Programa de doctorado en Deporte y Salud

SUPERVISED EXERCISE TRAINING PROGRAMMES IN BARIATRIC SURGERY CANDIDATES: EFFECTS AND IMPACT ON HEALTH.

Doctoral Thesis

A dissertation presented by

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- 2024 -

La presente tesis doctoral, con título "SUPERVISED EXERCISE TRAINING PROGRAMMES IN BARIATRIC SURGERY CANDIDATES: EFFECTS AND IMPACT ON HEALTH", es un compendio de tres artículos previamente publicados, de los cuáles uno está publicado en una revista indexada en el *Journal Citation Reports* de la *Web of Science.* La referencia completa es la siguiente:

1. Picó-Sirvent I, Manresa-Rocamora A, Aracil-Marco A, Moya-Ramón M. A Combination of Aerobic Exercise at Fatmax and Low Resistance Training Increases Fat Oxidation and Maintains Muscle Mass, in Women Waiting for Bariatric Surgery. Obes Surg. 2022 Apr;32(4):1130-1140. doi: 10.1007/s11695-022-05897-1. Epub 2022 Jan 20. PMID: 35048250; PMCID: PMC8933381 (JCR-SCIE 2022: Q2, JIF: 2.9; JIF rank: 63/213; JIF percentile: 70.7; SJR 2022: Q1; 1.13; 9 citas recibidas, Google Académico).

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1. Moya-Ramón M, Picó-Sirvent I, Aracil A. Effects of physical activity programmes in severe obesity before and after bariatric surgery: a current framework. Eur J Hum Mov. 2018;41:103–23. (Revista con sello FECYT; Q3; posición 42/56, área ciencias de la educación, 2018; 5 citas recibidas, Google Académico).
2. Picó-Sirvent I, Aracil-Marco A, Pastor D, Moya-Ramón M. Effects of a Combined High-Intensity Interval Training and Resistance Training Program in Patients Awaiting Bariatric Surgery: A Pilot Study. Sports (Basel). 2019 Mar 25;7(3):72. doi: 10.3390/sports7030072. PMID: 30934623; PMCID: PMC6473567. (JCR-ESCI 2019: Q3, JCI rank: 69/116; JCI percentile: 40,95; 24 citas recibidas, Google Académico).

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Prof. Dr. D. *Francisco J. Moreno Hernández*

Coordinador del Programa de Doctorado en Deporte y Salud

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AGRADECIMIENTOS

Agradecimientos

Los trabajos experimentales presentados en esta Tesis Doctoral se han realizado al amparo del convenio de colaboración científica entre el Hospital Vinalopó, el Hospital General Universitario de Elche, y la Universidad Miguel Hernández de Elche (FISABIO3.l5X), y han sido financiados parcialmente por los siguientes proyectos de investigación: "Efectos físicos y psicológicos de un programa de ejercicio en pacientes bariátricos" (UEM2.11X; Escuela de Estudios Universitarios Real Madrid-Universidad Europea de Madrid) y "Efectos fisiológicos y psicológicos de un programa de actividad física en pacientes bariátricos" (Fundación MAPFRE). La financiación de la publicación en Open Access se ha realizado gracias al acuerdo CRUE-CSIC con Springer Nature. Me gustaría expresar mi más sincero agradecimiento a todos ellos.

Del mismo modo, me gustaría dar las gracias especialmente a la Dra. Mª Isabel Pérez Soto del Hospital Vinalopó, tanto por recomendar el programa como por su disposición y colaboración en el seguimiento de los pacientes participantes, y a los Dres. José Luís López Elvira y Eduardo Cervelló, del Centro de Investigación del Deporte, por su apoyo en la tutela de esta tesis.

“Aprecia el momento que tienes a tu alcance,

siéntelo como único e irrepetible,

y luego, avanza hacia lo que te llena.

Hasta conseguirlo. Así es como el esfuerzo merecerá la pena.”

En el año 2015 empecé a interesarme por las bondades del ejercicio físico para la mejora de la salud en la obesidad. Recuerdo esa primera reunión con Manolo y Artur en la que se me abrían las puertas para participar en la fase experimental del proyecto como mis estancias del grado, aprendiendo de Artur y guiada por Manolo. Ahora, veo un propósito cumplido que me ha costado un esfuerzo que no se puede medir. Sin su confianza, tutela y ayuda para poder empezar a formarme en esta línea, jamás hubiese podido llegar hasta aquí, con todas las experiencias y aprendizajes que he tenido la suerte de adquirir.

Sin embargo, no siempre lo he visto así. El mundo investigador es un camino que te reta constantemente: te obliga a adaptarte a las exigencias académicas a un ritmo muy acelerado. Y a menudo, si te apasiona como llegó a apasionarme a mí, te absorbe a un nivel que dejas de ser consciente de las demás áreas de tu vida con tal de rendir al máximo. Por este motivo, me siento enormemente agradecida de tener unos amigos maravillosos, una familia emocionalmente entregada y una pareja tan incondicional que, por muchas líneas que escriba, jamás harán justicia a lo mucho que siento que les debo.

Por un lado, quiero dar las gracias a todas las personas que, en el CID, contribuyeron a que mi experiencia en cada laboratorio fuese enriquecedora y agradable: los pacientes participantes, Laura, Alejandro Jiménez, Alejandro Javaloyes, Iván, Silvia, Alba, Pedro, Alberto, Diego, Rafa, Juan Pedro, Dori, Susi… Todos vosotros, en alguno o varios momentos de la fase experimental de mi tesis me aportasteis y pude compartir y/o aprender de vosotros y vosotras. Pero, de forma especial, quiero mencionar a cuatro personas que no solo me han aportado académicamente, sino también a nivel personal.

En primer lugar, Agus, gracias por esas pausas de charla y café, por todas las veces que no perdiste los nervios conmigo intentando explicarme estadística avanzada mientras te miraba con cara de “*¿qué me estás contando?*”. También por ser mi compañero de cursos, seminarios y congresos, lo que jamás me hubiese imaginado en primero de grado, cuando lo único que hacía era molestarte por hablar en clase (perdóname, aún no había madurado). Te considero una persona muy luchadora, profesional y válida, además de buen compañero y me siento afortunada de haber podido compartir y aprender de ti.

En segundo lugar, Sarabia, por tu infinita, pero INFINITA, paciencia y tolerancia para no cerrarme la puerta de tu despacho cada vez que tenía una duda técnica, teórica o de gestión del PMC. Siempre me atendiste y asesoraste cuando lo necesité, con amabilidad y cercanía, lo que hizo que sintiese mucho respaldo durante mi aprendizaje. Aprendí muchísimo de tu forma de gestionar el trabajo en investigación. Tu actitud en un entorno

con tanta exigencia de productividad no es común, y te agradezco muchísimo toda la ayuda que me prestaste. Especialmente, en el diseño de las herramientas para prescribir ejercicio en la última intervención de la tesis. Sin ti, nunca lo hubiese podido llevar a cabo. Siempre te consideraré el "Simba" del CID. Gracias por dedicar parte de tu tiempo en ayudarme tantas veces.

En tercer lugar, Manolo, no tengo palabras para agradecerte el apoyo y comprensión que me has dado para poder llegar hasta aquí. Y aunque he de reconocer que tuve mis varios ataques de ansiedad por no saber gestionar la autonomía que me diste en la fase experimental de la tesis, lo cierto es que esa etapa de mi vida me permitió adquirir unas habilidades que, a día de hoy, me han enriquecido y hecho más competente en mi trabajo. Gracias por haberme dado tiempo, por haber empatizado con mi situación y haberme proporcionado espacio. Y aunque lo sabes, quiero materializarlo en el documento de esta tesis: te considero, literalmente, un director de tesis atípico pero en el buen sentido, porque me has demostrado tener una capacidad humana que dudo mucho que exista en todos los laboratorios de investigación. Me enorgullece poder decir que he sido tutelada por ti.

Por último, no podía olvidarme de ti, Fito, porque has sido el pilar fundamental para que esta tesis se haya terminado. No sé cómo lo hacías, pero cuando atravesaba una fase en la que la culpabilidad me quemaba por dentro y no era capaz de retomar la tesis de pura tristeza, recibía un mensaje tuyo y hacías que mi compromiso y motivación, de repente, floreciesen de nuevo. Literalmente, has sido la chispa que me ha ido recordando de vez en cuando lo mucho que me gusta la investigación. Y a la vez, me has incitado a escucharme, respetar mis tiempos y establecerme pequeños objetivos que no me permitiesen desengancharme del todo. Gracias por haberme guiado y acompañado cuando ni yo misma creía en que pudiese lograr llegar a este momento después de todo. Pero principalmente, gracias por tu empatía y por acompañarme en este proceso. Eres la sinergia perfecta de conocimiento, compañerismo, profesionalidad y humanidad.

Por otro lado, sois muchas las personas de mi entorno que habéis contribuido a hacerme la vida mucho más fácil en los últimos años. Gracias a Pablo, Paloma y a mis niñas Laura, Day, Cintia, Stefy y Lauri por ser de esos amigos con los que absolutamente nada cambia aunque no te veas en meses por vivir en otra ciudad y ser una "*friki estudiosa y ocupada*". Gracias a Pascual y a mi mesita infantil (Alba, Susi y Fran), por aparecer en el que sin duda ha sido el momento más duro de mi vida y haberme dado tanto amor, apoyo y compañía. Gracias a mis super compañeros de trabajo: Alberto, mi compi pro de ping-

pong, con un talento excelente para restarle importancia a las cosas y sacarme una sonrisa cuando entro en fase de indignación; mi José Manuel, que has hecho de mi hermano mayor estos cuatro últimos años a un nivel que cualquier descripción de mi agradecimiento se quedaría corta; y como no, a mi Flor, por tratarme con tanta dulzura y cariño y ayudarme tantísimo, sin ser consciente, a mejorar la autoconfianza.

También tengo mucho que agradecer a mis psicólogas, Gema Peñalver y Aldara Martos. A Gema, por acompañarme en mis primeras fases del duelo y enseñarme a establecer límites y a darme tiempo. Gracias a ti, supe pedir ayuda y enfrentar la conversación con Manolo y Fito para decir en voz alta "no puedo seguir", para explicar mi estado emocional y pedir ayuda al respecto. Me enseñaste a no escapar, a dar el 100% de mi energía en lo que hacía, aunque mi energía real fuese un 10%, y me diste herramientas para aceptarme y perdonarme tanto por mis decisiones pasadas como por no ser todo lo productiva que sentía, en ciertos momentos, que debía ser. A Aldara, por seguir enseñándome a perdonarme e integrar el dolor cuando aparece, a que no me paralice como antes y a hablarme con cariño y de forma positiva. Gracias por trabajar conmigo que pueda enfrentar este momento sin miedo y culpa, y por ser tan cercana y profesional.

Por supuesto, esta tesis no hubiese sido posible sin el apoyo incondicional de mi familia. Gracias a mis abuelos, por enseñarme el valor de la humildad y el esfuerzo. A mi madre, por preocuparse de que estudiase y tuviese un futuro mejor, por facilitarme tanto la vida cuando necesitaba tiempo para mi formación, y por quererme tanto aun con mis defectos. Gracias a ti, tata, por ser mi confidente, a la que quiero infinitamente. Eres de las personas más buenas, válidas, fieles e incondicionales que existen. No lo olvides nunca.

Y en especial, gracias a ti, papá, porque estés donde estés, esta tesis es para ti. Fuiste un ejemplo de superación: luchaste por mantener tu autonomía hasta el último suspiro, no dejaste que el cáncer condicionase tu vida y tuviste la capacidad de disimular tan, pero tan bien tu enfermedad que hasta llegué a dejar de ser consciente de que te podía perder en cualquier momento. Y así fue, ni siquiera lo vi venir. Así que no puedo dejar de darte las gracias por aceptar siempre mis decisiones, por no enfadarte ninguna de las veces que me decías de hacer un plan en familia y te decía que no porque "*tenía mediciones de la tesis*". Gracias por alentarme a seguir formándome, por hacer esfuerzos económicos para que pudiese seguir mis estudios tanto en la tesis como en las oposiciones, y por darme el más grande de los aprendizajes: **da igual lo que consigas en la vida, lo que le da realmente valor es poder compartirlo con <u>todas</u> las personas importantes para ti**.

Siento no haberme dado cuenta antes, pero te prometo que, al menos, haré que valga la pena el tiempo que perdí de estar contigo, y nunca volveré a cometer el mismo error en mis prioridades. Gracias por quererme, entenderme y respetarme siempre. Te quiero.

Para terminar, no me olvido de dar las gracias a la suerte de mi vida. Pedro, ya van casi 10 años desde que decidimos compartir un proyecto de vida juntos. En todo este tiempo, hemos vivido de todo: terminar estudios, trabajos mal pagados, vivir de alquiler, relación a distancia, reinventarnos, estudiar una tesis y oposiciones, mejorar profesionalmente, una pandemia mundial, perder a muchos seres queridos, una casa con su reforma… Y a todo hemos sobrevivido, apoyándonos, siempre juntos. Has sido y sigues siendo mi mayor soporte. Gracias por creer en mí cuando ni yo misma lo hago. Gracias por alentarme a estudiar la tesis y las oposiciones a la vez, a pesar de que yo lo viese una absoluta locura y no me considerase ni tan capaz ni tan inteligente. Gracias por quererme de una forma tan bonita e incondicional, por ayudarme a ser mejor persona, por aceptarme y comprenderme, y por compartir conmigo tantos principios éticos y morales. Gracias por todos esos abrazos en momentos de alegría y euforia, pero también de tristeza y sentimiento de soledad. Gracias por todas las conversaciones intensas y palabras de ánimo, por toda la responsabilidad que asumiste cuando me encontraba en el hoyo más profundo en el que he estado jamás, y por no abandonarme y hacerme sentir que podía con ello. Porque, si hoy estoy escribiendo estas líneas con entereza y resiliencia es por ti. Me has complementado: si no he tenido energía, me la has dado; si no he tenido ilusión, has intentado que la encontrase; y si no he querido seguir, me has dado motivos para que cambiase de opinión.

Dicen que las relaciones de hoy en día no son como las de antes, que las personas no se respetan sino que se controlan, sin embargo esa no es mi experiencia en absoluto. Solo nosotros sabemos las horas que hemos pasado, cada uno en su habitación, luchando por un futuro mejor, más estable y sano. Y solo nosotros sabemos lo mucho que nos hemos tenido que comprender, comunicándonos una y mil veces, para ayudarnos como necesitábamos hacerlo entre nosotros. De la forma que fuese. Por todo y mucho más, gran parte de esta tesis también es tuya. Gracias por recordarme las motivaciones que había olvidado. Gracias por estar, por darme paz y por contribuir tantísimo a hacerlo posible. Te quiero.

Un doctorado no es un camino fácil, pero rodeada de las mejores personas, no solo es posible, sino que vale la pena vivirlo. Y, sobre todo, compartirlo. GRACIAS.

ABBREVIATION LIST

Abbreviation list

1. Bariatric surgery (BS)
2. Body mass index (BMI)
3. Body weight (BW)
4. Carbohydrate oxidation (CHO)
5. Excess body weight (EBW)
6. Exercise-based training programme(s) (ETP)
7. Fat free mass (FFM)
8. Fat oxidation (FO)
9. First ventilatory threshold (VT1)
10. Glucagon-like peptide-1 (GLP-1)
11. Heart rate (HR)
12. High intensity interval training (HIIT)
13. Intensity in which maximal fat oxidation occurs (Fatmax)
14. Laparoscopic adjustable gastric band (LAGB)
15. Laparoscopic sleeve gastrectomy (LSG)
16. Maximal dynamic strength (MDS)
17. Maximal fat oxidation (MFO)
18. Maximal isometric strength (MIS)
19. Maximal oxygen uptake (VO_{2max})
20. Maximum Voluntary Contraction (MVC)
21. Metabolically healthy obese (MHO)
22. Moderate intensity continuous training (MICT)
23. Normal weight obesity (NWW)
24. Peak oxygen uptake (VO_{2peak})
25. Peak power output (PO_{peak})

26. Physical activity programmes (PAP)

27. Power output (PO)

28. Resting carbohydrate oxidation (RCHO)

29. Resting energy expenditure (REE)

30. Resting fat oxidation (RFO)

31. Resting metabolic rate (RMR)

32. Roux-en-Y gastric bypass (LRYGB)

33. Third polynomial equation (P3 model)

34. Waist circumference (WC)

35. Waist to height ratio (WHtR)

36. Waist to hip ratio (WHR)

37. Watts (W)

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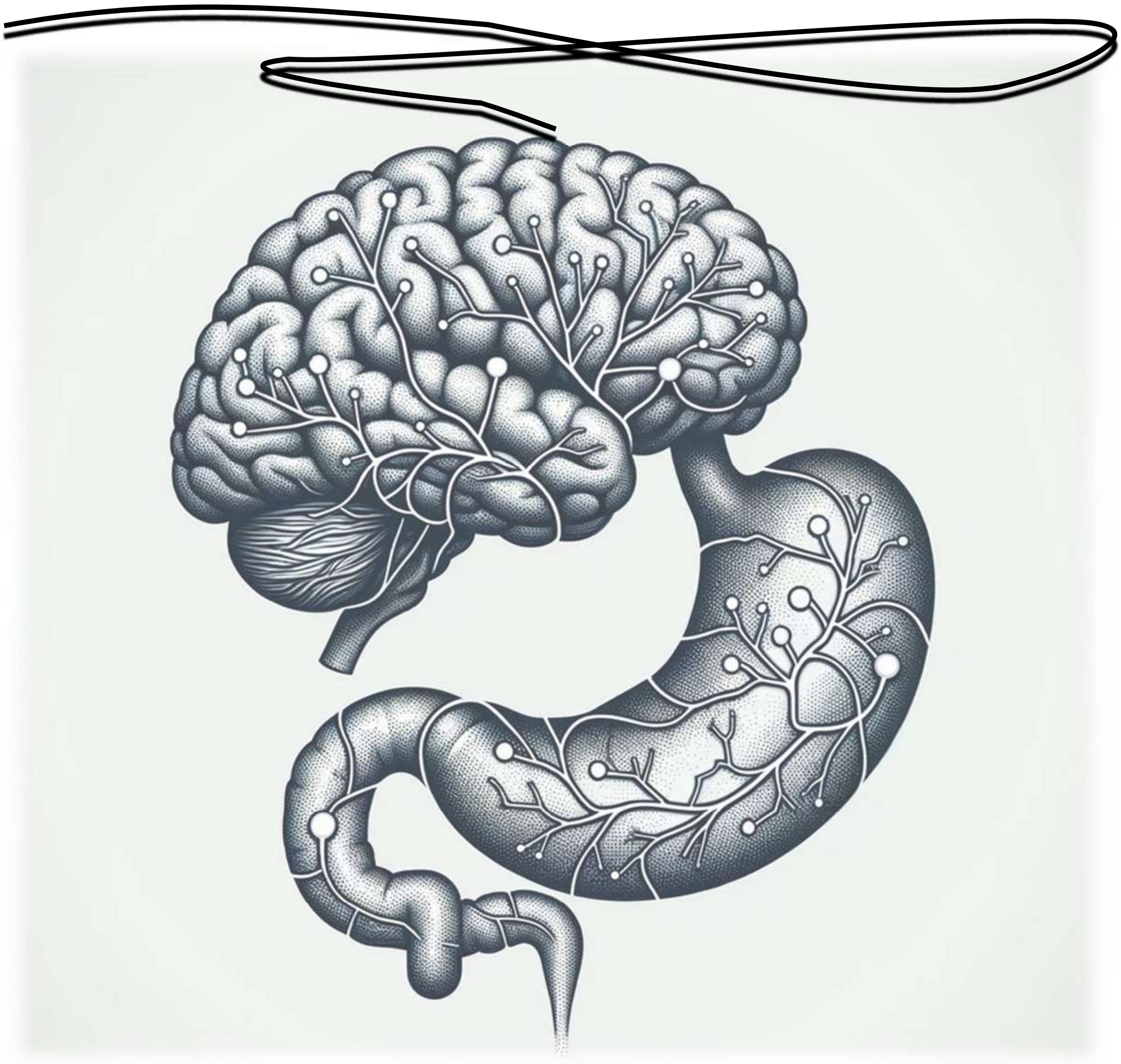
ABSTRACT



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Resumen

Antecedentes: La cirugía bariátrica (BS) se considera el tratamiento más efectivo en la obesidad mórbida, cuya prevalencia mundial ha ido aumentando en las últimas décadas. Sin embargo, su abordaje clínico se lleva a cabo a través de un tratamiento multimodal en el que se combinan terapias farmacológicas con intervenciones cuyo propósito es estimular cambios en el estilo de vida a tres niveles: nutricional, comportamental y de práctica de actividad física. Habitualmente, cuando las intervenciones en el estilo de vida no consiguen la pérdida de peso objetivo en un periodo de seis meses, se propone al paciente someterse a BS si presenta un Índice de Masa Corporal (BMI) $\geq$ 40 kg·m^{-2}, o bien si presenta un BMI $\geq$ 35 kg·m^{-2} con comorbilidades asociadas (p. ej. síndrome metabólico). No obstante, los resultados de estudios en pacientes sometidos a técnicas de BS han demostrado que el peso corporal previo a la cirugía se recupera a medio y largo plazo en muchos casos, provocando de nuevo problemas de salud y afectando negativamente a la autoestima de las personas intervenidas. En el corto plazo, uno de los problemas más subrayados es la pérdida de masa libre de grasa (FFM) tras la intervención quirúrgica, cuyas estrategias de prevención todavía siguen siendo objeto de estudio tanto desde un enfoque nutricional como de práctica de ejercicio físico, concretamente, basado en entrenamiento de fuerza. Existen evidencias significativas acerca de los beneficios de la práctica de actividad física en forma de ejercicio físico regular sobre la salud individual, ya sea ejercicio aeróbico o de fuerza, en población con obesidad por su impacto positivo en la pérdida de peso y la salud cardiometabólica. Sin embargo, cuestiones como su viabilidad o seguridad en casos de obesidad mórbida es una cuestión aún sin resolver. De igual modo, mientras que la mayoría de los estudios previos en pacientes de BS se han realizado post intervención, las evidencias acerca de los efectos derivados de programas de intervención de pérdida de peso previos a la cirugía son escasas. En relación con esto, considerando que el objetivo principal de la BS es la pérdida de peso y su consecuente mejora en la salud cardiometabólica, y que la práctica de ejercicio físico regular ha demostrado ampliamente ser útil en la consecución de este objetivo, resulta coherente cuestionarse por qué no se llevan a cabo programas de actividad física (PAPs), estructurados y monitorizados, tanto en la preparación como en el seguimiento post intervención de los pacientes con obesidad mórbida en el ámbito clínico. Además, los resultados de estudios previos sobre los efectos derivados de intervenciones basadas en

ejercicio físico en esta población no son concluyentes, demandando mayor investigación al respecto.

