at least 16 weeks or longer are recommended to increase caloric expenditure and induce lipolysis [143]. Exercise training in people with

obesity helps increase caloric expenditure [146,147], which in the long term will result in weight loss.

- Furthermore, in patients undergoing BS it is necessary to specifically clarify the appropriate time between BS and the start of the exercise intervention. Nowadays, the reviewed studies show such a great variability as from 1 to 102 months after the surgery (**study III)**

The significant increase in VO_{2max} / $_{peak}$ of the exercise groups versus the control groups observed in **study III** could be determined by increased lung diffusion capacity, pulmonary ventilation [148] and muscle capillary function [149], which seems to accompany physical training, which allows a higher saturation of O_2 in blood. Another reason may be the increase in stroke volume and the size of the heart caused by aerobic training in patients with obesity, since this increases the mass of the left ventricle, mass of the right ventricle, stroke volume of the left ventricle and the volume of the right ventricle [150]. Likewise, all these factors could be directly related to the decrease in RHR (ES=-0.438; p=0.007) observed in **study III.**

The effect of combining BS with exercise training is much greater on the VO_{2max} / $_{peak}$ relative to body weight (ES=0.673; p=0.001) than in the VO_{2max} / $_{peak}$ absolute (ES=0.317; p=0.014), what could be due to two reasons. First of all, as suggested by Bellicha et al. [80], the exercise intervention after BS seem to produce a greater weight loss and this could be positively affect the ratio VO2max / peak relative to body weight. On the contrary, if as suggested by our **study II**, exercise after BS does not produce a greater wight loss, it would be necessary to conduct studies involving fat-free mass (FFM), so that it could be discerned whether the improvement in VO_{2max} / $_{peak}$ comes from weight loss or from increasing / maintening muscle mass, as it occurs in other populations [151].

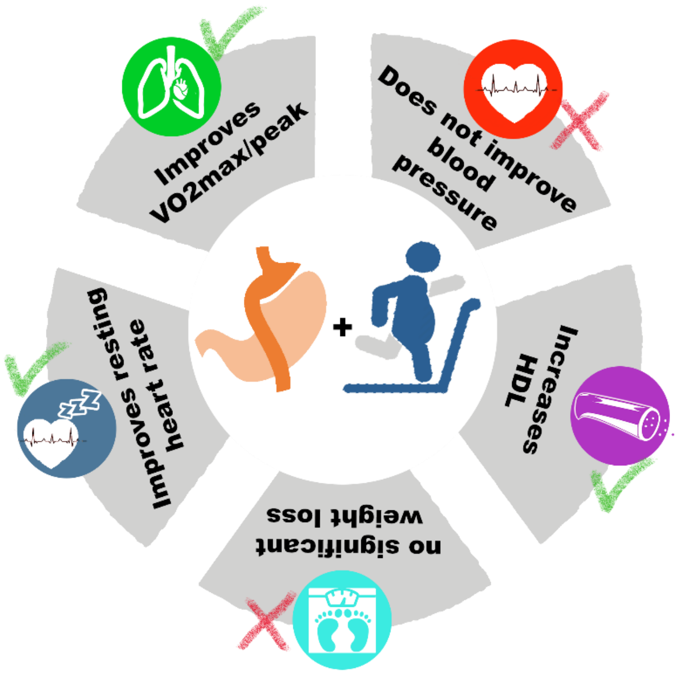


Figure 17. Graphic representation of the results obtained in studies II and III (systematic reviews).

Our results **(study III)** also show a significant increase in HDL concentrations (ES=0.22; p=0.041) in those patients undergoing BS who perform physical exercise versus those receiving only BS. The effycacy of PA to improve HDL concentrations have been long studied, with no clear conclussions yet. Some studies have found direct associations between PA and HDL concentration in people with obesity (not undergoing BS) [129] and in people with normal weight [130]. Similarly, there are also studies that have not found improvements in HDL concentrations with PA but showing positive results regarding its functions [152,153]. These studies propose to change the point of view about HDL, going from measuring it from a quantitative perspective to a qualitative one. Using the main protein component of HDL, apoA-I and ATP-dependent transporters or ABC transporters (ABCA1 y ABCG1) among other markers [152], we are able to quantify many of the functions of HDL such as the return of cholesterol to the liver [154], its ability to promote the release of cholesterol from macrophages [155] and other functions such as its anti-inflammatory / antioxidant capacity [156]. For these reasons, we hypothesize that, in addition to a possible increase in HDL concentration, there may be an improvement in its functions, as it has been observed in other populations [153]. Therefore, it would be convenient to measure these variables in future studies with patients performing exercise training after BS.

LIMITATIONS AND STRENGTHS

	Strengths	Limitations
Study I	• All the outcomes included in this cross-sectional study are of demonstrated interest for patients awating BS. • The study fills an existing gap, as there is little information on how patients arrive at BS, especially with regard to PA performed and its correlation with functional capacity. • The evaluation data have been obtained, stored, analyzed and reported using the corresponding protocols for each test.	• The sample is too small to represent the population of patients awaiting BS. • More than twice as many patients are women, which makes it difficult to reach general conclusions in men. • Some participants may have performed the functional capacity assessments not at the maximum extent due to mobility limitations or mechanical stress. • There is no real consensus to define the accelerometer-based cut-off points for the intensity of PA, especially in this population.
Study II	• All the information included in this systematic review and meta-analysis has been obtained and synthesized using Prisma and Cochrane protocols. • The information has been summarized and explained so that it is understandable for not specialized readers. • Up to 16 studies have been included in the quantitative analysis, helping to reach a stronger conclusion on the topic. In addition, subgroup and meta-regression analyses have been performed. • The heterogeneity of the reviewed studies is very low. • All the studies included in the systematic review and in the meta-analysis are	• 5 of the studies do not report the SD of body weight, which makes it difficult to estimate the correlation of pre-post intervention measures. • The sample size and characteristics, the inclusion / exclusion criteria and the follow-up time vary greatly between studies. • Studies with a moderate risk of bias have been included. • It has not been possible to analyze the intensity-related training variables because of the lack of standardized criteria.

	experimental with a physical exercise intervention after BS.	
Study III	• All the information included in the systematic review and meta-analysis has been obtained and synthesized using Prisma and Cochrane protocols. • A complete and exhaustive systematic review has been carried out for each of the outcomes, comprising a total of 942 participants, which allows us to adequately understand how the intervention affects patients undergoing BS and to draw solid conclusions. • All the studies included in the systematic review and in the meta-analysis are experimental with a physical exercise intervention after BS. • The heterogeneity of the reviewed studies is very low except for one of them.	• The meta-analyses of each outcome are based on few studies, between 4 and 6 studies in each case. • Due to the limited number of studies for each variable, it has not been possible to perform meta-regressions or subgroup analyses. • Only articles written in English and / or Spanish have been included and gray literature has not been consulted. • There is a great variability in the characteristics of the physical exercise interventions carried out.

BS: Bariatric surgery; PA: Physical activity; SD: standard deviation.

CONCLUSIONS

The results of the present Doctoral Thesis suggest that:

I. People who are awaiting BS spend most of their time doing sedentary and light activities. Although the majority of them comply with the recommendations of 150 min / week of MVPA, they present clearly altered cardiometabolic risk factors and poor results in functional capacity tests.

II. Performing an exercise program after BS does not translate into greater weight loss compared to those patients who only receive BS and routine postoperative care.

III. There does not appear to be any particularly effective type of training performed after BS to further increase weight loss.

IV. The number of controlled trials is insufficient, and the way of reporting and planning the training program in some studies is insufficient to fully conclude that exercise is not effective to achieve greater weight loss after BS.

V. Exercising after undergoing BS has a significant effect on improving VO_{2max}, HDL cholesterol, and reducing RHR, compared to routine postoperative care. In contrast, exercise training after BS seems to have no effect on BP, both SBP and DBP.

VI. Due to the limited number of studies and the characteristics of the interventions carried out, it may be too early to conclude that exercise does or does not significantly affect these cardiometabolic risk factors. Therefore, it would be wise to wait for more research to be done in the future.

CONCLUSIONES

Los resultados de la presente Tesis Doctoral sugieren que:

I. Las personas a la espera de ser sometidas a cirugía bariátrica pasan la mayor parte de su tiempo realizando actividades sedentarias y ligeras. A pesar de que la mayoría cumplen con las recomendaciones de 150 min / semana de AF moderada o vigorosa, estos pacientes presentan factores de riesgo cardiometabólico alterados y malos resultados en las pruebas de capacidad funcional.

II. Llevar a cabo un programa de ejercicio físico después de la cirugía bariátrica no se traduce en una mayor pérdida de peso en comparación con aquellos pacientes que únicamente reciben la cirugía bariátrica seguida de los cuidados postoperatorios habituales.

III. No parece haber ningún tipo de entrenamiento particularmente efectivo que realizado tras la cirugía bariátrica aumente en mayor medida la pérdida de peso.

IV. La cantidad de ensayos controlados es insuficiente, y la forma de reportar y planificar el programa de entrenamiento en algunos estudios es deficiente como para poder concluir totalmente que el ejercicio físico no produce una mayor pérdida de peso tras la cirugía bariátrica.

V. Realizar ejercicio después de someterse a cirugía bariátrica tiene un efecto significativo en la mejora del VO_{2max}, colesterol HDL y reducción de la frecuencia cardíaca en reposo, en comparación con los cuidados postoperatorios habituales. Por el contrario, el ejercicio físico después de la cirugía bariátrica parece no tener ningún efecto sobre la presión arterial, ni sistólica ni diastólica.

VI. Debido al número limitado de estudios y las características de las intervenciones realizadas, puede resultar arriesgado concluir que el ejercicio sí afecta -o no- significativamente a estos factores de riesgo cardiometabólicos. Por tanto, sería prudente esperar a más investigaciones futuras

FUTURE DIRECTIONS

Given the limitations of **study I** and previous ones, it seems of clinical interest to recruit larger sample sizes in subsequent studies of patients awaiting BS, in order to confirm the conclusions found and to be able to adequately examine if there is any influence of PA on body composition, BP or functional capacity in these patients. Also, further research on PA in people awaiting BS should not only measure the patients' amount and intensity of PA, but also the type of activity, in order to discern between the PA carried out in their day-to-day activities from the amount of time doing structured physical exercise. In addition, defining the accelerometer-based PA cut-off points in this population is particularly relevant for future studies, since there is no real consensus in patients with MO / SO, which can alter the results and introduce a serious bias in this topic.

The results of **studies II and III** indicate that it would be convenient to further explore the possible benefits of BS combined with exercise training, with the aim of determining the most appropriate prescription and design of the training programs and PA for this population (exercise technique, speed of execution, quantification of the load, intensity and types of exercises, among others). Therefore, in order to reach strong conclusions, further research should meet some basic characteristics, such as larger sample sizes, training programs designed (and reported) based on previous solid scientific knowledge in populations with similar characteristics, and implemented by specialized PA and sports scientists. In addition, in these patients who have undergone BS, another question arises when planning a training program, which is particularly relevant, and refers to the moment when the exercise program should start after the surgery. Future studies should begin to train immediately after surgery to take advantage of the window of opportunity that this offers us, given the motivation that patients present immediately after the operation, which could help to positively change eating habits and PA behaviours.

Likewise, based on what is discussed in **study III**, several questions remain that should be investigated in future studies:

1- How the combination of BS with exercise training affects VO_{2max} in relation to FFM, with the main purpose of clarifying whether the improvements in relative VO_{2max} in observed in these patients after exercising comes from the loss of body weight or from the maintenance of muscle mass.

2- Regarding the significant increase in HDL concentrations, future research should evaluate the effects of exercise after BS on the different functions and subclasses of HDL, to specifically test possible qualitative improvements and not just in the total amount of HDL.

DIRECCIONES FUTURAS

Dadas las limitaciones del **estudio I** y otros estudios previos, parece de interés clínico que los próximos estudios que se realicen en este campo se lleven a cabo con un mayor tamaño de muestra de pacientes a la espera de cirugía bariátrica, para poder confirmar las conclusiones halladas y poder examinar de forma adecuada si existe alguna influencia de la AF sobre la composición corporal, la presión arterial o la capacidad funcional en estos pacientes. En consecuencia, futuras investigaciones sobre la AF en personas a la espera de cirugía bariátrica no sólo tendrían que medir la cantidad e intensidad de AF que realizan los pacientes, sino también el tipo de actividad, para poder discernir entre la actividad que realizan en su día a día de la cantidad de tiempo dedicado al ejercicio físico estructurado. También, definir los puntos de corte de AF basados en acelerometría en esta población es particularmente relevante para futuros estudios, ya que no existe un consenso real en pacientes con obesidad severa / mórbida, lo cual puede alterar los resultados y suponer un sesgo en las publicaciones.

Los resultados de los **estudios II y III** indican que sería conveniente continuar con la línea de investigación que combina la cirugía bariátrica y el ejercicio físico, con la idea de determinar cuál sería la prescripción y diseño más adecuados de los programas de ejercicio físico y AF para esta población (técnica adecuada, velocidad de ejecución, cuantificación de la carga, intensidad y tipos de ejercicios, entre otros). Por lo tanto, para obtener unas conclusiones sólidas, las investigaciones futuras deberían cumplir unas caracterísiticas básicas, entre otras un mayor tamaño muestral, programas de entrenamiento diseñados (y reportados) a partir de conocimientos científicos sólidos previos en poblaciones con características similares, y ejecutados por personal especializado en ciencias de la AF y del Deporte. Además, en estos pacientes que han sido operados de cirugía bariátrica se abre otra incógnita a la hora de planificar un programa de entrenamiento, que es particularmente relevante y no existe en otras poblaciones, y que se refiere a cuándo comenzar a entrenar tras la cirugía. Próximos estudios deberían comenzar el entrenamiento inmediatamente tras la cirugía para poder aprovechar la ventana de oportunidad que esto nos brinda, dado que la motivación que presentan los pacientes inmediatamente después de la operación puede ayudar a conseguir cambios positivos en sus hábitos de alimentación y de AF.

También, a partir de lo discutido en el **estudio III,** quedan abiertas varias cuestiones que se deberían investigar en futuros estudios:

1- Cómo la combinación de la cirugía bariátrica con el ejercicio físico afecta al VO_{2max} relativo a la masa libre de grasa, con el objetivo de aclarar si las mejoras en el VO_{2max} relativo en estos pacientes tras realizar un programa de ejercicio físico son provocadas por la pérdida de peso o por el mantenimiento de la masa muscular.

2- Con respecto al aumento significativo del colesterol HDL, las futuras investigaciones deben evaluar los efectos del ejercicio después de la cirugía bariátrica en las diferentes funciones y subclases de HDL, para comprobar específicamente posibles mejoras cualitativas y no solo en la cantidad total de HDL.

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EDUCATION

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  University of Almería (UAL)
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  Catholic University of Murcia (UCAM)
- 2014-2015 — **Master degree in Training and Nutrition**
  European University of Madrid (UEM)
- 2017-2018 — **Master degree in Teacher Training in Obligatory Secondary Education (Physical Education Specialty).**
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  University of Castilla-La Mancha (UCLM)
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  Ruiz Sánchez Formación S.L.
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WORK EXPERIENCE

- **Primary education teacher in charter school Nuestra Señora del Milagro (2018-Present)**
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  University of Almería (UAL)
- **Member of the work team in the research project Physical exercise after bariatric surgery in the treatment of severe / morbid obesity: EIBAR randomized controlled trial (Present)**
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- **Collaborator as a researcher in the research contract "UAL ACTIVA". Sports research group CTS-1024 and Sports Service of the University of Almería (2018-2020).**
  University of Almería (UAL)
- **Collaboration in field work in research project: Longitudinal monitoring and genetic modulation in fibromyalgia. Effects of physical exercise and hydrotherapy on pain. Health and quality of life (october 2016)**
  University of Granada (UGR)
- **Personal trainer (18 months; years 2015-2016).**
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SCIENTIFIC PUBLICATIONS

- **"Supervised Exercise Immediately After Bariatric Surgery: the Study Protocol of the EFIBAR Randomized Controlled Trial"** (2021)
  DOI: 10.1007/s11695-021-05559-8

  Authors: Enrique G. Artero; Manuel Ferrez-Márquez; María José Torrente-Sánchez; Elena Martínez-Rosales; Alejandro Carretero-Ruiz; Alba Hernández-Martínez; Laura López-Sánchez; Alba Esteban-Simón; Andrea Romero del Rey; Manuel Alcaraz-Ibáñez; Manuel A. Rodríguez-Pérez; Emilio Villa-González; Yaira Barranco-Ruiz;

Sonia Martínez-Forte; Carlos Castillo8; Carlos Gómez Navarro; Jesús Aceituno Cubero; Raúl Reyes Parrilla; José A. Aparicio Gómez; Pedro Femia; Ana M. Fernández-Alonso; Alberto Soriano-Maldonado.

- **"Supervised exercise following bariatric surgery in morbid obese adults: CERT-based exercise study protocol of the EFIBAR randomised controlled trial"** (2019)
  DOI: 10.1186/s12893-019-0566-9

  Authors: Emilio Villa-González, Dr.; Yaira Barranco-Ruiz, Dr.; Manuel Rodríguez-Pérez, Dr.; Alejandro Carretero Ruiz; José María García-Martínez; Alba Martínez Hernández; María José Torrente; Manuel Ferrer-Márquez; Alberto Soriano-Maldonado, Dr.; Enrique G Artero, Dr.

- **" Effects of exercise training on weight loss in patients who have undergone bariatric surgery: a systematic review and meta-analysis of controlled trials."** (2019)
  Doi: 10.1007/s11695-019-04130-w

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- **"Physical Exercise following bariatric surgery in women with Morbid obesity Study protocol clinical trial (SPIRIT compliant)"** (2020)
  DOI: 10.1097/MD.0000000000019427

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- **"Impact of exercise training after bariatric surgery on cardiometabolic risk factors: a systematic review and meta-analysis of controlled trials"**
  DOI: 10.1007/s11154-021-09651-3

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- **"Effects of Bariatric Surgery on Cardiorespiratory Fitness: A Systematic Review and Meta-analysis"**
  DOI: 10.1111/obr.13408

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PRESENTATIONS / COMMUNICATIONS / ORGANIZING COMMITTEE

- **2017** X INTERNATIONAL SYMPOSIUM OF UPDATES IN STRENGTH TRAINING (MADRID)

Oral presentation: **"Exercise program immediately after bariatric surgery in severe/morbid obese adults: Rationale and design of the EFIBAR* Study Training Program based on CERT"**

- **2017** X INTERNATIONAL SYMPOSIUM OF UPDATES IN STRENGTH TRAINING (MADRID)

Poster: **"Exercise program immediately after bariatric surgery in severe/morbid obese adults: Rationale and design of the EFIBAR* Study Training Program based on CERT"**

- **2017** SADECA (ALMERÍA)

Oral presentation: **"Implantación y seguimiento comité bariátrico"**

- **2017** European researchers night 2017; Openresearchers Project.

Organizing Committee: "**La Ciencia en el Deporte y Ejercicio Físico"**

- **2017** **EJERCICIO FÍSICO Y OBESIDAD ¿QUÉ NOS DICE LA CIENCIA?**

Organizing Committee

- **2018** National Congress of the SPANISH SOCIETY OF SURGERY of the Obesity and METABOLIC DISEASES (Mallorca)

Poster: **"Programa de ejercicio físico individualizado y supervisado tras la cirugía bariátrica en adultos con obesidad severa/mórbida: Estudio EFIBAR"**

- **2018** European researchers night 2018; Openresearchers Project.

Organizing Committee: "**La Ciencia en el Deporte y Ejercicio Físico"**

- **2019** National Congress of Medicine and Sports Sciences

Poster: **"ADHERENCIA AL PROGRAMA DE INTERVENCIÓN EN EL ENSAYO CLÍNICO EFIBAR: EJERCICIO FÍSICO TRAS LA CIRUGÍA BARIÁTRICA"**

- **2020** Sexual medicine society 21st annual

Presentation: **"Association of Sexual Function with BMI and Cardiorespiratory Fitness in Morbid Obese Women awaiting Bariatric Surgery: EMOVAR study"**

- **2020** European researchers night 2020; Openresearchers Project.

Organizing Committee: "**La Ciencia en el Deporte y Ejercicio Físico"**

- **2021** VII EXERNET Symposium: "Prescripción del ejercicio físico basado en la evidencia"

Presentation: **"Ejercicio físico supervisado en pacientes con alto grado de obesidad sometidos a cirugía bariátrica: aprendizajes de un ensayo clínico (EFIBAR)"**

ACKNOWLEDGMENT (AGRADECIMIENTOS)

Llegados a este punto la gente que me conozca se preguntará cómo una persona que no destaca por sus notas y con una actitud pueril está defendiendo su tesis, habiendo publicado además algunos artículos. Tras pensarlo varias veces he llegado a dos conclusiones: una ser muy cabezón (si algo te cuesta dedícale más tiempo), y dos, tener la suerte de estar bien acompañado, tanto durante la tesis, como en el resto de mi vida. Por todo ello creo que tengo mucho que agradecer.

Cuando me planteé comenzar con el doctorado estuve preguntando a varias personas la mejor forma de hacerlo, en uno de estos rebotes y por suerte, acabé hablando con **Enrique**, el cual casi sin conocerme de nada me planteó que me uniera al proyecto que estaban preparando (proyecto EFIBAR). Únicamente por ese detalle ya tendría que darle las gracias una y otra vez, pero no ha sido solo eso, a lo largo de estos cuatros años siempre me ha facilitado las cosas, me ha ayudado en todo lo que he necesitado, me ha permitido formarme con el grupo de investigación, ha tenido paciencia infinita y aunque su tiempo es muy limitado siempre ha estado ahí cuando lo he necesitado.