Por ello, los principales objetivos de esta tesis doctoral fueron: 1) estudiar el impacto de los programas de actividad física (PAPs) realizados en pacientes bariátricos, tanto en la preparación como en el seguimiento post cirugía, sobre la salud; y 2) explorar los efectos de distintos programas de entrenamiento basados en ejercicio físico (ETP) en pacientes a la espera de BS.

Métodos: Para abordar los objetivos planteados en esta tesis doctoral se utilizaron métodos de revisión y métodos experimentales. Por un lado, en el estudio 1 se utilizaron métodos de revisión en los que se realizaron búsquedas electrónicas en dos bases de datos distintas. Por otro lado, en los estudios 2 y 3 se utilizaron métodos experimentales. Los pacientes, derivados desde el hospital por estar a la espera de someterse a una BS, contactaban voluntariamente y se sometían a una anamnesis en la que se comprobaba la ausencia de criterios de exclusión: asma, enfermedad pulmonar obstructiva crónica, enfermedad cardiovascular, hipotiroidismo o limitaciones funcionales para realizar un PAP. Se asignaban a un grupo experimental o a un grupo control en función de sus posibilidades individuales para asistir regularmente a las sesiones de entrenamiento. Todos los participantes se evaluaban al inicio y al final de la intervención: en concreto, a los tres y seis meses en los estudios 2 y 3, respectivamente. Se registraban parámetros antropométricos y de fitness cardiorrespiratorio en ambos estudios, además de registros de fuerza muscular en el estudio 2 y de oxidación de sustratos en reposo en el estudio 3. En ambas intervenciones, los participantes del grupo experimental realizaron un ETP en el que las sesiones semanales progresaron mensualmente hasta el tercer mes en ambos estudios, manteniéndose en 4 sesiones semanales hasta finalizar la intervención en el estudio 2. Además, mientras que en el estudio 2 se realizaron sesiones de entrenamiento interválico de alta intensidad (HIIT) combinado con entrenamiento de fuerza a cargas altas e intercaladas con sesiones de entrenamiento continuo de intensidad moderada (MICT), en el estudio 3 se llevaron a cabo sesiones de entrenamiento aeróbico a intensidad de máxima oxidación de grasas (Fatmax) e intercaladas con sesiones de entrenamiento de fuerza a cargas bajas. Las comparaciones entre los grupos se reportaron como la diferencia de medias con un intervalo de confianza al 95%, junto con su significación práctica reportada con valores de tamaño del efecto.

Resultados: El estudio 1 de revisión mostró la heterogeneidad entre los distintos estudios realizados en pacientes tanto a la espera como intervenidos de BS, en aspectos como el diseño del estudio, las características de la muestra, o los componentes del programa de actividad física, entre otros. Sin embargo, los hallazgos mostraron que el rol de los PAP se había estudiado hasta el momento en mayor medida post BS que en los meses previos a la intervención quirúrgica. Además, se observó que a pesar de las recomendaciones de práctica de actividad física previas a la cirugía, los efectos derivados de los PAP requerían mayor investigación por varias razones: 1) ni los instrumentos de medida ni los protocolos aplicados estaban estandarizados; y 2) existía discrepancia entre el momento más apropiado para introducir un PAP en pacientes de BS. En consecuencia, en el primer estudio experimental (estudio 2) se registraron cambios significativos en BMI, así como cambios positivos en la composición corporal, la salud cardiometabólica y el fitness cardiorrespiratorio. Se observaron reducciones en la grasa visceral (VF) y en la masa grasa (FM) tanto en valores absolutos (kg) como relativos al peso corporal total (%), acompañados del mantenimiento de la FFM en el grupo experimental. Además, se registró una alta tasa de participación (> 90% del total de las sesiones de entrenamiento supervisadas), sin incidentes registrados. Finalmente, en el segundo estudio experimental (estudio 3) no se registraron cambios significativos en la composición corporal pero la oxidación máxima de grasas (MFO) registrada durante el ejercicio aumentó, manteniéndose constante en reposo. De igual modo, la tasa metabólica basal (RMR) no sufrió modificaciones en los participantes del grupo experimental.

Conclusión: Las intervenciones preoperatorias con ETP, estructurados y monitorizados, parecen ser viables y seguras en adultos con obesidad a la espera de cirugía bariátrica sin incidentes registrados. Respecto al tipo de entrenamiento, combinar HIIT con entrenamiento de fuerza a cargas altas parece que podría proporcionar cambios positivos sobre la composición corporal, y en especial, sobre la VF. Por otra parte, los valores de MFO parecen mejorar con independencia de cambios en la composición corporal, lo que puede resultar muy relevante en el tratamiento de las comorbilidades asociadas a la obesidad. Los resultados de esta tesis doctoral muestran la viabilidad de llevar a cabo un ETP en pacientes a la espera de BS, sí como la importancia de protocolizar y monitorizar tanto las pruebas de valoración como la prescripción y control de los ETP, aportando dos cuestiones: 1) mayor seguridad en la práctica; y 2) mayor reproducibilidad de los diseños experimentales en futuras investigaciones en las que se apliquen intervenciones de ETP similares que confirmen los resultados obtenidos.

Palabras clave: *obesidad mórbida; cirugía bariátrica; prescripción de ejercicio; entrenamiento; ejercicio físico; entrenamiento de fuerza; HIIT; Fatmax; composición corporal; riesgo cardiometabólico; fitness cardiorrespiratorio; oxidación de grasas; tasa metabólica en reposo.*

Resum

Antecedents: La cirurgia bariàtrica (BS) es considera el tractament més efectiu en l'obesitat mòrbida, la prevalença mundial de la qual ha anat augmentant en les últimes dècades. No obstant això, el seu abordatge clínic es du a terme a través d'un tractament multimodal en el qual es combinen teràpies farmacològiques amb intervencions el propòsit de les quals és estimular canvis en l'estil de vida a tres nivells: nutricional, comportamental i de pràctica d'activitat física. Habitualment, quan les intervencions en l'estil de vida no aconsegueixen la pèrdua de pes objectiu en un període de sis mesos, es proposa al pacient sotmetre's a BS si presenta un Índex de Massa Corporal (BMI) $\geq$ 40 $kg \cdot m^{-2}$, o bé si presenta un BMI $\geq$ 35 $kg \cdot m^{-2}$ amb comorbiditats associades (p. ex. síndrome metabòlica). No obstant això, els resultats d'estudis en pacients sotmesos a tècniques de BS han demostrat que el pes corporal previ a la cirurgia es recupera a mitjà i llarg termini en molts casos, provocant de nou problemes de salut i afectant negativament l'autoestima de les persones intervingudes. En el curt termini, un dels problemes més subratllats és la pèrdua de massa lliure de greix (FFM) després de la intervenció quirúrgica, les estratègies de prevenció de la qual encara continuen sent objecte d'estudi tant des d'un enfocament nutricional com de pràctica d'exercici físic, concretament, basat en entrenament de força. Existeixen evidències significatives sobre els beneficis de la pràctica d'activitat física en forma d'exercici físic regular sobre la salut individual, ja sigui exercici aeròbic o de força, en població amb obesitat pel seu impacte positiu en la pèrdua de pes i la salut cardiometabólica. No obstant això, qüestions com la seva viabilitat o seguretat en casos d'obesitat mòrbida és una qüestió encara sense resoldre. D'igual mode, mentre que la majoria dels estudis previs en pacients de BS s'han realitzat post intervenció, les evidències sobre els efectes derivats de programes d'intervenció de pèrdua de pes previs a la cirurgia són escasses. En relació amb això, considerant que l'objectiu principal de la BS és la pèrdua de pes i la seva conseqüent millora en la salut cardiometabólica, i que la pràctica d'exercici físic regular ha demostrat àmpliament ser útil en la consecució d'aquest objectiu, resulta coherent qüestionar-se per què no es duen a terme programes d'activitat física (PAPs), estructurats i monitorats, tant en la preparació com en el seguiment post intervenció dels pacients amb obesitat mòrbida en l'àmbit clínic. A més, els resultats d'estudis previs sobre els efectes derivats d'intervencions basades en exercici físic en aquesta població no són concloents, demandant major recerca sobre aquest tema.

Per això, els principals objectius d'aquesta tesi doctoral van ser: 1) estudiar l'impacte dels programes d'activitat física (PAPs) realitzats en pacients bariàtrics, tant en la preparació com en el seguiment post cirurgia, sobre la salut; i 2) explorar els efectes de diferents programes d'entrenament basats en exercici físic (ETP) en pacients a l'espera de BS.

Mètodes: Per a abordar els objectius plantejats en aquesta tesi doctoral es van utilitzar mètodes de revisió i mètodes experimentals. D'una banda, en l'estudi 1 es van utilitzar mètodes de revisió en els quals es van realitzar cerques electròniques en dues bases de dades diferents. D'altra banda, en els estudis 2 i 3 es van utilitzar mètodes experimentals. Els pacients, derivats des de l'hospital per estar a l'espera de sotmetre's a una BS, contactaven voluntàriament i se sotmetien a una anamnesi en la qual es comprovava l'absència de criteris d'exclusió: asma, malaltia pulmonar obstructiva crònica, malaltia cardiovascular, hipotiroïdisme o limitacions funcionals per a realitzar un PAP. S'assignaven a un grup experimental o a un grup control en funció de les seves possibilitats individuals per a assistir regularment a les sessions d'entrenament. Tots els participants s'avaluaven a l'inici i al final de la intervenció: en concret, als tres i sis mesos en els estudis 2 i 3, respectivament. Es registraven paràmetres antropomètrics i de fitnes cardiorespiratori en tots dos estudis, a més de registres de força muscular en l'estudi 2 i d'oxidació de substrats en repòs en l'estudi 3. En totes dues intervencions, els participants del grup experimental van realitzar un ETP en el qual les sessions setmanals van progressar mensualment fins al tercer mes en tots dos estudis, mantenint-se en 4 sessions setmanals fins a finalitzar la intervenció en l'estudi 2. A més, mentre que en l'estudi 2 es van realitzar sessions d'entrenament intervàl·lic d'alta intensitat (HIIT) combinat amb entrenament de força a càrregues altes i intercalades amb sessions d'entrenament continu d'intensitat moderada (MICT), en l'estudi 3 es van dur a terme sessions d'entrenament aeròbic a intensitat de màxima oxidació de greixos (Fatmax) i intercalades amb sessions d'entrenament de força a càrregues baixes. Les comparacions entre els grups es van reportar com la diferència de mitjanes amb un interval de confiança al 95%, juntament amb la seva significació pràctica reportada amb valors de grandària de l'efecte.

Resultats: L'estudi 1 de revisió va mostrar l'heterogeneïtat entre els diferents estudis realitzats en pacients tant a l'espera com intervinguts de BS, en aspectes com el disseny de l'estudi, les característiques de la mostra, o els components del PAP, entre altres. No obstant això, les troballes van mostrar que el rol dels PAPs s'havia estudiat fins al moment en grau més alt post BS que en els mesos previs a la intervenció quirúrgica. A més, es va observar que malgrat les recomanacions de pràctica d'activitat física prèvies a la cirurgia, els efectes derivats dels PAPs requerien major recerca per diverses raons: 1) ni els instruments de mesura ni els protocols aplicats estaven estandarditzats; i 2) existia discrepància entre el moment més apropiat per a introduir un PAP en pacients de BS. En conseqüència, en el primer estudi experimental (estudi 2) es van registrar canvis significatius en BMI, així com canvis positius en la composició corporal, la salut cardiometabòlica i el fitnes cardiorespiratori. Es van observar reduccions en el greix visceral (VF) i en la massa grassa (FM) tant en valors absoluts (kg) com a relatius al pes corporal total (%), acompanyats del manteniment de la FFM en el grup experimental. A més, es va registrar una alta taxa de participació (> 90% del total de les sessions d'entrenament supervisades). Finalment, en el segon estudi experimental (estudi 3) no es van registrar canvis significatius en la composició corporal però l'oxidació màxima de greixos (MFO) registrada durant l'exercici va augmentar, mantenint-se constant en repòs. D'igual mode, la taxa metabòlica basal (RMR) no va sofrir modificacions en els participants del grup experimental.

Conclusió: Les intervencions preoperatòries amb ETP, estructurats i monitorats, semblen ser viables i segures en adults amb obesitat a l'espera de BS sense incidents registrats. Respecte al tipus d'entrenament, combinar HIIT amb entrenament de força a càrregues altes sembla que podria proporcionar canvis positius sobre la composició corporal, i especialment, sobre la VF. D'altra banda, els valors de MFO semblen millorar amb independència de canvis en la composició corporal, la qual cosa pot resultar molt rellevant en el tractament de les comorbiditats associades a l'obesitat. Els resultats d'aquesta tesi doctoral mostren la viabilitat de dur a terme un ETP en pacients a l'espera de BS, sí com la importància de protocol·litzar i monitorar tant les proves de valoració com la prescripció i control dels ETP, aportant dues qüestions: 1) major seguretat en la pràctica; i 2) major reproducibilidad dels dissenys experimentals en futures recerques en les quals s'apliquin intervencions de ETP similars que confirmin els resultats obtinguts.

Paraules clau: *obesitat mòrbida; cirugia bariàtrica; prescripció d'exercici; entrenament; exercici físic; entrenament de força; HIIT; Fatmax; composició corporal; risc cardiometabolic; fitness cardiorrespiratori; oxidació de grases; tasa metabòlica en repos.*

Abstract

Background: Bariatric surgery (BS) is considered the most effective treatment for morbid obesity, whose global prevalence has been increasing in recent decades. However, its clinical approach is carried out through multimodal treatment, combining pharmacological therapies with interventions aimed at stimulating lifestyle changes at three levels: nutritional, behavioural, and physical activity practice. Typically, when lifestyle interventions do not achieve the targeted weight loss within a six-month period, the patient is considered for BS if they have a Body Mass Index (BMI) $\geq$ 40 $kg{\cdot}m^{-2}$, or a BMI $\geq$ 35 $kg{\cdot}m^{-2}$ with associated comorbidities (e.g., metabolic syndrome). However, study results in patients undergoing BS techniques have shown that the weight prior to surgery is regained in the medium and long term in many cases, causing health problems and negatively affecting the self-esteem of those treated. In the short term, one of the most highlighted problems is the loss of fat-free mass (FFM) following the surgical intervention, whose prevention strategies are still being studied from both a nutritional and physical exercise perspective, specifically strength training. There is significant evidence about the benefits of physical activity in the form of regular physical exercise on individual health, whether it is aerobic or strength exercise, in the obese population due to its positive impact on weight loss and cardiometabolic health. However, issues such as its feasibility or safety in cases of morbid obesity remain unsolved. Similarly, while most previous studies in BS patients have been conducted post-surgery, evidence on the effects of pre-surgical weight loss intervention programs is scarce. In this regard, considering that the main goal of BS is weight loss and consequent improvement in cardiometabolic health, and that regular physical exercise has been widely demonstrated to be useful in achieving this goal, it is logical to question why physical activity programmes (PAPs), structured and monitored, are not carried out both in preparation and in post-surgical follow-up of patients with morbid obesity in the clinical setting. Additionally, the results of previous studies on the effects of exercise-based interventions in this population are not conclusive, demanding further research in this area.

Therefore, the main objectives of this doctoral thesis were: 1) to study the impact of physical activity programs (PAPs) conducted in bariatric patients, both in preparation and in post-surgery follow-up, on health; and 2) to explore the effects of different exercise-based training programs (ETPs) in patients awaiting BS.

Methods: To address the objectives set out in this Doctoral Thesis, both review methods and experimental methods were used. On one hand, in study 1, review methods were employed, involving electronic searches in two different databases. On the other hand, in studies 2 and 3, experimental methods were used. Patients, referred from the hospital as they were awaiting BS, voluntarily contacted and underwent an anamnesis to ensure the absence of exclusion criteria: asthma, obstructive pulmonary disease, cardiovascular disease, hypothyroidism, or functional limitations for carrying out a PAP. They were assigned to either an experimental group or a control group based on their individual availability to regularly attend training sessions. All participants were assessed at the beginning and end of the intervention: specifically, at three and six months in studies 2 and 3, respectively. Anthropometric parameters and cardiorespiratory fitness were recorded in both studies, in addition to muscular strength measurements in study 2 and substrate oxidation at rest in study 3. In both interventions, participants in the experimental group underwent an ETP where the weekly sessions progressed monthly up to the third month in both studies, maintaining four weekly sessions until the end of the intervention in study 2. Furthermore, while in study 2, high-intensity interval training (HIIT) sessions combined with resistance training at high loads were alternated with moderate-intensity continuous training (MICT) sessions, in study 3, aerobic training sessions at the intensity of maximum fat oxidation (Fatmax) were alternated with resistance training sessions at low loads. Comparisons between the groups were reported as the mean difference with a 95% confidence interval, along with its practical significance reported with effect size values.

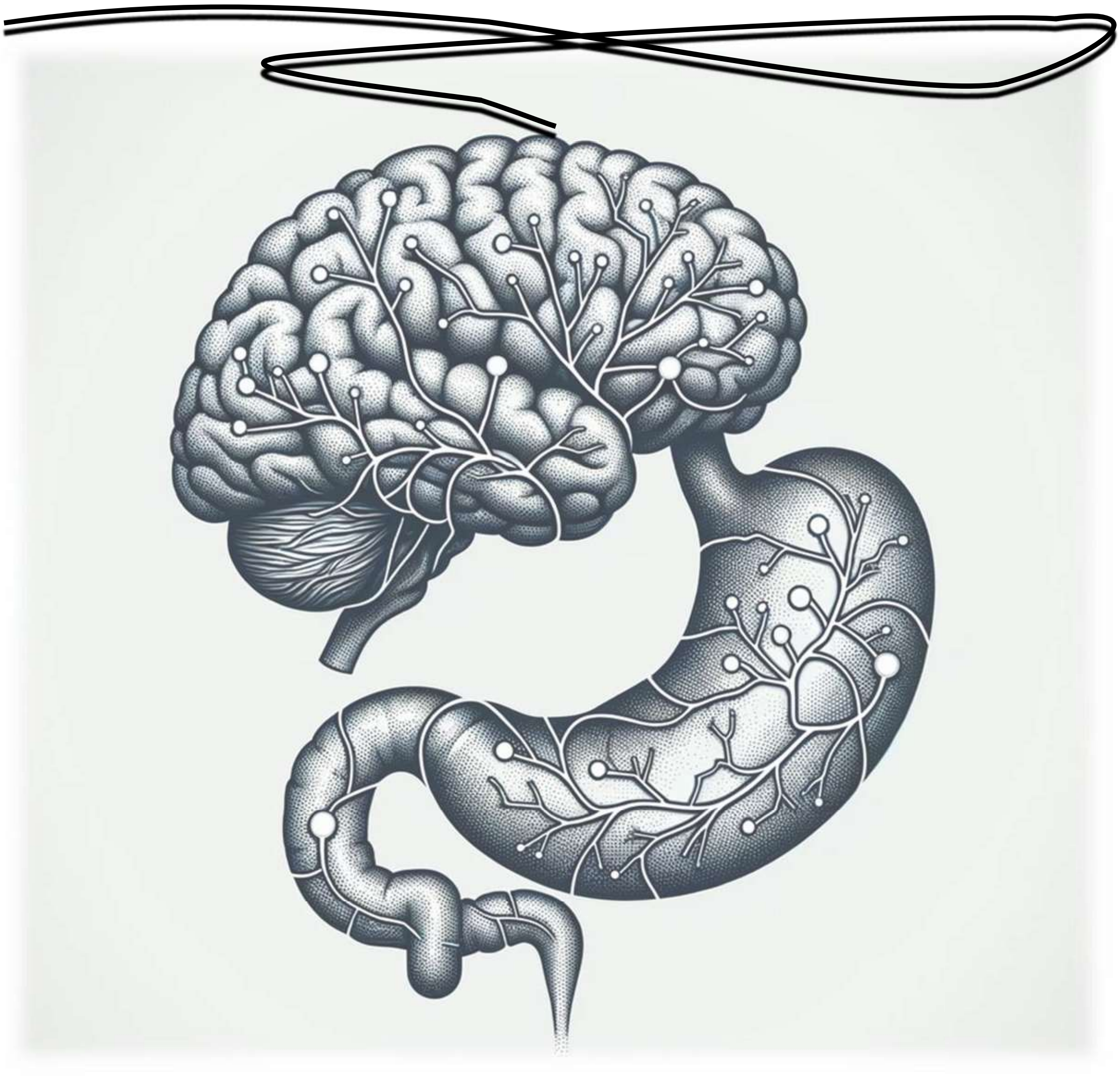
Results: Study 1, a review, demonstrated heterogeneity among various studies conducted on patients both awaiting and having undergone BS, in aspects such as study design, sample characteristics, or components of the PAP, among others. However, the findings indicated that the role of PAPs had been studied to a greater extent post-BS than in the months prior to the surgical intervention. Moreover, it was observed that despite recommendations for physical activity practice prior to surgery, the effects derived from PAPs required further research for several reasons: 1) neither the measurement instruments nor the applied protocols were standardized; and 2) there was discrepancy regarding the most appropriate time to introduce a PAP in BS patients. Consequently, in the first experimental study (study 2), significant changes were registered in BMI, as well as positive changes in body composition, cardiometabolic health, and cardiorespiratory

fitness. Reductions in visceral fat (VF) and fat mass (FM) were observed both in absolute values (kg) and relative to total body weight (%), accompanied by the maintenance of FFM in the experimental group. In addition, a high participation rate (> 90% of all supervised training sessions) was registered. Finally, in the second experimental study (study 3), no significant changes in body composition were shown, but the maximal fat oxidation (MFO) registered during exercise increased, remaining constant at rest. Similarly, the resting metabolic rate (RMR) did not change in participants of the experimental group.