Como decía, tuve la suerte de formar parte del proyecto EFIBAR cuando aún se estaba organizando, de esta primera etapa guardo grandes recuerdos de las reuniones en casa de **Manu,** co-tutor de la tesis, la persona que conozco que más sabe de cirugía bariátrica y a la cuál solo puedo agradecerle que incluso después de todas las horas de trabajo en el hospital le dedique tiempo al proyecto y a resolver todas las dudas que se nos plantean a los que no tenemos mucha idea, como yo. Además, en estas reuniones tuve la suerte de conocer a muchísima gente con una gran pasión por la investigación, entre ellos al otro co-tutor de la tesis **Alberto**, un enamorado de la ciencia de pies a cabeza que exige a los demás tanto como se exige a sí mismo, y al igual que ocurre con Enrique, sin él seguramente la tesis no habría salido adelante.

En el grupo de investigación CTS-1024 he ido conociendo a mucha gente, a **Carles** que se comía todos los marrones de lo que metíamos mal en las bases de datos y de la gestión de todas las citas con los pacientes del estudio. **Jose María**, que empezamos juntos el doctorado, a veces pasaba más rato con él que con mi pareja. Sobre todo, **Alba** y **Elena**, que teóricamente tenía que ser yo el que les echase una mano con las cosas del estudio porque llevaba más tiempo en el grupo de investigación, pero siempre ha sido al revés, me han ayudado con las bases de datos, la estadística, los entrenamientos y me han resuelto dudas de la cuales yo no tenía ni idea. Creo que tendré que invitarles a unas cervezas.

Empezar el segundo artículo de esta tesis (primero realizado en orden cronológico) fue un punto de inflexión durante el desarrollo del doctorado, ahí me ves sin tener datos del proyecto, con poca idea de estadística y Enrique me plantea realizar un meta-análisis (concepto que había escuchado cero veces hasta ese momento). Tras pasar dos meses buscando información y llorando por las esquinas, entran en la ecuación cuatro personas sin las cuales no podría haber realizado los meta-análisis. El equipo de Cuenca, formado por **Iván**, **Celia** y **Vicente**, quienes han tenido que soportar mi patanismo en todo su esplendor con una batería de correos formados por una duda detrás de otra y a los que solo puedo darles las gracias por su paciencia infinita. Y por otro lado **Mamen**, de ella he aprendido todo lo que sé de estadística y también tuvo que aguantar que subiera al hospital una vez semanal a ayudarme con el meta-análisis.

Sobrepasando el segundo año de doctorado mi vida dio un pequeño vuelco y conseguí el trabajo soñado, maestro de primaria. No puedo hacer otra cosa que darle las gracias a todo el equipo de trabajo por acogerme tan bien y permitirme dedicar tiempo de forma simultánea al doctorado, especialmente a **Inma**, **María del Mar** y **Carmen** por enseñarme a diario a ser mejor profesor.

Ahora toca hablar de la familia que se elige, mis amigos. Por suerte tengo un grupo de amigos que siempre que hace falta están cerca, ya sea para echarte una mano, tomarse "algo" o para meterse contigo. Me gustaría agradecer a **Marta** y **Oliver** su ayuda con el inglés, a **Germán** haber hecho una portada tan chula, a los **Jorges**, **Raúl** y **Willy** por estar siempre cuando los necesito y ser capaces de sacarme una sonrisa cuando uno peor está. En este apartado hay una mención especial, mi primo y mejor amigo **Pablo**, la persona que me llama cuando sabe que estoy mal y que me lleva aguantando toda la vida, hemos aprendido juntos a hacer deporte, a ser scout y a disfrutar de las pequeñas cosas.

Hay alguien a quien tengo que agradecerle que me haya aguantado todos los días desde que comenzó esta andadura del doctorado, a mi novia y directora artística de la tesis **Rocío**. Ha estado siempre al pie del cañón, ha confiado en que podía hacerlo más que yo mismo y ahora que ella empieza una nueva etapa quiero que sepa que yo también confío en que va a sacarla adelante. ¡Te quiero muchísimo y nos quedan muchos objetivos por cumplir juntos!

Me gustaría también agradecer a mis tíos **Rafa** e **Inma**, y a mi hermano **Tali**, por estar apoyándome en todo momento, quererme incondicionalmente y ser pilares fundamentales en todo lo que hago. En esta montaña rusa que ha sido el doctorado mi hermano me ha escuchado, ha aguantado todas las quejas y ha sido clave en todos los "problemas" que han aparecido, ya sean del doctorado o de la vida cotidiana. Si necesitas ayuda para arreglar el coche, ahí está él. Si necesitas ayuda con los papeles de la casa, ahí está él. Qué necesitas sacar unos papeles para los entrenamientos, ahí está él.

¿Sabéis que en la vida todos tenemos una persona en la que mirarnos y seguir sus pasos? Pues en mi caso yo tengo tres, personas que han hecho cosas que sabes nunca vas a ser capaz de alcanzar, que te inspiran a esforzarte y darlo todo. Estos tres nos son otros que mi madre y mis abuelos. Mi madre, **Eloisa**, la persona que me ha motivado en todo momento a hacer lo que más me gustara, que me ha levantado cuando me he caído, que me ha apoyado en todos los proyectos que he empezado en la vida; desde la nada y teniendo dos hijos aprobó su carrera, cuatro oposiciones, que ha trabajado como nadie y de la cual no puedo estar más orgulloso. Mis abuelos no son personas comunes, no solo por lo que han conseguido en la vida, mi **abuelo Pepe** dejó los estudios a los 6 años y ha llegado a base de esfuerzo a ser jefe de taller de marcas como Renault y Volvo, mi **abuela María Benita** ha sido junto a mi madre la que me ha enseñado el significado de ser una mujer empoderada, la primera mujer de Granada en aprobar una oposición. Pero esas cosas son sus hitos personales, a mi me gustaría decirles que los quiero y que sin ellos no sería la persona que soy hoy; no es suficiente darles únicamente las gracias, para ellos necesitaría otras 150 páginas para agradecerles todo lo que han hecho por mí.

ANNEXES (ANEXOS)

Los anexos están formados por los artículos científicos que han derivado de la presente tesis.

I

I. Association of physical activity with blood pressure, arterial stiffness, body composition and functional capacity in patients awaiting bariatric surgery: baseline results from the EFIBAR Study

(Pending to publish)

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Title: Association of physical activity with blood pressure, arterial stiffness, body composition and functional capacity in patients awaiting bariatric surgery: baseline results from the EFIBAR Study

Short title: Physical activity, blood pressure, arterial stiffness, body composition and functional capacity in patients awaiting bariatric surgery

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KEY WORDS:

Obesity, bariatric surgery, physical activity, functional capacity, blood pressure, accelerometer

CLINICAL TRIAL REGISTRATION:

NCT03497546

WORD COUNT:

3261

DECLARATIONS

Informed consent

Informed consent was obtained from all individual participants included in the study.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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Author contributions

ACR and EGA designed the cross-sectional study. ACR and EMR wrote the article with the support of EGA, LL-S, MF-M, and AS-M, while EGA provided clinical and epidemiological support. EGA was the principal investigator and guarantor. All authors reviewed and approved the final version of the manuscript.

BULLET-POINTS

What is already known about this subject?

- An adequate physical condition prior to undergoing Bariatric Surgery translates into better post-intervention recovery.
- Patients with obesity awaiting bariatric surgery spend most of their time doing sedentary activities and light intensity activities.

What are the new findings in your manuscript?

- Patients with obesity awaiting Bariatric Surgery have cardiometabolic risk markers well above normal (such as neck circumference, waist circumference, fat mass, body weight, and BMI)
- Despite complying with the weekly MVPA recommendations, no direct relationship has been found between the amount of MVPA performed by obese patients awaiting bariatric surgery and body composition, nor functional capacity.

How might your results change the direction of research or the focus of clinical practice?

- We know that patients with obesity awaiting Bariatric Surgery, thanks to their daily activity, comply with the MVPA recommendations, but this is insufficient to produce improvements in their functional capacity and body composition. It seems necessary to improve the eating habits of patients and perform specific exercise training.
- Many of the patients were unable to achieve 100% effort on the evaluations due to mobility problems or increased blood pressure during exercise. It would be convenient to adapt the functional capacity tests to the special characteristics of these patients in order to evaluate them properly.

ABSTRACT

Objective

The purpose of this cross-sectional study was to describe physical activity (PA) levels, body composition, blood pressure, arterial stiffness and functional capacity in obese adults awaiting bariatric surgery (BS), as well as to analyse the association of PA with these health indicators.

Methods

68 patients underwent pre-surgery clinical evaluations as part of the EFIBAR randomized controlled trial, between 5 and 12 days before the surgery (ClinicalTrials.gov Identifier: NCT03497546). A selection of the outcomes measured in EFIBAR were used in this study: body composition, blood pressure, arterial stiffness, functional capacity, and objectively measured physical activity.

Results

75.4% of the participants met the recommendation of 150 min/wk of moderate-to-vigorous PA (MVPA). There was no significant association between PA and body composition. On the other hand, those patients who spent more time in sedentary activities showed a higher arm circumference (r = 0.31; $p < 0.01$) and less perceived effort on the Borg scale during the maximal treadmill test (r = -0.5; p = 0.009).

Conclusions

People awaiting BS spend most of their time performing sedentary and light activities. All this means that these patients, who despite the fact that most comply with the recommendations of 150 min / week of MVPA, present altered cardiometabolic risk factors and poor results in functional capacity tests.

INTRODUCTION

The prevalence of severe / morbid obesity has doubled globally in adults in the last 40 years, especially in middle- and high-income regions [1]. It is currently one of the main health problems worldwide [2], which means a high annual economic cost for health systems [3]. In people with severe obesity, the cardiometabolic risk factors are altered to a greater extent than in people with type 1 obesity or people with normal weight [4], both in men and women. This actually leads to comorbidities such as hypertension, hyperlipidemia, type 2 diabetes, respiratory problems, chronic inflammation [5] and metabolic syndrome [6]. Cardiovascular risk is directly influenced by arterial stiffness [7], and pulse wave velocity (PWV) is the gold standard for measuring arterial stiffness [8]. A high PWV level is directly associated with cardiovascular disease and hypertension. Furthermore, PWV has been suggested as an independent predictor of mortality [9]. High levels of obesity, like those we can find in patients awaiting bariatric surgery (BS), are directly related to higher levels of PWV [10].

The World Health Organization (WHO), as well as the US Department of Health and Human Services, recommend that adults aged 18-64 years should do at least 150 minutes of moderate-intensity aerobic physical activity (PA) throughout the week, or at least 75 minutes of vigorous-intensity aerobic PA, or an equivalent combination of moderate- and vigorous-intensity activity (MVPA) [11]. Low PA levels and a sedentary lifestyle are associated with an increase in obesity, worsening of functional capacity [12], deterioration in body composition indicators and an increased cardiometabolic risk [13].

High levels of PA and an adequate physical condition prior to undergoing BS translate into better post-intervention recovery, improvements in body composition and functional capacity [14], in addition to changes in behavioral habits that produce a better adaptation to exercise and higher levels of PA after surgery [14,15]. Previous studies have shown that PA levels in people with obesity are below the recommended amount and intensity [12]. However, there is scarce research on the relationship of PA with functional capacity and body composition in people with high degrees of obesity awaiting BS. The aim of this cross-sectional study was to describe PA levels, body composition, blood pressure, arterial stiffness and functional capacity in obese adults awaiting BS, as well as to analyze the association of PA with these health indicators.

METHODS

Study design and procedures

This report is a cross-sectional analysis of baseline results (i.e., pre-surgery examinations) of patients participating in the EFIBAR randomized controlled trial (ClinicalTrials.gov ID: NCT03497546), at the University of Almería. The study protocol was reviewed and approved by the Ethics Committee of the Torrecárdenas University Hospital, prior to the start of the recruitment process (case N° 76/2016). A detailed description of the study design and methods has been published elsewhere[16]. The STROBE guidelines and checklist have been strictly followed in this report [17].

Participants were recruited at Torrecárdenas University Hospital and HLA Mediterráneo Hospital (Almería, Spain). Participants included in this EFIBAR analysis are those recruited and examined from May 2018 to January 2021. All participants completed and signed the informed consent. The eligibility (inclusion and exclusion) criteria are detailed in Table 1.

Pre-surgery examinations were conducted between 5 and 12 days before the surgery during 3 days, and were performed by the same blind evaluators. Data was compiled in record sheets and/or digital archives with a security password, and later entered into the database.

Table 1. EFIBAR inclusion and exclusion criteria.

Inclusion criteria
• Males or females aged between 16 and 60 years old.
• Body mass index ≥40 (or ≥ 35 kg/m2 with comorbidities).
• Acceptable surgical risk (defined by the approval of anesthetist).
• Obesity maintained at least 5 years.
• Ineffective previous treatments.
• Informed consent signed before surgical treatment.
• Not having contraindications for supervised physical exercise.
Exclusion criteria
• Severe psychiatric or neurological disorders such as schizophrenia, epilepsy, Alzheimer, Parkinson, personality disorders, eating behavior disorders, untreated depression or suicidal tendencies.
• Adrenal or thyroid pathology that may be the cause of obesity.
• Addiction to alcohol or drugs.

Variables/Outcomes

Anthropometric measurements and body composition

Height (in cm) was measured with a portable stadiometer (SECA 213; Hamburg, Germany), adjusting the closest measurement to 0.1 cm. The position of the subjects was standing, barefoot, with their heels glued to the base of the height bar and with their heads in the Frankfort plane [18].

Different body circumferences were measured using an anthropometric tape measure (Cescorf) and following the standardized guidelines [19]. All measurements were carried out consecutively (neck, relaxed arm, waist and hip) from proximal to distal, bringing the measurement closer to 0.1 cm. The measurements were repeated twice, and if these two measurements were separated by more than 0.5 cm from each other, a third measurement was performed, taking for analysis the mean between the two closest measurements.

Body composition (% body fat, fat mass in kg, fat free mass in kg), body weight and BMI were assessed with a bioelectrical impedance device (Inbody 270, Biospace Co, USA). This measurement took place in the morning, with patients wearing underwear that occupied the least possible body surface, after at least 2 hours of fasting, not having exercised in the previous 24 hours, and were asked to urinate before the evaluation [20,21].

Functional capacity

Participants' functional capacity was measured using handgrip strength test, 30-second chair stand test, back scratch test and maximal treadmill test. Handgrip test (in kg) was carried out using a digital dynamometer (T.K.K. 540; Takei, Tokyo, Japan) with a precision to the nearest 0.1 kg to assess upper limb isometric strength adjusted for hand size (25). Participants were asked to perform the test twice with each hand, alternating between sides and with a rest period of 1 minute between repetitions. Participants performed the trial in a standing position, with the elbow fully extended, the arm relaxed in a neutral position and encouraged by the evaluators to exert themselves to their maximal effort for a couple of seconds. The best attempt from each hand was recorded, and the average of them used for analysis [22].

30-second chair stand test was used to measure lower-body muscular strength. This test was performed with the subject seated with the back resting on the chair back. The participants were instructed to stand up and sit down on a chair as fast as possible during 30 seconds with arms folded across the chest, with a straight back and feet flat. The total number of repetitions was registered. Only one attempt was allowed [22].

The back scratch test was used to quantify upper body (shoulder girdle) range of motion [22]. The patient, standing, placed the non-dominant hand on the back above the shoulder and the dominant hand on the lower part of the back with the palm of the hand out and extended, while he/she tried to touch fingertips. In the case of not touching, the value in cm was negative and if the middle fingers overlapped, the value in cm was positive. Two attempts were allowed and the best was used in analysis [22].

Cardiorespiratory fitness was assessed on a treadmill using the Bruce protocol [23], one of the most used protocols [24] consisting of a maximum test, up to complete exhaustion, in which speed and incline increase every 3 minutes [23]. Total time on the treadmill was registered, together with blood pressure, heart rate and rate of perceived exertion (RPE, Borg $_{1-10}$) in each 3-min stage.

Blood pressure and arterial stiffness

The oscillometry-based pulse analysis system Mobil-O-Graph® (IEM GmbH, Stolberg, Germany) was used to measure blood pressure and arterial stiffness [PWV (m/seg)] [25,26]. The test was carried out with the patient sitting for 10 minutes, for 5 minutes with the cuff placed on the upper arm around the brachial artery and with the palm facing up [27]. Three readings were made, using the average for statistical analysis.

Objectively measured physical activity

The data was collected using a triaxial accelerometer GT3X+ (Actigraph Pensacola, Florida, USA) at a rate of 30 Hz and stored at an epoch length of 60 seconds. The participants wore the device on the right hip, near the center of gravity, underneath their clothes and secured with an elastic belt. The accelerometer wearing time was calculated by subtracting the sleeping time from each day (registered by the patients in a diary where they reported the time they went to sleep and the time they woke up). The bouts of 90 continuous minutes of 0 counts were excluded from the analyses, considered as non-wear periods (a valid "wear time" is considered when it measures at least 4 out of 7 days). The data was recorded up to 7 days, starting from the day the patients received the accelerometers until the day they returned the devices. As an overall measure of PA, average counts per minute (cpm) in each independent axis and the vector magnitude were calculated for each patient. Sedentary time, light, moderate, and vigorous PA intensity levels were calculated based on the recommended PA vector magnitude cut points: 0–199, 200–2689, 2690–6166, and ≥6167, respectively, and were expressed as minutes per day. Total PA was calculated as the sum of light, moderate, and vigorous PA (min/day). A bout of moderate-to-vigorous PA (MVPA) was defined as spending ≥10 continuous minutes in MVPA (≥2690 cpm). The total time in MVPA in bouts of ≥10 minutes was also calculated. Meeting the bouted PA recommendations required engaging in at least 150 min/week of MVPA accumulated in bouts ≥10 min; conversely, non-bouted PA recommendations did not need to accumulate MVPA in bouts ≥10 min. We used the manufacturer software ActilifeTM v.6.13.3 desktop for data download, reduction, cleaning, and analyses purposes.

Statistical analysis

The different data collected in this study is shown as frequency and percentage, or mean and standard deviation (SD). Both parametric and non-parametric tests were performed. To verify normality in the distribution the Kolmogorov-Smirnov test was used, while one-way ANOVA test was used to determine homogeneity of variance. T test for independent samples was used to compare men and women means in data with normal distribution, and the Mann-Whitney U test for variables with non-parametric distribution. In addition, to analyze correlation between variables, P-Pearson was used for variables with parametric distribution and Spearman's rank correlation for variables with non-parametric distribution. Statistical analyses were performed using the SPSS V.23.0 statistical software package (IBM SPSS Statistics, Chicago, IL, USA), and statistical significance was determined at $p < 0.05$.

RESULTS

Out of 70 participants who completed pre-surgery examinations, 2 were excluded due to not meeting the accelerometer wear-time criterion. Thus, a total of 68 patients (47 women, 69%) were included in this analysis (Figure 1). Descriptive characteristics of the study participants are shown in Table 2. Mean age was 42.4 ± 9.6 years, with an average weight of 129.7 ± 22.5 kg, a BMI of 47.4 ± 7.1 kg/m^2, fat free mass (FFM) of 64.0 ± 12.8 kg, and percentage body fat of 50.8 ± 5.3 %. The average neck circumference (NC) was 42.4 ± 6.1 cm and waist circumference (WC) 126.7 ± 15.9 cm. Significant differences between men and women were observed in all parameters except in age, systolic blood pressure (SBP), BMI, fat mass (kg), mid-upper arm circumference (MUAC) and hip circumference (HC).

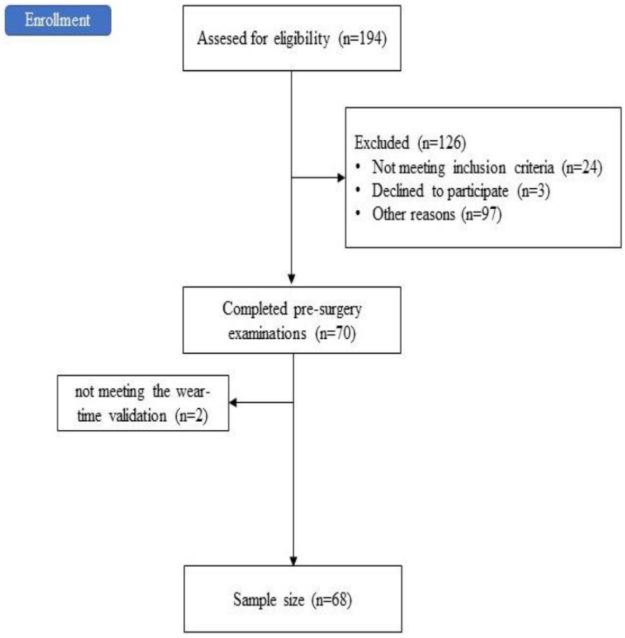

Figure 1. Enrollment flow-chart

Average scores for functional capacity tests were as follows: the back scratch test -13.8 ± 8.3 cm; chair stand test 10.7 ± 2.8 repetitions in 30 seconds; hand grip test 34.8 ± 10.3 kg; and estimated METs in the maximal treadmill test 6.1 ± 2.3. Significant differences were observed between men and women in the back scratch test, hand grip and estimated METS.

Table 2. Basic characteristics, body composition and blood pressure.