Conclusions: Preoperative interventions with structured and monitored ETPs appear to be viable and safe for adults with obesity awaiting bariatric surgery, with no incidents registered. Regarding the type of training, combining HIIT with resistance training at high loads seems to potentially provide positive changes in body composition, particularly in VF. Furthermore, values of MFO seem to improve regardless of changes in body composition, which may be highly relevant in the treatment of comorbidities associated with obesity. The results of this Doctoral Thesis demonstrate the feasibility of conducting an ETP in patients awaiting BS, as well as the importance of standardizing and monitoring both the assessment tests and the prescription and control of the ETPs, contributing two aspects: 1) greater safety in practice; and 2) greater reproducibility of experimental designs in future research where similar ETP interventions are applied to confirm the obtained results.

Keywords: *morbid obesity; bariatric surgery; exercise prescription; exercise training; physical exercise; resistance training; HIIT; Fatmax; body composition; cardiometabolic risk; cardiorespiratory fitness; fat oxidation; resting metabolic rate.*

GENERAL INTRODUCTION



OpenAI. (2024). *DALL-E* [text-to-image model]. https://openai.com/dall-e-3

1. General introduction

Morbid obesity represents a growing public health challenge worldwide. With an increasing prevalence, this condition has become a true pandemic with significant consequences for both individual health and society at large. In this context, bariatric surgery (BS) has emerged as an effective intervention for managing morbid obesity. However, it is crucial to recognize that BS is a valuable but not risk-free tool and optimizing health prior to the intervention is of paramount importance. In this regard, research in the field of obesity prevention and treatment has expanded its interest towards examining the impact of programmed physical exercise on preparing patients for BS, a concept known as prehabilitation. Recently, exercise in adults awaiting or having undergone BS has been considered as feasible and acceptable, although more indicators are required yet to establish methodologies and practical approaches (Baillot et al., 2022).

The research work summarized in this Doctoral Thesis was carried out within the research line on '*Physiological and psychological effects of a physical activity program in bariatric patients*', which was in progress in the research group '*Grupo de Investigación en Acondicionamiento Físico y Salud*' (GIAFIS) when I joined the group. The three research papers included in this Doctoral Thesis entail a temporary evolution of research goals established within the aforementioned research line. Particularly, the previous works of the group were focused mainly on the effects of exercise programmes implemented at different timings after surgery. When I joined the research group the research interest was changing to describe the effects of preoperative exercise programmes, and this is the main topic of this Doctoral Thesis. Thus, the first article consists of a narrative review focused on updating the field of knowledge, while both the second and the third ones show the effects of two exercise-based training programmes (ETPs) in which training methods are different.

The first article focuses on summarizing the current scientific evidence related to physical activity programmes (PAPs) in patients both awaiting and undergone BS. The aim of this narrative review was to establish a starting point to continue this Doctoral Thesis after finishing the previous research project by GIAFIS.

The second article is the first interventional one and consists of a pilot study aimed to analyse the effect of a systematic and periodized six-months ETP based on high workloads. Participants carried out alternated weekly sessions of concurrent training to perform short-interval high intensity interval training (HIIT) combined with resistance training, with moderate intensity continuous training (MICT) sessions. So, the aim of this article shows the results of a 6-months ETP as well as analyse differences between participants, specially related to individually body changes.

Last, the third article is the second interventional paper and consists of an experimental study as well. Study design is the same of the second article, but training methods and some protocol tests are different. The ETP is based on low workloads, so participants performed alternated weekly sessions of aerobic continuous training at intensity in which maximal fat oxidation occurs (Fatmax) with resistance training. Thus, while the second article is based on intensity to stimulate health improvements, the third one progress depending on the training volume.

To contextualize the research included in this Doctoral Thesis in the field of exercise and obesity research, the following points are disclosed: what is morbid obesity, a summary of how it is diagnosed and managed, and which could be the role of physical activity and ETP in the preparation of patients who are waiting for BS.

1.1 Morbid obesity in the context of the global obesity pandemic.

Along with undernutrition and climate change, obesity is mentioned as the first one of the three global pandemics (Swinburn et al., 2019), with significant implications for public health worldwide. This condition, characterized by excess body fat, has been on the rise in recent decades, negatively affecting health status and life expectancy of individuals of all ages and socioeconomic groups (Afshin, A., Forouzanfar, M. H., Reitsma, M. B., Sur, P., Estep, K., Lee, A., ... & Murray, 2017; Bray & Bellanger, 2006). So first, it is relevant to explore the magnitude of obesity as a global public health issue and examine its impact on quality of life and morbidity.

In this regard, obesity has reached alarming proportions. According to the 2021 Global Nutrition Report (*2021 Global Nutrition Report: The state of global nutrition*, 2021), it is estimated that 2.2 billion people worldwide are overweight or obese, of whom around 772 million are classified as obese. Consequently, its target 7 is focused on stopping the rise in obesity and diabetes in adults, emphasizing the link between poor diets and poor metabolic health as a highlighted challenge to change worldwide (*2021 Global Nutrition Report: The state of global nutrition*, 2021).

These findings reflect an alarming trend that has increased significantly in recent decades, representing a globally obesity prevalence of 12.0% among adults, which is generally higher among women than men in all age and sociodemographic ranges (Afshin, A., Forouzanfar, M. H., Reitsma, M. B., Sur, P., Estep, K., Lee, A., ... & Murray, 2017). Specifically, high body mass index (BMI) has directly been related to morbidity burden from 1990 to 2015 and, although the rates of increase in deaths from cardiovascular disease have decreased in this time, elevated BMI has not shown the same trend (Afshin, A., Forouzanfar, M. H., Reitsma, M. B., Sur, P., Estep, K., Lee, A., ... & Murray, 2017).

Concerning sociodemographic level, the highest prevalence of obesity has been shown among women aged 60 to 64 in high-developed countries. In fact, obesity rates have generally increased in high-developed countries, except for women in low-developed nations over age 55. In contrast, men aged 25 to 29 in low-middle-developed countries have shown a fast increase in obesity, while children of both genders have represented a 20.0% relative increase in obesity prevalence in low-developed countries, with significant increases in middle-developed nations (Afshin, A., Forouzanfar, M. H., Reitsma, M. B., Sur, P., Estep, K., Lee, A., ... & Murray, 2017). In this line, from 1975 to 2016 it has been observed that the upward trends in BMI of children and adolescent have slowed down in many high-income countries, although Asian zones have tended to rise faster and not to be correlated with those of adults. In fact, high levels BMI have not be diminished anywhere (Abarca-Gómez et al., 2017). Hence, it could be assumed that the trend towards increasing obesity prevalence at younger and younger ages is undeniable: it's a fact which is occurring globally regardless of the sociodemographic level, at different levels of prevalence though.

Also, obesity is linked to a range of severe health issues, including cardiovascular diseases, type 2 diabetes, hypertension, sleep apnoea, liver diseases, and certain types of cancer (Malik, Willett, & Hu, 2013). In addition to the increased risk of chronic diseases, obesity is also associated with social and mental problems, as well as comorbidities such as the metabolic syndrome and musculoskeletal disorders, which all together represent high costs for health care systems, reduced work capacity and, a reduced quality of life of those affected (Herzog, 2020). Currently, it has been estimated that obesity costs about $2 trillion annually from direct health-care costs and lost economic productivity, representing 2.8% of the world's gross domestic product. These data are significant since they are roughly the equivalent of the costs linked to smoking or armed violence and war (Swinburn et al., 2019).

Obesity results from a complex interplay of genetic, environmental, and behavioural factors. Changes in diet, lack of physical activity, and the obesogenic environment, which promotes excessive food intake and inactivity, are key factors that have contributed to this pandemic (Egger & Swinburn, 1997). These factors that have a mass exposure in population, are widely distributed and act with short time-lags (Rodgers, Woodward, Swinburn, & Dietz, 2018). Consequently, addressing obesity is a complex challenge that requires a multidisciplinary approach. First, prevention and treatment strategies must focus on promoting healthy eating and regular physical activity from early ages, as well as creating environments that facilitate healthy decision-making (Swinburn et al., 2019). And second, developing new medical protocols and analysing factors that limit current clinical treatments efficacy are imperative to deal with the becoming unsustainability in health care systems, mainly in developed countries (Gul, Balkhi, & Haq, 2018).

Specifically to Spain, the National Health Survey (ENSE) registered a prevalence of obesity in adults of 17.4%, and of 54.5% when taking together both, overweight and obesity (Ministerio de Sanidad, 2017). Compared to these data, adult obesity has shown a slightly decrease in the last European Health Survey (EESE) since it reported a prevalence of 16.50% (Ministerio de Sanidad, 2020). Last, Valencian Community -the location at which the experimental interventions described in this Doctoral Thesis were performed- registered an obesity prevalence of 18.75% in 2017 (Portal Estadístico de la Generalitat Valenciana, 2017), according to the latest available data.

1.1.1 Definition of morbid obesity: diagnosis criteria.

Generally, obesity is defined as excess body weight (EBW) for a given height (Gadde, Martin, Berthoud, & Heymsfield, 2018), and more specifically, as ‘a condition in which percentage body fat is increased to an extent in which health and well-being are impaired’ (World Health Organization, 2000). Concretely, it implies an excessive accumulation of triglycerides in the adipose tissue that leads to a detrimental rise in fat mass, which finally cause hypertrophy or hyperplasia of fat cells. These cell changes are what is eventually known as the pathological lesion of obesity (Gul et al., 2018).

The diagnosis of obesity is based in the BMI. Although BMI is not a specific measure of adiposity (Gadde et al., 2018), the degree of adiposity is related to BMI though, so it let classify overweight and obesity levels and predict information about increasing body fatness (Gul et al., 2018). There are several classifications of obesity levels which are summarized in Table 1.

BMI values are independent of age and gender, but different populations might show differences in the same degree of fatness due to different body proportions (NIH Report, 1998). Thus, this fact should be considered when health risk would be assessed to give a clinical diagnosis. Specifically, this Doctoral Thesis is focused on the most severe grade of obesity according to the WHO International Classification of adult underweight, overweight and obesity (WHO Expert Committee, 1995; World Health Organization, 2000), named as morbid obesity. This condition implies a BMI above 40 $kg \cdot m^{-2}$, and thus, being a candidate for BS (Herpertz, Kessler, & Jongen, 2017).

There are few current analyses concerning trends in severe and morbid obesity. This fact could be explained by relatively uncommon presence of class III obesity in the recent past, and consequently, sample sizes in research studies were limited or not assessed risks of death for extremely high BMI (Kitahara et al., 2014). The last widely become known epidemiological research showed that global prevalence of morbid obesity was 0.64% in men and 1.6% in women in 2014 (Di Cesare et al., 2016). However, previous studies have already shown the growing tendency of obesity prevalence worldwide (Abarca-Gómez et al., 2017; Afshin, A., Forouzanfar, M. H., Reitsma, M. B., Sur, P., Estep, K., Lee, A., ... & Murray, 2017), so it is not wrong to presume that these data could be currently even higher.

Table 1

Summary of classifications of adult body weight condition according to BMI.

BMI ($kg \cdot m^{-2}$)	**Classification**	**Description**
< 18.5	Underweight	Thin
18.5 - 24.9	Healthy	Normal Weight
25.0 - 29.9	Class I obesity - Grade 1 overweight Pre-obese	Overweight
30.0 - 39.9	Class II obesity - Grade 2 overweight	Obesity
≥ 35		Severe obesity
≥ 40.0	Class III obesity - Grade 3 overweight	Extreme obesity Morbid obesity
≥ 50.0	Class IV	Not defined
≥ 60.0	Class V	Not defined

Note. According to: (Kitahara et al., 2014; Poirier et al., 2011; WHO Expert Committee, 1995; World Health Organization, 2000).

Although the diagnosis of obesity is generally based on the individual's BMI, other variables are also becoming potential diagnosis criteria, since they have been independently associated to several health risks:

1. Visceral fat is defined as fat accumulation around the viscera and inside the intraabdominal solid organs (Osama Hamdy, Sriurai Porramatikul, 2006). It is considered an independent cardiovascular risk factor (NIH Report, 1998) since it has been seen that obese people with intra-abdominal visceral fat accumulation are more related to glucose and lipid metabolism dysfunctions than those with subcutaneous fat accumulation due to an excess of free fatty acids into the circulation (Matsuzawa et al., 1995). In fact, it is well-known that obesity leads to a mix of liver dysfunctions referred as a Non-alcoholic fatty liver disease (NAFLD), one of the most relevant risk factors associated with obesity (Gul et al.,

2018). However, measuring total visceral fat by computed tomography or magnetic resonance imaging is not commonly used because of: a) the cost and radiation exposure; and, b) although Dual-Energy X-Ray Absorptiometry is accurate enough to measure total body fat and its distribution, it cannot distinguish between visceral fat and subcutaneous fat accumulation (Osama Hamdy, Sriurai Porramatikul, 2006).

2. The higher BMI is, the higher risk of suffering diseases and comorbidities associated is, but BMI is not enough a precise indicator of FM (Gadde et al., 2018). However, it is the abdominal or central distribution of adiposity the more strongly associated with high-risk diseases such as type 2 diabetes, hypertension, atherosclerosis, and coronary artery disease, and not total adiposity (Osama Hamdy, Sriurai Porramatikul, 2006). For these reason, since central adiposity can be considered as surrogate of visceral fat, anthropometric measurements are clinically used to diagnose abdominal obesity (Gul et al., 2018; Osama Hamdy, Sriurai Porramatikul, 2006). The measures most closely related to cardiometabolic risk factors and incidence of cardiovascular disease events are the waist circumference (WC), the waist to hip ratio (WHR) and the waist to height ratio (WHtR) (World Health Organization, 2011). They are illustrated in Figure 1. Depending on the demographic region, specific classifications are clinically used. To this Doctoral Thesis, the most relevant are summarized and shown in Table 2. In the last years, it has been shown that WHtR perform better than BMI, being suggested as more useful clinical screening tool because of having stronger association with adiposity (Salmón-Gómez, Catalán, Frühbeck, & Gómez-Ambrosi, 2023).

Table 2

Anthropometric measurements to diagnose abdominal obesity.

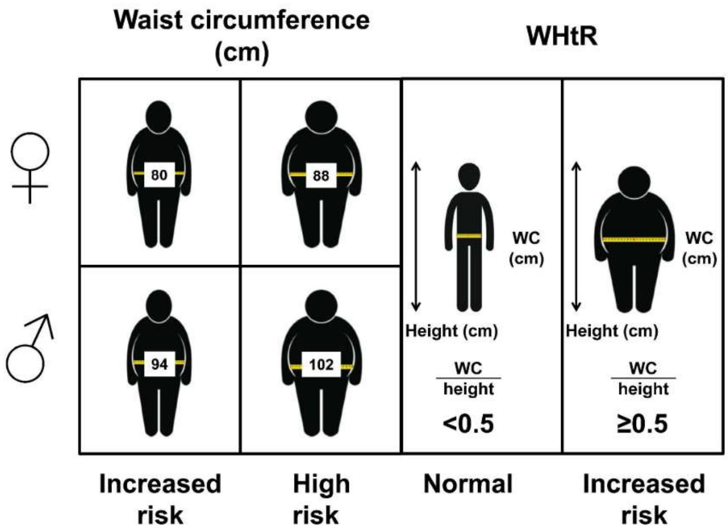
Gender	**Waist circumference (cm)**			**WHR (cm)**
	Spain	**Europe**	**USA**	
Men	≥ 94.5	> 94	≥ 102	≥ 1.0
Women	≥ 89.5	> 80	≥ 88	≥ 0.85

Note. According to: (Han, Van Leer, Seidell, & Lean, 1995; Martínez-Larrad et al., 2011; WHO Expert Committee, 1995; World Health Organization, 2011).

Therefore, it is imperative that protocols to measure and describe individual health status would be optimized in the future to prioritize in clinical treatment those patients who may benefit the most (Kitahara et al., 2014).

Figure 1

Threshold values to estimate cardiometabolic risk according to WC for females and males (left) and WHtR (right).



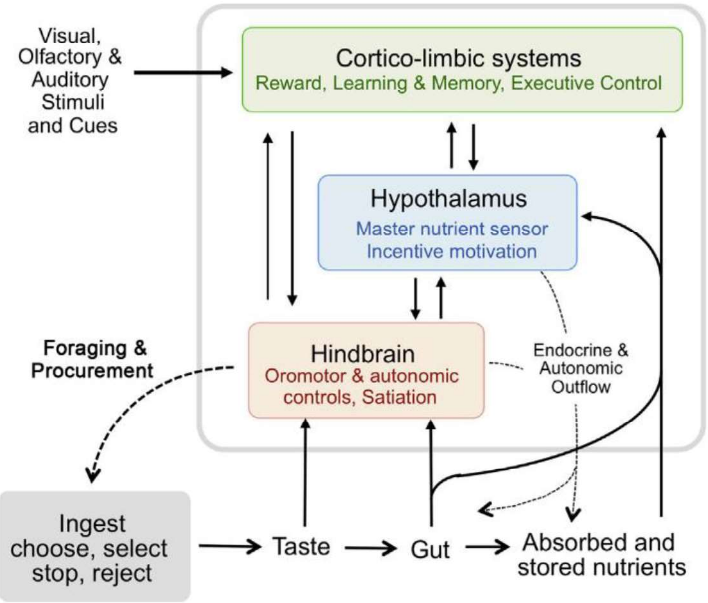
Note. Extracted from "Relevance of body composition in phenotyping the obesities" (p.814), by Salmón-Gómez et al., 2023, Reviews in Endocrine & Metabolic Disorders, 24 (5). Creative Commons Attribution 4.0 International License (CC BY 4.0). (http://creativecommons.org/licenses/by/4.0/).

1.1.2 Pathophysiological framework of morbid obesity.

It is generally believed that obesity emerges because of an imbalance of energy homeostasis. While individual cells and tissues have their own energy sensors, the hypothalamus serves as a master energy sensor, integrating the body's energy requirements in any time with environmental conditions. The hypothalamus, a vital component in detecting hunger and organizing eating behaviour, has been extensively studied, and a crosstalk between the hypothalamus, other brain regions such as the cortex and limbic system, and the periphery is now recognized (Berthoud, Münzberg, & Morrison, 2017; Gadde et al., 2018). The basomedial hypothalamus specifically detects nutrient shortages, with distinct neuron groups responding to signals from circulating metabolites and hormones such as leptin, ghrelin, insulin, and glucose, as well as neural signals reflecting gut nutrition through the vagus nerve and brainstem, processes that can be seen graphically in Figure 2. So, it is believed that disruptions in this complex set of interactions, that are far to be fully understood, result in impaired energy balance regulation that ultimately cause the abnormal accumulation of FM (Gadde et al., 2018).

Figure 2

Neural pathways and systems controlling ingestive behaviour and energy balance.



Note. Extracted from "Blaming the Brain for Obesity: Integration of Hedonic and Homeostatic Mechanisms" (p.1732), by Berthoud et al., 2017, *Gastroenterology, 152 (7). Creative Commons Attribution – NonCommercial – NoDerivs (CC BY-NC-ND 4.0). (https://creativecommons.org/licenses/by-nc-nd/4.0/)*

Once stablished, obesity is related to metabolic impairments, such as higher blood free fatty acids, triglycerides, and glucose levels, and reduced circulating HDL-cholesterol and adiponectin. These facts are especially relevant due to two mainly associated health risks. First, a decline in HDL level related to an increased heart demand to provide enough blood to organs may ease the progression of cardiovascular disease. And second, insulin resistance clinically stated by higher insulin levels in blood may deriver in pancreas dysfunction and, finally, in type 2 diabetes. All these metabolic changes may also cause modifications in the sympathetic nervous system activity, as well as a chronic low-grade inflammation (Gul et al., 2018) that, in cases, may lead to adverse effects such as glucotoxicity and lipotoxicity (Lorenzo, 2016). Moreover, chronic inflammation has also been suggested in accelerating cancer development in genetically susceptible individuals by mechanisms which are currently not completely understood (Aminian et al., 2022). In fact, it has shown that avoiding an excess of body fatness reduces the risk of most cancers such as the colon, kidney, corpus uteri, breast and oesophagus, and more interestingly, studies in experimental animals has already suggested that intentional weight loss could be causal-related to a preventive effect of developing cancer, not established in humans trials yet (Lauby-Secretan, B., Scoccianti, C., Loomis, D., Benbrahim-Tallaa, L., Bouvard, V., Bianchini, F., & Straif, 2016). Therefore, to counteract the abovementioned health risks associated with obesity, the National Institutes of Health recommend that surgical intervention should be propose to obese patients both classified as morbid (BMI >40 $kg{\cdot}m^{-2}$) and severe (>35 $kg{\cdot}m^{-2}$) with obesity-related comorbidities (Herpertz et al., 2017; Poirier et al., 2011).

However, there is a controversy in the literature called the 'obesity paradox' which complicates medical choices to treat severe and morbid obesity based on very objective criteria. According to this medical hypothesis, obesity seems to exhibit a protective effect in certain chronic diseases, but this observation is based on associations between the BMI and clinical outcomes related to diseases which implies some limitations and it is considered not appropriate. To the contrary, determining body composition by specific FM and fat free mass (FFM) is mentioned of huge importance (Simati, Kokkinos, Dalamaga, & Argyrakopoulou, 2023) to clearly understand this paradoxical association.

Body composition assessment is being presented as a new way to classify obese patients. Around 80% of total fat is stored in subcutaneous adipose tissue. Otherwise, visceral adipose tissue implies accumulated visceral fat around internal organs and represents 20% of total fat. Some organs are closely related to BS interventions, not only directly such as the mesenteric depot around the intestines or the omental depot, but also indirectly such as liver, skeletal muscle, or pancreas (Pandžić Jakšić & Grizelj, 2016). Metabolic impairments previously described are due to the involvement of adipose tissue and skeletal muscle in lipid and glucose metabolism. These tissues release bioactive proteins associated with cardiometabolic risk factors, referred to as adipokines and myokines. With the expansion of adipose tissue, there is an increase in the infiltration of macrophages and T-cells, resulting in a pro-inflammatory phenotype (Lorenzo, 2016). While macrophages' dispersion among adipose tissue cells is about 5% in normal weight people, in obesity it rises to 50% since macrophages tend to form crown-like structures that surround apoptotic or necrotic adipocytes. This surrounding phenomenon is produced quicker in visceral adipose tissue than in subcutaneous adipose tissue because of higher rates of macrophages in the tissue (Pandžić Jakšić & Grizelj, 2016). Lastly, when infiltration occurs and the interaction between immune cells and adipocytes residing in the adipose tissue is in process, this leads to the secretion of adipokines, cytokines, chemokines, and lipids predominantly exhibiting a proinflammatory character (Lorenzo, 2016). This could be related to the 'obesity paradox' since the functional state of adipose tissue seems to be the main factor in explaining the survival benefits associated with obesity. Interestingly, it has been hypothesized that subcutaneous fat accumulation, but not visceral fat, is not related to dysfunctional changes and, consequently, may account for protective metabolic changes in people with obesity (Pandžić Jakšić & Grizelj, 2016).

All the mechanisms previously described are associated with a term which is rising interest during the lasts years and that focuses on the pathogenic role of adipose tissue. It is the adiposopathy, also called 'sick fat', a crucial condition to consider both recommending a BS intervention itself and selecting the best technique (Lorenzo, 2016). It is defined as 'pathogenic adipose tissue that is promoted by positive caloric balance, increased energy storage and sedentary lifestyle in genetically and environmentally susceptible patients' (Bays et al., 2009). Adipose tissue is an active endocrine and immune organ, among whose anatomical symptoms are visceral adiposity (Bays et al., 2009) previously explained. Then, any impairment in its function and structure will directly affect metabolic health. So, considering adiposopathy, a new classification of obesity has been proposed. This classification is closely linked to sarcopenic obesity -'the combination of sarcopenia and obesity' (Papadopetraki, A., Giannopoulos, A., Maridaki, M., Zagouri, F., Droufakou, S., Koutsilieris, M., & Philippou, 2023)-, and it defines four distinct obesity phenotypes based on body fat composition and distribution: 1) normal weight obese, 2) metabolically obese normal weight, 3) metabolically healthy obese, and 4) metabolically unhealthy obese (Lorenzo, 2016). Sarcopenic obesity is referred to the influence that inflammatory cytokines, produced by adipose tissue and more specifically by visceral adipose tissue, could have to accelerate the muscle catabolism. Cytokines, such as IL-6 and C-reactive protein, play a significant role in influencing appetite, carbohydrate and fat metabolism, and lastly energy balance, negatively affecting various organs. Increased FM elevates cytokine levels as it is mentioned previously, affecting protein metabolism and insulin sensitivity. Moreover, regarding linking among central obesity and visceral adipose tissue, which directly contributes to inflammation, its negative impact on muscle strength and its influence in development of sarcopenic obesity has been suggested (Lorenzo, 2016).

In this context, the current clinical approach to treating morbid obesity needs to be explained, with a particular emphasis on contemporary medical follow-up and surgical therapies throughout a review of common BS techniques. In this line, it is equally imperative to analyse their effectiveness in long-term weight loss and the improvement of associated comorbidities.

1.1.3 Clinical approach of morbid obesity: medical treatment.

Conservative weight loss programmes continue to emphasize lifestyle interventions centred around dietary and eating behaviour modifications, increased physical activity, and behavioural therapy. However, when these programmes prove ineffective in achieving long-term reductions in body weight (BW) or addressing obesity-related comorbidities, BS is proposed as a treatment for severe and morbid cases (Herpertz et al., 2017). As lifestyle interventions will be accurately described in a specific section below, this section is focused on the two main medical alternatives to treat severe obesity from the clinical field: pharmacotherapy and BS.

BS ultimately serves to enhance psychosocial functioning and overall quality of life. A 5-10% weight loss during the immediate perioperative period is considered clinically relevant. While lifestyle interventions have demonstrated these outcomes, a substantial portion of patients are categorized as non-responders. Furthermore, one-third to half of responders experience weight regain after initial loss. This phenomenon is even more pronounced in cases of morbid obesity, since weight loss ranges from 2% to 6.9%, becoming BS the best alternative proposed by clinicians (Herpertz et al., 2017). In fact, some current studies do not support the hypothesis that weight loss preoperatively may improve weight loss after BS, as well as they highlight the lack of medical evidence linked to support the weight loss criteria to be eligible for BS (Bettini, Belligoli, Fabris, & Busetto, 2020).

In this context, acknowledging the significance of visceral fat as a cardiometabolic risk factors it has been highlighted that BMI and other anthropometric classification methods do not precisely reflect the presence or severity of obesity-related risks, comorbidities or quality of life individually (Sharma & Kushner, 2009). This fact has leaded to propose clinical staging systems for obesity-related conditions and comorbidities whose should be considered to decide individual treatment for patients. These systems aim to adopt a more comprehensive approach to describe health status of each patient, facilitating the definition of clear indications for obesity treatment and identifying those patients who would derive the greatest benefit from BS (Valderhaug et al., 2016).

The Edmonton's Obesity Staging System (EOSS) and King's Obesity Staging Criteria (KOSC) have been spreading from recent years. Interestingly, while EOSS has been recommended to be used together with the anthropometric classification, KOSC has shown that BMI is the strongest domain to influence the clinical decision to propose a BS to patients, without enough information to recommend its use in practical field (Valderhaug et al., 2016). Thus, to the date, both the 'obesity paradox' and adiposopathy seems to be partially unsolved, so they are not included in the clinical criteria of the surgical decision-making process to treat morbid obesity despite of its influence on disease development.

So, it has been widely recognized that weight is not a direct indicator of health status or excess adiposity. While BMI is often employed as a cost-effective and straightforward tool to identify potential health risks, it is shown that relying solely on BMI is inadequate for assessing the risk associated with increased adiposity. BMI does not consider individual factors, so there is a critical need for a more precise measurement that may be implemented. In this context, anthropometric measurements such as WC, WHtR, and, when available, body composition assessment, are suitable for assessing each patient's health and may also to choose for the best treatment (Perdomo, Cohen, Sumithran, Clément, & Frühbeck, 2023).

1.1.3.1 *Pharmacotherapy: a first step combined with lifestyle interventions.*

As explained previously, several neural pathways and systems control eating behaviour patterns and energy balance (Berthoud et al., 2017). To modify their activity, several anti-obesity medications are in development or already in use. The most common is orlistat, leaded to inactivate gastric and pancreatic lipase, but there are currently some different anti-obesity medications approved which act throughout effects on neurotransmitters in central nervous system pathways. These vias regulate food intake to decrease hunger and food reward, promote satiation, or to reach a combination of these three effects (Perdomo et al., 2023).

To select pharmacological therapies as treatment, the most value outcomes to each patient, as well as factors such as comorbidities, cardiometabolic risk factors, age, and body fat distribution should be considered in decision-making. Patients that are unable to reach or maintain a 5-10% weight loss clinically required by multimodal management over 6 to 12 months, as well as those who present any metabolic dysfunction or extremely risked comorbidity, might be eligible for pharmacological treatment (Gul et al., 2018; Perdomo et al., 2023). Thus, it is relevant to consider the significant advances in antiobesity medications such as glucose-dependent insulinotropic polypeptide and glucagon-like peptide-1 (GLP-1) receptor agonists (semaglutide and liraglutide). The latter affects appetite, gastric emptying, glucose-dependent insulin release, glucagon secretion and pancreatic β-cell growth, with a positive impact on reducing body weight and diminishing risk of cardiovascular events in obese adults without diabetes (Elmaleh-Sachs et al., 2023).

Recommending pharmacotherapy has been only proposed as a complementary treatment due to its limited evidence of efficacy, its lack of evidence related to the effect on cardiovascular events, and inter-individual variation in weight loss response (Bray, Frühbeck, Ryan, & Wilding, 2016; Perdomo et al., 2023). Even so, current evidence shows that GLP-1 receptor agonists achieve roughly 8% to 21% weight loss, compared to the 25% to 30% weight loss attained by BS (Elmaleh-Sachs et al., 2023). In any case, it is counselled that comprehensive obesity treatment combines behavioural, nutritional and physical activity interventions, as well as bariatric procedures depending on individual needs for patients (Elmaleh-Sachs et al., 2023).

1.1.3.2 *Bariatric surgery: clinical criteria and preoperatively general management.*

BS is typically considered for patients with a BMI ≥ 40 $kg \cdot m^{-2}$ alone or ≥ 35 $kg \cdot m^{-2}$ when accompanied by severe comorbid conditions like type 2 diabetes, obstructive sleep apnoea or coronary heart disease. This recommendation is applicable when a dedicated six-month medical treatment or lifestyle modification fails to achieve and maintain sufficient weight loss. But, for patients categorized as class IV or higher (BMI ≥ 50 $kg \cdot m^{-2}$) the option of BS may be proposed without the prerequisite of prior lifestyle intervention (Khwaja & Bonanomi, 2010; Neylan, Kannan, Dempsey, Williams, & Dumon, 2016). In practice, the percentage excess weight loss is a relative outcome measure in the context of BS. To control the progress, EBW is considered and clinically followed since is the weight exceeding the ideal BW, commonly determined by BMI ≥ 25 $kg \cdot m^{-2}$ (Herpertz et al., 2017). However, long-term maintenance of weight loss is still challenging for most people currently. To assist patients in reaching and sustaining sufficient weight loss to the management goal, a multimodal approach to treatment is recommended. If the management do not lead to reach the medical outcomes, BS would be proposed (Perdomo et al., 2023).

In this context, preoperative multimodal management should be mentioned. In terms of diet and behaviour therapy, medical supervision and follow-up is currently administrated to BS patients. On one hand, low-calorie diets are designed to stimulate weight loss based on proportioning less energy than required for daily maintenance. Thus, there are two protocols in field to accomplish the main weight loss goal which are feasibly proposed to BS patients. First, a reduction of 500 kcal/day below energy requirements, and second, using a dietary plan that has 1200-1500 kcal/day for women or 1500-1800 kcal/day for men, which could be increased in 300 kcal/day if BW exceeds 150 kg (Bray et al., 2016). However, when weight loss goal is not achieved, patients are recommended to follow a very low-calorie diet which comprise 200-800 kcal/day and enough protein (70-100 g/day) to preserve FFM (Bray et al., 2016; Gul et al., 2018). Traditionally, a 2-week liquid protein diet is prescribed to induce weight loss before BS (Parikh et al., 2012).

On the other hand, in reference to behaviour therapy, it is widely demonstrated that performing the preoperative diagnostics is determinant to assess psychosomatic or psychosocial issues in patients waiting for BS. Its predictive value is essential to offer an early treatment to ensure the benefits in weight loss and quality of life after BS. In this regard, it has been shown that preoperative depression correlates negatively with the percentage weight loss after surgery, as well as preoperative eating disorder leads to a high risk of problematic eating behaviour after BS (Herpertz et al., 2017).

1.1.3.3 *Bariatric surgery: procedures and techniques.*

Distinct surgical procedures to treat severe and morbid obesity have been widely used over decades. They are classified depending on: a) techniques that cause a restriction of food intake; and b) techniques that cause the malabsorption of food. In turn, they give rise to three categories: restrictive operations, malabsorptive operations, and combined operations (Poirier et al., 2011).

Each procedure results in a degree of weight loss, with its particular risks and benefits which should be considered (Bray et al., 2016). Although there is no consensus concerning the best procedure overall, restrictive operations have shown to have a lower mortality with a lower rate of surgical and nutritional complications compared with the other procedures. But, on the opposite, they causes less WL, which is achieved more slowly than other surgical interventions, and additionally, require more postoperative medical visits (Poirier et al., 2011). Based on this classification, there are six techniques could be clearly distinguished (Khwaja & Bonanomi, 2010) (Table 3).

Table 3

Classification of bariatric surgery procedures.

PROCEDURE	TECHNIQUE
Restrictive operations	Laparoscopic adjustable gastric band (LAGB) Laparoscopic sleeve gastrectomy (LSG) Vertical banded gastroplasty
Malabsorptive operations	Bilio-pancreatic diversion Bilio-pancreatic diversion with duodenal switch
Combined operations	Roux-en-Y gastric bypass (LRYGB)

Note. According to: (Khwaja & Bonanomi, 2010)

However, regarding the quickly development of laparoscopic technique in recent decades, the most common surgical techniques are LSG, LRYGB and LAGB (Khwaja & Bonanomi, 2010; Neylan et al., 2016).

LSG combines a restrictive mechanism in the stomach and a reduction of the appetite-related gastric hormones ghrelin and peptide YY levels (Poirier et al., 2011). Previously, LSG was the first stage of other surgical technique which modifies the duodenum, but because of its easier implementation and benefits in weight loss and comorbidity improvement, it is suggested as highly effective to loss BW (Khwaja & Bonanomi, 2010), but not superior to LRYGB for now (Neylan et al., 2016).

LRYGB is considered the gold standard of BS (Khwaja & Bonanomi, 2010; Poirier et al., 2011). This technique not only does present the same benefits as LSG, but also increase the level of GLP-1 and glucose-dependent insulinotropic peptide (GIP), which might contribute to treat type 2 diabetes and satiety by restrictive and hormonal mechanisms (Khwaja & Bonanomi, 2010). Moreover, it produces a reduction of intestinal food absorption. This fact seems to make this technique be lightly superior to LSG. However, its surgical complexity influences in its application and, in field, LSG is currently more performed (Khwaja & Bonanomi, 2010; Neylan et al., 2016).

Last, LAGB technique creates a 10-15 ml gastric pouch, reducing the rate of food entry, which provoke that the stomach wall is stretched and causes early satiety perceived by the hypothalamus, and thus, the appetite decreases. It is a totally reversible procedure but its effects are dependent on the maintenance of the gastric pouch diameter (Khwaja & Bonanomi, 2010). In addition, due to its higher complication rate and inferior results in weight loss compared to LSG and LRYGB in the long term (44% vs 56% vs 67%, respectively)(Neylan et al., 2016), it is currently less performed. But interestingly, it is associated with less loss of FFM (Poirier et al., 2011).

Regarding improvements in comorbidity and mortality in long term, LRYGB has shown benefits on several comorbidities. First, dyslipidaemia improves due to triglycerides and LDL decrease, as well as HDL levels rises. Second, in cases of hypertension, obstructive sleep apnoea and/or NAFLD, few medications used and/or lower risk of incident and symptoms have been reported. Third, benefits in type 2 diabetes such as less use of glucose-lowering medications or reduction in microvascular and macrovascular complications have been shown. And lastly, a decrease in adverse cardiovascular events has been observed (Perdomo et al., 2023).

It is relevant to note its association with a lower cancer-related mortality, which it has been recently observed and analysed but not enough to differentiate between types of cancer. In this line, researching the link between obesity and cancer risk reduction after BS has been suggested by focusing on types of cancer causally related to obesity (Aminian et al., 2022).

In any case, weight regain is one of the biggest clinical challenges in long-term care (Monaco-Ferreira & Leandro-Merhi, 2017; Perdomo et al., 2023). Thus, to the date, these surgeries have only demonstrated to be useful to sustainably reduce BW whether patient change diet habits, practice regular exercise and an exhaustive bariatric follow-up is carried out (Khwaja & Bonanomi, 2010).

1.1.4 Multimodal management of morbid obesity: a lifestyle and behavioural intervention.

BS is considered the most effective treatment to induce weight loss and reduce morbimortality in severe obese patients, but it may be related to clinical problems and side effects, especially in the nutritional status (Bettini et al., 2020) and the psychological process required to be adapted to changes in eating behaviour and body image (Bettini et al., 2020). In this line, the importance of behavioural intervention in the treatment of morbid obesity is undeniable. However, the isolated effect of psychological strategies and behaviour modification techniques used to improve health status, prepare patients for BS and maintain long-term results are considerably discussed. This point includes diet, physical activity and behavioural therapy.

In terms of decision-making, a guideline for the management of overweight and obesity in adults related to reduce cardiometabolic risk factors was published both in USA (Jensen et al., 2014) and Europe (Yumuk et al., 2015). Through their treatment algorithms to be carried out in clinical care, weight loss options include comprehensive lifestyle intervention alone or with adjunctive therapies to treat morbid obesity. Generally, BS is no mentioned unless patients have not responded to behavioural treatment to achieve enough weight loss, with presence or not of pharmacotherapy. In fact, it is recommended to encourage patients to undertake a comprehensive lifestyle treatment alone as a first step to get weight loss if this option has not been tested previously, with no link to be a BS candidate in the future unless clinical criteria regarding comorbidities and BMI are presented (Jensen et al., 2014; Yumuk et al., 2015).

Independent of their eligibility for BS, multimodal interventions focused on modifying lifestyle is the core of obesity treatment, specially by practising regular physical activity, since most patients are insufficiently active both pre and postoperatively (King & Bond, 2014). It seems that weight loss before BS may be positive to surgical outcomes, reducing both surgical problems such as anastomotic leakage, bleeding and infections, and post-intervention risks (e.g. protein and micronutrient deficiencies), as well as improving short-term efficacy (Bettini et al., 2020; Tabesh, Maleklou, Ejtehadi, & Alizadeh, 2019).

Generally, as it is mentioned before, preoperatively behavioural interventions are based on modifying lifestyle of individuals with obesity by provoking a negative energy homeostasis imbalance to stimulate weight loss both by caloric-restriction diets and recommending practicing regular physical activity (Bettini et al., 2020; Gul et al., 2018; Parikh et al., 2012; Tabesh et al., 2019). Additionally, behaviour therapy includes advice tips and strategies to help patients to adhere both to the diet and the PA programmes (Gul et al., 2018).

1.1.4.1 *Nutritional approach: effects, controversies and problems after BS*

Regarding eating behaviours and diet approach, the role of very low-calorie diet interventions in preoperative period is consolidated (Gul et al., 2018; Tabesh et al., 2019). However, it is crucial to consider that it leads to an increased oxidative stress and a catabolic state that induce to negative impact on surgical outcomes. Among them, FFM loss is highlighted because it could drive to a decrease on resting energy expenditure (REE), what in turn may predispose patients to weight regain, and finally, to impair the long-term success of BS. When many patients experience difficulties to accomplish the recommended daily protein intake of 1.5-2.1 g/kg ideal weight, this fact turns highly worrying since malnutrition may further worsen FFM loss (Guida et al., 2018). To deal with this issue, it has been recently suggested an alternative to induce weight loss through a very low-calorie ketogenic diet. Reductions in liver and visceral fat volume have been shown, as well as improvements in clinical parameters such as glycaemic and lipid profiles, and post-operative haemoglobin levels. However, its wholesome prescription in preoperative patients is under debate. Very low-calorie ketogenic diet is based only on a protein substrate, so it has been suggested that changes in liver and visceral fat volumes need to be accurately measured to know its effect, especially regarding physiological changes in some organs (Bettini et al., 2020).

Skeletal muscle represents the most of FFM, and the contribution of skeletal muscle metabolism in REE is determinant. Surprisingly, a previous study showed that the higher FFM before BS, the higher FFM loss registered 1 year after LSG, especially in males (Guida et al., 2018). Also, type II fibres are mentioned as the most susceptible to suffer atrophy by lack of nutrient availability, since the predominant metabolism is glycolytic and oxidative in subtype IIa and IIb, respectively. Then, it was hypothesized they would be seriously affected because of their impossibility to adapt by burning fatty acids to obtain enough energy. Consequently, preoperative FFM was considered a risk factor for losing more FFM, at least, after LSG (Guida et al., 2018). So, this finding may ease the early diagnose of patients with specific nutritional needs of support to keep FFM after BS, being in turn a determinant of the preoperative nutritional approach.

Generally, an excess weight loss ≥ 50% is clinically considered an indicator of success in BS (Larrad & Sánchez-Cabezudo, 2004), but as it has been mentioned previously, determining body composition by specific FM and FFM is relevant to make a suitable approach. In this regard, a previous study showed that lower preoperative %FM was associated with a higher probability of success in weight loss of patients 1 year after RYGB. So, the assessment of body composition has already specified as indispensable to stablish new definition criteria of success in BS (Vázquez-velázquez et al., 2018), although the diet and exercise protocols are not well-stablished to achieve this goal yet.

The nutritional impact of the BS techniques is imperative. After the intervention, patients should gradually and progressively change the food consistency based on dietary instructions received by clinicians. Next, diet management transforms dietary counselling focused on guarantee the adaptation of patients eating behaviour to the digestive effects of BS, as well as the general recommendations of a healthy nutrient dense diet (Bettini et al., 2020). In this process, sufficient protein intake is considered to prevent FFM loss in weight loss process, but its accomplishment is usually reduced after BS due to the difficulties in reaching it with natural foods. This context leads to using protein supplementation to preserve FFM (Bettini et al., 2020). And interestingly, regarding multimodal approach after BS, the importance of strength training has already been emphasized to increase muscle strength (Tabesh et al., 2019) and keep FFM (Bettini et al., 2020).

1.1.4.2 *Behavioural items: what is relevant to consider*

Currently, research has tried to identify several predictors of success after BS but it has emerged tough. Most of factors are characterized as barriers to the treatment due to being non-modifiable, so interest is now focusing on detecting modifiable preoperative predictors such as weight loss, FFM and psychosocial factors like eating behaviours or physical activity (Guida et al., 2018; Livhits et al., 2012). All that leads to rise knowledge in the area and, subsequently, facilitate its application in proposing lifestyle interventions similar to prehabilitation programmes already used in other surgical specialities. Prehabilitation is a complex intervention aimed to prescribed exercise in healthcare systems throughout profound understanding behavioural, psychological, physiological, environmental, and social factors to be successful in adherence of patients, and consequently, in postoperative outcomes (Wynter-Blyth & Moorthy, 2017). Ultimately, prehabilitation implies a multimodal, interdisciplinary management of patients.