	Total (n=68)	Men (n=21)	Women (n=47)	*p*
Age	42.4 (9.6)	44.7 (10.4)	41.4 (9.2)	0.19
Body composition				
Height (cm)	165.8 (9.1)	175.3 (6.4)	161.5 (6.6)	**< 0.01**
Weight (Kg)	129.7 (22.5)	147.8 (21.0)	121.2 (17.8)	**< 0.01**
BMI (Kg/m^2)	47.4 (7.1)	48.8 (8.8)	46.7 (6.1)	0.28
Fat mass (Kg)	66 (13.9)	68.8 (18.4)	64.7 (11.1)	0.27
Fat mass (%)	50.8 (5.3)	46.2 (6.6)	53.1 (2.3)	**< 0.01**
FFM (kg)	64 (12.8)	78.3 (7.4)	56.9 (7.9)	**< 0.01**
Blood pressure and arterial stiffness				
SBP (mmHg)	131.4 (16.1)	136.5 (15.7)	128.9 (15.8)	0.08
DBP (mmHg)	83.4 (10.3)	87.6 (11.3)	81.3 (9.1)	**0.02**
PWV (m/s)	6.7 (1.0)	7.1 (0.9)	6.5 (1.0)	**0.04**
Circumferences				
NC (cm)	42.4 (6.1)	49.3 (3.9)	39.4 (4)	**< 0.01**
MUAC (cm)	41.6 (4.8)	42.0 (2.3)	41.5 (5.5)	0.76
WC (cm)	126.7 (15.9)	138.9 (14)	121.8 (13.6)	**< 0.01**
HC (cm)	140.3 (15.4)	140.0 (16.0)	140.4 (15.3)	0.91
Functional capacity				
Back Scratch (cm)	-13.8 (8.3)	-23.0 (11.5)	-13.8 (8.3)	**< 0.01**
30sec-chair Stand (reps)	10.7 (2.8)	11.2 (2.4)	10.5 (2.9)	0.4
Hand Grip (kg)	34.8 (10.3)	47.3 (7.2)	29 (5.1)	**< 0.01**
Maximal treadmill test				
Total time (min)	5.1 (2.3)	4.9 (1.9)	5.3 (2.3)	0.49
HR max	160.8 (14.4)	156.8 (18.3)	161.8 (11.7)	0.21
Borg scale	7.1 (1.1)	7 (1.1)	7.2 (1.1)	0.64
Estimated METS	6.1 (2.3)	5.5 (2.2)	6.9 (2.4)	0.2
Physical activity levels				
Sedentary (%)	65.8 (12.5)	64.9 (14.4)	66.2 (10.1)	0.71
Light (%)	29.7 (10.6)	30.0 (12.0)	29.6 (10.1)	0.88
Moderate (%)	4.4 (2.8)	5.0 (3.2)	4.1 (2.5)	0.22
Vigorous (%)	0.1 (0.4)	0.1 (0.1)	0.2 (0.4)	0.39
Total MVPA (min/day)	45.7 (29.1)	49.2 (34.3)	44.2 (26.8)	0.52
Steps per day	5518 (2512)	5760 (3019)	5408 (2277)	0.61

Data are shown as mean (standard deviation). BMI: Body Mass Index; FFM: fat-free mass; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PWV: Pulse wave velocity; NC: Neck circumference; MUAC: Mid-upper arm circumference; WC: Waist circumference; HC: Hip circumference; HR: Heart rate; MVPA: Moderate to vigorous physical activity.

75.4% of the participants met the recommendations of 150 min/wk of MVPA. Furthermore, no significant differences were observed between men and women in any PA parameter, as seen in Table 2. The average time in sedentary activities per day was 687.0 ± 226.1 min (65.8 ± 12.5 %), in light activities 300.1 ± 107.6 min (29.7 ± 10.6 %), in moderate activities 44.3 ± 27.5 min (4.4 ± 2.8 %), and in vigorous activities 1.4 ± 3.5 min (0.1 ± 0.4 %). Women performed on average 5407.9 ± 2276.7 steps per day, while men performed 5760.3 ± 3019.3 steps.

Table 3. Correlations of physical activity with functional capacity.

Physical activity	Back Scratch (cm)	Hand Grip (Kg)	Chair Stand (reps/30seg)	Total time (min)	HR max	Borg scale	METS
Sedentary (%)	r: -0.15	r: 0.03	r: 0.09	r: -0.25	r: 0.02	r: -0.50 **	r: 0.00
Light (%)	r: 0.13	r: 0.00	r: -0.12	r: 0.01	r: -0.02	r: -0.51	r: -0.40
Moderate (%)	r: 0.17	r: 0.12	r: 0.02	r: 0.07	r: 0.04	r: 0.39 *	r: 0.14
Total MVPA/day	r: 0.15	r: 0.11	r: 0.04	r: 0.08	r: 0.04	r: 0.40	r: 0.19
Steps per day	r: 0.07	r: 0.15	r: 0.05	r: 0.14	r: -0.01	r: 0.42 *	r: 0.23

* $p < 0.05$; ** $p < 0.01$; MVPA: moderate-to-vigorous physical activity; HR: heart rate.

Table 3 shows correlations between PA and functional capacity. More time spent in sedentary activities was correlated with a lower perceived effort (Borg scale) during the maximal treadmill test (r: -0.5; *p*: 0.009). On the other hand, those participants who performed more steps per day perceived a greater effort (Borg scale) during the treadmill test (r: 0.42; *p*: 0.04), the same occurs with patients who perform a more moderate PA (r: 0.39; *p*: 0.04). Correlation analysis between PA and body composition are presented in Table 4, with none of them achieving statistical significance.

Table 4. Correlations of physical activity with body composition.

Physical activity	BMI (Kg/m^2)	Fat mass (%)	FFM (kg)
Sedentary (%)	r: 0.03	r: -0.4	r: 0.03
Light (%)	r: -0.08	r: 0.09	r: -0.1
Moderate (%)	r: -0.03	r: -0.19	r: 0.11
Total MVPA/day	r: -0.02	r: -0.01	r: 0.086
Steps per day	r: 0.08	r: -0.08	r: 0.07

None of the correlations were significant. BMI: body mass index; FFM: fat-free mass.

Correlation analysis of PA with body circumferences, blood pressure and arterial stiffness is shown in table 5. A significant positive correlation was observed between the arm circumference (MUAC) and time spent in sedentary activities (R: 0.31; *p*: 0.01). Negative significant correlations were between arm circumference (MUAC) and number of steps per day MUAC (R: -0.29; *p*: 0.02), furthermore between MUAC and light PA (R: -0.34; *p*: <0.01).

Table 5. Correlation analysis of physical activity with body circumferences, blood pressure and arterial stiffness.

Physical activity	NC	MUAC	WC	HC	SBP (mmHg)	DBP (mmHg)	PWV (m/s)
Sedentary (%)	r: 0.14	r: 0.31 **	r: 0.08	r: -0.04	r: -0.06	r: -0.16	r: -0.08
Light (%)	r: -0.15	r: -0.34 **	r: -0.08	r: 0.05	r: 0.14	r: 0.16	r: 0.14
Moderate (%)	r: -0.02	r: -0.10	r: -0.03	r: -0.01	r: -0.2	r: 0.14	r: -0.12
Total MVPA/day	r: -0.07	r: -0.05	r: -0.50	r: -0.03	r: -0.21	r: 0.13	r: -0.13
Steps per day	r: -0.19	r: -0.29*	r: -0.14	r: -0.09	r: -0.09	r: 0.07	r: 0.01

* p < 0.05; ** p < 0.01. MUAC: mid-upper arm circumference; WC: Waist circumference; HC: Hip circumference; NC: Neck circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; PWV: Pulse wave velocity

DISCUSSION

The aim of this study was to describe PA levels, body composition, blood pressure, arterial stiffness and functional capacity in obese adults awaiting BS, as well as to analyze the association of PA with these health indicators. Our male patients weighed on average about 25 kg more than our female patients (148 vs. 121 kg, respectively), also presenting corresponding differences in FFM (78 vs. 57 kg). Differences were also evident in height (men, 175 cm; women, 162 cm) but not in BMI (49 vs. 47 kg/m^2). In a recent study by Serafim et al. [28] in candidate patients for BS, authors reported similar results before patients went on a carbohydrate-restricted diet.

Roughly half of our patients' body weight was fat mass (51 %). Such high levels of fat mass are directly related to foot pain [29] as well as cardiometabolic risk factors, especially abdominal fat mass [30], which is especially relevant because our sample presented notably high values of WC (men, 139 cm; women, 122 cm), well over the WC cut-off levels that define abdominal obesity [102 cm for men and 88 cm for women [31]]. As in the study by Serafim et al. [28], our patients presented high values of NC in both sexes (men, 49 cm; women, 40 cm). Although the NC cut-off points are still being defined for each comorbidity, an abnormal NC is considered ≥37 cm in men and ≥34 cm in women [32]. "Neck obesity" has been directly related to hyperuricemia [33], cardiometabolic risk factors [34,35] and metabolic syndrome [36].

High levels of sedentary time (65 %) and light activity (30 %) were observed in our participants, which is in line with the data provided by Rioux et al [12], where patients awaiting BS spent on average 70 % of the time in sedentary activities. Such low levels of PA have been directly related to metabolic syndrome as well as mortality from cardiovascular diseases and from all causes [37]. In our study, no significant correlation was observed between BMI and time spent in sedentary activities, although according to Bond et al. [38], BS candidates with a BMI greater than 50 spent significantly more time in sedentary activities. In contrast, we observed a significant positive correlation between sedentary time and arm circumference: those patients who spent more time in sedentary activities also presented a higher MUAC. On the other hand, patients who performed more steps per day presented a lower arm circumference. It has been stated that a greater MUAC is positively associated with an increased risk of cardiometabolic disorders [39].

A person is considered to be hypertensive when his/her systolic and/or diastolic blood pressure values are over 140 and 90 mmHg, respectively [40,41]. Our patients presented both systolic and diastolic blood pressures within normal limits (131 and 83 mmHg, respectively). These results are in line with those found by Oliveras et al. [42] in their patients awaiting BS. Something similar occurred with arterial stiffness (PWV), as our patients (6.7 ± 1 m/s) are within the normal values established by the ESC guidelines [a cut-off point of 10 m/s has been established to define abnormal PWV [41]]. Again, our results are similar to those previously found in the literature [42,43] in patients before undergoing BS.

We did not observe any significant correlation between sedentary time and functional capacity, which goes in line with the study of Rioux et al. [12]. However, it should be noted that Sellberg et al. [44] reported that patients who spent more time in sedentary activities presented worse results in the SF-36's sections of functional capacity, vitality and social function. In our study, patients who performed more sedentary and light activities reported a lower perceived exertion (Borg scale) in the maximal treadmill test. We hypothesize this could be due to the fact that many of the patients may not be able to reach 100% of effort due to mobility problems, or to increased blood pressure during exercise, or maybe it was related to the subjectivity of the scale itself, as occurs in other sedentary patients with little previous experience in exertion, who tend to give answers with little consistency [45].

According to our results, vigorous PA did not correlate with a better result in the chair stand test. Opposing results were obtained by Rioux et al. [12], as they found a positive relationship between moderate PA and the chair stand test in patients with obesity awaiting BS. 75.4% of our patients comply with the recommendations of 150 min/wk of MVPA or 75 min/wk of vigorous-intensity PA [11]. These results are similar to those previously reported in the study of Sellberg et al. [44], in which more than 50% of the patients awaiting BS complied with the PA recommendations, which according to their results led those patients to better physical function, as well as more vitality and mental health in the SF-36 test, it should be noted that mean BMI in that study (41 kg/m_2) is clearly lower than in our sample (47 kg/m_2). However, this did not occur in other studies in which no one single patient [46] or only 1 out of twenty [47] met the PA recommendations. Despite the fact that most patients comply with the recommendations of 150 min / week of MVPA, they present high levels of cardiometabolic risk factors, body perimeters and difficulties when performing functional capacity evaluations, this may be due to various causes: I) Although they comply with the recommendations, most of the time they spend them doing sedentary and light activities, also, since they only get 1.4 ± 3.5 min per day of vigorous activity, they meet the recommendations only for the amount of moderate activity they do each day; II) These patients do not have an adequate diet, which generates serious health problems [48]; III) We hypothesize that many of them perform MVPA throughout the day due to their work routine or daily routine, but they do not invest their time in physical training.

Although the activity of a moderate nature carried out by our patients is within the international recommendations, in any case, the vigorous PA levels observed in our participants are well below international recommendations, so it would be daring to conclude that the amount of vigorous PA performed does not affect body composition, functional capacity or blood pressure in patients awaiting surgery BS.

Limitations

Our relatively small sample size (n=68) limited the correlation analyses and may not represent the entire population of people awaiting BS. It's also important to note that more than twice as many participants were women, making it difficult to generalize or obtain conclusive results in men. However, this sex distribution is confirmed by the literature, as more than 70% of bariatric procedures are performed on women [49]. Another limitation to note is that some of the functional tests may not have been performed at maximum effort, due to mobility limitations or mechanical stress. Finally, the lack of consensus when defining accelerometer-based cut points for PA intensities may limit comparability and replicability in other studies that use different thresholds or even different PA methodologies.

CONCLUSIONS

Our results indicate that people awaiting BS spend most of their time performing sedentary activities, and more sedentary time seems to be related to a higher arm circumference. On the other hand, always according to our results, those patients who walk more steps per day seem to present a lower arm circumference. Although most patients comply with the recommendations of 150 min/week of MVPA, no direct relationship was found between the amount of MVPA performed by the patients and body composition or functional capacity, probably due to their high levels of sedentary and light PA. Additionally, our patients awaiting BS present altered cardiometabolic risk factors, such as elevated fat mass, and waist and neck circumferences well above the recommended levels.

Future directions

Future research should establish correlations between BP and physical condition, body composition, as well as other variables, in larger sample sizes of patients awaiting BS, to confirm the results obtained in the present study and to better understand in which clinical state patients face the surgery and the causes that can lead them there. It would also be interesting in future studies to compare whether the level of PA, functional capacity and body composition at which obese people reach BS is different from that of the rest of the obese population. Furthermore, future papers would not only have the amount and intensity of PA performed by the patients, but also the type of activity, in order to be able to discern between the activity carried out in the patients' day-to-day life and the amount of time dedicated to specific exercise training.

LIST OF ABBREVIATIONS

PWV: Pulse wave velocity; BS: Bariatric surgery; PA: Physical activity; MUAC: Mid-upper arm circumference; WC: Waist circumference; HC: Hip circumference; NC: Neck circumference; SBP: Systolic blood pressure; DBP: Diastolic blood pressure.

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II

II. Effects of exercise training on weight loss in patients who have undergone bariatric surgery: a systematic review and meta-analysis of controlled trials.

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REVIEW

Effects of Exercise Training on Weight Loss in Patients Who Have Undergone Bariatric Surgery: a Systematic Review and Meta-Analysis of Controlled Trials

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Abstract

The combination of bariatric surgery and physical exercise has been suggested as a promising strategy to positively influence obesity, not only body weight but also all associated comorbidities. An electronic search of intervention studies was carried out in which an exercise training program was implemented after bariatric surgery. The quality of each study was assessed and the data were meta-analyzed using a random effect model. Twenty-six articles were included in the systematic review and 16 in the meta-analysis. As the main conclusion, exercise in patients who have undergone bariatric surgery does not seem to be effective in enhancing weight loss (SMD = 0.15; 95% CI = −0.02, 0.32; p = 0.094). However, the variability in the protocols used makes it too early to reach a definite conclusion.

Keywords Bariatric surgery · Weight loss · Physical activity · Exercise

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Background

The World Health Organization considers people with class I obesity if they have a body mass index (BMI) ≥ 30 kg/m^2, class II obesity if they have a BMI ≥ 35 kg/m^2, and class III obesity with a BMI ≥ 40 kg/m^2 [1]. Obesity is considered a risk factor for diseases such as hypertension, heart failure, coronary heart disease [2], diabetes mellitus [2, 3], sleep apnea, and osteoarthritis [3]. Compared to normal weight, class II and III obesity are related to higher mortality rates from all causes [4]; the average survival rate is reduced by 2–4 years for people with class II obesity and by 8–10 years for people with class III obesity [5]. In economic terms, obese people have worse results in the world of work, lower wages, and higher health costs [6].

Weight and fat loss are related to improvements in obese people's health, a reduction in the inflammatory markers associated with diabetes [7], a decrease in blood pressure [8], and improvements in terms of cardiovascular diseases [7]. Bariatric surgery is an effective treatment option for reducing weight in people with morbid obesity [9], on average losing around 12% of total body weight in the 6 months after surgery, and up to 45% over 3 years [10]. Physical activity (PA) is also one of the main approaches that influences and improves people's health [11], decreasing cardiovascular risks [12] and coronary heart diseases [13]. Exercise training diminishes comorbidities related to obesity, such as asthma and sleep problems [14] as well as reducing insulin resistance, hypertension, and blood lipids [15]. Furthermore, PA plays an important role in the amount of weight recovered after weight loss and helps reduce weight progressively [16].

Given the increased number of people with morbid obesity [17], the proven short- and long-term effectiveness of bariatric surgery [18] and the possibilities presented by PA in relation to maintenance and improvement of risk factors suggest that PA could help those patients who suffer weight regain after bariatric surgery [19]. The present review and meta-analysis arise from the need to accurately assess whether PA following bariatric surgery has a positive effect on weight loss and to try to determine what type of exercise is most effective for that purpose. Previous systematic reviews [20, 21] and one meta-analysis [22] have studied weight loss caused by exercise following bariatric surgery, although the authors failed to take into account the specific characteristics of each training program, which can undoubtedly influence their effect.

The aims of this systematic review and meta-analysis were (a) to analyze the effects of exercise training after bariatric surgery in relation to weight loss; and, in case of being effective for a higher weight loss, (b) to determine what type of training is the most appropriate for weight loss in people undergoing bariatric surgery.

Material and Methods

Protocol and Registration

This study has been carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, the PRISMA Statement [23], using the PRISMA checklist as a reference (Table A supplementary files), and the Cochrane Handbook for Systematic Reviews of Interventions [24]. This systematic review and meta-analysis has been registered in PROSPERO, the International Prospective Register of Systematic Reviews, with the ID CRD42018097444.

Searches

The literature search was performed systematically using the MEDLINE, EMBASE, Scopus, Cochrane, and Web of Science databases, with the deadline of May 23, 2019.

The following equation was used for the search ("Bariatric Surgery" OR "stapling stomach" OR "weight loss surgery" OR "obesity surgery" OR "weight reduction surgery" OR "Biliopancreatic Diversion" OR "Duodenal switch" OR "laparoscopic band" OR "lap band" OR "gastric band" OR "gastric banding" OR "Gastric Bypass" OR "Gastroplasty" OR "gastric sleeve" OR "sleeve gastrectomy" OR "gastric bypass surgery" OR "gastric bypass" OR "Roux-en-Y Gastric Bypass" OR "Maestro Rechargeable System" OR "gastric balloon" OR "gastric bubble" OR "ballobes balloon" OR "Greenville gastric bypass") AND ("physical exercise" OR "Physical Therapy" OR "physical activity" OR "physical education" OR "physical training" OR exercise OR fitness OR sport OR "Exercise Movement" OR "exercise program" OR "Complementary Therapies" OR "physiotherapy" OR "physio therapy" OR "therapeutic exercise" OR "Occupational Therapy" OR "Exercise therapy") AND ("body mass index change" OR "weight maintenance" OR "weight loss" OR "weight regain" OR obesity OR overweight).

Eligibility Criteria

Articles showing either the effect of physical activity on patients who had undergone bariatric surgery or which carried out an experimental intervention were included as eligible for further review.

The exclusion criteria for this systematic review were (a) papers not written in English or Spanish; (b) studies that do not report the outcome weight; (c) studies in which the intervention is performed before bariatric surgery; (d) studies in which the population investigated are non-humans; (e) studies in which participants are under 18 years old; (f) papers that combine physical activity with other types of intervention, medications, and nutrition among others; (g) retracted studies;

(h) duplicate studies; and (i) non-selectable publications, as in the case of reviews, guidelines, interviews, comments, or case studies.

The literature review was independently and simultaneously performed by two reviewers (AC and IC-R). Disagreements were sorted out either through consensus or with the participation of a third party (EG).

Data Selection

The data gathered from the selected studies were as follows: (a) the year of the study; (b) the study design; (c) the main features and the type of physical activity intervention; (d) the population's characteristics, number, sex, and age; and (e) the pre- and post-surgery weight.

Assessment of the Risk of Bias

For randomized controlled trials (RCTs), the Cochrane Collaboration's tool was used for assessing risk of bias in randomized trials [25]. This tool measures the risk of bias based on six domains: selection bias, performance bias, detection bias, attrition bias, reporting bias, and other biases. For non-randomized control trials (non-RCTs), the quality assessment tool for quantitative studies [26] was used. This tool considers seven domains: selection bias, study design, confounders, blinding, the data collection method, and withdrawals and dropouts.

To combine both tools for evaluating the risk of bias for the reviewed articles, each of the sections to be evaluated was designated as strong, moderate, or weak, and the articles were classified as having a low risk of bias (without weak ratings), a moderate risk of bias (one weak rating), or a high risk of bias (two or more weak ratings) [27, 28].

Quality assessment and data extraction were carried out independently and simultaneously by two reviewers (AC and IC-R). Any differences were sorted out either through consensus or with the participation of a third researcher (EG).

Statistical Analyses

The software used to perform the statistical analyses of the meta-analysis was StataSE V.14.0 (StataCorp LP., College Station, TX, USA). The analysis variable (the result) was the weight loss at the end of the treatment in each of the groups; the quantification of the effect was calculated through the standardized mean difference (SMD) and through the unbiased Hedges estimator [29]. Weightings and standard deviations (SDs) were extracted for each study and group before and at the end of the treatment. In the case of not having the SD values, these were imputed as the average value of each group [30]. On the other hand, the differences of the weight means and the standard deviation of the difference for each of the articles were calculated; for the latter, a correlation of 0.59 was considered between the values before and after starting the treatment [31]. A positive SMD value indicated greater weight loss in the intervention group compared to the control group. The DerSimonian-Laird random effects method was used and the 95% confidence intervals (CI) were calculated [32].

As a test to evaluate heterogeneity, we estimated the I^2 statistic [25]—values of 0% indicated non-heterogeneity, whereas values of 25%, 50%, and 75% were interpreted as having a low, moderate, and high level of heterogeneity, respectively. In addition, the Q statistic and its P value were calculated.

The publication bias was evaluated by the funnel plot and the Egger test was performed.

To complete the statistical analysis, certain details were contemplated: (I) when two or more studies obtained the data from the same database, only the main study was taken into account; (II) those papers with two intervention groups were analyzed as two individual studies; and (III) pre-operative body weight data were collected using the baseline and post-intervention data from the evaluation performed immediately after the surgery.

Subgroups analyses were carried out considering the following characteristics of the training intervention protocols: (I) the type of physical activity intervention, (II) the start of the intervention after the surgery, (III) the duration of the intervention, (IV) the type of exercise, and (V) the total exercise time per week.

Meta-regressions with random effects were employed using the aggregate level data to know the effect of the intervention and the heterogeneity in relation to (I) the average age of the participants, (II) the time per session, and (III) the length of the intervention.

Finally, a sensitivity analysis was conducted by performing the calculations again, without each of the studies, to know the robustness of that particular study.

Results

Systematic Review

Of the 10543 studies obtained in the search, 26 documents were finally selected (Fig. 1). These were carried out in different countries—10 from the United States, 6 from Brazil, 2 from Iran, 4 from Denmark, and 1 from Belgium, Sweden, Italy, and the UK, respectively. All the studies included were experimental, most of them with an RCT design (21) while 5 were non-RCTs. All 26 studies were published between 2011 and 2018 (Table 1).

The internationally accepted criteria to undergo bariatric surgery are a BMI $\geq$ 40 kg/m^2 or a BMI $\geq$ 35 kg/m^2 if comorbidities are present that put the patient's health at risk. Most of

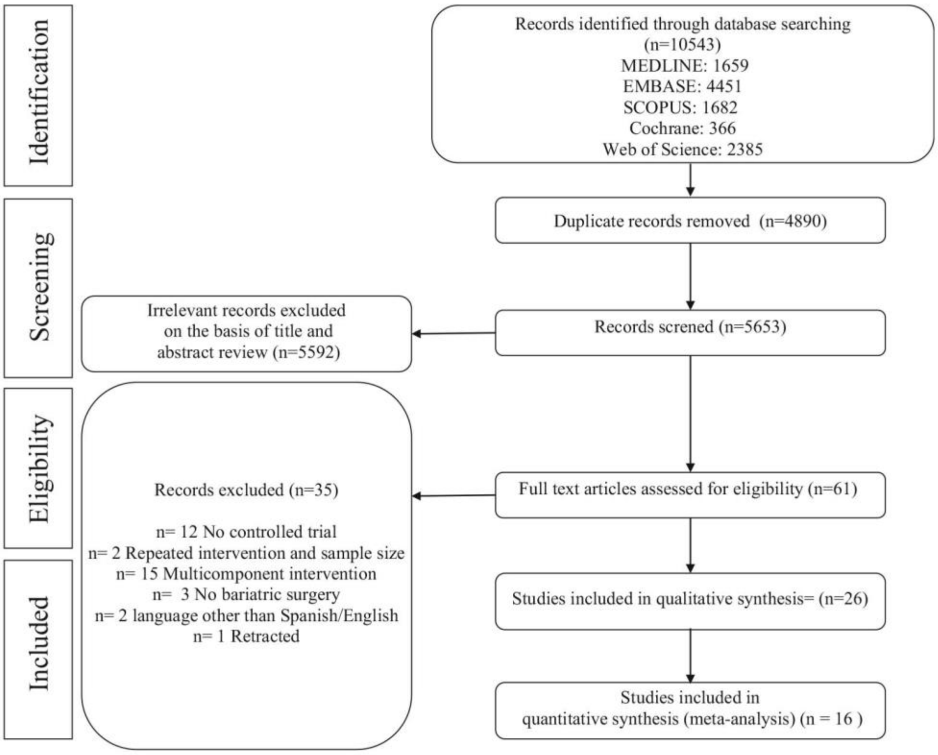

Fig. 1 Literature search preferred reporting items for systematic reviews and meta-analyses consort diagram

the selected studies included any type of surgical technique, apart from nine of them which included only laparoscopic surgery with RYGB, and one study on the sleeve gastrectomy technique. The sample size of the studies varied between 12 and 120 subjects, most of them including participants of both sexes, except for 5 studies in which only women participated.

The physical activity interventions carried out were supervised in 12 of the studies, programmed in 4, while 8 were mixed interventions, combining programmed and supervised. Only 1 study used a counseling intervention type. Aerobic exercise alone was used in 11 studies, resistance exercise alone in 2 of them, whereas a combination of both was used in 10 studies, and other alternative types of exercise in 3 studies. The reviewed studies used exercise durations between 20 and 85 min per session. The maximum length of the intervention was 40 weeks and the shortest was 1 week. The start of the intervention varied between 5 days and 24 months after surgery.

Risk of Bias

Regarding the risk of bias, as can be seen in Tables 2 and 3, from the 26 studies analyzed, 10 of them (38.5%) show a high risk of bias, 6 (23.1%) show a moderate risk of bias, and the other 10 (38.5%) show a low risk of bias. Analyzing the sections considered in both assessment tools individually, we can observe that all non-RCTs ($n = 5$, 100%) present deficiencies (i.e., scored as weak) in the blinding domain study, while in the case of RCTs, 38.1% ($n = 8$) and 14.3% ($n = 3$) show detection bias and performance bias, respectively. Among the non-RCT studies, deficiencies in the selection bias and the design of the study were present in 40% of the studies ($n = 2$) compared to 5.3% ($n = 1$) showing selection bias among the RCTs.

Meta-Analyses

The pooled SMD estimate did not show a greater significant weight loss in favor of the intervention (exercise) group, with a small effect size and no significant differences (SMD = 0.15; 95% CI = − 0.02, 0.32; $p = 0.094$), as well as low heterogeneity ($I^2 = 0\%$; $p = 0.999$) (Fig. 2).

Subgroup Analyses

When considering the specific characteristics of the physical activity intervention (i.e., type of intervention, start of the intervention after surgery, duration, type of exercise, and total time per week), none of the subgroups analyses showed a significant difference in favor of the control group or the intervention group, with heterogeneity being very low in all cases ($I^2 = 0.0\%$) (Table 4).

Meta-Regressions

The meta-regression analyses showed no heterogeneity based on the participants' mean age ($p = 0.902$), nor on the length of

Table 1 Studies included in the systematic review

Reference	Country	Study design	Population Characteristics: Age	Sample size (%W)	BMI	Pre-surgery weight	Intervention: Type of population	Type of intervention/Start of intervention	Physical activity characteristics
Campanha-Versiani et al. 2017 [42]	Brazil	NON-RCT	I.G: 37.2 ± 9.3 C.G: 37.0 ± 10.8	I.G: 30 (83%) C.G: 30 (83%)	I.G: 42.5 ± 4 C.G: 41.7 ± 4.6	I.G: 111.2 ± 10.8 C.G: 112.7 ± 14	Have undergone bariatric surgery	I.G: Physical activity supervised 3 months after surgery	I.G: Resistance + Endurance training - 36 weeks - 2 days/week - 85 min - 1–3 sets - 10–12 reps - Load correspondent to 10 RM - 70 to 80% HRmax
Carnero et al. 2017 [43]	USA	RCT	I.G: 39.4 ± 9.7 C.G:41.7 ± 9.8	I.G: 46 (91.3%) C.G: 50 (86%)	I.G: 45.8 ± 7.4 C.G: 44.4 ± 7.5	I.G: 127.9 ± 23.9 C.G: 122.6 ± 27.3	Not diabetic Have undergone bariatric surgery	I.G: Physical activity supervised/programme 11 weeks after surgery	I.G: Cycling or walking endurance training - 26 weeks (6 months) - 3–5 days/week - Minimum of 120 m/week
Casali et al. 2011 [44]	Brazil	RCT	I.G: 37.6 ± 10.9 C.G: 35.1 ± 10.7	I.G: 15 (73.3%) C.G: 15 (73.3%)	I.G: 42.8 ± 4.2 C.G:43.6 ± 3.9	I.G:115.2 ± 19 C.G: 120.3 ± 14.1	Have undergone bariatric surgery	I.G: Physical activity supervised 1 day after surgery	I.G: Respiratory training - 4 weeks - Daily 29 days - 30 min - 40% of MIP
Castello et al. 2011 [45]	Brazil	RCT	I.G: 38.0 ± 4 C.G: 36.0 ± 4	I.G: 16 (100%) C.G: 16 (100%)	I.G: 45.64 ± 1.54 C.G: 44.46 ± 0.96	I.G: 117.6 ± 4 C.G: 117 ± 6	Women who have undergone bariatric surgery	I.G: Physical activity supervised 1 months after surgery	I.G: Endurance training - 12 weeks - 3 days/week - 60 min - 50 to 70% HR peak
Castello-Simoes et al. 2013 [46]	Brazil	RCT	I.G: 32.0 ± 4.0 C.G: 31 ± 2.0	I.G: 16 (100%) C.G: 16 (100%)	I.G: 45.5 ± 1.7 C.G: 43.6 ± 1	I.G: 115 ± 6.9 C.G: 113 ± 4.7	Women who have undergone bariatric surgery	I.G: Physical activity supervised 1 months after surgery	I.G: Endurance training - 12 weeks - 3 days/week - 60 min - 50 to 70% HR peak
Coen et al. 2015 [47]	USA	RCT	I.G: 41.3 ± 9.7 C.G: 41.9 ± 10.3	I.G: 66 (89.4%) C.G: 62 (87.1%)	I.G: 38.8 ± 6.1 C.G: 38.3 ± 6.9	I.G: 127.2 ± 22.6 C.G:121.8 ± 25.7	Have undergone bariatric surgery	I.G: Physical activity supervised/programme Between 1 and 3 months after surgery	I.G: Endurance training - 26 weeks (6 months) - 3 to 5 days/week - 30 min - 60 to 70% HR
Coen et al. 2015 (2) [48]	USA	RCT	I.G: 41.6 ± 9.3 C.G: 42.1 ± 9.9	I.G: 51 (88%) C.G: 50 (84.3%)	I.G: 38.8 ± 5.6 C.G: 38.1 ± 6.9	I.G:108.2 ± 20.2 C.G:106.8 ± 25.4	Have undergone bariatric surgery Volunteered to undergo muscle biopsy before and after the intervention	I.G: Physical activity supervised/programme Between 1 and 3 months after surgery	I.G: Endurance training - 26 weeks (6 months) - 3 to 5 days/week - 30 min - 60 to 70% HR
Coleman et al. 2016 [49]	USA	RCT	I.G: 52.0 ± 10.9 C.G: 46.6 ± 12.0	I.G: 26 (84%) C.G: 25 (84.6%)	I.G: 45.0 ± 7.6 C.G: 44.5 ± 5.5	I.G: 90.8 ± 23.0 C.G: 93.4 ± 19.8	Have undergone bariatric surgery	I.G: Physical activity supervised/programme Between 6 and 24 months after surgery	I.G: Endurance + resistance training - 26 weeks (6 months) + 26 weeks of maintenance

Table 1 (continued)

Reference	Country	Study design	Population Characteristics: Age	Sample size (%W)	BMI	Pre-surgery weight	Intervention: Type of population	Type of intervention/Start of intervention	Physical activity characteristics
									- 5 dayd/week - 60 min
Creel et al. 2016 [50]	USA	RCT	C.G: 44.2 ± 11.0 I.G1: 41.8 ± 10.8 I.G2: 43.6 ± 12.2	C.G: 50 (84.0%) I.G1: 52 (84.6%) I.G2: 48 (83.3%)	C.G: 47.6 ± 8.0 I.G1: 48.4 ± 9.5 I.G2: 46.9 ± 7.8	132.1 ± 2.7	Morbidly obese Have undergone bariatric surgery	I.G1: Physical activity programme NR I.G2: Physical activity counseling NR	I.G1: Walking endurance - 26 weeks (6 months) - 7 days/week - Up to 10,000 steps per day I.G2: Walking endurance - 26 weeks (6 months) - 7 days/week
Daniels et al. 2018 [51]	USA	RCT	44.9 ± 10.2	I.G: 8 (100%) C.G: 8 (100%)	NR NR	I.G: 134.8 ± 23.6 C.G: 135.4 ± 17.1	Women who have undergone RYGB	I.G: NR 8 weeks post-surgery	I.G: Resistance training - 12 weeks - 3 days/week - 60–80 min - Period 1: 8–10 exercise; 1 set; 10–15 reps; 50–60% RM - Period 2: Progressive increased of volume; 10–15 reps; 50–60% to 70–80% RM - Period 3: Maintains sets of period 2; 8–10 reps; > 80% RM
Hassannejad et al. 2017 [52]	IRAN	RCT	I.G. 1: 33.3 ± 8.4 I.G. 2:35.5 ± 8.1 C.G:36.7 ± 6.2	I.G. 1: 20 (75%) I.G. 2: 20 (70%) C.G: 20 (80%)	I.G. 1: 47.9 ± 6.7 I.G. 2: 42.9 ± 3.9 C.G: 46.6 ± 6.9	I.G. 1: 129.6 ± 19.2 I.G. 2: 119.8 ± 15.3 C.G: 122.4 ± 24.9	Patients with BMI ≥ 35 Have undergone bariatric surgery	I.G. 1: Physical activity programme I.G. 2: Physical activity programme During first week after surgery	- The first 4 weeks, in both groups, patients should walk 150 min/week with a progressive increase in intensity I.G. 1: Endurance training - 5–12 weeks - 3–5 days/week - 150–200 min/week - 12–14 Borg Scale I.G. 2: Endurance + resistance training - 5–12 weeks - 3–5 days/week - 150–200 min/week - 12-14 Borg Scale Resistance training - 3 days/week - 20–30 min - Elastic bands with different resistances
Herring et al. 2017 [52]	UK	RCT	I.G: 44.3 ± 7.9 C.G:52.4 ± 81	I.G: 12 (91.7%) C.G: 12 (91.7%)	I.G: 38.2 ± 6.1 C.G: 39.4 ± 4.3	I.G: 106.5 ± 16.4 C.G: 106 ± 17.5	Inactive people Have undergone RYGB	I.G: Physical programme 12–24 months after operation	I.G: Resistance + Endurance training - 12 weeks - 3 days/week - 60 min - 2 exercise per session

Table 1 (continued)

Reference	Country	Study design	Population Characteristics: Age	Sample size (%W)	BMI	Pre-surgery weight	Intervention: Type of population	Type of intervention/Start of intervention	Physical activity characteristics
									- 3 sets - 12 reps - 60% RM 64–77% HRmax
Huck 2015 [53]	USA	NON-RCT	I.G: 53.6 ± 8.2 C.G: 44.0 ± 9.7	I.G: 7 (85.7%) C.G: 8 (75%)	I.G: 37.7 ± 6.3 C.G: 32.7 ± 4.2	I.G: 101.6 ± 19.8 C.G: 92.5 ± 15.5	Have undergone bariatric surgery	I.G: Physical programme NR	I.G: Small groups resistance training - 12 weeks - 2 days/week first 6 weeks and 3 days/week last 6 weeks - 60 min 60% to 75% RM
López et al. 2017 [54]	USA	RCT	I.G:38.5 ± 16.3 C.G: 43 ± 12.6	I.G: 11 (81.8%) C.G: 11 (81.8%)	I.G: 39.5 ± 6.7 C.G: 40.8 ± 7.9	I.G: 106.9 ± 19.9 C.G: 111.1 ± 21.3	Have undergone laparoscopic RYGB	I.G: Physical programme/programme Between 1 to 3 months after surgery	I.G: Endurance training - 26 weeks (6 months) - 3 to 5 days/week - 30 min - 60 to 70% HR
Marchesi et al. 2015 [55]	Italy	NON-RCT	I.G: 43.1 C.G:39.1	I.G: 10 (100%) C.G: 10 (100%)	I.G:29.57 C.G:30.07	I.G: 81.3 C.G: 80.2	Women who have undergone bariatric surgery	I.G: Physical activity supervised/programme Between 1 to 3 years after surgery	I.G: Endurance training - 40 weeks - 3 days/week for 6 first months and 4 days/week last 4 months - 60 min - 3 first months 55–65% and 65–75% HRmax, middle 3 months 55–65% and 65–85% HRmax and last 4 months 60–70% and 70–90% HRmax
Mundbjerg et al. 2018 [56]	Denmark	RCT	I.G: 42.3 ± 9.4 C.G: 42.4 ± 9	I.G: 32 (66.6%) C.G: 28 (75%)	I.G: 43.1 ± 6.7 C.G:42.8 ± 5.5	I.G:129.1 ± 19.9 C.G:123.7 ± 22	Have undergone RYGB	I.G: Physical activity supervised 6 months after surgery	I.G: Resistance + Endurance training - 26 weeks - 2 days/week - 40 min - Borg Sacale 15 to 17/ 50 to 70% VO_2max Encouraged to do 210 m/w of extra exercise
Mundbjerg et al. 2018 (2) [57]	Denmark	RCT	42.3 ± 9.1	I.G: 32 (66.6%) C.G: 28 (75%)	43 ± 6.1	126.6 ± 20.9	Have undergone RYGB	I.G: Physical activity supervised 6 months after surgery	I.G: Resistance + endurance training - 26 weeks - 2 days/week - 40 min - Borg Scale 15 to 17/ 50 to 70% VO_2max encouraged to do 210 min/week of extra exercise
Oliveira et al. 2016 [58]	Brazil	RCT	I.G: NR C.G: NR	I.G: 20 (%NR) C.G: 23 (%NR)	I.G: 44.7 ± 4.7 C.G: 46.4.7 ± 5.4	I.G: 113.6 ± 12.3 C.G: 122.4 ± 19.6	Have undergone bariatric surgery	I.G: Physical activity supervised 1 months after surgery (30 days)	I.G: Resistance + breathing training - 4 weeks (30 days)

Table 1 (continued)

Reference	Country	Study design	Population Characteristics: Age	Sample size (%W)	BMI	Pre-surgery weight	Intervention: Type of population	Type of intervention/Start of intervention	Physical activity characteristics
									- 2 days/week - 40 min - 15 reps per exercise
Onofre et al. 2017 [59]	Brazil	NON-RCT	I.G: 40.3 ± 10.7 C.G:39.5 ± 7.2	I.G: 6 (100%) C.G:6 (100%)	I.G: 46.1 ± 7.0 C.G: 44.9 ± 9.0	I.G: 118.4 ± 21.6 C.G: 117.6 ± 7.2	Women with Obesity type II or III who have undergone bariatric surgery	I.G: Supervised training 3 months after surgery	I.G: Resistance + endurance training - 12 weeks - 3 days/week - 60 min - 60–80% RM - 40–60% intercalated with 85–90% HRR reserve
Rojhani-Shirazi et al. 2015 [60]	Iran	RCT	I.G: 36.1 ± 6.7 C.G: 36.6 ± 7.8	I.G: 16 (%NR) C.G: 16 (%NR)	I.G: 40.5 ± 5.4 C.G: 44.0 ± 7.2	I.G: 109.1 ± 13.4 C.G: 117.3 ± 22.2	Have undergone sleeve gastrectomy To be between 20 and 50 years old	I.G: Physical activity programme 5 days after surgery	I.G: Balance training - 4 weeks - 4 days/week - 45 min
Shah et al. 2011 [61]	USA	RCT	I.G: 47.3 ± 10.0 C.G:53.9 ± 8.8	I.G: 21 (90%) C.G: 12 (92%)	I.G: 42.4 ± 6.9 C.G: 41.0 ± 3.7	I.G: 110.3 ± 16.6 C.G: 101.4 ± 8.7	Class 2 obesity Have undergone bariatric surgery	I.G: Physical activity supervised/programme More than 3 months after surgery	I.G: Endurance training - 12 weeks - 5 days/week - 60 min - 60% to 70% VO_2max
Stegen et al. 2011 [62]	Belgium	NON-RCT	I.G: 39.9 ± 9.9 C.G: 43.1 ± 5.6	I.G: 8 (87.5%) C.G: 7 (57.1%)	I.G: 45.3 ± 2.7 C.G: 40.4 ± 8.1	I.G: 130.8 ± 17.8 C.G: 126.5 ± 24.7	Have undergone RYGB	I.G: Physical activity supervised 1 months after surgery	I.G: Resistance + endurance training - 12 weeks - 3 days/week - 75 min - 60%-75% RM - 60% to 75% HRR reserve
Stolberg et al. 2018 [63]	DENMARK	RCT	I.G: 43.0 ± 9.4 C.G:42.8 ± 9.4	I.G: 32 (65.6%) C.G: 28 (75%)	I.G: 33.3 ± 6.2 C.G: 34.1 ± 5.4	126.6 ± 20.9	Have undergone laparoscopic RYGB	I.G: Physical activity supervised/counseling 6 months after surgery	I.G: Resistance + endurance training - 26 weeks - 2 days/week - 40 min - Endurance: moderate intensity
Stolberg et al. 2018 (2) [64]	DENMARK	RCT	I.G: 42.4 ± 9.0 C.G:42.3 ± 9.4	I.G: 32 (65.6%) C.G: 28 (75%)	I.G: 33.3 ± 6.2 C.G: 34.1 ± 5.4	126.6 ± 20.9	Have undergone laparoscopic RYGB	I.G: Physical activity supervised/counseling 6 months after surgery	I.G: Resistance + endurance training - 26 weeks - 2 days/week - 40 min - Endurance: moderate intensity
Wiklund et al. 2015 [65]	Sweden	RCT	I.G: 39.9 ± 11.7 C.G: 44.6 ± 12.9	I.G: 30 (53.3%) C.G:25 (56%)	I.G: 45.4 ± 8.0 C.G: 42 ± 2.4	I.G: 123.8 ± 15.2 C.G: 133.7 ± 31.3	Have undergone laparoscopic RYGB	I.G: Physical activity programme During first week after surgery	I.G: Walking endurance training - 1 week - 7 days/week
Woodlief et al. 2015 [66]	USA	RCT	I.G. Low-ex: 39 ± 2 I.G. Med-ex: 43 ± 2	I.G. Low-ex: 18 I.G. Med-ex: 19	I.G. Low-ex: 38.9 ± 1.6 I.G. Med-ex: 37.8 ± 1.5	I.G. Low-ex: 127.8 ± 3.8 I.G. Med-ex: 120.9 ± 3.5	Have undergone bariatric surgery	I.G: Physical activity supervised/programme Between 1 and 3 months after surgery	I.G: Endurance training - 26 weeks (6 months) - 3 to 5 days/week - 30 min

Table 1 (continued)

Reference	Country	Study design	Population Characteristics: Age	Sample size (%W)	BMI	Pre-surgery weight	Intervention: Type of population	Type of intervention/Start of intervention	Physical activity characteristics
			I.G. High-ex: 41 ± 2	I.G. High-ex:19	I.G. High-ex: 39.7 ± 1.4	I.G. High-ex: 132.7 ± 6.9			- 60 to 70% HR
			C.G: 43 ± 2	C.G: 42	C.G: 38.5 ± 0.9	C.G: 123.9 ± 4.4			

RCT randomized controlled trial, *NON-RCT* non-randomized controlled trial, *I.G* intervention group, *C.G* control group; NR: Not reported; HR: Heart Rate; RM: Repetition Maximum; VO_2max: Maximum oxygen consumption; D/W: Day per Week; BMI: Body Mass Index; RYGB: Roux-en-Y gastric bypass. M/W: Minutes per week; MIP: maximum inspiratory pressure. %W: percentage of women in each study or group

the intervention ($p = 0.377$) or the time devoted to each exercise session ($p = 0.807$) (Table 5).