In this regard, a recent study in which a 24-36 month's follow-up was carried out, suggested the influence of preoperatively psychological issues such as alexithymia, anxiety and depression as likely predictors of a lower weight loss after BS (Lai et al., 2021). Moreover, a recent systematic review analysed preoperative behaviour factors related to weight loss outcomes in at least of two years after BS and concluded that more research is required (Kourounis, Kong, Logue, & Gibson, 2020). Both weight loss and maladaptive eating behaviour prior to BS might be positive or non-predictor of weight loss after BS, while regarding physical activity, lacking data made difficult to conclude its influence and impact on postoperative outcomes. In fact, it suggested that although preoperative weight loss seems to be positive, considering the rigorous use of maladaptive eating behaviours before BS as a barrier to BS could be not suitable for all patients (Kourounis et al., 2020).

Again, getting common predictor and outcome measures is imperative in clinical management of patients waiting for BS due to the heterogeneity of studies. Knowing these parameters would let to design more suitable preoperative programmes to improve current lifestyle interventions.

1.1.4.3 *Sedentary lifestyles and physical inactivity: clinical approach*

The beneficial role of being physically active is unquestionable, especially in preventing chronic diseases (e.g. obesity, diabetes mellitus, and cardiovascular disease), by reducing its morbimortality, and the most widely spread in society, by enhancing weight loss (King & Bond, 2014). These benefits become more relevant in patients with morbid obesity, candidates to undergone a BS, since these surgical procedures are often related to musculoskeletal problems which affect their exercise tolerance and functional capacity (Tabesh et al., 2019). For these patients, it is determinant to improve their quality of life prior BS (Bond, Thomas, et al., 2015).

Most of preoperative patients are insufficiently active and not accomplish general physical activity recommendations for health, a condition linked to fail in their attempt to change after BS without support nor guidance (King & Bond, 2014). However, this sedentary lifestyle is not exclusive to BS patients, but also people with obesity in all-grades classification. A recent systematic review showed the weight management as the key physical activity motive to be physically active, while lack of motivation and pain was mentioned as barriers (Aurélie Baillot, Stéphanie chenail, Naiara Barros Polita, Mylène Simoneau, Mathilde Libourel, Evy Nazon, Eléonor Riesco, Dale S. Bond, 2021). In fact, other research showed that postoperatively patients who participated in a supervised PAP did not change their behaviour of physical activity although their future intention at the end of the programme were to be active. Then, it suggested that the end of a PAP symbolised a key barrier for taking an active lifestyle (Beltrán-Carrillo et al., 2019). These results drive to reflect on the relevance of dealing with stimulating an active lifestyle prior to BS and not to merely provide general recommendations of physical activity to be achieved in the long-term postoperatively. Especially, because both weight regain (Livhits et al., 2012), and raised energy consumption occur in long-term (Christou, N. V., Look, D., & MacLean, 2006; Monaco-Ferreira & Leandro-Merhi, 2017). Therefore, stimulating healthy habits associated with physical activity seems to be determinant and dependent of individual preferences to keep its benefits in long-term.

Regarding clinical goals linked to weight loss in BS candidates, current evidence shows that preoperative lifestyle interventions in which physical activity is included are associated with significantly greater weight loss (Bond, Vithiananthan, et al., 2015; Marcon et al., 2017; Papalazarou et al., 2010; Tabesh et al., 2019) compared to usual care, but its contribution in weight regain prevention and weight loss after BS are still not clear enough (Kalarchian, Marcus, Courcoulas, Cheng, & Levine, 2016; Pouwels, Sanches, Cagiltay, Severin, & Philips, 2020). However, a lifestyle intervention based on physical activity should be not confused with other interventions in which physical exercise is carried out by specific and individualised training methodologies. This difference would help to contemplate a suitable clinical approach to settle more specific protocols in preparation of patients waiting for BS.

Despite current research, clinical approaches only include general recommendations to increase physical activity that are usually reported to patients. These usually include mentioning programmed activities (e.g. walking, biking, aerobic classes or similar) and lifestyle activities present in daily habits (e.g. using stairs, lower time for watching TV, etc.) (Gul et al., 2018). Any of different alternatives of physical activity or exercise practice is directly dependent on individual patients' factors such as motivation, economic resources or personal circumstances.

Recently, prehabilitation programmes has been offered as a feasible pathway for stimulating active lifestyles and optimising outcomes after surgical procedures (Wynter-Blyth & Moorthy, 2017). However, regarding the inclusion of prehabilitation and exercise in perioperative care of BS, the level of current evidence is considered low, and consequently, the grade of recommendation is also qualified as weak (Stenberg, E., dos Reis Falcao, L. F., O'Kane, M., Liem, R., Pournaras, D. J., Salminen, P., ... & Thorell, 2022).

Therefore, although physical activity is at the core of interdisciplinary obesity management, specific PAP are not included in clinical approaches nowadays. So, the only management available is recommending 150 min per week of moderate aerobic exercise combined with 1-3 sessions per week of resistance exercise (Yumuk et al., 2015). The most suitable type of exercise and combinations, as well as its variables to prescribe accurately in preoperative obese patients, have been gathered in a recent study (Tabesh et al., 2019), but it is a question still under research.

1.2 Physical activity and exercise programmes before BS: the current framework.

Just as food marketing practices, the institutionally driven decrease in physical activity is known as one of 'the big two' factors that contribute to the obesity epidemic (Mcallister et al., 2009). However, they are not isolated since some complementary hypotheses are under debate on that subject: e.g. the gut microbiome, social-psychological factors, or environmental exposures such as endocrine disruptors (Davis, Plaisance, & Allison, 2018). Then, some data are relevant to summarise before describing exercise programmes currently carried out by patients awaiting BS for a better understanding. As it is mentioned before, adiposopathy is related to sarcopenic obesity and, both terms together, lead the obesity classification to consider differences between healthy and unhealthy obese people (Lorenzo, 2016). This fact is especially important due to the previously described relevance of accumulation of visceral fat as an independent cardiovascular risk factor (NIH Report, 1998).

Rising knowledge of weight gain pathophysiology and endocrinologic factors is paving the way for enhanced obesity management strategies. The concept of 'metabolic obesity' has emerged as a valuable tool for identifying individuals with obesity associated with an increased risk of cardiovascular disease (Osama Hamdy, Sriurai Porramatikul, 2006). Additionally, 'metabolic healthy obesity' should be considered as this phenotype exhibits distinct characteristics compared to unhealthy obesity including normal glucose and lipid metabolism levels, preserved β-cell function, and improved cardiorespiratory fitness (Blüher, 2020). These critical distinctions pose challenges in accurately assessing the effectiveness of exercise programmes in preoperative obese patient research studies. So, it is relevant to know the variables to prescribe exercise in terms of frequency, intensity, type and volume that are commonly used in current research.

Preoperatively people with obesity are recommended to practice physical activity regularly as part of multimodal management. Its positive impact on physical fitness, muscle strength and coordination is well-known (Aurélie Baillot, Stéphanie chenail, Naiara Barros Polita, Mylène Simoneau, Mathilde Libourel, Evy Nazon, Eléonor Riesco, Dale S. Bond, 2021). However, although feasibility of presurgical interventions based on physical activity has been demonstrated, its most effective prescription needs to be elucidated in obese patients waiting for BS (Al-Hazzaa, 2016). And more specifically, its impact on postsurgery outcomes, and consequently, in the long-term management of patients (Bellicha et al., 2021a).

1.2.1 Training methods in preoperative obese adults

One of the main problems in BS candidates is the time availability to adhere to physical activity, so choosing the appropriate type of activity depending on personal preferences, age, current weight, aerobic fitness level, range of motion and comorbidity results fundamental (Al-Hazzaa, 2016). In obese patients, aerobic exercise has been the most recommended over the years, and in terms of clinical weight loss, the American College of Sports Medicine considers to get this goal the practice of moderate physical activity above 250 min per week (Donnelly et al., 2009). Now then, selection among HIIT or MICT is under debate since, both training protocols seem to be related to improvements in body fat, lipid profile, insulin sensitivity and aerobic power though, HIIT seems to be not suitable for all patients (Al-Hazzaa, 2016). Additionally, a recent review concluded that programmes in which aerobic and resistance training were combined seem to be the most promising and usually recommended in the context of BS to improve both muscular and cardiorespiratory fitness (Bellicha et al., 2021a).

Besides, regarding aerobic exercise, training performed at Fatmax is also considered, although there is few evidence in obese adults, with no mention in patients waiting for BS. In this line, metabolic flexibility, defined as the ability to adapt substrate oxidation rates in response to changes in fuel availability (Rynders, Blanc, DeJong, Bessesen, & Bergouignan, 2018), needs to be mentioned since it has been shown that plays an important role in regulation of fuel homeostasis and metabolic health. Likewise, it is also relevant to consider that regulation of macronutrient oxidative balance depends on the storage and oxidative capacity of them (Rynders et al., 2018). When these aspects fail, they are closely associated with a metabolic phenomenon known as lipotoxicity, which consists of the inability of adipose tissue to meet the demand of storing the excess of energy, and its consequent accumulation as ectopic fat, negatively affecting to many organ systems such as skeletal muscle or heart (Lorenzo, 2016). Therefore, determining guidelines to train at Fatmax is currently difficult due to the lack of knowledge and research regarding metabolic state and acute macronutrient consumption in obese adults, which could influence fat oxidation rates performing exercise (Chávez-Guevara, Amaro-Gahete, Ramos-Jiménez, & Brun, 2023).

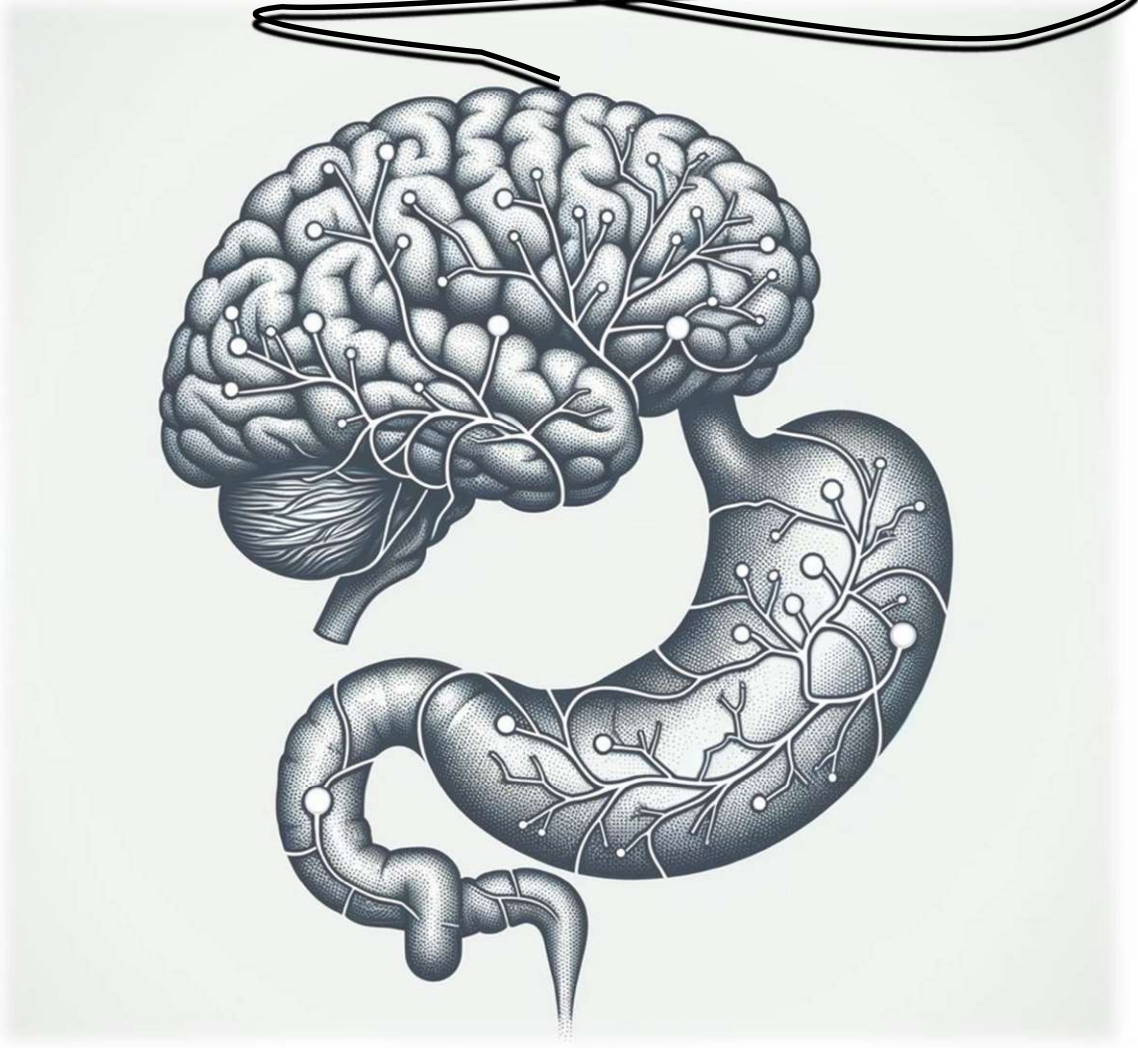
Concerning resistance training, a systematic review has been suggested that it may be useful to prevent loss of strength and muscle mass after BS, although there is not shown any intervention prior to BS focused on strength training accurately prescribed (Schurmans, Caty, & Reychler, 2022). This is interesting to note since impaired strength have been shown in obesity, linked to impaired work capacity as well (Marks & Rippe, 1996).

1.2.2 Exercise prescription in preoperative obese adults

Particularly for candidates for BS, a recent review (Baillot et al., 2022) that compiled controlled trials with interventions carried out before BS, demonstrated that are scarce and heterogeneous. Duration between interventions varies from 4 weeks to 26 weeks, being the longest one the study 2 included in this Doctoral Thesis. Regarding type of exercise, both strength exercise based on a core stabilization exercise programme and endurance and resistance training with an accurate prescription in terms of volume and intensity have been tried. Other interventions are based on home walking or aquatic exercises, only specifying session total time and weekly frequency. Ultimately, the limited and heterogeneous nature of the available data complicates decision-making aimed at establishing exercise training protocols under real-life conditions that can be tailored to the clinical requirements of candidates for BS.

Positive effects on health linked to following a supervised exercise training programme are plausible but also premature about to identify the most beneficial intervention. First, both cardiorespiratory and anthropometrical improvements have been shown, and in terms of keeping FFM, the type of training has been mentioned as relevant to explain the absence of significant results since aerobic exercise is more frequent in most of the interventions. Besides, muscle training increases strength and slows down muscle atrophy in obese adults (Schurmans et al., 2022), so further research is needed in BS context that could confirm these results preoperatively. Second, functional capacity seems to improve and it might be related to induce a moderate weight loss, as well as maximal oxygen uptake (VO_{2max}), that increase with exercise training and is associated with a shorter hospital staying (Bellicha et al., 2021a). Third, there is not enough evidence regarding the effect of exercise in quality of life before BS. Surprisingly, exercise itself has not shown additional significantly benefits on health postoperatively, that which could be explained with the fact that BS is independently associated with considerable improvement in quality of life. And last, there are insufficient studies in which the impact of preoperative exercise on cardiometabolic health has been assessed (Bellicha et al., 2021a).

RESEARCH STUDIES



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2. Research studies: the rationale behind incorporating each article in this thesis

This Doctoral Thesis belongs to the project titled '*Physiological and psychological effects of a physical activity program in bariatric patients*', carried out collaboratively by GIAFIS and '*Grupo de Investigación en Comportamiento Motor*' (GICOM) at Sports Research Centre at Miguel Hernández University. Study design is highly influenced by previous research developed in the context of the effects of physical activity in BS. To a better understanding, it is crucial summarizing previous research presented and linked to this project, since this Doctoral Thesis follows the same research line and aims to complement their results.

As mentioned earlier, the focus of the project by GIAFIS was on the effect of different ETP implemented at different timing after surgery. In one of the works (Marc-Hernández, Ruiz-Tovar, Aracil, Guillén, & Moya-Ramón, 2020), the impact of a supervised 5-month ETP developed three years after BS in postoperative patients experiencing weight regain, was studied. In a second work (Marc-Hernández García, 2017), an ETP was carried out immediately postsurgery. When I joined the group, the focus was turning to the effects of presurgical ETP, and a first work, consisting of a short-time intervention was in development (Marc-Hernández, Ruiz-Tovar, Aracil, Guillén, & Moya-Ramón, 2019).

In parallel, other colleagues from the GICOM were studying the motivational and psychological traits of this population (Jiménez Loaisa, 2021). Employing qualitative research methodology, weight stigma, healthism and facilitators and barriers perceived to practice physical activity were explored (Beltrán-Carrillo et al., 2019; Jiménez-Loaisa, Beltrán-Carrillo, González-Cutre, & Jennings, 2020). Besides, levels of physical activity, quality of life and motivation to be physically active postoperatively were also analysed after a physical activity intervention based on self-determination theory (González-Cutre et al., 2020; Jiménez-Loaisa, González-Cutre, Beltrán-Carrillo, & Alcaraz-Ibáñez, 2020). Their results highlighted the importance of weight stigmatization and discrimination in the daily life of obese people, as well as the huge difficult to change habits of physical activity independently of improving levels of satisfaction in autonomy, competence and relatedness after participating in the physical activity intervention. Likewise, their results were mainly focused on assessing and understanding of their own context perception by

BS patients, with and without physical activity intervention, from a psychological perspective (Jiménez Loaisa, 2021).

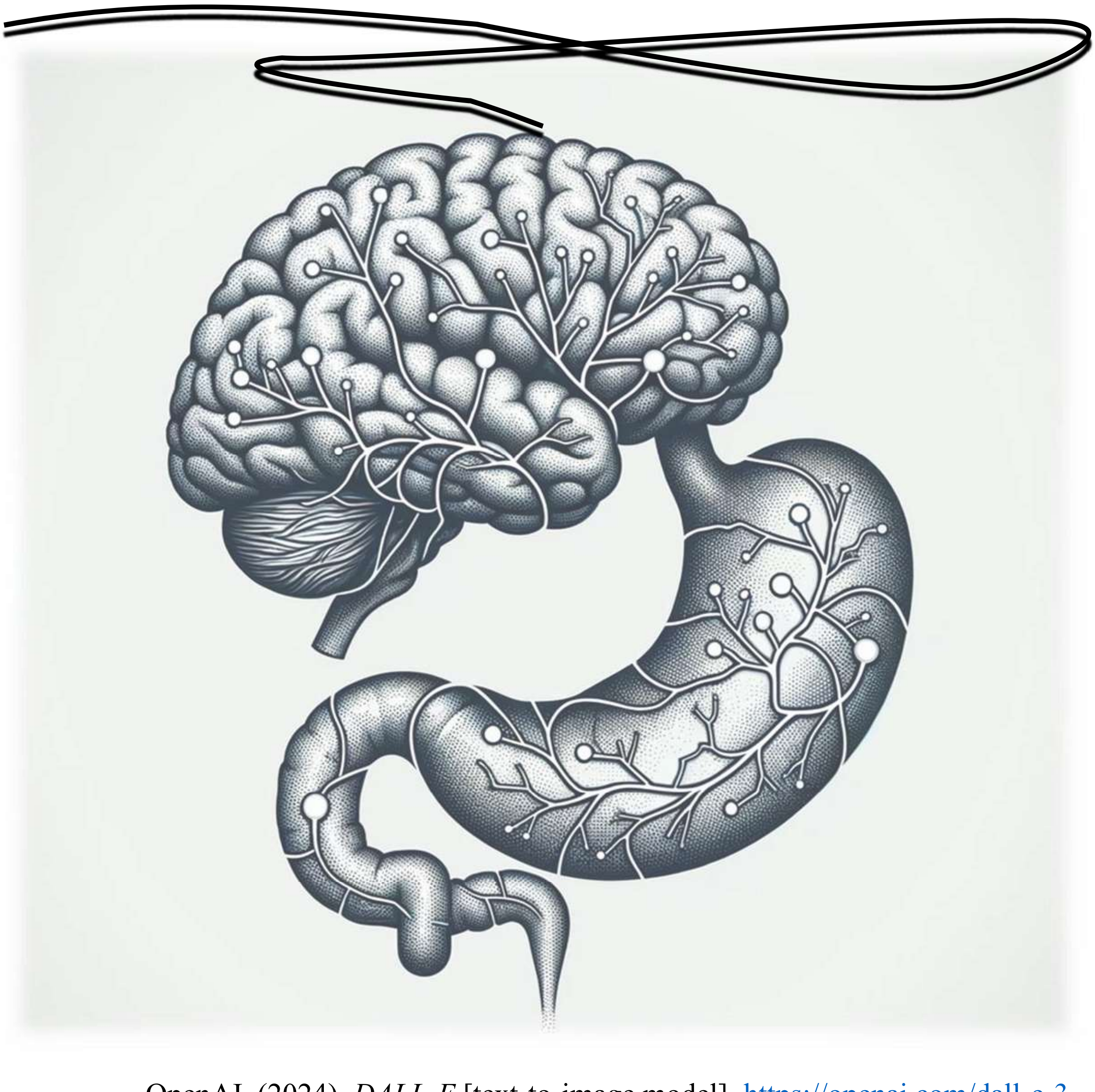
Therefore, my research work is specifically focused in implementing different types of ETP in patients waiting for BS, and it is composed of the following works:

Study 1 is carried out to explore the state of knowledge regarding physical activity in the context of BS (Moya-Ramón Manuel, Picó-Sirvent, Inés, Aracil, 2018). Heterogeneity in type of physical activity and its prescription, lack of research in preoperative physical activity field, and short duration of the interventions influence the design of the experimental studies that are shown in this thesis.

Study 2 is a pilot study in which a combined ETP with high workloads is prescribed, with an accurate prescription in terms of volume, intensity and workload control during a six-months intervention. The length of the study is justified because BS is recommended when a six-month medical treatment or lifestyle modification fails to loss enough total body weight, as it is described previously. Considering recovery between sessions, HIIT and MICT methodologies to train endurance are alternated, considering MICT as a recovery session with lower workloads prescribed based just on aerobic exercise (Picó-Sirvent, Aracil-Marco, Pastor, & Moya-Ramón, 2019).