Sensitivity Analysis and Publication Bias

Once the impact of each study was verified in the final result, eliminating each study individually, no changes were observed in the overall results. As seen in the funnel plot (Fig. 3) and once the Egger test was performed, there was no evidence of significant publication bias risk ($p = 0.208$).

Discussion

Our systematic review and meta-analysis provide insight into how a physical activity program performed after bariatric surgery can affect weight loss. The data obtained from the analysis of a total of 749 pooled bariatric surgeries did not show significant positive results in favor of exercise for people who underwent bariatric surgery. No significant results were found in terms of weight loss in favor of physical exercise after bariatric surgery when compared to the usual postoperative care.

Three previous systematic reviews [20, 21, 33] concluded that exercise following bariatric surgery is positive in increasing weight loss and improving other factors such as muscle loss or cardiovascular risk. Similarly, a recent meta-analysis [22] obtained significant results in favor of physical exercise, in contrast to our results, which are slightly positive for the intervention group, although not significant. This might be because some of the studies included in these previous reviews carried out multi-component interventions; meaning that physical exercise was accompanied by something else. Also, discrepancy between our results and those from previous systematic reviews and meta-analysis may be due to the fact that other authors directly calculated the difference in means between the groups, instead of calculating the difference in the standardized means. In addition, the number of articles included in our meta-analysis is higher than in previous weight-loss reviews, and the studies included in this meta-analysis only performed exercise, without any other type of intervention, such as diet or psychological support.

The results obtained in our systematic review and meta-analysis slightly disagree with the conclusions of previous reviews, showing no significant differences in favor of physical exercise once the bariatric surgery has been completed successfully. The effect (standardized mean difference, SMD) does not achieve statistical significance, which could indicate that (i) longer/more intense/better designed physical exercise programs are needed to elicit greater weight loss after bariatric surgery, or (ii) physical

Table 2 The Cochrane collaboration's tool for assessing the risk of bias in randomized trials

RCTs	Selection bias	Performance bias	Detection bias	Attrition bias	Reporting bias	Other bias	Risk of bias
Carnero et al. 2017 [43]	Strong	Strong	Strong	Moderate	Strong	Strong	Low
Casali et al. 2011 [44]	Moderate	Moderate	Weak	Moderate	Moderate	Strong	Moderate
Castello et al. 2011 [45]	Moderate	Weak	Weak	Moderate	Moderate	Strong	High
Castello-Simoes et al. 2013 [46]	Moderate	Weak	Weak	Moderate	Moderate	Strong	High
Coen et al. 2015 [47]	Strong	Moderate	Strong	Strong	Strong	Strong	Low
Coen et al. 2015 (2) [48]	Strong	Moderate	Strong	Strong	Strong	Strong	Low
Coleman et al. 2017 [49]	Strong	Moderate	Moderate	Weak	Moderate	Strong	Moderate
Creel et al. 2016 [50]	Strong	Weak	Moderate	Weak	Moderate	Strong	High
Daniels et al. 2018 [51]	Strong	Strong	Strong	Moderate	Strong	Strong	Low
Hassannejad et al. 2017 [52]	Strong	Moderate	Weak	Strong	Strong	Strong	Moderate
Herring et al. 2017 [67]	Strong	Moderate	Weak	Strong	Strong	Strong	Moderate
López et al. 2017 [54]	Strong	Strong	Moderate	Moderate	Strong	Strong	Low
Mundbjerg et al. 2018 [56]	Strong	Strong	Moderate	Strong	Strong	Strong	Low
Mundbjerg et al. 2018 (2) [65]	Strong	Strong	Moderate	Strong	Strong	Strong	Low
Oliveira et al. 2016 [58]	Moderate	Moderate	Weak	Weak	Weak	Moderate	High
Rojhani et al. 2016 [60]	Moderate	Moderate	Weak	Weak	Moderate	Moderate	High
Shah et al. 2011 [61]	Strong	Moderate	Moderate	Moderate	Weak	Strong	Moderate
Stolberg et al. 2018 [63]	Strong	Strong	Moderate	Strong	Strong	Strong	Low
Stolberg et al. 2018 (2) [64]	Strong	Strong	Moderate	Strong	Strong	Strong	Low
Wiklund et al. 2015 [65]	Weak	Moderate	Weak	Weak	Weak	Strong	High
Woodlief et al. 2015 [66]	Strong	Moderate	Strong	Strong	Strong	Strong	Low

RCTs randomized controlled trials

exercise after bariatric surgery must be accompanied by long-term changes in eating habits [16].

In a previous randomized controlled trial by Creasy et al. [34], obese/overweight participants lost on average 3.8 ± 3.0 kg when performing supervised physical activity, compared to an average weight loss of 5.1 ± 3.3 kg among those who were in the programmed (unsupervised) physical activity group. In our meta-analysis, the data reveal a non-significant trend toward greater weight reduction in those studies carrying out programmed (unsupervised) physical activity. This may occur due to an improvement in the psychological processes, self-efficacy, and autonomous motivation produced by performing physical activity after bariatric surgery [35].

Regarding the type of exercise, aerobic training shows the highest effect size, although this is also not significant. In contrast, previous studies on obese and overweight people (not bariatric patients) showed that a combination of resistance and aerobic training is the most effective way to lose weight [36]. Furthermore, a minimum of 150 min/week of moderate intensity physical activity has been proposed for developing and maintaining fitness [37]. In our results, however, the greatest weight loss was observed (although again not significant) in those interventions lasting less than 150 min/week. These two results might be related to the scarcity of studies containing sufficient samples combining aerobic and resistance exercise that entailed more than 150 min/week of exercise in patients who had undergone bariatric surgery. In addition, the studies did not control other factors that may affect weight loss, such as sleep, physical activity outside the program, or

Table 3 The quality assessment tool for quantitative studies

Non-RCTs	Selection bias	Study design	Confounders	Blinding	Data collection	Withdrawals/ drop-outs	Risk of bias
Campanha-Versiani et al. 2017 [42]	Weak	Moderate	Strong	Weak	Strong	Strong	High
Huck et al. 2015 [53]	Moderate	Moderate	Moderate	Weak	Strong	Strong	Moderate
Marchesi et al. 2015 [55]	Moderate	Weak	Strong	Weak	Strong	Moderate	High
Onofre et al. 2017 [59]	Weak	Moderate	Moderate	Weak	Strong	Strong	High
Stegen et al. 2011 [62]	Moderate	Weak	Strong	Weak	Strong	Strong	High

Non-RCTs non-randomized controlled trials

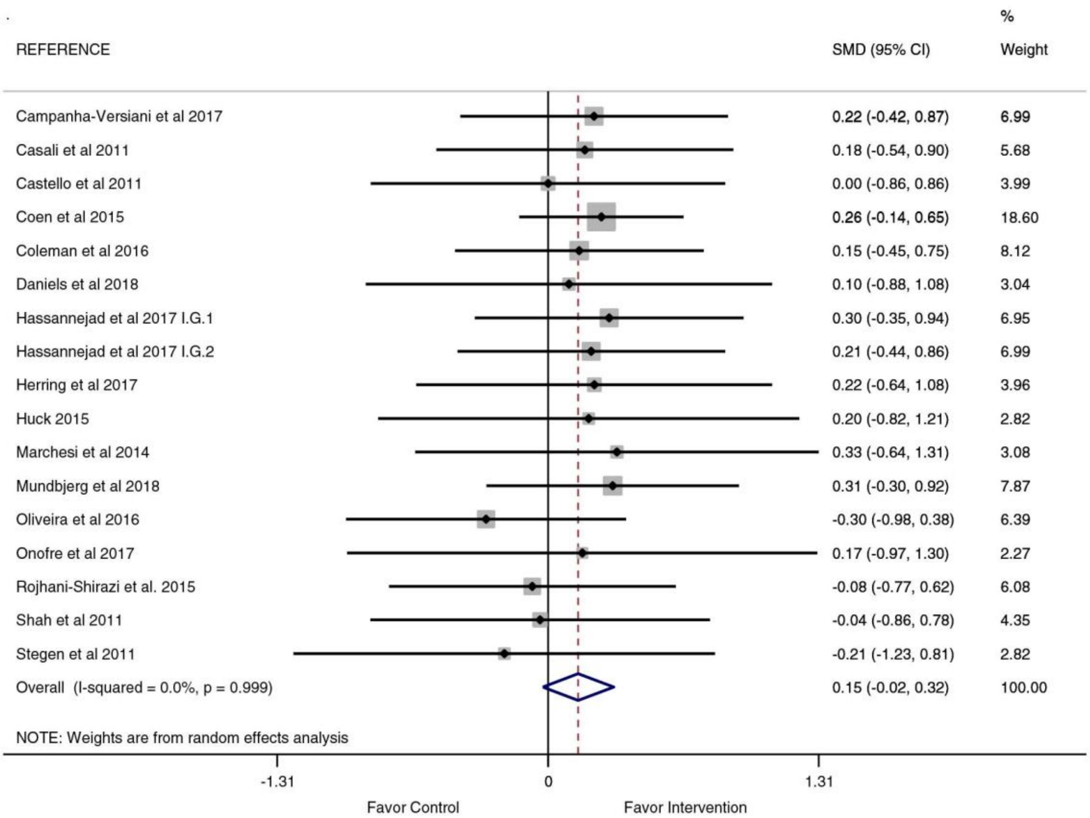

Fig. 2 Forest plot of the weight loss standardized mean difference between the control group and the intervention group. *SMD* standardized mean difference, *CI* confidence interval

Table 4 Stratified analysis according to the characteristics of the exercise program

Subgroups analysis	Control group vs. intervention group				
	Number of studies	Pooled SMD (95%CI)	I^2	X^2	*P*
Type of intervention					
Physical activity programmed	3	0.153 (−0.229, 0.535)	0.0	0.63	0.434
Physical activity supervised	9	0.101 (−0.160, 0.363)	0.0	2.53	0.447
Physical activity programmed/supervised	4	*0.202 (−0.091, 0.495)*	*0.0*	*0.50*	*0.176*
Start of intervention after the surgery					
≤3 months	11	0.123 (−0.081, 0.328)	0.0	3.21	0.238
>3 months	5	*0.199 (−0.128, 0.526)*	*0.0*	*0.55*	*0.234*
Duration of the intervention					
≤16 weeks	12	0.064 (−0.166, 0.294)	0.0	2.64	0.587
>16 weeks	5	*0.248 (−0.008, 0.504)*	*0.0*	*0.18*	*0.057*
Type of exercise					
Aerobic training	5	*0.209 (−0.073, 0.490)*	*0.0*	*0.77*	*0.146*
Resistance training	2	0.147 (−0.559, 0.853)	0.0	0.02	0.683
Aerobic/resistance combination	7	0.189 (−0.085, 0.463)	0.0	0.79	0.176
Alternative training	3	−0.075 (−0.476, 0.327)	0.0	0.90	0.715
Time of exercise					
≤150 min/week	4	*0.165 (−0.110, 0.441)*	*0.0*	*2.24*	*0.240*
>150 min/week	13	0.134 (−0.084, 0.352)	0.0	1.64	0.228

SMD standardized mean difference, *CI* confidence interval

Positive SMD values indicate a higher score in outcomes favoring the intervention group

Results in italic are those that show a higher SMD

Table 5 Meta-regression of weight loss with mean age, length of intervention, and time per session

	Mean age			Length of intervention			Time per session		
	I^2	β (95% CI)	*p*	I^2	β (95% CI)	*p*	I^2	β (95% CI)	*P*
SMD weight loss	0%	− 0.002 (− 0.042, 0.037)	*0.902*	0%	0.006 (− 0.008, 0.002)	*0.377*	0%	− 0.001 (− 0.013, 0.01)	*0.807*

CI confidence interval, *SMD* standardized mean difference

nutritional habits, which may condition the study results in relation to weight loss.

Physical activity interventions in obese people lasting less than 16 weeks were associated with increased energy expenditure but not with a reduction in body weight [38, 39]. According to our analysis, interventions lasting more than 16 weeks seem to produce greater weight loss, although this effect was not statistically significant compared to the control groups (no exercise). This might occur due to the increase in energy expenditure and the induction of lipolysis [40]. Some evidence suggests that weight loss could be higher if physical activity were combined with dietetic education, caloric reduction, or changes in eating habits [38, 40].

Limitations

Certain limitations that may have affected the results should be considered. First of all, some studies (five of them) did not report the standard deviation for body weight after the intervention. Secondly, not having the correlation between pre- and post-measures to estimate the standard deviation of the difference—it was for this reason that 0.59 was used. Thirdly, the samples, the inclusion/exclusion criteria, and the follow-up time varied greatly across studies. Moreover, there was a moderate risk of bias for the studies included. Finally, we could not analyze the exercise intensity performed in the reviewed programs because it was not possible to unify the criteria.

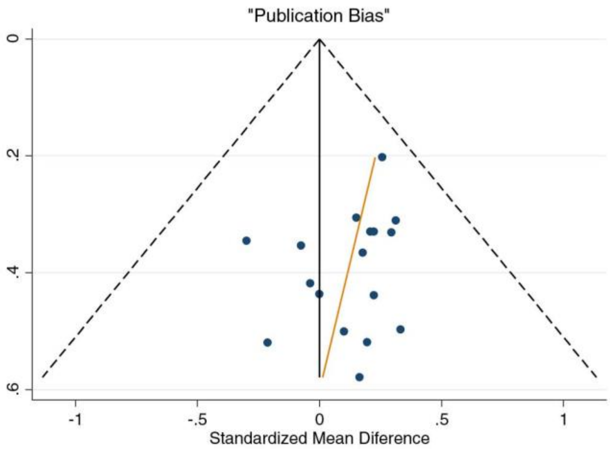

Fig. 3 Funnel plot with Egger test

Conclusions

Based on the results of our meta-analysis, one can conclude that exercise training in patients who have undergone bariatric surgery does not seem to be effective in achieving greater weight loss compared to the usual postoperative care, and no particular training is more effective than another for losing weight in patients who have undergone bariatric surgery. There is, however, a consensus that large enough RCTs of exercise have yet to be done—so doing meta-analyses of early, small cohorts can be misleading. The reviewed studies used different surgery types, exercise types, exercise durations, and interventions were in general poorly reported, making them difficult to be properly combined. It may be too early to make any conclusions, and reporting null findings could possibly dissuade people from adding exercise to their postoperative lifestyle changes, which could take them away from the myriad of positive effects of exercise. Even if the lack of effects on weight loss could be rigorously confirmed, exercise after bariatric surgery may help maintain lean body mass, improve cardiovascular health, psychological well-being, and increase adherence to training, among other benefits [41].

Future Directions

This line of research, which combines bariatric surgery and exercise training, should continue in order to elucidate the most appropriate type of exercise, as well as to determine the design and implementation of training programs with greater frequency, volume, intensity, and/or with different types of exercises, in such a way that is most appropriate for this population. Studies are also necessary in which patients begin to train straight after surgery to take advantage of the window of opportunity for behavioral change as soon as possible, not only to achieve greater weight loss but also to improve other parameters that affect these patients' health status such as muscle mass loss, cardiovascular parameters, biochemical markers, and respiratory parameters, among others. As demonstrated in our weight loss meta-analysis, all these research areas require better designed (and better reported) studies with sufficient sample sizes.

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Compliance with Ethical Standards

Ethics Approval and Consent to Participate Not applicable.

Conflict of Interest The authors declare that they have no conflict of interest.

Abbreviations 95% CI, 95% confidence intervals; BMI, Body mass index; C.G, Control group; D/W, Days per week; HR, Heart rate; I.G, Intervention group; M/W, Minutes per week; MIP, Maximum inspiratory pressure; non-RCTs, Non-randomized control trials; NR, Not reported; PA, Physical activity; RCTs, Randomized controlled trials; RM, Repetition maximum; RYGB, Roux-en-Y gastric bypass; SDs, Standard deviations; SMD, Standardized mean difference; VO2max, Maximum oxygen consumption

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III

III. Impact of exercise training after bariatric surgery on cardiometabolic risk factors: a systematic review and meta-analysis of controlled trials.

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Impact of exercise training after bariatric surgery on cardiometabolic risk factors: a systematic review and meta-analysis of controlled trials

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Abstract

The purpose of this systematic review was to provide updated evidence synthesis of the effectiveness of exercise training in patients with obesity undergoing bariatric surgery to improve cardio-metabolic risk. We systematically searched the MEDLINE, EMBASE, Scopus, Cochrane, and Web of Science databases. The studies selected were those in which an exercise-based intervention was performed after bariatric surgery, a control group was present, and at least one of the following outcomes was investigated: VO_{2max} or VO_{2peak}, resting heart rate (RHR), blood pressure, lipid profile, glucose, and insulin. The study quality was assessed using the PEDro scale and the data were meta-analyzed with a random effects model, comparing control groups to intervention groups using standardized measurements. Twenty articles were included in the systematic review and fourteen (70%) in the meta-analysis. Significant differences were observed between the control and intervention groups (always in favor of exercise) for absolute VO_{2max} / VO_{2peak} (ES = 0.317; 95% CI = 0.065, 0.569; p = 0.014), VO_{2max} / peak relative to body weight (ES = 0.673; 95% CI = 0.287, 1.060; p = 0.001), HDL cholesterol (ES = 0.22; 95% CI = 0.009, 0.430; p = 0.041) and RHR (ES = -0.438; 95% CI = -0.753, -0.022; p = 0.007). No effects were observed for either systolic or diastolic blood pressure. Exercise training for patients undergoing bariatric surgery appears to be effective in improving absolute and relative VO_{2max} / VO_{2peak}, HDL cholesterol and reducing the RHR. More intervention studies using (better) exercise interventions are needed before discarding their effects on other cardiometabolic risk factors. This systematic review and meta-analysis has been registered in Prospero (CRD42020153398).

Keywords Bariatric surgery · Exercise training · Cardiovascular · Blood pressure · VO_{2max}

1 Introduction

Between 1975 and 2016, the obesity rate has tripled, affecting more than 650 million people worldwide [1]. Obesity is associated with an increased mortality risk since it directly affects cardiometabolic health markers [2], causing comorbidities such as hypertension, hyperlipidemia, type 2 diabetes, respiratory problems, and metabolic syndrome [3]. It has also been shown that many cardiometabolic risk factors are significantly more impaired as the severity of obesity increases, both in men and women [4].

Bariatric surgery is presented as an effective strategy for weight loss [5] and for treating comorbidities related to severe obesity [6]. Massive weight loss results in hemodynamic, structural and metabolic changes [7], due to several factors such as improved left ventricle geometry, diastolic function and reduced left atrial size [8], decreased

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inflammation and changes in existing genetic alterations in adipose tissue [9]. Exercise training programs have been demonstrated to be feasible and safe for bariatric surgery patients, helping to maintain long-term weight loss [10] and to improve walking function [11], although the replicability of these exercise programs is challenging [12]. At the same time, in non-operated patients, physical activity has been shown to improve cardiometabolic risk factors [13] such as high total cholesterol or LDL [14, 15], and cardiorespiratory biomarkers [13], such as mitochondrial oxidation capacity [16]. Therefore, we hypothesized that exercise training could be an effective adjunct therapy to bariatric surgery for improving cardiometabolic health [10].

Once the literature is reviewed, it seems necessary to clarify how exercise interventions following bariatric surgery affect markers related to cardiometabolic health, given that this is an under investigated area of knowledge since most recent reviews have focused on the effect of an exercise program on weight loss following bariatric surgery [11, 17].

The aim of the present systematic review and meta-analysis was review the evidence on the effectiveness of exercise training to improve cardiometabolic risk in patients with obesity who are undergoing bariatric surgery.

2 Material and methods

2.1 Protocol and registration

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses, PRISMA Statement and checklist [18], along with the Cochrane Handbook for Systematic Reviews of Interventions [19], have been strictly followed in the design and reporting of this study (Table A COMPLEMENTARY FILES). Additionally, this systematic review and meta-analysis has been registered in PROSPERO, the International Prospective Register of Systematic Reviews (ID CRD42020153398).

2.2 Searches

The systematic search was performed using the MEDLINE, EMBASE, Scopus, Cochrane, and Web of Science databases, with the deadline of December 6, 2020.

The search strategy is described in the Table 1:

2.3 Eligibility criteria

The systematic review was independently and simultaneously performed by two reviewers (ACR and EM-R). In the case of disagreement, an impartial third party (EGA) would resolve the issue.

All articles that clearly indicated, both in the abstract and in the title, that they had performed an experimental intervention based on physical activity on patients who had already undergone bariatric surgery were included as suitable for further in-depth review.

The systematic review ‘s exclusion criteria were: a) articles not written in English or Spanish; b) studies that did not report at least one of the selected outcomes (i.e., VO_{2max} or VO_{2peak}, heart rate, blood pressure, lipid profile, glucose or insulin); c) studies in which the intervention was performed before bariatric surgery; d) studies using animals; e) studies in which the participants were younger than 18 years old; f) articles combining physical activity with other types of intervention, such as medications + exercise, nutrition + exercise, other surgeries + exercise and lifestyle interventions + exercise; g) retracted studies; h) duplicate studies; and i) ineligible publications such as reviews, guidelines, interviews, comments or case studies.

The final inclusion criteria were: a) Randomized or not randomized controls trials; b) intervention based on physical activity on patients who had already undergone bariatric surgery; c) Written in Spanish or English; d) At least measure one outcome related to metabolic risk (VO_{2max} or peak, heart rate, blood pressure, lipid profile, glucose, insulin or inflammation markers).

2.4 Data selection

The following data were reported for each of the studies finally selected in the systematic review: a) first author, b) publication year, c) country in which the study was conducted, d) study design, e) population characteristics such as age, sample size and gender, f) intervention characteristics (type of bariatric surgery and physical activity-related characteristics), g) outcomes assessment, and h) intervention group (IG) results.

2.5 Measurement of the quality of the reports

The PEDro scale, based on the Delphi scale, was used to assess the quality of the selected studies (https://www.pedro.org.au) [20]. This scale considers 11 criteria answered “yes” or “no”: eligibility criteria, random allocation, concealed allocation, similarity groups’ baseline, blinding subjects, blinding therapist/trainers, blinding assessors, measured more than 85% of subjects, intention to treat and point measure. From these 11 criteria, the first one is not considered when adding up the total score, meaning that the quality of the articles will be assessed from 0 to 10. Articles of poor methodological quality would be ranked below 4 points, those of fair quality between 4 and 5, those of good quality from 6 to 8 and those of excellent quality would be scored either 9 or 10 [21].

Table 1 Search Strategy

Surgery Mode		Risk Factors		Exercise
("Bariatric Surgery" OR "stapling stomach" OR "weight loss surgery" OR "obesity surgery" OR "weight reduction surgery" OR "Biliopancreatic Diversion" OR "Duodenal switch" OR "laparoscopic band" OR "lap band" OR "gastric band" OR "gastric banding" OR "Gastric Bypass" OR "Gastroplasty" OR "gastric sleeve" OR "sleeve gastrectomy" OR "gastric bypass surgery" OR "gastric bypass" OR "Roux-en-Y Gastric Bypass" OR "Maestro Rechargeable System" OR "gastric balloon" OR "gastric bubble" OR "ballobes balloon" OR "Greenville gastric bypass")	AND	("Risk factors" OR "biomarkers")	AND	("physical exercise" OR "Physical Therapy" OR "physical activity" OR "physical education" OR "physical training" OR exercise OR fitness OR sport OR "Exercise Movement" OR "exercise program" OR "Complementary Therapies" OR "physiotherapy" OR "manual therapy" OR "therapeutic exercise" OR "Occupational Therapy" OR "Exercise therapy" OR "Physical Fitness" OR "Resistance Training" OR "rehabilitation")
		OR		
		("glycemic control" OR "metabolic outcomes" OR "diabetes" OR "diabetes mellitus" OR "type II Diabetes" OR "peptide c" OR "glycemia" OR "glucose" OR "hemoglobin level" OR "glycated hemoglobin" OR "hba1c" OR "insulin resistance" OR "fasting insulin" OR "fasting glucose")		
		OR		
		("Hypertension" OR "heart rate" OR "arterial hypertension" OR "blood pressure" OR "endothelial function" OR "hypertensive" OR "systolic blood pressure" OR "diastolic blood pressure" OR "diastolic" OR "systolic" OR "blood")		
		OR		
		("Hyperlipidemia" OR " lipids" OR "lipoproteins" OR "dyslipidemia" OR "high cholesterol" OR "high density lipoprotein" OR "low density lipoproteins" OR "cholesterol" OR "HDL" OR "LDL" OR "blood markers" OR "triglycerides" OR "cardiometabolic risk" OR "cardiovascular diseases")		
		OR		
		("Inflammation" OR "Interleukin 6" OR "IL-6" OR "C-reactive protein" OR "CRP" OR "alfa1-acid glycoprotein" OR "AGP" OR "adipokines" OR "adiponectin" OR "cytokines")		

Data extraction and quality assessment were independently performed by two reviewers at the same time (ACR and EM-R). Differences of opinion were resolved by consensus or by the involvement of a third neutral researcher (EGA).

2.6 Statistical analyses

The comprehensive MetaAnalysis 2.0 software was used to perform the main statistical analysis as well as the sensitivity analysis. The outcomes were HDL, systolic blood pressure (SBP) and diastolic blood pressure (DBP), resting heart rate (RHR), fasting glucose, absolute VO_{2max}, and VO_2max relative to weight. The size effect, which quantifies the degree to which the sample results diverge from the expectations specified in the null hypothesis [22], was calculated using the standardized mean difference (SMD) and the Hedge´s g estimator [23]. Furthermore, sizes effect were expressed as the weighted mean difference between control and intervention group when the results of the evaluations were performed with the same units of measurement and the evaluation tests were similar, such as VO_{2max} / VO_{2peak} relative to weight, RHR, SBP and DBP. Random-effects meta-analysis using the DerSimonian-Laird method was used and the 95% confidence intervals were calculated (95% CI) [24]. The direction of the effects in the funnel plot was positive when it favored the intervention group and negative when it favored the control group.

Two-sided $P < 0.05$ were calculated as the significance level. In addition, The Q-value and the I^2 statistic were used to assess heterogeneity between the studies included in the different forest plots [25, 26]. A I^2 value of 0–40% indicates non-important heterogeneity, 30–60% moderate heterogeneity, 50–90% substantial heterogeneity, and 75–100% considerable heterogeneity [19].

When performing the statistical analyses and extracting the data from each study, the following criteria were applied: I) if two or more studies used an identical intervention taken from the same database to achieve an outcome, only the data from the main study were used; and II) outcome data were collected using the pre- and post-intervention evaluations (i.e., before and after the physical activity program). Only in the absence of a pre-intervention assessment were the pre-surgery data used as a proxy.

Sensitivity analyses were conducted by removing each study one by one to observe possible variations. Funnel plots and the Egger test were performed to check for the presence of publication bias [27], $P \leq 0.1$ was used as the Egger test significance level [28]. Meta-regressions and subgroup analyses could not be performed because there were not enough studies (at least 10 studies for meta-regressions and 4 for subgroup analyses).

3 Results

3.1 Systematic review

Out of a total of 10,123 articles obtained in the search, 2,466 were eliminated once all the titles and abstracts were reviewed, and 20 articles were included after meeting all the selection criteria (Fig. 1). All the included studies had an experimental design with the participants of the intervention group performing an exercise program after the bariatric surgery, 16 of them being randomized (RCTs) and four non-randomized (non-RCTs). Finally, 14 of them could be used for the meta-analysis.

All the studies were published between 2011 and 2020 and were conducted in different countries: six in the USA, five in Brazil, three in Denmark, two in Canada, one in Belgium, one in Italy, one in Spain and one in the United Kingdom (Table 2). A wide variety of bariatric surgery techniques were performed: 16 (80%) studies used gastric bypass, four (20%) sleeve gastrectomy, two (20%) gastric band and two (20%) biliopancreatic diversion with duodenal switch (BPD/DS). Of these studies, 14 (70%) used one single type of surgery, five (25%) used two different types, and one (5%) study used any type of bariatric surgery.

All the articles included in this review (n = 20) provided at least one outcome related to cardiometabolic risk: HDL were reported in 9 studies (45%); fasting insulin, VO_{2max} or VO_{2peak} in ml / min and LDL in 8 studies (40%); total cholesterol, triglycerides, fasting glucose, SBP, and DBP in 7 of the studies (35%); VO_{2max} or VO_{2peak} in ml / min / kg in 6 (30%); VO_{2max} or VO_{2peak} in ml / min / FFM in 5 studies (25%); HR_{max} or peak and RHR in 3 studies (15%); $HR_{reserve}$, mean

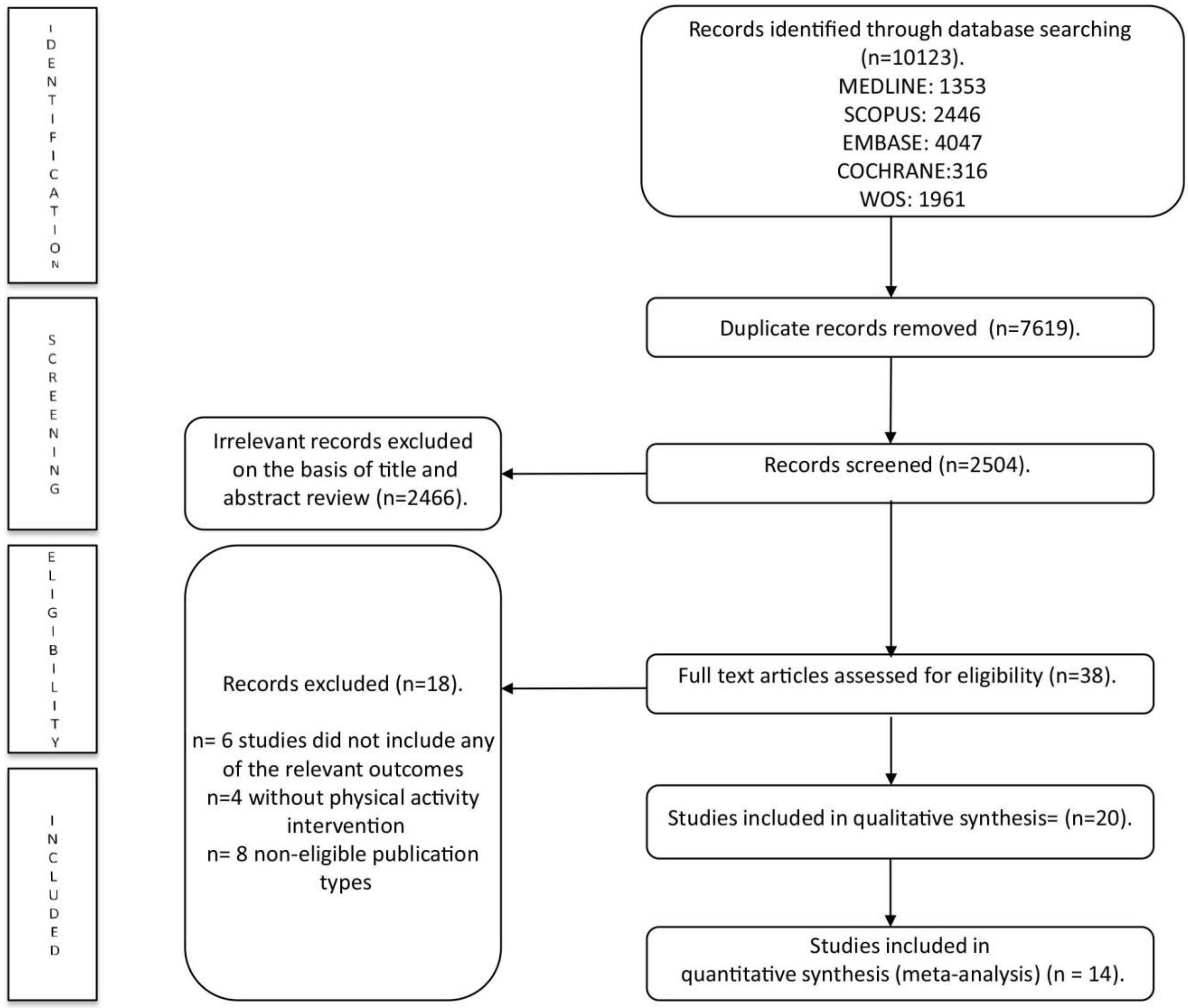


Fig. 1 Literature search Preferred Reporting Items for Systematic Reviews and Meta-Analyses consort diagram

Table 2 Studies included in the systematic review

Reference	Country	Study Design	Age	Sample Size (%W)	Type of Bariatric Surgery	Intervention Physical Activity Characteristics	Outcomes assessment	I.G. Results (before-after intervention)
Auclair et al. [30]	Canada	RCT	I.G: 42±12 C.G: 42±12	I.G: 39 (82%) C.G: 19 (74%)	Sleeve gastrectomy BPD/DS	I.G: Supervised Endurance + Resistance training - 12 weeks - 3 d/w - 60 min - 3-5 min warm-up - 35 min of endurance training 60 to 75% HR Reserve - 25 min resistance, 3 sets of 10-12 reps of the largest muscle groups	-Cardiopulmonary exercise test were performed on an electromagnetic ergometer (Corival Recumbent) through a ramp protocol which started with 1 min of unload pedaling (0 W) and gradually increased each minute between 10-30 W • Resting data were obtained with the subject sitting in the ergometer. • The expired gas analysis was measured via breath-by-breath metabolic measurement system (Ultima Cardio O2; MGC Diagnosis). • Heart rate by 12 lead electrocardiography (Cardioperfect; Welch-Allyn). • Blood pressure (STBP-780; Colin).	= HR max = HR Reserve = SBP max = DBP max ↑ V O2peak (ml/kg/min) ↑ VO2peak (ml/kg/min Indexed to the muscle mass of the middle thigh) ↑ VO2peak (ml/min)
Castello et al. [40]	Brazil	RCT	I.G: 38.0±4 C.G: 36.0±4	I.G: 16 (100%) C.G: 16 (100%)	Gastric bypass	I.G: Supervised Endurance training - 12 weeks - 3 d/w - 60 min - 50 to 70% HR peak	- HR and R-Ri records were taken with a 10-minute-rest supine test (Polar S810i) - HR (Polar S810i) and BP were obtained immediately before and after 6MWT.	↓ Mean Heart Rate (HRV) ↓Systolic Blood Pressure ↓ Diastolic Blood Pressure = Mean Heart Rate (during 6MWT)
Castello-Simoes et al. [41]	Brazil	RCT	I.G: 32.0±4.0 C.G: 31±2.0	I.G: 16 (100%) C.G: 16 (100%)	Gastric bypass	I.G: Supervised Endurance training - 12 weeks - 3 d/w - 60 min - 50 to 70% HR peak	- HR (Polar S810i) was obtained immediately before and after 6MWT	↓ Mean Heart Rate (during 6MWT)

Table 2 (continued)

Reference	Country	Study Design	Age	Sample Size (%W)	Type of Bariatic Surgery	Intervention Physical Activity Characteristics	Outcomes assessment	I.G. Results (before-after intervention)
Coen et al. [31]	USA	USA RCT	I.G: 41.3±9.7 C.G: 41.9±10.3	I.G: 66 (89.4%) C.G: 62 (87.1%)	Gastric bypass	I.G: Supervised/programmed Endurance training - 26 weeks (6 months) - 3 to 5 d/w - 30 min - 60 to 70% HR	- A 3-hour insulin-modified IVGTT after a 12-hour fast based on the Bergman minimal model calculations. • Blood samples were collected in EDTA tubes at different times during the test. • Plasma insulin was determined by enzyme immunoassay and glucose by the oxidation reaction - BP was measured using standard clinical protocols	= LDL ↑ HDL ↓ Triglycerides = Total cholesterol ↓ Systolic Blood Pressure = Diastolic Blood Pressure ↓ Fasting Insulin = Fasting Glucose
Coen et al. (2) [32]	USA	RCT	I.G: 41.6±9.3 C.G:42.1±9.9	I.G: 51 (88%) C.G: 50 (84.3%)	Gastric bypass	I.G: Supervised/programmed Endurance training - 26 weeks (6 months) - 3 to 5 d/w - 30 min - 60 to 70% HR	- A 3-hour insulin-modified IVGTT after a 12-hour fast based on the Bergman minimal model calculations. • Plasma insulin was determined by enzyme immunoassay and glucose by the oxidation reaction. -VO2peak was measured by indirect calorimetry during a 5- to 12-minute graded exercise test on a cycle ergometer.	↓ Fasting Insulin ↓ Fasting Glucose ↑ VO2peak (ml/kg/min FFM) ↑ VO2peak (ml/min)
Dantas et al. [39]	Brazil	RCT	I.G: 39±7 C.G: 42.±7	I.G: 31 (100%) C.G: 31 (100%)	Gastric bypass	I.G: Supervised Endurance + Resistance training. - 26 weeks (6 months) - 3 d/w - 5 min warm up - 30-60 min endurance training (10 min progression every 4 weeks) at 50% of difference between the ventilator threshold and respiratory compensation - Resistance training 3 sets 8-12 reps with 60 sec of rest (Exercises for major muscle groups).	- Insulin sensitivity were measured via a tolerance test (OGTT) - Plasma glucose, triglycerides, LDL, HDL and total cholesterol were assessed using an automatic analyzer (SBA-200; CELM) through enzymatic methods, after 12 h overnight fast.	↑ HDL ↓ LDL ↓ Triglycerides = Total cholesterol = Fasting Insulin = Fasting Glucose

Table 2 (continued)

Reference	Country	Study Design	Age	Sample Size (%W)	Type of Bariatic Surgery	Intervention Physical Activity Characteristics	Outcomes assessment	I.G. Results (before-after intervention)
Gil et al. [38]	Brazil	RCT	I.G: 39±7 C.G: 42.±7	I.G: 31 (100%) C.G: 31 (100%)	Gastric bypass	I.G: Supervised Endurance + Resistance training. - 26 weeks (6 months) - 3 d/w - 5 min warm up - 30-60 min endurance training (10 min progression every 4 weeks) at 50% of difference between the ventilator threshold and respiratory compensation Resistance training 3 sets 8-12 reps with 60 sec of rest (Exercises for major muscle groups).	- Maximal exercise test was performed with a treadmill (Centurion 200, micromed), the velocity and/or grade were incremented every minute. • VO2 was assessed using a calorimetric system (Cortex-Metalyzer) • HRrest were measured before the test standing on the treadmill and the HR peak during the test (ErgoPCElite, micromed)	↑ Heart rate peak ↑ Heart rate reserve ↓ Resting Heart Rate
Herring et al. [42]	UK	RCT	I.G: 44.3±7.9 C.G:52.4±81	I.G: 12 (91.7%) C.G: 12 (91.7%)	Any type	I.G: Supervised Resistance + Endurance training - 12 weeks - 3 d/w - 60 min. - 2 exercises per session - 3 sets - 12 reps - 60% RM - 64-77% HRmax	- Resting HR was measured using the Contec Full-Color OLED USB Finger Pulse Oximeter. - BP was measured three times; the first measurement was discarded and a mean of the following two measurements was reported (Omron Intellisense M7)	↓ Systolic Blood Pressure ↓ Diastolic Blood Pressure ↓ Resting Heart Rate
Huck [43]	USA	Non RCT	I.G: 53.6±8.2 C.G: 44.0±9.7	I.G: 7 (85.7%) C.G: 8 (75%)	Gastric bypass Banding/gastroplasty	I.G: Supervised small groups resistance training 12 weeks 2 d/w first 6 weeks and 3 d/w last 6 weeks 60 min 60% to 75% RM	- HR and BP were measured after 5 minutes of seated rest (automated cuff, OMRON) - Aerobic capacity was measured using the submaximal Ebbeling treadmill protocol and VO2 max was estimated	

Table 2 (continued)