In contrast, ***Study 3*** is an experimental study in which study design is similar to study 2 but prescribing low workloads both in endurance and resistance training. In this study, length is shorter due to limitations out of our control. This study aims to improve the limitations detected in the assessment protocol, as well as considering individual metabolic differences related to fat oxidation (Picó-Sirvent, Manresa-Rocamora, Aracil-Marco, & Moya-Ramón, 2022)

HYPOTHESIS



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3. Hypothesis

Throughout this introduction, the context and relevance of the research presented in this compendium of articles are established. According to the previously reported scientific evidence, this Doctoral Thesis relies in the general hypothesis that the introduction of different PAPs in patients awaiting BS will result in improvements in their BW, BMI, body composition, physical functioning and energy expenditure.

More specifically, the following hypotheses were established in each of the studies:

Study 1

Considering that study 1 is a review article, no hypothesis was formulated. Later, it served to generate them for studies 2 and 3, as well as to identify aspects of interesting relevance to future research.

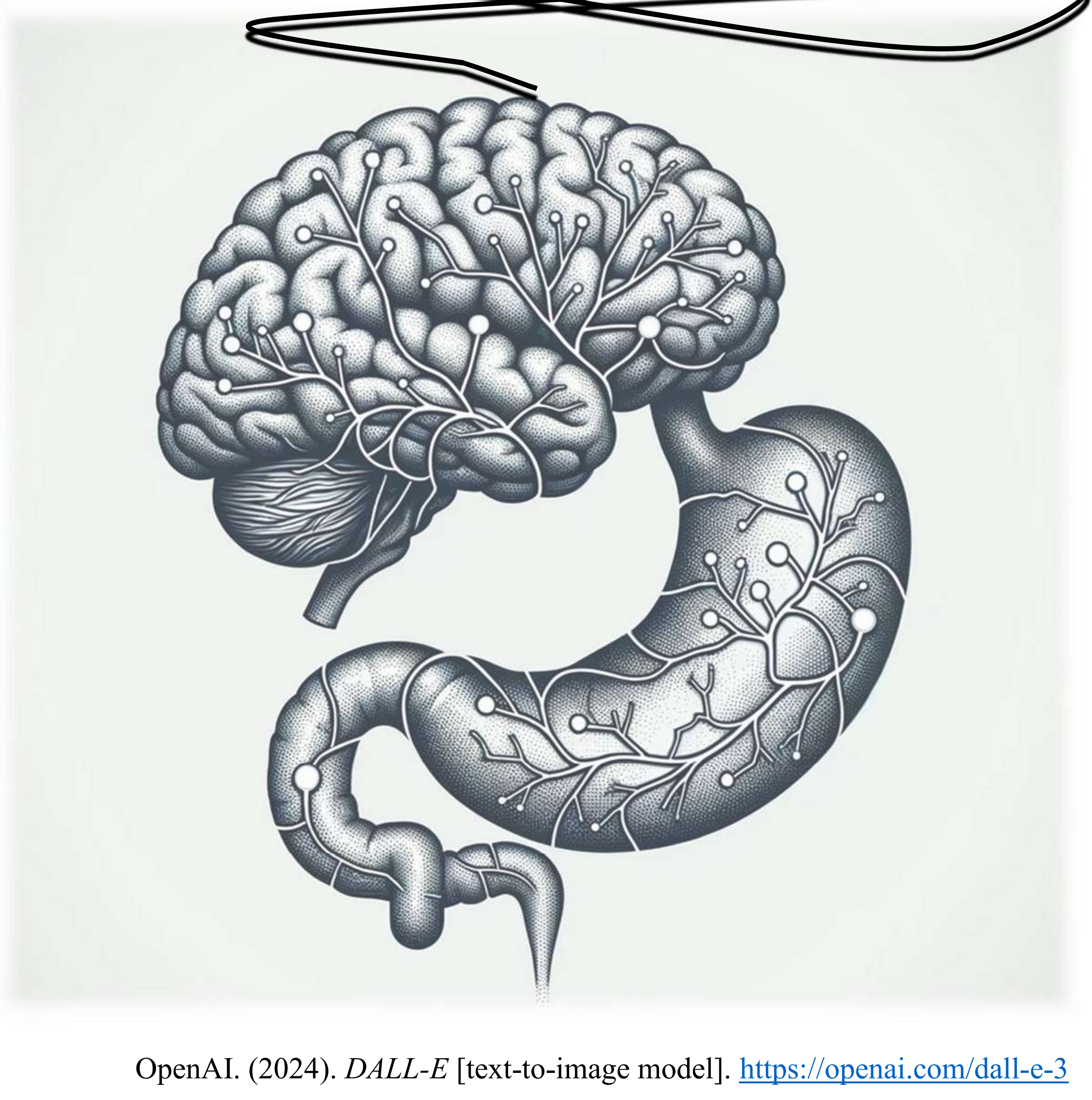
Study 2

1) An ETP in which HIIT and high-workloads resistance training are combined will benefit weight loss and health status in preoperative class IV obese patients.
2) Including resistance training will positively contribute to maintain FFM in this population.
3) Despite its long-duration, a high-workload ETP, individualized and monitored, will be well-tolerated and feasible to be performed by obese patients awaiting BS.

Study 3

4) Substrate oxidation will be positively influenced by an ETP based on aerobic training at individual Fatmax and low-intensity resistance training in obese women awaiting BS.
5) Resistance training at low workloads will be equally effective to preserve FFM in women patients for BS.
6) Fat oxidation will improve both at rest and during exercise after performing an ETP in women awaiting BS, associated with an improvement in body composition.

GENERAL AND SPECIFIC OBJECTIVES



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4. General and specific objectives

4.1 General objective.

Individual, periodized and monitored ETP in morbid obese adults need to be researched to know how to design effective protocols and interventions. Then, this Doctoral Thesis is aimed to explore the effects of different ETP in patients awaiting BS, trying to overcome the limitations of previous published works in the field. Therefore, the ultimate aim of this Doctoral Thesis is to contribute to generate evidence that could clarify in the future the role of periodized and personalized ETPs during the clinical management of patients before BS.

4.2 Specific objectives of each research article.

With the aim to contribute to the general objective of this Doctoral Thesis, the following specific objectives were addressed at each study:

Study 1

1) To update the field of knowledge regarding the impact of physical activity programmes in BS patients, both in preparation and follow-up after surgical interventions, on anthropometric and fitness status.
2) To summarise methodologies and protocols of physical activity programmes carried out in previous research.
3) To identify potential knowledge gaps that could be the subject of future research.

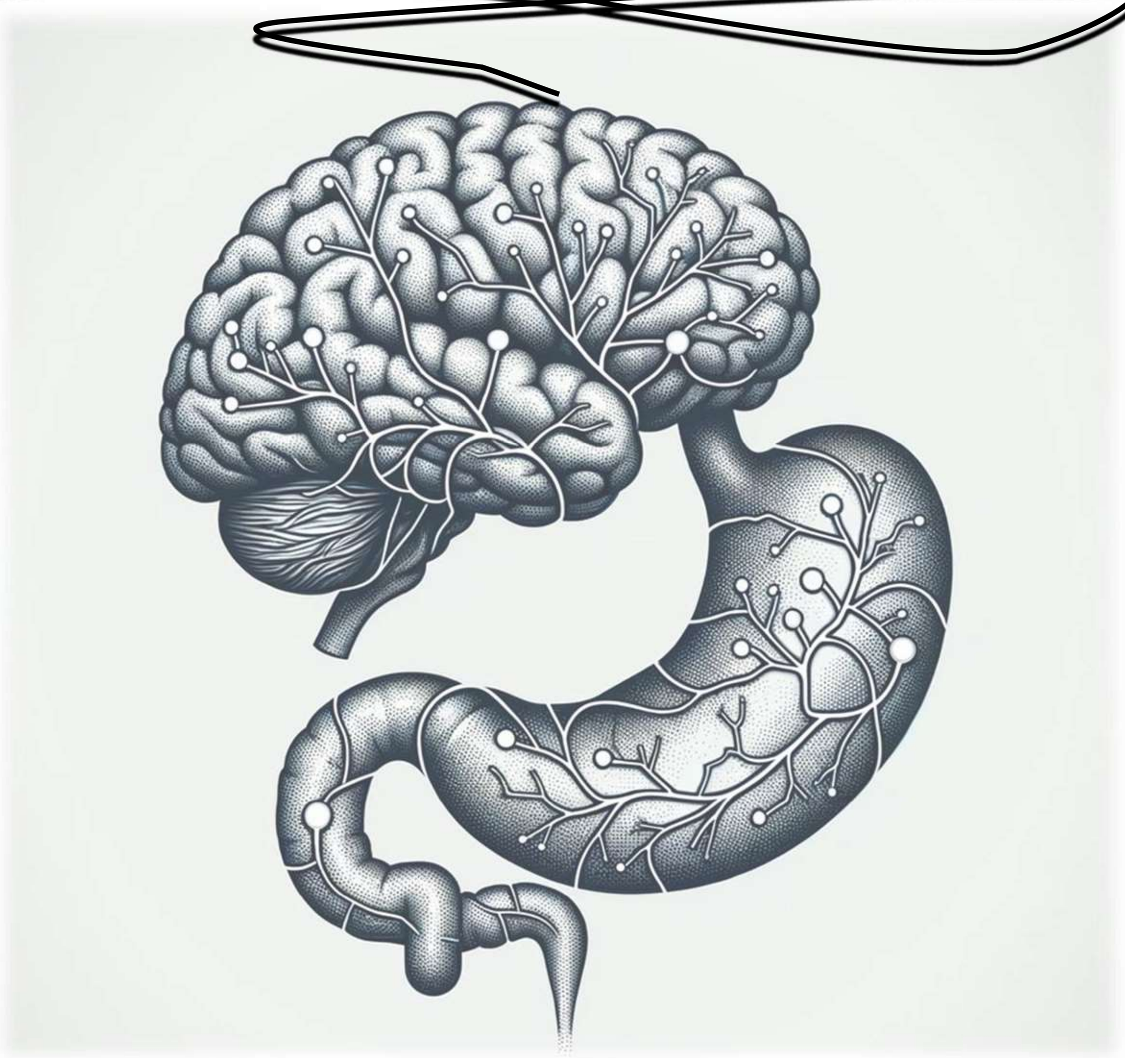
Study 2

4) To describe the changes in anthropometric profile, cardiometabolic risk factors, cardiorespiratory fitness and strength levels of patients awaiting BS, caused by a long-duration, high-workload ETP.
5) To analyse the impact of a high-workload ETP on tolerance and load-adjustment in patients awaiting BS.
6) To know if a high-workload ETP is feasible to be carried out by patients waiting for BS

Study 3

7) To assess the effectiveness of aerobic training at Fatmax combined with low-intensity resistance training in weight loss and physical fitness, in patients awaiting BS
8) To study the impact of a supervised and monitored ETP on visceral fat in patients waiting for BS
9) To know whether improvements in fat oxidation, both at rest and during exercise, are related to changes in body composition, in patients awaiting BS.

SUMMARY OF THE MATERIALS AND METHODS



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5. Summary of the material and methods

To tackle the aims previously described, experimental methods and narrative review were used depending on the phase of the research project in which this Doctoral Thesis is delimited. The summary of mentioned methods will be shown enumerated in sections below.

5.1 Review methods. Study 1.

The aim of the ***Study 1*** was to update the state of knowledge regarding PAP in BS patients to establish general and specific research objectives, as well as hypothesis, to continue the research project by GIAFIS. Due to the scarcity of clinical trials in which PAP programmed and monitored have been carried out to the date of the narrative review was written, it was decided to approach the Study 2 as a summarize of the role of physical activity in the management of morbid obesity linked to bariatric procedures. Hence, neither statistical data analysis nor systematic review were made, but available literature was carefully read, analysed and classified to provide a better understanding of the theoretical framework.

5.1.1 Data search terms and sources

The electronic search was performed using the MEDLINE and SCOPUS databases up to August 2018. The terms used in the search were the following: “bariatric surgery”, “obesity surgery”, “obesity management”, “bariatric surgery management”, “multidisciplinary programme”, “interdisciplinary programme”, “physical activity”, “physical activity programme”, “physical exercise”, “aerobic exercise”, “strength exercise”, “exercise programme”, “physical exercise programme”, “resistance training”, “strength training”. Several combinations were made using terms “AND” and “OR”.

5.1.2 Literature screening

To establish inclusion criteria, both sample characteristics and study design aspects were considered. First, regarding sample characteristics, males and females who were patients awaiting or undergone BS (participants) were included. Second, any study design was included: randomized, non-randomized, controlled and uncontrolled trial. However, it was imperative that studies had carried out an intervention in which physical activity or exercise was present to be included. It could be performed isolated or combining diet and/or behavioural therapy as well, but type of exercise should be clearly identified: that is mainly aerobic, strength or resistance exercise. Also, clinical trials did not necessary included a control group since the aim of the review was to sum up the current knowledge regarding the role of physical activity on anthropometry, health status, fitness and quality of life.

5.2 Experimental methods.

5.2.1 Participants.

Twenty-six participants awaiting BS (BMI ≥ 45 $kg \cdot m^{-2}$; obesity class IV) were voluntary eligible for taking part in our two interventions. In both cases, exclusion criteria were to be affected by asthma, obstructive pulmonary disease, cardiovascular diseases, hypothyroidism, or functional limitations to perform a physical activity program. Volunteers were recruited from two University Hospitals of an urban area serving 230.000 residents approximately.

5.2.2 Allocation.

Allocation to a control group or an experimental group depended on volunteers' possibilities to assist regularly to the training weekly sessions. Six participants took part in the study 2, while the twenty's remaining participated in the study 3.

5.2.3 Intervention and measurements.

All participants in both studies followed the presurgical care indications from their medical team. Furthermore, experimental group carried out an ETP which lasted 6 months and 12 weeks in study 2 and 3, respectively. Participants were assessed before and after the intervention for each study.

5.2.3.1 *Study 2. ETP based on concurrent training and high workloads.*

Participants attended to controlled and monitored training sessions in small groups. Weekly frequency was progressively increased. Hence, the first month consisted of 2 weekly sessions in which concurrent training was performed. The second month rise up to 3 sessions per week, with the intermediate session aimed to perform MICT. Finally, from the third to the sixth month, participants performed 4 sessions in which concurrent training and MICT were carried out in alternative sessions. Also, to ensure that training was accurately individualised and well-monitored, participants were assessed at the end of the third month to control the progress and update the training workloads. In this study, the intervention was designed based on increasing progressively individual training intensity both HIIT, MICT and resistance training.

Anthropometry and body composition.

Anthropometric measurements were taken between 07:00 and 09:00 A.M., after 12 hours overnight fasting and with and empty bladder (Kyle et al., 2004). Restriction of caffeine or alcohol intake, as well as physical exercise during the previous 48 hours were demanded. Body composition and total BW were registered by bioimpedance analysis (Tanita BC-420MA, Tanita, Tokyo, Japan), the ISAK protocol was applied to measure waist and hip circumferences (Marfell-Jones, M.; Stewart, A.; de Ridder, 2012) and BMI was calculated and expressed as kilograms per square meter ($kg \cdot m^{-2}$).

Cardiorespiratory fitness measurements and substrate oxidation during exercise.

This article is focused on determining the peak oxygen uptake (VO_{2peak}), carbohydrate and fat oxidation (CHO and FO, respectively) through a two-phase protocol on a cycle ergometer (Technogym Bike Med, Technogym, Gambettola, Italy) adapted from a previous study (Achten, Gleeson, & Jeukendrup, 2002). The test consisted of increasing intensity from 40 watts (W) to the peak power output (PO_{peak}) participants were able to achieve until volitional fatigue. Power steps were applied every 3 min or each minute depending on the protocol's phase, and cadence should be kept at 60 rpm or higher. However, this protocol showed issues since it was too short to register both fat oxidation and the first ventilatory threshold (VT1).

The test was performed under continuous respiratory gas analysis (Oxycon Pro, Jaeger, Friedberg, Germany) and heart rate (HR) register.

Muscle strength measurements

Maximal isometric and dynamic strength (MIS and MDS, respectively) of the hamstrings and quadriceps were tested by an isokinetic dynamometer (Biodex System 4; Biodex Medical Systems, New York, NY, USA). Three unilateral tests were carried out with each limb, two isometric tests in which four repetitions of Maximum Voluntary Contraction (MVC) were performed for quadriceps and hamstrings separately, and one isokinetic test to assess the same muscles in which four sets of four concentric contractions (knee flexion-extension) were performed to keep their maximal effort in every repetition (Symons, Vandervoort, Rice, Overend, & Marsh, 2005). All protocols were performed by dominant limb first, followed by the non-dominant limb. At least, the highest value of the last three sets was chosen to analyse the peak torque (N·m) in isokinetic protocol, while maximal muscle strength in any moment during each repetition was chosen in isometric protocol (Drouin, Valovich-McLeod, Shultz, Gansneder, & Perrin, 2004).

5.2.3.2 *Study 3. ETP based on low intensity and aerobic training volume individually prescribed.*

Regarding intervention design, Study 3 follows the same progress in weekly frequency than Study 1. However, training methodologies were antagonistic. Participants started the programme with a single individual aerobic continuous training at Fatmax intensity combined with another weekly session of resistance training at low workloads (20% RM). Then, a second weekly Fatmax session was introduced, while resistance training intensity rise to 25% RM. Finally, participants performed 2 weekly Fatmax sessions alternated to 2 weekly resistance training at 30% RM. Similarly, to individualise and well-monitor all training sessions, individual Fatmax was updated throughout a control assessment carried out at sixth week of the ETP. Hence, in this study, the intervention was designed based on increasing progressively individual training volume.

Anthropometry and body composition.

Anthropometric measurements were assessed with the same conditions and protocols carried out in the study 2 previously detailed.

Cardiorespiratory fitness measurements and substrate oxidation during exercise.

In the third article, two ergoespirometric incremental tests up to exhaustion on a cycle ergometer were performed, separated by 48 hours. This protocol included a verification test in the first test and the determination of Fatmax in the second one based on previous studies (Lanzi et al., 2015; Sawyer, B. J., Tucker, W. J., Bhammar, D. M., & Gaesser, 2015). The first test allowed for registering the PO_{peak}, which was used to determine the intensity of the second one depending on individual outcomes. The second test specified two phases in which the power output (PO) increased by 10% PO_{peak} every 5 min and 15 W every minute, respectively. Cadence was controlled in both tests, fat oxidation rates were calculated according to Frayn's equations (Frayn, 1983) and Fatmax was estimated using a third polynomial equation (P3 model) (Stisen et al., 2006).All tests were performed under continuous respiratory gas analysis (Oxycon Pro, Jaeger, Friedberg, Germany) and heart rate (HR) register.

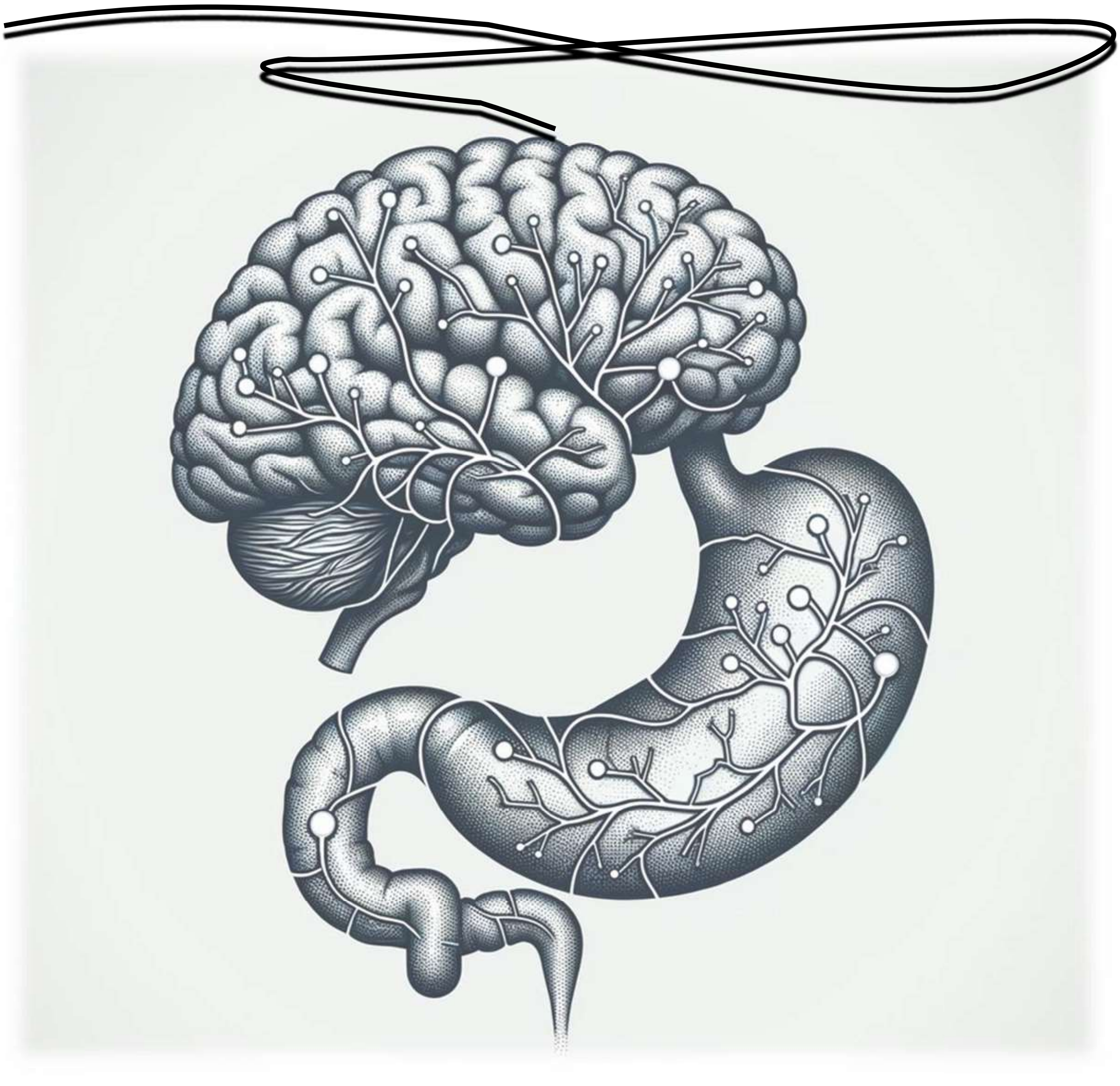
Resting metabolic rate and substrate oxidation.