Reference	Country	Study Design	Age	Sample Size (%W)	Type of Bariatic Surgery	Intervention Physical Activity Characteristics	Outcomes assessment	I.G. Results (before-after intervention)
Marc-Hernández et al. [47]	Spain	RCT	I.G: 47.3±6.5 C.G: 43.7±11.4	I.G: 11 (72.7%) C.G. 10 (80%)	Sleeve gastrectomy	I.G: Supervised Resistance + endurance training - 20 weeks / 5 blocks. Block 1 - Resistance (50% RM) and endurance (60-70% HRmax) the same session - 2 d/w - 35´continous endurance training. Block 2 - 2d/w Resistance (60% RM) and HIIT (60- 70% VO2 peak) in the same session. - 1 d/w 50´ of continuous endurance training (70-80% HRmax) Block 3 - 2d/w Resistance (65% RM) and HIIT (70- 80% VO2 peak) in the same session. - 2 d/w 50´ of continuous endurance training (70-80% HRmax) Block 4 - 2d/w Resistance (70% RM) and HIIT (75- 85% VO2 peak) in the same session. - 2 d/w 50´ of continuous endurance training (70-80% HRmax) Block 5 - 2d/w Resistance (75% RM) and HIIT (80-95% VO2 peak) in the same session. 2 d/w 50´ of continuous endurance training (70-80% HRmax)	- VO2peak was measured using a cycle ergometer (Technogym) and a gas analyser (Oxycon Pro, Jaeger). Performing a graded exercise test to exhaustion: ● First phase had 3-min stages and 20-W increments until respiratory exchange ratio 1. ● Second phase 1 min stages and 20-W increments. - To analyze blood glucose and total cholesterol, a portable multi analyser (Accutrend GCT) was used. The patients spent at least 10 hours fasting and 48 hours without exercising - Blood pressure was measured using a digital sphygmomanometer (Microlife WatchBP Home, Heerbrugg, Switzerland	↑ VO2peak (ml/kg/min) ↑ VO2peak (ml/min) = SBP = DBP ↓ Fasting glucose ↓ Cholesterol

Table 2 (continued)

Reference	Country	Study Design	Age	Sample Size (%W)	Type of Bariatic Surgery	Intervention Physical Activity Characteristics	Outcomes assessment	I.G. Results (before-after intervention)
Marchesi et al. [48]	Italy	Non- RCT	I.G: 43.1 C.G:39.1	I.G: 10 (100%) C.G: 10 (100%)	Gastric bypass	I.G: Supervised/programmed Endurance training - 40 weeks - 3 d/w for 6 first months and 4 d/w last 4 months - 60 min. - 3 first months 55-65% and 65-75% HRmax, middle 3 months 55-65% and 65-85% HRmax and last 4 months 60-70% and 70-90% HRmax	- To determine VO2max, a cardiopulmonary exercise test (CPET) was performed.	= Total Cholesterol = HDL = Triglycerides = Glucose = Resting heart rate ↑ VO2 max (ml/min/kg)
Mundbjerg et al [33]	Denmark	RCT	I.G: 42.3±9.4 C.G: 42.4 ±9	I.G: 32 (66.6%) C.G: 28 (75%)	Gastric bypass	I.G: Supervised Resistance + Endurance training - 26 weeks - 2 d/w - 40 min. - Borg Scale 15 to 17/ 50 to 70% VO2max. Encouraged to do 210 m/w of extra. Exercise	- Blood samples were measured after 10 hours fasting and 15 minutes of supine rest. • Plasma glucose was determined enzymatically (Architect C16000) and insulin was measured using electrochemiluminescence immunoassay (COBAS). • Lipid samples were measured using an Architect C16000. - BP and HR were measured in a 10- minute supine position and the mean of 3 to 5 measurements was taken (DINAMAP V100 monitor)	= LDL ↑ HDL = Triglycerides = Total cholesterol = Systolic Blood Pressure = Diastolic Blood Pressure ↓ Fasting Insulin = Fasting Glucose = Resting Heart Rate
Mundbjerg et al. (2) [34]	Denmark	RCT	42.3 ±9.1	I.G: 32 (66.6%) C.G: 28 (75%)	Gastric bypass	I.G: Supervised Resistance + Endurance training - 26 weeks - 2 d/w - 40 min. Borg Scale 15 to 17/ 50 to 70% VO2max. Encouraged to do 210 m/w of extra exercise	- Aerobic capacity was measured using the Astrand one-point submaximal bicycle test. VO2max was estimated using sex, workload, and mean steady-state heart rate during the test.	↑ VO2max (l/min)

Table 2 (continued)

Reference	Country	Study Design	Age	Sample Size (%W)	Type of Bariatric Surgery	Intervention Physical Activity Characteristics	Outcomes assessment	I.G. Results (before-after intervention)
Nunez Lopez et al. [35]	USA	RCT	I.G: 53.6±8.2 C.G: 44.0±9.7	I.G: 7 (85.7%) C.G: 8 (75%)	Gastric bypass	I.G:Supervised/Programmed Endurance training - 26 weeks (6 months) - 3 to 5 d/w - 30 min - 60 to 70% HR	-A 3-hours insulin-modified IVGTT after a 12-hours fast based on the Bergman minimal model calculations. • Blood samples were collected in EDTA tubes at different times during the test. • Plasma insulin was determined by enzyme immunoassay and glucose by the oxidation reaction - VO2peak was measured by indirect calorimetry during a 5- to 12-minutes graded exercise test on a cycle ergometer	↑ VO2max (ml/min/kg FFM) ↑ VO2max (ml/min) = LDL ↑ HDL ↓ Triglycerides = Total cholesterol ↓ Fasting Insulin = Fasting Glucose
Onofre et al. [44]	Brazil	Non-RCT	I.G: 43 C.G:38.5	I.G: 11 (81%) C.G:11 (81%)	Gastric bypass Sleeve gastrectomy	I.G: Supervised Resistance + Endurance training - 12 weeks - 3 d/w - 60 min. - 60%-80% RM - 40%-60% intercalated with 85-90% HR Reserve	- VO2peak was determined by the highest 10 seconds value during a symptom-limited cardiopulmonary exercise, testing until physical exhaustion with a ramp protocol. (Centurion 300 Micromed treadmill) - Blood Pressure and HR were measured every 2 minutes during the CPX.	↑ VO2peak (ml/min/kg) = VO2peak (ml/min) = Systolic blood pressure = Diastolic blood pressure = HRmax
Shah et al. [46]	USA	RCT	I.G:47.3±10.0 C.G:53.9±8.8	I.G: 21 (90%) C.G: 12 (92%)	Gastric bypass Gastric banding	I.G: Supervised/programmed endurance training - 12 weeks - 5 d/w - 60 min. - 60% to 70% VO2max	-VO2max was measured with a graded maximal exercise test on a treadmill. BP and HR were measured during the last 30 seconds of each stage. - Rest BP was assessed 3 times. - A blood sample was taken after 12 hours of overnight fasting. Plasma lipids were analyzed using enzymatic methods. - Plasma insulin was measured using radioimmunoassay kits.	= Systolic blood pressure = Diastolic blood pressure = Fasting HDL = Fasting LDL ↓ Fasting Triglycerides = Fasting Glucose = Fasting Insulin ↑ VO2max (ml/min/kg)

Table 2 (continued)

Reference	Country	Study Design	Age	Sample Size (%W)	Type of Bariatric Surgery	Intervention Physical Activity Characteristics	Outcomes assessment	I.G. Results (before-after intervention)
Stegen et al. [45]	Belgium	Non-RCT	I.G: 39.9±9.9 C.G: 43.1±5.6	I.G: 8 (87.5%) C.G: 7 (57.1%)	Gastric bypass	I.G: Supervised Resistance + Endurance training - 12 weeks - 3 d/w - 75 min. - 60%-75% RM - 60% to 75% HR Reserve	- VO2peak was measured by means of a maximal cardiopulmonary test on a cycle ergometer (Gymna) using a portable mixing chamber system (MetaLyzer II) - Heart rate was monitored during the 6MWD test (Polar heart watch)	= VO2peak/FFM (ml/min/kg) ↑ VO2 peak/BW (ml/kg/min) = VO2peak (ml/min) ↓ Heart rate during 6MWD
Stolberg et al. [36]	Denmark	RCT	I.G: 43.0±9.4 C.G:42.8±9.4	I.G: 32 (65.6%) C.G: 28 (75%)	Gastric bypass	I.G: Supervised/Counselling Resistance + Endurance training - 26 weeks - 2 d/w - 40 min. - Endurance: Moderate intensity	- Blood samples were measured after 10 hours fasting and 15 minutes of supine rest. • Plasma glucose was determined enzymatically (Architect C16000). • Insulin was measured using electrochemiluminescence immunoassay (COBAS).	= Glucose = Insulin
Tardif et al. [29]	Canada	RCT	I.G:41.6±11.7 C.G: 39.3±10.7	I.G: 34 (76%) C.G: 15 (73%)	Sleeve gastric omy BPD/DS	I.G: Supervised Endurance + Resistancetraining - 12 weeks - 3 d/w - 60 min - 3-5 min warm-up - 35 min of endurance training 60 to 75% HR Reserve - 25 min resistance, 3 sets of 10-12 reps of the largest muscle groups	- Blood samples were collected after 12 hours overnight fast from an antecubial vein into Vancutainer tubes containing EDTA. Total cholesterol and triglycerides were determined enzymatically in plasma using Technicons RA 500 analyzer (Bayer, Tarrytown)	= Total cholesterol = Triglycerides = LDL C.G ↑ HDL

Table 2 (continued)

Reference	Country	Study Design	Age	Sample Size (%W)	Type of Bariatic Surgery	Intervention Physical Activity Characteristics	Outcomes assessment	I.G. Results (before-after intervention)
Woodlief et al. [37]	USA	RCT	I.G. Low-ex: 39±2 I.G. Med-ex: 43±2 I.G. High-ex: 41±2 C.G:43±2	I.G. Low-ex: 18(NR) .G. Med-ex: 19(NR) I.G. High-ex:19 (NR) C.G:42(NR)	Gastric bypass	I.G:Supervised/programmed Endurance training - 26 weeks (6 months) - 3 to 5 d/w - 30 min - 60 to 70% HR	- A 3-hour insulin-modified IVGTT after a 12-hours fast based on the Bergman minimal model calculations. • Blood samples were collected in EDTA tubes at different times during the test • Plasma insulin was determined by enzyme immunoassay and glucose by the oxidation reaction - VO2peak was measured by indirect calorimetry during a 5- to 12-minutes graded exercise test on a cycle ergometer	↑ VO2max (ml/min/kg FFM) high time intervention group ↑ VO2max (ml/min) high time intervention group ↑ Insulin Sensitive in all intervention groups

RCT Randomized Controlled Trial, *non-RCT*, non-Randomized Controlled Trial, *I.G* Intervention Group, *C.G* Control Group, *HR* Heart Rate, *BP* Blood Pressure, *SBP* Systolic Blood Pressure, *DBP* Diastolic Blood Pressure, *BPD/DS* Biliopancreatic diversion with duodenal switch, *FFM* Fat-Free Mass, *6MWT* 6-Minute-Walk Test, *d/w* Days per Week, *HIIT* High-Intensity Interval Training, *IVGTT* Intravenous Glucose Tolerance Test, *NR* Not Reported

HR (from HRV) and mean HR (from 6MWT) in 2 studies (10%); insulin sensitivity, SBP_{max}, DBP_{max} and VO_2 relative to the muscle mass of the middle thigh in one study (5%).

3.2 Participants' characteristics

The study samples ranged from 15 to 134 patients and among the 20 articles it comprises a total of 942 participants (88% women), with a mean age of 42.6 ± 4 years old. Most of them (12 studies, 60%) included participants of both sexes, although in 8 studies (40%), only women participated.

3.3 Intervention characteristics

As described in Fig. 2, the exercise programs started between one and 102 months after surgery. The most frequent intervention durations were 6 months used in nine studies [29–38] and 3 months in other nine interventions [30, 39–46], except for two studies in which the intervention lasted 5 months [47] or 10 months [48].

The characteristics of the physical exercise interventions are summarized in Table 2. Eight of the studies conducted an endurance training[31, 32, 35, 37, 40, 41, 46, 48]. Endurance training was done in different ways. Two studies with the same protocol did incremental treadmill training in which they did 5 min of stretching and diaphragmatic breathing, 5 min of treadmill warm up, 4 steps of 10 min, the 1st at 50%, the 2nd at 60% and the 3rd—4th at 70% of the HR_{peak} and 10 min of stretching and diaphragmatic breathing again, 3 days per week always by a physiotherapist [40, 41]. Four studies carried out the same intervention, 3 to 5 days a week (of which at least one must be supervised), training on a treadmill or bicycle between 60–70% HR_{max}. Participants progressed over 3 months to a minimum of 120 min/week of exercise, they were encouraged to get at least 30 min of exercise a day [31, 32, 35, 37]. Marchesi et al. [48] conducted a training program with 3 supervised hours per week in the first three weeks and 1 additional self-managed hour from the third to the sixth week; the intensity was increased, the first 3 months alternation of slow walking 55–65% and fast walking 65–75% HR_{max} then 3 intermediate months running 55–65% and fast walking 65–85% HR_{max} and the last 4 months 70 min of continuous running at 70–90% HR_{max} interweaving short stretches of slow walking between 60–70% HR_{max}.

Nine studies conducted a resistance plus endurance training [29, 30, 33, 34, 36, 38, 39, 42, 44, 45, 47]. Three of them performed the same protocol [33, 34, 36], two weekly sessions of 40 min, always supervised by a physiotherapist which consisted of 10 min of bicycle training, 10 min of upper resistance training and 15 of endurance training; the subjects could choose stair climbing, treadmill, or rowing. The training programme was divide in three phases. Phase 1: endurance training at 50% of VO_{2max} and resistance at 60% 1 RM (20 repetitions); Phase 2: endurance training at 50–70% of VO_{2max} and resistance at 65% 1 RM (15 repetitions); Phase 3:

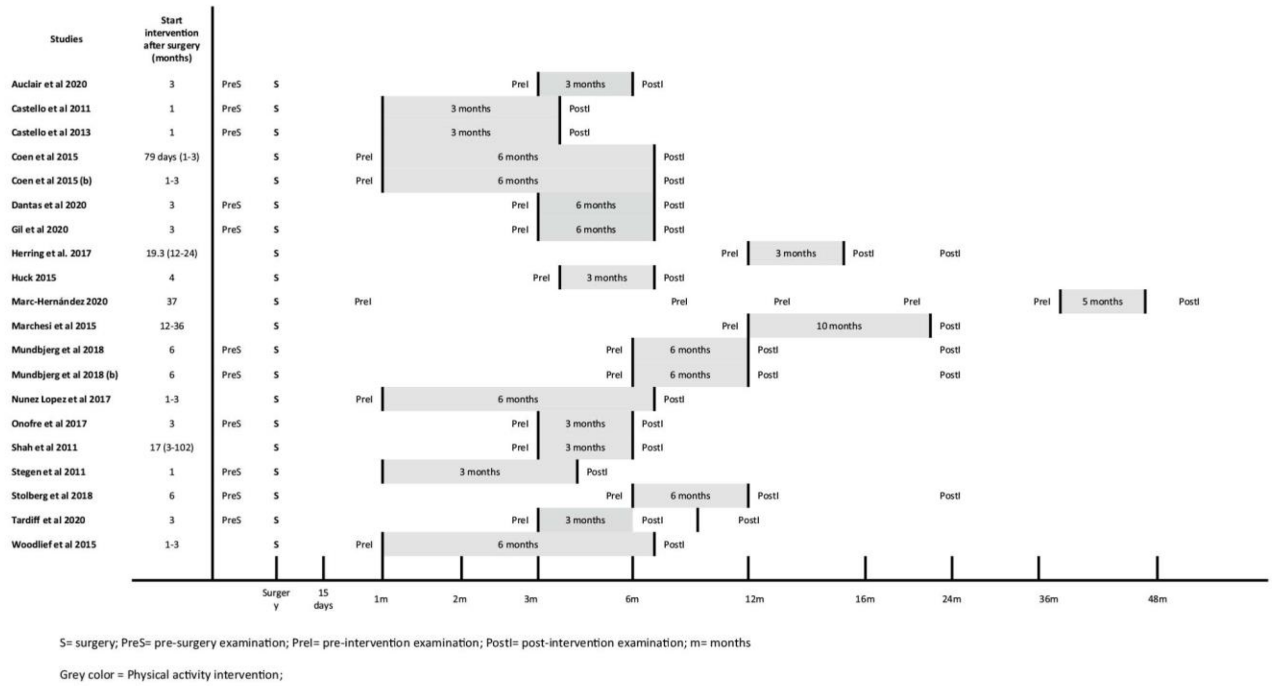


Fig. 2 Temporalization of the interventions carried out in each study. S= surgery; PreS= pre-surgery examination; PreI= pre-intervention examination; PostI= post-intervention examination; m= months. Grey color = Physical activity intervention

endurance training at 70% of VO_{2max} and resistance at 75% 1 RM (10 repetitions). Onofre et al. [44] did 3 weekly sessions of one hour, divided into 5 min of warm-up, 30 min of resistance training on a treadmill; periods of 40–60% HRR interspersed with periods of 85–90% HRR, 20 min of upper and lower limb resistance training at 60–80% of 1 RM, and 5 min of stretching. Marc-Hernández et al. [47] proposes sessions between 35 and 50 min supervised by graduates in sports science, in addition, volume and intensity progressively increases in blocks as shown in Table 3. Herring et al. [42] and Stegen et al. [45] effectuated 2 weekly supervised sessions. Stegen et al. [45] divided sessions in 10 min of cardiovascular warm up, 25 min of resistance training at 60% RM, 30 min of endurance (10 min cycling, 10 min walking, 10 min stepping) at 64 -77% HR_{max}. Finally 4 studies [29, 30, 38, 39] carried out 3 weekly sessions that began 3 months after surgery, Gil et al. [38] and Dantas et al. [39] divided the sessions into a 5-min warm-up, 30 to 60 min (10-min progression every 4 weeks) of treadmill training at a 50% difference between the ventilatory threshold and the respiratory compensation point, and 3 sets of 8–12 reps of strength training on major muscle groups with 60 s rest. On the other hand, Auclair et al.[30] and Tardif et al. [29] performed 60-min sessions divided into 5-min warm-up, 35-min resistance training at 60–75% $HR_{reserve}$, and 25-min strength training (3 sets of 10–12 reps).

One study performs resistance training only [43]. They performed 2 weekly sessions the first 6 weeks and 3 weekly sessions the last 3 weeks. Each session consisted of 5 min of cardio warm-up, 45 min of resistance training, and 5 min of stretching. The resistance training had an initial intensity of 60% of the estimated 1 RM and was gradually increased to 75%, performing between 8 and 12 repetitions of the main muscle groups.

3.4 Quality assessment

As shown in Table 4, the methodological quality was classified as good in 65% of cases (thirteen studies), fair in 25% (five studies), and poor in 10% (two studies). All the studies showed deficiencies (or no information) in the type of intervention performed, in the fields of blinding therapist / trainers and in blinding subjects. Due to the intervention being physical exercise, it is not possible to blind the patients or therapists/trainers. In addition, 55% of the studies (n = 11) had shortcomings (or no information) in the blinding of the evaluators/assessors. The remaining quality items on the PEDro scale were generally achieved.

3.5 Outcomes

3.5.1 Cardiorespiratory fitness and heart rate

Cardiorespiratory fitness was examined in twelve of the twenty trials. Four studies reported it as absolute VO_{2peak} [30, 32, 44, 45, 47], three as absolute VO_{2max} [33, 35, 37], three as VO_{2peak} relative to body weight [30, 44, 45, 47], three as VO_{2peak} relative to FFM [32, 35, 45], three as VO_{2max} relative to body weight [43, 46, 48], Woodlife et al. [37] reported it as VO_{2pmax} relative to FFM and, Auclair et al. [30] as $VO_{2\ indexed}$ to the muscle mass of the middle thigh. Of these, ten measured cardiorespiratory fitness using a gas analyzer or indirect calorimetry [29, 30, 35, 37, 44–48], and two by indirect formulas after a submaximal stress test [34, 43].

Exercise in patients undergoing bariatric surgery show an increase in the absolute cardiorespiratory fitness (VO_{2max} or VO_{2peak}) with significant changes in six trials [29, 32, 34, 35, 37, 47]. Although Onofre et al. [44] and Stegen et al. [45] show no significant changes. Similarly, positive changes are reported in cardiorespiratory fitness in relation to body weight (VO_{2max}/BW or VO_{2peak}/BW) in six studies [29, 44–48]. All the studies that measure cardiorespiratory fitness in relation to fat-free mass (VO_{2max} / FFM or VO_{2peak} / FFM) show a significant improvement [35, 37], except Stegen et al. [45], who showed no changes in the intervention group.

Heart rate was measured in different ways in eight of the seventeen studies [33, 38, 40–45, 48]. Five of them measured RHR [33, 38, 42, 43, 48]. Three of the tests evaluate the mean HR during the 6MWT test [40, 41, 45]. Castello et al. [40] reported it as mean HR during the heart rate variability (HRV) test, Onofre et al. [44] and Gil et al.[38] reported maximum HR in a cardiopulmonary exercise testing until physical exhaustion. Only Gil et al. [38] reported the $HR_{reserve}$.