Resting metabolic rate (RMR) and resting energetic substrate oxidation were estimated from an indirect calorimetry performed immediately after the anthropometric measurements. The respiratory gases were analysed during 30 min (Oxycon Pro, Jaeger, Friedberg, Germany) and the last 10 min data were used to calculate the RMR according to Weir's equation (Weir, 1948). Both resting fat oxidation (RFO) and resting carbohydrate oxidation (RCHO) were calculated based on Frayn's equation (Frayn, 1983).

5.2.4 Ethics.

Participants were carefully informed about the risks associated with the intervention and they were asked to sign an informed consent based on the Helsinki Declaration and approved by the University Ethical Committee (DPS.MMR.01.15).

DISCUSSION



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6. Discussion

This thesis comprises three studies whose results are complementary. The first one is a literature review that allowed us to identify lacks in previous published works that were addressed in the other two, experimental interventions.

The review study showed that by the date of its completion, most of the exercise-based interventions in the context of BS were developed post-operatively, and that the role of pre-operative exercise programs was mostly unknown. We found that the introduction of exercise programs before BS was in the context of "prehabilitating" the patients, i.e., exercise was aimed to reduce weight for improving the patients' cardiorespiratory function before surgery, and, in turn, reduce their surgical associated risks. The exercise-based interventions before BS described at the literature by that moment included face-to-face educational programs to encourage unsupervised home-based walking, supervised physical activity programmes combining endurance and resistance training, that were developed with or without accompanying hypocaloric diets. All of these interventions showed reductions in body weight, BMI, fat mass, etc., as well as reduced indicators of cardiovascular risk, such the Framingham Risk Score. The specific role of resistance training in the context of pre-surgical exercise programs was starting by that moment. A lack of knowledge both on the role of high-intensity exercise and on the potential effects of training at maximal fat oxidation intensity in patients awaiting BS were noticed. This lack of knowledge was the starting point for the two experimental interventions that follow.

In the first experimental study (study 2), a pilot intervention was performed in a small sample of volunteers (83% women). Since we were not sure of the acceptability of high-intensity exercise in the population of patients awaiting BS, a limited number of volunteers were recruited. The participants were randomly allocated to an exercise group or to a control group. The exercise group performed a six-month exercise program combining MICT, HIIT, resistance training and stretching. The volume and intensity of the HIIT and resistance components of the program increased progressively along the intervention period. One of the major findings of this work was that the participants allocated to the exercise-group performed >90% of the sessions without complaints. After the training program, this group exhibited a reduction of BMI and excess body weight, as well as an increase in maximal dynamic and isokinetic strength in several muscle groups of the non-dominant limb when compared to the control group.

Similarly, as stated above, we didn't find any previous work in which an exercise program performed at the maximal fat oxidation intensity in the population of patients waiting for BS had been carried out by the time at which our review was performed. Therefore, in the third study the effect of a three-month exercise programme combining endurance training at maximal fat oxidation intensity combined with low intensity resistance training on fat oxidation was tested. The main findings of this intervention were: a) that fat oxidation during exercise, but not at rest, increased in the volunteers included in the exercise group and not in the control group, that solely followed the usual care guidelines; and, b) that resting metabolic rate of the subjects included in the exercise group was unchanged, a finding that could be related to the maintenance of the fat-free mass in these individuals.

The main strength of the interventional studies included in this Doctoral Thesis is their protocolised and monitored design. Surprisingly, some gaps in evidence have been identified in current research (Oppert et al., 2021) but no mention regarding optimal prescription and programming of exercise training interventions before BS have been found, possibly due to the lack of interventional studies in this population. In fact, although aerobic training is recognised as more effective than resistance training on weight and fat mass losses in obesity, only HIIT and MICT are mentioned to be equally effective at the same level of energy expenditure, with no data or mention linked to training at Fatmax (Bellicha et al., 2021b). This fact shows that more research in the field is required. Regarding this, a recent review has mentioned that training at Fatmax has proven to be more efficient than MICT to weight management and cardiometabolic health in obesity, but its impact on muscle mass is absent, so its combination with resistance training to improve muscle strength seems to be required (Chávez-Guevara et al., 2023). However, a systematic review with meta-analysis showed that both HIIT and MICT improve maximal fat oxidation (MFO), with a remarkable inability to establish training protocols due to the heterogeneity between study designs and the lack of research about the impact of HIIT on MFO (Yin et al., 2023). Consequently, future research interventions need to be focused on monitoring and analysing the impact of well-designed ETP on health status in this specific population. Specially, because interindividual variability in response to exercise has been considered another gap in current knowledge regarding management of obesity (Oppert et al., 2021), and fat oxidation is highly influenced by metabolic disorders. Then, it could be coherent to consider MFO as key in protocols for measuring the effectiveness of a training program in people with obesity, and even more, in patients awaiting BS because it is currently considered an indicator of metabolic flexibility (Amaro-Gahete, Acosta, Migueles, Ponce González, & Ruiz, 2020).

Considering additional contributions of exercise training before BS on weight loss and level of physical activity postoperatively, the strength of evidence is currently low (Oppert et al., 2021). A question highly relevant could be the heterogeneity in assessment protocols, which is as important as exercise prescription to give recommendations directly applicable in clinical practice. To the best of our knowledge, no systematic review nor meta-analysis has been focused on analysing measurement protocols in cardiorespiratory fitness, substrate oxidation and muscle strength to assess its reliability in research interventions. In fact, there is no evidence regarding the most suitable protocols to assess these variables accurately in patients awaiting BS. Trying to improve this limitation, protocols carried out in this Doctoral Thesis were carefully designed based on previous research (Achten et al., 2002; Lanzi et al., 2015; Sawyer, B. J., Tucker, W. J., Bhammar, D. M., & Gaesser, 2015; Symons et al., 2005). However, future studies need to validate them to confirm that its application is suitable and reliable in this population.

Volume required to acquire benefits linked to exercise is also a question unsolved (Oppert et al., 2021), especially in terms of time intervention with exercise training in patients waiting for BS. In the moment of carrying out the study 2 included in this Doctoral Thesis, no preoperative exercise interventions were found of over few months. Currently, the state of knowledge has progressed and a recent review showed interventions from 4 weeks to 161 weeks, but with a significant limitation to compare study designs between them: time duration was summarized considering pre and postsurgical intervention (Baillot et al., 2022).

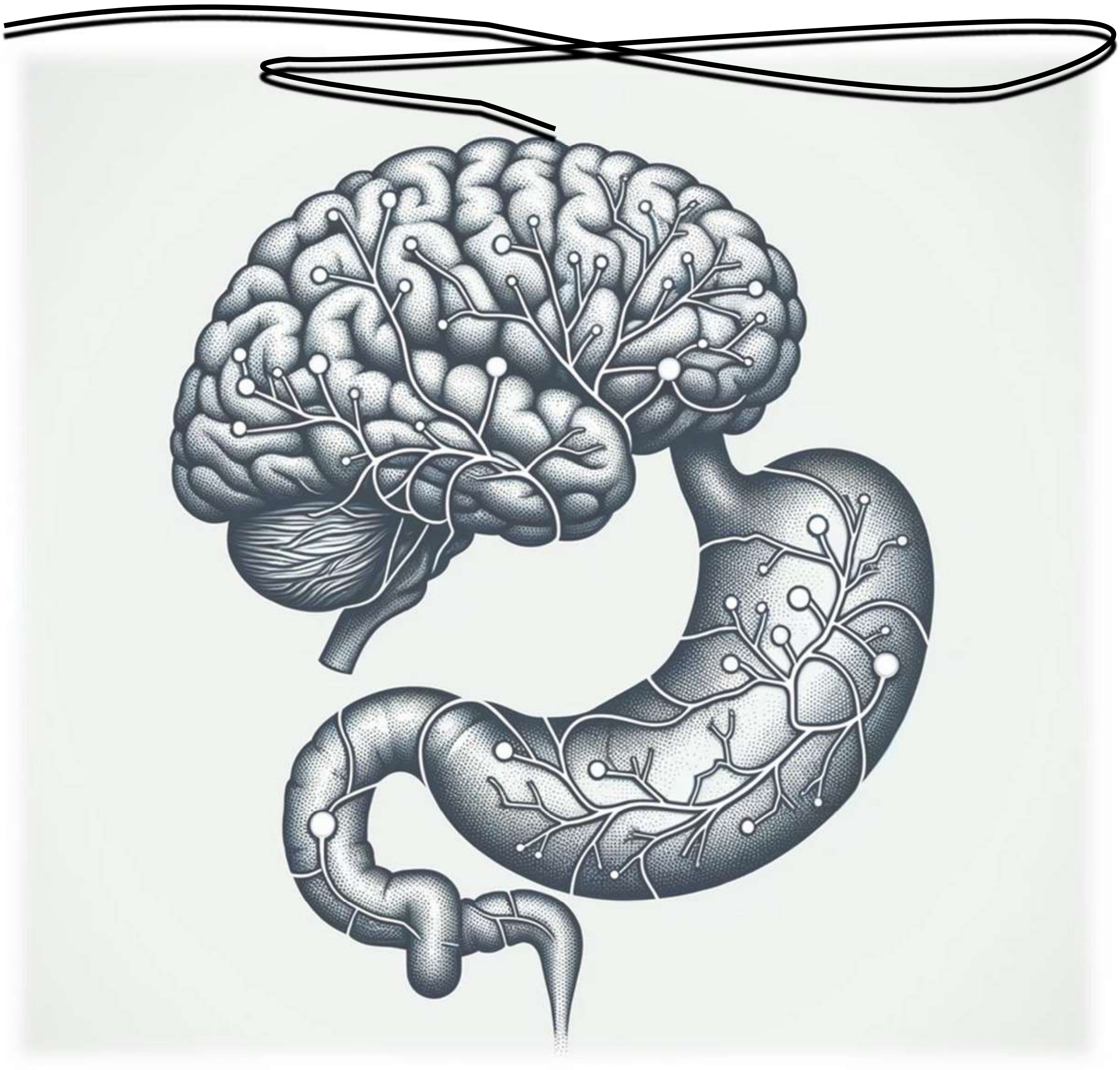
Regarding the main outcome linked to morbid obesity management, pharmacotherapy should be considered since, as it has mentioned before, antiobesity medications have improved to be capable of achieving weight loss outcomes similar to those acquired with physical activity interventions (Elmaleh-Sachs et al., 2023). However, the effect of its combination with exercise training on weight loss, body composition, cardiometabolic health and physical fitness have not been researched until the date. In fact, another gap to persist unsolved is how different types and timing of exercise could influence eating behaviour, and more interestingly, appetite control (Oppert et al., 2021). Thus, future studies could be aimed to compare different groups of adults waiting for BS in which exercise training and antiobesity medications (i.e. GLP-1 receptor agonists) are assessed both combined and separately to a better understanding of their effects on health.

Besides, when exercise training is proposed to obese adults, the question linked to security in patients is highlighted and raises concerns, especially related to musculoskeletal injuries and adverse cardiac events (Oppert et al., 2021). However, this issue is considerably difficult to assess due to some reasons: 1) current research only shows too short interventions carried out in preoperative obese adults; 2) medical protocols to prepare candidates to undergo a BS could be diverse among patients, depending on factors such as medical criteria or different hospitals with their own protocols; and 3) participation in an ETP is usually voluntary, but adherence in this population is a well-known limitation and needs also to be explored. Based on it, no information regarding incidence of musculoskeletal injury or cardiac events in obese population directly related to exercise training may be shown since long-term interventions are required but non-easily accessible to research nowadays. However, study 2 included in this Doctoral Thesis performed an ETP with high workloads for 24 weeks, no adverse events and a participation up to 90% of the total supervised exercise training sessions proposed. Small sample size of study 2 is a strong limitation to stablish general recommendations, but these data suggest that the ETP in which HIIT and resistance training with high workloads are combined could be feasible in obese adults waiting for BS. The main factors that might have been determinant in obtaining these positive results in security, adherence and participation are the following: 1) an accurate monitorization of workloads in which monotony and strain indexes are considered; and 2) the guidance, attention and supervision of the ETP by sport science professionals who adapted both the type of exercise and intensity level to the needs and capabilities of participants who were waiting for a BS. In fact, the latter has already been mentioned as a priority research need aimed to establish exercise training guidelines in obese population (Oppert et al., 2021). In this context, multidisciplinary prehabilitation programmes seem to be the key to future research in exercise on health, subject to the implementation of close collaborations between professionals from clinical, behavioural and fitness fields. Exercise intervention before BS has been recently considered feasible and acceptable, but their protocols in real life are still unsolved (Baillot et al., 2022).

Benefits of exercise on health are well-known, so it could accept that its correct prescription and application in the preparation of obese adults candidates for a BS could always contribute positively on health, independently of weight loss. These benefits could be related to improvements in body composition, visceral fat, insulin sensitivity, systolic and diastolic blood pressure, and definitely, cardiometabolic health (Bellicha et al., 2021b; Oppert et al., 2021). Regarding this, two new concepts have been proposed that it is relevant to mention: normal weight obesity (NWO) and metabolically healthy obese (MHO) (Lorenzo, 2016). Its use aims to improve BS recommendations for each patient considering factors such as adiposopathy and sick fat, closely related to inflammation level and metabolic profile of each patient. Thus, NWO adults are characterized by normal BMI and highest body fat percentage, associated with high risk for cardiometabolic disease and vascular inflammation, while MHO implies a subject who may exhibit an obese phenotype with no metabolic abnormalities (Lorenzo, 2016). In fact, MHO subjects have high insulin sensitivity, no hypertension and healthy lipid profile (Seo & Rhee, 2014). Consequently, this new obesity classification shows a better understanding of improvements on health that any obesity management can pursue, whether from clinical, nutritional, behavioural and/or exercise interventions, with independence of weight loss. Both study 2 and study 3 included in this Doctoral Thesis registered changes in body composition due to FFM maintenance and fat mass losses after exercise interventions in EG, although not enough data were available to assess their impact on cardiometabolic health completely. However, changes in work efficiency observed in study 3 should be mentioned since they were registered without significant body weight reductions, a condition previously described (Hames et al., 2016). Interestingly, after ETP performed in study 3, participants showed higher MFO during exercise, which could be related to improvements in metabolic flexibility but more identification of molecular and cellular mechanisms needs to be determined.

In summary, all these findings together could have the potential to significantly impact on healthcare and the quality of life of individuals facing BS if ETP, well-designed and monitored, instead of general recommendations to physical activity practice, were available to patients in public healthcare national systems. Future studies need to be aimed to validate and unify assessment protocols, to compare different types of exercise, well prescribed and monitored, in larger sample size and longer exercise interventions, with or without other approaches that are clinically followed nowadays.

CONCLUSIONS



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7. Conclusions of the thesis

Obesity is considered a global pandemic with a prevalence which seems to be constantly rising up (Abarca-Gómez et al., 2017; Swinburn et al., 2019). Spain, and more specifically, the Valencian Community are not an exception

The diagnosis of obesity is based in the BMI, although current research shows that other factors such as body composition seems to be more relevant (Salmón-Gómez et al., 2023). Regarding multimodal management which usually accompanied clinical criteria in severe obesity treatment, some key points such as preserving FFM (Bettini et al., 2020; Tabesh et al., 2019), being more physically active (King & Bond, 2014; Tabesh et al., 2019) or assessing metabolic health versus weight loss (Lorenzo, 2016) are under research aimed to improve clinical decision-making for each patient's condition. In this context, physical activity has been widely researched but type of exercise or its specific prescription in terms of volume and intensity is still not determined (Oppert et al., 2021). Especially, because both questions linked to security and long-term feasibility of ETP are also unsolved.

To the aim of contributing to improve obesity management in adults with obesity who are waiting for a BS, this Doctoral Thesis was focused on exploring the effects of different ETP in this population. The conclusions extracted from the studies included in this Doctoral Thesis are the following:

Study 1:

1. There was noticeable absence of knowledge on the role and characteristics of exercise programs in patients awaiting BS. Heterogeneity in previous interventional works in this population, and the absence of control groups in many of them was also noticed.
2. Aerobic exercise was the most frequent form of physical activity/exercise prescribed to patients waiting for BS. However, the specific role of resistance training had been starting to be explored by the time of the review, and more research was needed.
3. Similarly, the role of HIIT in patients awaiting BS was mostly unknown since it was assumed as not suitable for moderate-to high cardiovascular risk individuals.

4. Last, but not least, the effect of exercise on fat oxidation in patients waiting for BS, specifically during exercise had not been studied.

Study 2:

5. In patients waiting for BS, a six-month exercise program that combined HIIT with resistance training that progresses from 55% to 75% 1RM is well tolerated.
6. This sort of program improved body composition, including a reduction of body weight, BMI, fat mass and visceral fat.
7. CRF and physical condition were also improved by this intervention.

Study 3:

8. Lipid oxidation during exercise, but not at rest, increased after a 12-week exercise program that combined endurance training performed at Fatmax intensity and low intensity resistance training, in women waiting for BS.
9. FFM loss in this population can be prevented by the low intensity resistance training component of the program.

8. Conclusiones de la tesis

La obesidad se considera una pandemia global con una prevalencia que parece estar en aumento constantemente (Abarca-Gómez et al., 2017; Swinburn et al., 2019). España, y de forma más específica, la Comunidad Valenciana no son una excepción.

El diagnóstico de la obesidad se basa en el BMI, aunque la investigación actual muestra que otros factores como la composición corporal parecen ser más relevantes (Salmón-Gómez et al., 2023). En cuanto al manejo multimodal que suele acompañar los criterios clínicos en el tratamiento de la obesidad severa, algunos puntos clave como preservar la masa libre de grasa (Bettini et al., 2020; Tabesh et al., 2019), ser físicamente más active (King & Bond, 2014; Tabesh et al., 2019) o evaluar la salud metabólica frente a la pérdida de peso (Lorenzo, 2016) son objeto de investigación con el fin de mejorar la toma de decisiones clínicas en función del estado de cada paciente. En este contexto, la actividad física ha sido ampliamente investigada, pero el tipo de ejercicio o su prescripción específica en términos de volumen e intensidad aún no se ha determinado (Oppert et al., 2021). Sobre todo, porque tampoco se han resuelto las cuestiones relacionadas con la seguridad y la viabilidad a largo plazo de los programas de entrenamiento basados en ejercicio.

Con el objetivo de contribuir a mejorar el manejo de la obesidad en adultos con obesidad que se encuentran a la espera de una cirugía bariátrica, esta Tesis Doctoral se centró en explorar los efectos de diferentes programas de entrenamiento basados en ejercicio en esta población. Las conclusiones extraídas de los estudios incluidos en esta Tesis Doctoral son las siguientes:

Estudio 1:

1. Se observó una ausencia notable de conocimiento sobre el papel y las características de los programas de ejercicio en pacientes a la espera de cirugía bariátrica. También se observó heterogeneidad en los trabajos de intervención previos en esta población, y la ausencia de grupos control en muchos de ellos.
2. El ejercicio aeróbico fue la forma más frecuente de actividad física/ejercicio prescrita a los pacientes en espera de cirugía bariátrica. Sin embargo, el papel específico del entrenamiento de fuerza había empezado a explorarse en el momento de la revisión, y se necesitaba más investigación.

3. Del mismo modo, el papel del HIIT en pacientes a la espera de una cirugía bariátrica era en su mayor parte desconocido, ya que se suponía que no era adecuado para personas con un riesgo cardiovascular de moderado a alto.
4. Por último, pero no por ello menos importante, no se había estudiado el efecto del ejercicio sobre la oxidación de grasas en pacientes en espera de cirugía bariátrica, específicamente durante el ejercicio.

Estudio 2:

5. En pacientes a la espera de una cirugía bariátrica, se tolera bien un programa de ejercicio de seis meses que combina HIIT con entrenamiento de fuerza que progresa del 55% al 75% RM.
6. Este tipo de programa mejoró la composición corporal, incluyendo una reducción del peso corporal, el BMI, la masa grasa y la grasa visceral.
7. Factores de riesgo cardiometabólico y la condición física también mejoraron con esta intervención.

Estudio 3:

8. La oxidación lipídica durante el ejercicio, pero no en reposo, aumentó tras un programa de ejercicio de 12 semanas que combinaba entrenamiento de resistencia realizado a intensidad Fatmax y entrenamiento de fuerza de baja intensidad, en mujeres a la espera de cirugía bariátrica.
9. La pérdida de FFM en esta población puede prevenirse mediante el componente de entrenamiento de fuerza a baja intensidad del programa.