None of the articles indicate significant variations in RHR [33, 42, 43, 48], with the exception of Gil et al. [38], with the same happening in the trial evaluating HR_{max} [44]. In contrast, there is a significant decrease in mean heart rate during 6MWT of the intervention group in two of the studies [41, 45], but the same does not happen in Castello et al. [40], who do not report any significant difference. During the HRV measurement, Castello et al. [40] showed a significant decrease in mean HR in the intervention group.

3.5.2 Blood pressure

Blood pressure was measured in eight of the sixteen trials [30, 31, 33, 40, 42–44, 46, 47], all reported data for both systolic and diastolic blood pressure. In all the studies, they took a rest period of 5 to 10 min prior to taking the blood pressure s, except Auclair et al.[30] and Onofre et al. [44], who did it during the stress test, and Castello et al. [40], who took the measurements during the 6MWT test.

Interventions showed positive results decreasing the systolic BP in three of the studies [31, 40, 42], whereas in the other five studies [33, 43, 44, 46, 47], no significant effects were found in the intervention group. The same occurs with

Table 3 PEDRo *scale* to measure the *quality of the studies*

	Eligibility Criteria	Random allocation	Concealed Allocation	Similarity groups' baseline	Blinding Subjects	Blinding therapist/trainers	Blinding assessor	Measured more than 85% of subjects	Intention to treat	Between groups statistical	Point measure	Score
Castello et al. [40]	1	1	1	1	0	0	0	0	0	1	1	5/10
Castello et al. [41]	1	1	1	1	0	0	0	0	0	1	1	5/10
Coen et al. [31]	1	1	1	1	0	0	1	0	1	1	1	7/10
Coen et al. [32]	1	1	1	1	0	0	1	1	1	1	1	8/10
Herring et al. [42]	1	1	1	1	0	0	0	1	1	1	1	7/10
Huck [43]	1	0	0	1	0	0	1	1	0	1	1	5/10
Marc-Hernández [47]	1	1	1	1	0	0	1	1	0	1	1	8/10
Marchesi et al. [48]	1	0	0	1	0	0	0	0	0	1	1	3/10
Mundberj et al. [33]	1	1	1	1	0	0	0	1	1	1	1	7/10
Mundberj et al. [34]	1	1	1	1	0	0	0	1	1	1	1	7/10
Nunez Lopez et al. [35]	1	1	1	1	0	0	1	1	1	1	1	8/10
Onofre et al. [44]	1	0	0	1	0	0	0	1	1	1	1	4/10
Shah et al. [46]	1	1	0	1	0	0	0	0	1	1	1	5/10
Stegen et al. [45]	1	0	0	1	0	0	0	0	0	1	1	3/10
Stolberg et al. [36]	1	1	1	1	0	0	0	1	1	1	1	7/10
Woodlief et al. [37]	1	1	1	1	0	0	1	0	1	1	1	7/10

1= reported; 0= not reported

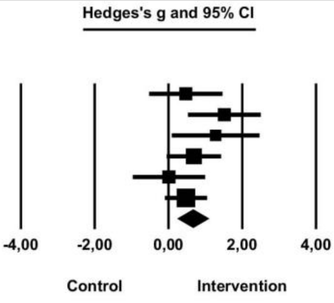
Table 4 PEDRo *scale* to measure the *quality of the studies*

	Eligibility Criteria	Random allocation	Concealed Allocation	Similarity groups' baseline	Blinding Subjects	Blinding therapist/trainers	Blinding assessors	Measured more than 85% of subjects	Intention to treat	Between groups statistical	Point measure	Score
Auclair et al. [30]	1	1	1	1	0	0	1	1	1	1	1	8/10
Castello et al. [40]	1	1	1	1	0	0	0	0	0	1	1	5/10
Castello et al. [41]	1	1	1	1	0	0	0	0	0	1	1	5/10
Coen et al. [31]	1	1	1	1	0	0	1	0	1	1	1	7/10
Coen et al. [32]	1	1	1	1	0	0	1	1	1	1	1	8/10
Dantas et al. [39]	1	1	1	1	0	0	1	1	1	1	1	9/10
Gil et al. [38]	1	1	1	0	0	0	1	1	1	1	1	8/10
Herring et al. [42]	1	1	1	1	0	0	0	1	1	1	1	7/10
Huck [43]	1	0	0	1	0	0	1	1	0	1	1	5/10
Marc-Hernández [47]	1	1	1	1	0	0	1	1	0	1	1	8/10
Marchesi et al. [48]	1	0	0	1	0	0	0	0	0	1	1	3/10
Mundberj et al. [33]	1	1	1	1	0	0	0	1	1	1	1	7/10
Mundberj et al. [34]	1	1	1	1	0	0	0	1	1	1	1	7/10
Nunez Lopez et al. [35]	1	1	1	1	0	0	1	1	1	1	1	8/10
Onofre et al. [44]	1	0	0	1	0	0	0	1	1	1	1	4/10
Shah et al. [46]	1	1	0	1	0	0	0	0	1	1	1	5/10
Stegen et al. [45]	1	0	0	1	0	0	0	0	0	1	1	3/10
Stolberg et al. [36]	1	1	1	1	0	0	0	1	1	1	1	7/10
Tardif et al. [29]	1	1	1	1	0	0	0	1	1	1	1	8/10
Woodlief et al. [37]	1	1	1	1	0	0	1	0	1	1	1	7/10

1= reported; 0= not reported

Fig. 3 Forest plot of VO2max-VO2peak in relation to body weight between intervention and control groups

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Huck 2015	0,471	0,495	0,245	-0,499	1,440	0,952	0,341
Marchesi et al 2015	1,516	0,491	0,241	0,554	2,478	3,088	0,002
Onofre et al 2017	1,280	0,594	0,352	0,117	2,443	2,156	0,031
Shah et al 2011	0,691	0,363	0,132	-0,021	1,403	1,903	0,057
Stegen et al 2011	0,014	0,487	0,237	-0,940	0,969	0,029	0,977
Auclair et al 2020	0,475	0,280	0,078	-0,073	1,023	1,700	0,089
	0,673	0,197	0,039	0,287	1,060	3,413	0,001



diastolic blood pressure, there are two trials that report a significant decrease in it [40, 42] and six that do not report significant changes [31, 33, 43, 44, 46, 47].

3.5.3 Lipid profile

Eight of the twenty studies included in this systematic review provided results related to the lipid profile [29, 31, 33, 35, 39, 46–48] All of them, except Shah et al.[46], reported the total cholesterol [29, 31, 33, 35, 39, 47, 48], seven the HDL and the triglycerides [29, 31, 33, 35, 39, 46–48], and six the LDL [29, 31, 33, 35, 39, 46–48]. All blood tests were performed with at least 10 h of fasting.

Six of the studies that measure total cholesterol do not show significant changes in patients undergoing bariatric surgery who perform physical exercise after the operation [29, 31, 33, 35, 39, 48], only Marc-Hernández et al. [47] shows a significant decrease in it. Four articles indicate a positive effect on the reduction of triglycerides in the blood [31, 35, 39, 46], while three other studies indicate that there are no significant changes[29, 33, 48] All studies, except Marchesi et al. [48] and Shah et al. [46], report a significant increase in HDL in the intervention group [29, 31, 33, 35, 39]. None of the studies found significant results in LDL in the intervention group [29, 31, 33, 35, 46], except Dantas et al. [39].

3.5.4 Glucose and insulin concentrations

Among the twenty trials included in the systematic review, eight report fasting glucose [31–33, 35, 39, 46–48] and five report fasting insulin [31–33, 35, 39, 46]. In all cases the blood tests or analyses were performed after at least 10 h of fasting.

There is agreement in all the studies that measure fasting insulin [31–33, 35], since all show a significant reduction in the group that performed physical exercise, except Shah et al. [46] and Dantas et al.[39]. On the other hand, in fasting glucose only Coen et al. (2) [32] and Marc-Hernández et al. [47] report significant changes indicating that there is a reduction in blood glucose in the intervention group.

3.6 Meta-analyses

The meta-analyses revealed a large size effect and a significant difference regarding VO_2max / peak in relation to body weight in favor of the experimental groups (ES = 0.673; 95% CI = 0.287, 1.060; p = 0.001) (Fig. 3) (Mean Difference = 1.250 ml/kg/min; 95% CI = 0.480, 2.019; p = 0.001). Significant differences and sizes effect were also observed regarding VO_2max / peak (ES = 0.317; 95% CI = 0.065, 0.569; p = 0.014) (Fig. 4), HDL (ES = 0.22; 95% CI = 0.009, 0.430; p = 0.041) (Fig. 5) and RHR (ES = -0.438; 95% CI = -0.753, -0.022; p = 0.007) (Fig. 6)

Fig. 4 Forest plot of vo2max-VO2peak between intervention and control groups

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Coen et al 2015 (b)	0,297	0,199	0,039	-0,093	0,686	1,493	0,135
Mundberj et al 2018 (b)	0,263	0,257	0,066	-0,240	0,766	1,024	0,306
Onofre et al 2017	1,468	0,611	0,374	0,269	2,666	2,401	0,016
Stegen et al 2011	0,108	0,488	0,238	-0,847	1,064	0,222	0,824
Auclair et al 2021	0,251	0,277	0,077	-0,292	0,794	0,907	0,364
	0,317	0,129	0,017	0,065	0,569	2,465	0,014

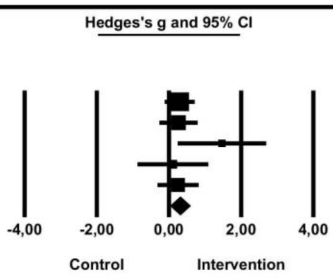
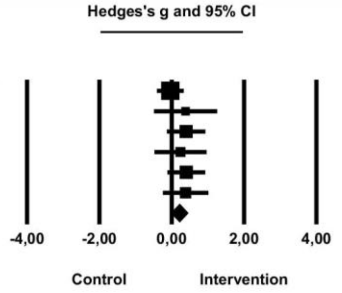


Fig. 5 Forest plot of HDL cholesterol between intervention and control groups

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Coen et al 2015 (a)	-0,038	0,176	0,031	-0,383	0,306	-0,217	0,828
Marchesi et al 2015	0,383	0,433	0,187	-0,465	1,230	0,885	0,376
Mundberj et al 2018 (b)	0,398	0,258	0,067	-0,108	0,904	1,543	0,123
Shah et al 2011	0,243	0,354	0,126	-0,452	0,937	0,685	0,493
Dantas et al 2020	0,404	0,253	0,064	-0,093	0,901	1,594	0,111
Tardif et al 2020	0,384	0,307	0,095	-0,218	0,987	1,250	0,211
	0,220	0,107	0,012	0,009	0,430	2,047	0,041



(Mean Difference = -3.925 BPM; 95% CI = -6.536, -1.313; p = 0.003), in favor of the experimental groups.

On the other hand, no significant differences were observed in either SBP (ES = -0.157; 95% CI = -0.399, 0.084; p = 0.202) (Fig. 6) (Mean Difference = -2.646 mmHg; 95% CI = -7.321, -1.109; p = 0.267) or DBP (ES = -0.117; 95% CI = -0.446, 0.212; p = 0.485) (Fig. 7) (Mean Difference = -1.405 mmHg; 95% CI = -5.559, 2.749; p = 0.507).

3.7 Heterogeneity

From the six meta-analyses performed, four of them showed non-significant heterogeneity: VO_2max / peak in relation to body weight (I^2 = 22.8%; p = 0.26) (Fig. 3), VO_2max / peak (I^2 = 0%; p = 0.43) (Fig. 4), HDL (I^2 = 0%; p = 0.61) (Fig. 5), SBP (I^2 = 0%; p = 0.54) (Fig. 7), and RHR (I^2 = 0%; p = 0.66). (Figure 6) In contrast, a significant heterogeneity was observed regarding DBP (I^2 = 34%; p = 0.19) (Fig. 8)

3.8 Sensitivity analysis

Once each study was individually removed and each ES was re-calculated, no changes in ES, effect direction or p-values were observed compared to those obtained in the original forest plots. The largest change was observed in the HDL when eliminating the Coen et al. study [49] (original p = 0.042; re-calculated p = 0.006).

3.9 Publication bias

In all the funnel plots performed, a symmetrical study distribution was observed, leaving all the studies within the limits of the funnel plot. In all cases, the Egger's statistics were not significant.

4 Discussion

The present systematic review and meta-analysis provides insight into how physical exercise affects certain cardio metabolic risk markers following bariatric surgery. Exercise interventions were effective in improving absolute VO_{2max} / $_{peak}$ (ES = 0.317; p = 0.014) and VO_{2max} / $_{peak}$ relative to body weight (ES = 0.673; p = 0.001), when compared to the usual care control groups. Previous meta-analyses performed by Silva et al. [50] and Bellicha et al. [11] showed similar results in terms of VO_{2max} improvement.

The increase in VO_{2max} can be due to several reasons. Firstly, the increase in lung diffusion capacity and pulmonary ventilation that training appears to produce [51], allowing greater O_2 saturation in the blood. Second, endurance training increases left ventricular mass, right ventricular mass, left ventricular systolic volume and right ventricular systolic volume in patients with obesity [52], which may result in increased stroke volume and increased heart size. All these factors would also be directly related to the significant decrease in RHR that we observed (ES = -0.438;

Fig. 6 Forest plot of resting heart rate between intervention and control groups

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Castello et al 2011	-0,644	0,354	0,125	-1,338	0,050	-1,819	0,069
Herring et al 2017	-0,546	0,402	0,162	-1,334	0,242	-1,359	0,174
Huck 2015	-0,326	0,491	0,241	-1,288	0,635	-0,665	0,506
Marchesi et al 2015	-0,855	0,449	0,202	-1,735	0,025	-1,904	0,057
Mundberj et al 2018	-0,181	0,256	0,066	-0,683	0,321	-0,707	0,480
	-0,438	0,161	0,026	-0,753	-0,122	-2,718	0,007

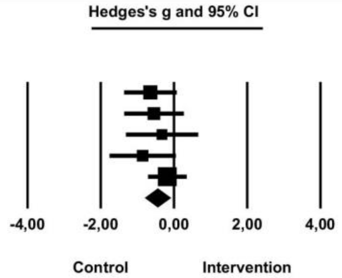
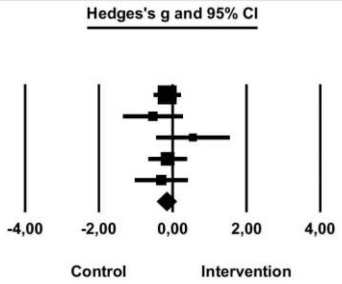


Fig. 7 Forest plot of systolic blood pressure between intervention and control groups

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Coen et al 2015 (a)	-0,146	0,176	0,031	-0,491	0,199	-0,832	0,406
Herring et al 2017	-0,536	0,402	0,161	-1,324	0,251	-1,335	0,182
Huck 2015	0,550	0,497	0,247	-0,425	1,524	1,105	0,269
Mundberj et al 2018	-0,135	0,256	0,065	-0,636	0,366	-0,529	0,597
Shah et al 2011	-0,308	0,355	0,126	-1,004	0,388	-0,868	0,385
	-0,157	0,123	0,015	-0,399	0,084	-1,275	0,202



p = 0.007). Finally, in people with obesity, exercise improves muscle capillary function [53], which actually improves muscle O_2 use.

A much larger effect was observed on the VO_{2max} / $_{peak}$ in relation to body weight (ES = 0.673; p = 0.001) when compared to that of the absolute VO_{2max} / $_{peak}$ (ES = 0.317; p = 0.014). This may be caused by the drastic weight loss that occurs when bariatric surgery and physical activity are combined [11]. Although some studies do not confirm further weight loss through exercise after bariatric surgery [54], if this were the case, more knowledge regarding VO_{2max} in relation to fat-free mass (FFM) in this population would be needed to discern whether the VO_{2max} improvement was more affected by body weight loss and/or muscle gain/maintenance, as occurs in populations with other characteristics [55].

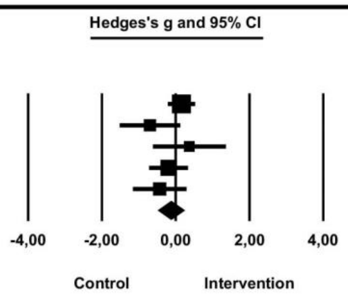
We observed significant increase in HDL concentrations (ES = 0.22; p = 0.041) in patients who exercised after bariatric surgery, compared to the control groups. These results are part of the existing controversy in the literature on this topic. There are studies associating physical activity with significant improvement in HDL in people with obesity who have not undergone bariatric surgery [56], or in normal weight people [57], in contrast to people who do not exercise. However, other studies do not indicate improvements in HDL concentration, but rather in its functions [58, 59], measured using HDL's main protein component, apoA-I, and by the ATP-binding cassette transporters ABCA1 and ABCG1, among other markers [58]. One of the main functions of HDL is the return of cholesterol to the liver [60] and the ability to promote cellular cholesterol efflux [61]. These and other functions such as its anti-inflammatory and antioxidant capacity have been favorably quantified in other studies, showing that HDL is not only a quantitative variable, and that its qualitative aspect must be taken into account [62]. For example, Woudberg et al.[59] observed that performing resistance training combined with endurance exercise in women with obesity improved HDL function as an antioxidant and antithrombotic. For all these reasons, we hypothesize that, furthermore of a quantitative increase in HDL concentration, there may be an improvement in its functions, as has been observed in other populations. Therefore, it would be convenient to measure these variables in future studies with patients who exercise after bariatric surgery.

Our results do not suggest any exercise effect after bariatric surgery on blood pressure, regardless of whether it is the SBP (ES = -0.157; p = 0.202) or the DBP (ES = -0.117; p = 0.485). Recent studies have found that exercise has a protective effect on endothelial function, reducing inflammation and increasing insulin sensitivity in people with obesity who are undergoing bariatric surgery [63]. It would therefore be convenient to wait until more studies are published (ideally those with a previous registry, and adequate design and reporting) before concluding that exercise following bariatric surgery does not affect blood pressure.

There is great variability in the start of training programs, between one and 102 months after surgery (Table 2). This is one of the main variables that has not yet been clarified

Fig. 8 Forest plot of diastolic blood pressure between intervention and control groups

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Coen et al 2015 (a)	0,157	0,176	0,031	-0,188	0,502	0,892	0,372
Herring et al 2017	-0,696	0,407	0,165	-1,493	0,101	-1,711	0,087
Huck 2015	0,372	0,492	0,242	-0,592	1,336	0,757	0,449
Mundberj et al 2018	-0,192	0,256	0,066	-0,694	0,310	-0,749	0,454
Shah et al 2011	-0,433	0,357	0,127	-1,133	0,266	-1,214	0,225
	-0,117	0,168	0,028	-0,446	0,212	-0,698	0,485



in order to create specific PA guidelines in people who have undergone bariatric surgery. As indicated by Coen et al. [10], we believe that more RCTs are needed to be able to accurately indicate the dose of PA (intensity, volume, duration), and the adequate time between bariatric surgery and the start of the intervention.

4.1 Limitations

The results presented in this study should be interpreted with caution because certain limitations exist. Firstly, although the systematic review included 20 studies, the meta-analysis for each outcome only included 4–6 studies. Secondly, as there were only a small number of studies available to analyze each outcome, it was impossible to perform meta-regressions or subgroup analysis; therefore, it was not possible to analyze the influence of different training variables or other types of biases. Thirdly, the methodological quality of the studies reviewed varied between good and fair. Fourthly, we have only reviewed articles in English or Spanish, and we have not consulted gray literature (resources not published or published in a non-commercial way). Finally, there was considerable variability between the included studies regarding the exercise interventions performed (i.e., duration of training, type of training, start time and follow-up measures, etc.).

5 Conclusions

The results from this systematic review and meta-analysis indicate that exercise after undergoing bariatric surgery has a significant effect on improving VO_2max, HDL cholesterol and lowering the resting heart rate (RHR), when compared to usual post-surgery care. In contrast, exercise training after bariatric surgery seems to have no effect on blood pressure. However, due to the limited number of studies and the characteristics of the interventions performed, it may be too early to conclude that exercise does not positively affect these cardio metabolic risk factors. Therefore, it would be prudent to wait for further research.

5.1 Future directions

The current prescription for physical activity in patients undergoing bariatric surgery is far from optimal. Studies using exercise-based interventions should be designed (and reported) on the basis of sound and current scientific evidence [64], as is the case for other clinical populations. This will ultimately allow us to find effective exercise strategies to employ in the post-operative period following bariatric surgery. Critical factors that should be considered when exercising with these patients include when to start the intervention after surgery, the appropriate technique and movement velocity, the correct quantification of the training load, and the combination of endurance and resistance training, amongst others.

Future studies should also investigate how bariatric surgery, in combination with physical exercise, affects VO_2max in relation to FFM; this will elucidate the connection between weight loss, muscle mass maintenance and VO_2max in these patients. Regarding the significant HDL improvements observed in this study, future research should evaluate the effects of exercise after bariatric surgery on the different functions and sub-classes of HDL, to specifically test for possible improvements in its functions, not only in the total amount of HDL.

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Author's Contribution ACR, IC-R, CA-B and EGA designed the review and meta-analysis. ACR and EMR conducted the review and carried out the meta-analysis. ACR wrote the article with the support of EGA, VM-V, MF-M, and AS-M, while EGA provided clinical and epidemiological support. EGA was the principal investigator and guarantor. All authors reviewed and approved the final version of the manuscript.

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Data Availability Data exchange is not applicable since no databases were generated during the present study.

Code availability Comprehensive Meta Analysis V2.0.

Declarations

Conflict of interest The authors declare that they have no conflict of interest.

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