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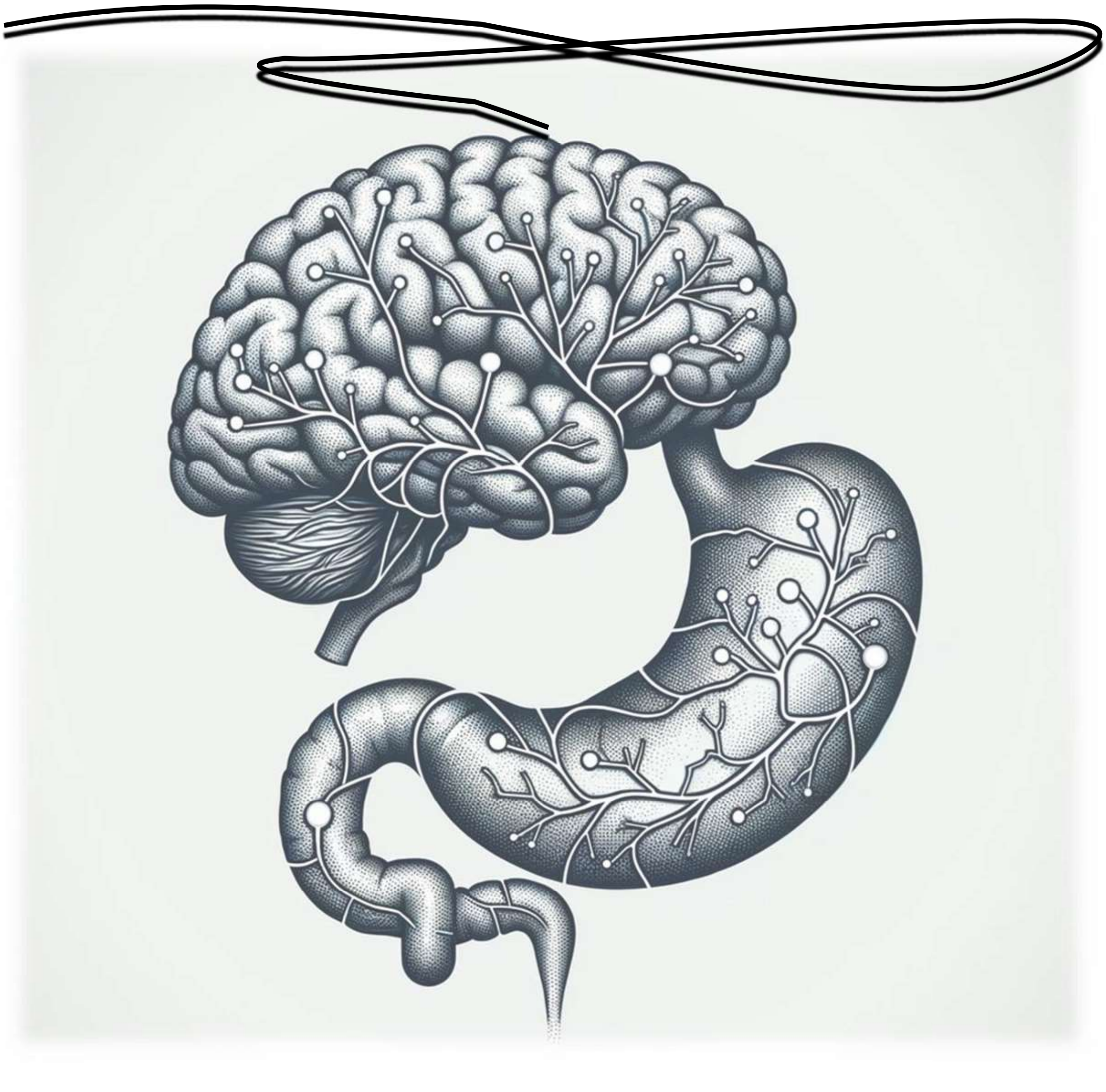

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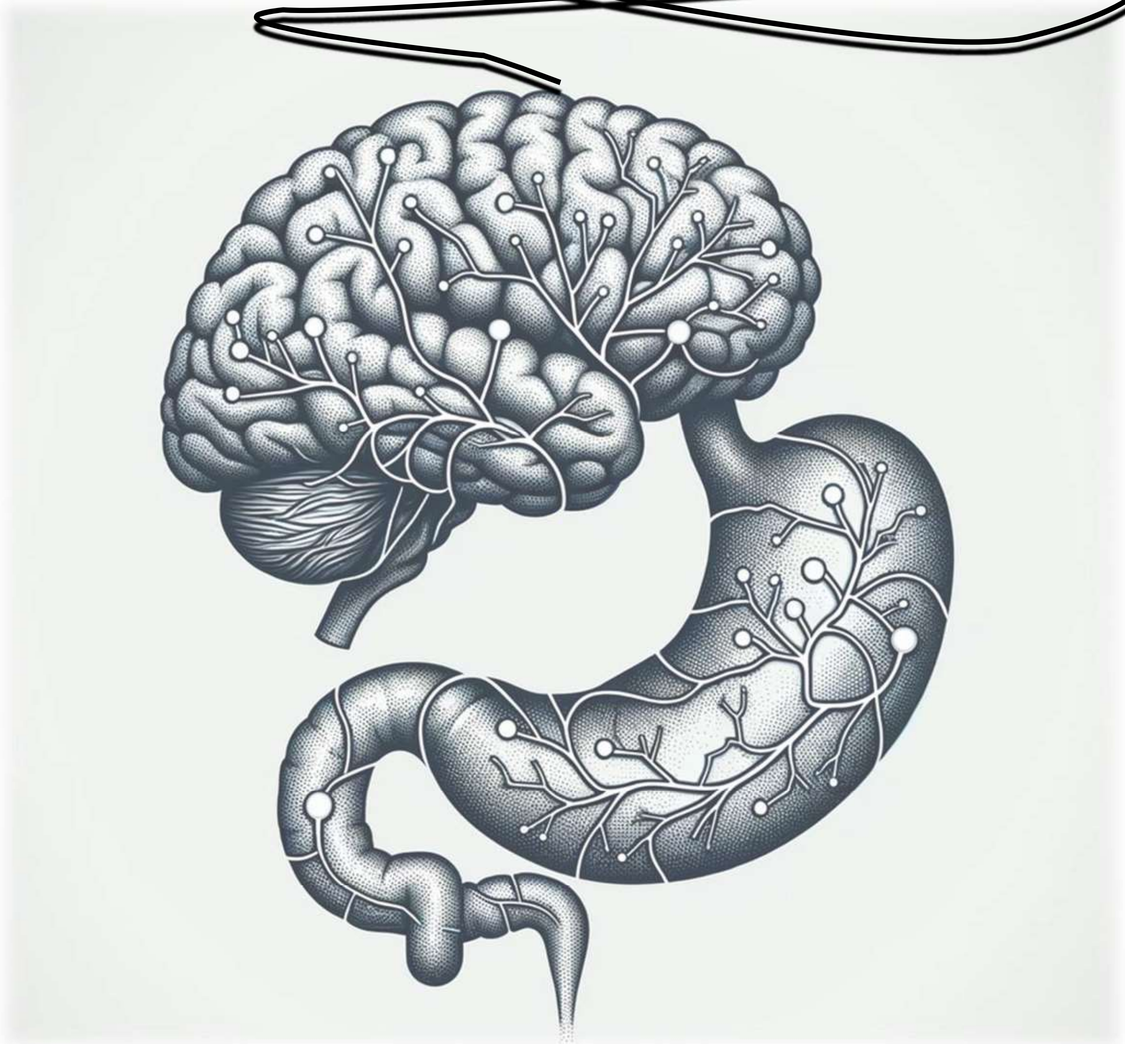
ANNEXES



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ANNEXE 1

STUDY 1

Effects of physical activity programmes in severe obesity before and after bariatric surgery: a current framework.

Note. This article was published.

Moya-Ramón M, Picó-Sirvent I, Aracil A. Effects of physical activity programmes in severe obesity before and after bariatric surgery: a current framework. Eur J Hum Mov. 2018;41:103–23.

European Journal of Human Movement, 2018: **41**, 103-123

EFFECTS OF PHYSICAL ACTIVITY PROGRAMS IN SEVERE OBESITY, BEFORE AND AFTER BARIATRIC SURGERY: A CURRENT FRAMEWORK

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ABSTRACT

Bariatric surgery is considered the gold-standard therapeutic intervention for severe obesity, a form of obesity that is steadily increasing in Western societies. However, surgery must be accompanied by interventions aimed at changing the patients' lifestyle, with special emphasis on increasing their physical activity levels. The optimal characteristics of physical activity programs for bariatric surgery patients are largely unknown. This review summarizes the main effects on body composition and physical condition of physical activity programs developed, both in patients awaiting bariatric surgery or after surgery. Recent research shows that in addition to moderate-to-vigorous aerobic exercise (the form of exercise commonly recommended for this population), strength training may help to avoid the loss of fat-free mass associated to surgery and the extreme dietetic restrictions usually prescribed to these patients. However, heterogeneity in: a) study design; b) components of the physical activity program; c) sample characteristics; d) outcomes measured; and e) time of recruitment, still limits the possibility of obtaining a clear picture of the effects of physical activity programs in this population.

Keywords: severe obesity, bariatric surgery, physical activity, exercise, weight loss

EFECTOS DE LOS PROGRAMAS DE ACTIVIDAD FÍSICA EN LA OBESIDAD SEVERA, ANTES Y DESPUÉS DE LA CIRUGÍA BARIÁTRICA: UNA VISIÓN ACTUAL

RESUMEN

La cirugía bariátrica se considera la intervención terapéutica por excelencia para la obesidad severa, un tipo de obesidad que continúa incrementando en las sociedades occidentales. Sin embargo, la cirugía debe acompañarse con intervenciones cuyo objetivo sea el cambio de estilo de vida de los pacientes, con especial atención en el incremento de sus niveles de actividad física. Las características óptimas de los programas de actividad física en pacientes bariátricos son en gran parte desconocidas. En esta revisión, se resumen los principales efectos sobre la composición corporal y la condición física de programas de actividad física desarrollados en pacientes a la espera de cirugía bariátrica y después de la cirugía. Investigaciones recientes muestran que, junto al ejercicio aeróbico de intensidad moderada a vigorosa (el tipo de ejercicio comúnmente recomendado en esta población), el entrenamiento de fuerza podría ayudar a evitar la pérdida de masa libre de grasa asociada con la cirugía y las restricciones dietéticas extremas normalmente prescritas en estos pacientes. Sin embargo, la heterogeneidad en: a) el diseño del estudio; b) los componentes del programa de actividad física; c) las características de la muestra; d) los resultados medidos; y e) el momento de reclutamiento, todavía limitan las posibilidades de obtener una visión clara de los efectos derivados de programas de actividad física en esta población.

Palabras clave: obesidad severa, cirugía bariátrica, actividad física, ejercicio, pérdida de peso

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Submitted: 09/10/2018 *Accepted:* 09/12/2018

INTRODUCTION

Severe obesity in the context of the current "obesity pandemic"

Obesity, defined as a body mass index (BMI) equal or above 30 kg·m^{-2} of body surface, is a non-communicable disease which develops due to the interaction of individual genetic, environmental and behavioural factors (Egger & Swinburn, 1997). In the last decades, Western societies have suffered a global phenomenon characterized by an increase in technological advances, economic growth and global trade liberalization. However, although globalization has improved quality of life and reduced the level of poverty in many countries, it has promoted a more sedentary lifestyle and a greater consumption of carbonated beverages and processed foods which are high in energy but low in nutritional value (Popkin, Adair, & Ng, 2017). The sudden environmental massive exposure of population to these potentially "obesogenic" factors, among others, has caused a sustained increase of mean BMI since the 70's, changing the trends existing up to that moment (Rodgers, Woodward, Swinburn, & Dietz, 2018). The Non-Communicable Disease Risk Factor Collaboration (2017) has recently reported that during the last 30 years the mean BMI of the global population has been consistently increasing worldwide. Consequently, the current prevalence of obesity estimated in one out of every three individuals of the world's population, especially in women (The Non-Communicable Disease Risk Factor Collaboration, 2017; Hruby & Hu, 2015), is reaching alarming values.

Obesity is commonly associated with several comorbidities, such as type 2 diabetes mellitus (T2DM), hypertension, dyslipidaemia, hypercholesterolemia, altered immune response, and several types of cancer. Together, obesity and its associated comorbidities increase the risk of both all-cause and cause-specific mortality (Gul, Balkhi, & Haq, 2018), therefore reducing life expectancy and quality of life. Consequently, this "obesity pandemic" is also contributing to the continuous rise of economic costs of health care systems. According to Von Lengerke and Krauth (2011), obesity accounted for excess health care costs between 117 and 1,873 euros per person in European countries, which particularly increased due to severe obesity (Von Lengerke & Krauth, 2011).

Severe obesity (or class III obesity) is defined by a BMI ≥ 40 kg·m^{-2} of body surface. Its prevalence has increased over time paralleling the prevalence of obesity. Nowadays, the global prevalence of severe obesity ranges between 0.6 and 1.6% for men and women, respectively. Therefore, if current trends continue, it is expected that in less than 10 years the prevalence of severe obesity will surpass 6 and 9% (men and women, respectively) of the global population (The Non-Communicable Disease Risk Factor Collaboration, 2017; Thomas et al., 2014). This would menace the economic sustainability of health care systems. While at the moment preventive global actions are claimed to reduce the obesity pandemic (Rodgers et al., 2018; The Lancet Public Health, 2018), efforts are being also directed to treat the already obese patients due to the failure of these global actions. Obesity management is particularly challenging in the case of severe obesity.

Current management of severe obesity: bariatric surgery

The current management of severe obesity in clinical settings relies mostly on the combination of bariatric surgery (BS) and interventions aimed at modifying the individual's lifestyle. Several drugs are also being studied to treat obesity, with limited evidence of efficacy (Bray, Frühbeck, Ryan, & Wilding, 2016). Consequently, obesity pharmacotherapy is only recommended as and adjunctive treatment in selected patients (Jensen et al., 2014).

Since the advancement of laparoscopic surgical techniques, BS has become the gold-standard therapeutic option for patients with severe obesity (Herpertz, Kessler, & Jongen, 2017), or for patients with BMI ranging between 30-35 kg·m^2 with associated T2DM (Bray et al., 2016). BS not only causes weight loss but also a remission of the associated metabolic alterations, thus also being called "metabolic surgery". The most common surgical techniques are sleeve gastrectomy and Roux-en-Y gastric bypass. While sleeve gastrectomy combines a restrictive mechanism and a reduction of the appetite-related gastric hormones ghrelin and/or glucagon-like peptide 1 (Puzziferri & Almandoz, 2018), gastric bypass also produces a reduction of intestinal food absorption (Khwaja & Bonanomi, 2010). In terms of excess weight loss, gastric bypass seems to be slightly superior to gastrectomy (Khwaja & Bonanomi, 2010; Neylan, Kannan, Dempsey, Williams, & Dumon, 2016), but due to the surgical complexity of the former, the latter is gaining momentum (Neylan et al., 2016).

Effects on body composition and physical condition of physical activity programs applied to bariatric surgery patients

Independent of their eligibility for BS, interventions aimed at modifying the lifestyle of severely obese individuals remain a cornerstone of the treatment, both before and after surgery. Behavioural interventions comprise one or more components relating to diet, physical activity and/or behaviour change therapies (Bray et al., 2016; Stewart & Avenell, 2016). Given that most patients show an insufficient level of preoperative physical activity and remain insufficiently active postoperatively, increasing physical activity is one of the major aims common to all these interventions.

The characteristics of physical activity programs (PAPs), including the frequency, intensity, type and duration of exercise remain largely undefined. The general recommendations of physical activity for health are used instead, i.e., ≥ 150 min·week^{-1} of moderate-to-vigorous aerobic exercise is set as a common target to be attained (Bray et al., 2016; Jensen et al., 2014). Although emphasis is placed on aerobic exercise, recent systematic reviews have shown that other modalities of exercise have been tried (Al-Hazzaa, 2016; Filou et al., 2017; Moya et al., 2014) in the context of BS. However, due to the wide heterogeneity of study design, sample characteristics, surgical procedures used, time of recruitment, and outcomes measured, only a patchy, superficial picture of the effects of PAPs in BS can be obtained. Given that PAPs can be introduced before BS or postoperatively, in this non-exhaustive narrative review we summarize the main effects of PAPs depending on the moment of their implementation.

Physical activity programs in patients awaiting bariatric surgery.

Although the evidence is still limited, the introduction of PAPs in patients awaiting for BS has been suggested because it is expected that: a) they may decrease the risk of intraoperative complications through preoperative weight loss (Hutcheon et al., 2018); and, b) they may reduce the hospital stay and postsurgical complications associated with a reduced cardiorespiratory fitness (Al-Hazzaa, 2016; Baillot et al., 2014). Additionally, it has been reported that one year after surgery, a preoperative PAP can increase the engagement in physical activity and maintain the weight loss caused by the BS (Baillotet al., 2017a).

Simple interventions, such as a 6 session face-to-face educational program on behavioural strategies to perform home-based walking exercise, can increase moderate-to-vigorous daily physical activity in patients awaiting for BS (Bond et al., 2015a; Bond et al., 2015b). However, severe obese adults awaiting BS usually present physical and psychological barriers that prevent them from exercising (such as chronic knee pain, breathing arrhythmia or exercise intolerance) which limit them to engage in and maintain a regular autonomous physical activity (King & Bond, 2014). Consequently, supervision of PAPs by exercise professionals seems to be needed for this population.

Other modalities of exercise different from aerobic exercise have been tried in patients awaiting BS in the last years. For example, in a series of studies by Baillot et al. (2013, 2014, 2016, 2017a & 2017b) the effect of a PAP combining endurance and strength exercise on weight loss before BS was studied. A pilot study (Baillot, Mampuya, Comeau, Méziat-Burdin, & Langlois, 2013) analysed the effect of a 12-week PAP combining 30 min of endurance activities at an intensity ranging 55-85% of heart rate reserve (HRR) with 20-30 min of strength exercises. Participants attended 3 sessions per week, and missed sessions were completed at home. Results showed that PAP alone induced significant weight loss (0.1 - 5.2 kg), decreased fat mass (FM) and BMI, and increased physical fitness before BS. Besides, they mentioned that the motivation to participate in regular moderate physical activity and the involvement in various intensities of physical activity seem to increase close to the date of the BS. Similar effects on body composition were obtained in their later studies, in which they applied the same PAP in a larger sample size (Baillot et al., 2016) and via a "telehealth" system (Baillot, Boissy, Tousignant, & Langlois, 2017b), although they didn't find differences in the physical condition among intervention groups in the latter. The results of Baillot et al. (2013) are also supported by independent observations by Sánchez Ortega, Sánchez Juan and Alfonso García (2014). They carried out a structured program consisting in aerobic and strength exercises sessions combined with a hypocaloric diet and a weekly food educational talk. Their results showed significant weight loss, and reductions in BMI, fat mass percentage (FM%) and visceral fat percentage, thereby reducing cardiometabolic risk before BS. Besides, fat-free mass percentage (FFM%) significantly increased, but non-significant improvements were shown in physical fitness. Similarly, Marcon et al. (2017) demonstrated that after a twice a week, 4-month supervised PAP of low-intensity aerobic exercise combined with stretching exercises, participants showed significant reductions in body weight, BMI, systolic blood pressure, Framingham Risk Score and glycaemia, while physical fitness also improved significantly before BS. In contrast, in a control group that received only a behavioural intervention all these variables worsened.

The effects of resistance training in patients awaiting BS have been recently studied in a series of papers by Delgado Floody et al. (2015a, 2015b, 2015c & 2015d). They implemented a PAP with overload until muscle failure in 60 min sessions and analysed its effects on lipid profile and glycaemia (Delgado Floody et al., 2015a), preoperative conditions (Delgado Floody et al., 2015b, 2015c), and anthropometric variables (Delgado Floody et al., 2015d). The PAP was combined with psychological therapy and diet recommendations. Their results showed significant improvements in weight loss, FM% and physical fitness, but non-significant reductions were obtained in BMI, waist and hip circumferences, basal glycaemic and lipid profile. Paradoxically, HDL-cholesterol decreased. Consequently, PAPs aimed at increasing muscle mass seem effective in the maintenance of body weight in the medium and long term. At our group we are also starting to investigate these effects (Picó-Sirvent & Moya-Ramón, 2018). A detailed summary of all these interventions may be found in table 1.

TABLE 1
Summary of the studies analysed in this review in which a physical activity program before bariatric surgery is applied.

Ref.	**Sample**	**Physical activity program**				**Multidisciplinary intervention**	**Results**	
		Volume	**Intensity**	**Frequency**	**Type**		**Anthropometry & health status**	**Fitness & quality of life**
Baillot et al., 2013	PreSET W (n=8) M (n=4)	12 weeks, or 2 weeks preBS due to specific diet Warm-up: 10 min AE: 20-30 min SE: 2-3x12-15 reps Cool-down: 10 min	AE: 55 to 85% HRR SE: lb progression for men and woman	3 sessions Missed sessions completed at home	AE: dance and aerobic exercises, ball games, badminton SE: 3 mini-circuits (upper/lower body, and trunk) with dumbbells, elastic bands, and sticks Monthly aquagym session included in PreSET	Weekly group educational sessions. Individual counselling sessions of 15' with the dietician and PA specialist every 6-8 weeks	*↓ BW, FM, BMI	*↑ PF6, ACT, HST; *↓ FI, EMBPA; *↑ QL, EM, SI, SL
Baillot et al., 2016	PreSET (n=15) UC (n=14)						PreSET$_{C}$: *↓ FM% PreSET$_{NC}$: *↓ FM% SC: ≠	PreSET$_{C}$: **↑ PF6, HST, ACT, SI, EMBPA; *↑ VPA PreSET$_{NC}$: *↑ VPA SC: ≠
Baillot et al., 2017b	TelePreSET (n=6) PreSET (n=12) UC (n=11)			2 supervised sessions in telehealth 1 unsupervised session			TelePreSET: ≠ PreSET: *↓ FM% UC: ↓ PF6; ≠	TelePreSET: ↑ PF6, ACT, STS PreSET: ↑ PF6, ACT, HST UC: ↓ PF6
Sánchez Ortega et al., 2014	W (n=6) M (n=4)	8 weeks Session: 60 min SE: 2-3 series of 10-15 reps	Not reported	2 sessions	AE: climbing stairs, games, "functional" exercises SE: self-load and dumbbells	Weekly food educational talk Hypocaloric diet of 1250-1800 kcal/day, with 500-1000 kcal restriction	*↓ BW, BMI, FM%, VF%; *↑ FFM%	*↑ PF6

TABLE 1 (CONT.)

Ref.	Sample	Physical activity program				Multidisciplinary intervention	Results	
		Volume	Intensity	Frequency	Type		Anthropometry & health status	Fitness & quality of life
Marcon et al., 2017	EX (n=22) EXCBT (n=17) CG (n=18)	4 months AE: 20 min STCH: 5 min	RPE from 2 to 4	2 supervised sessions	AE: walking STCH: arm, leg, trunk and neck muscles	Exer + CBT group participated in a support group program for lifestyle modification, once a week (1 h) immediately after the exercise session	EX: **↓ BW, BMI; *↑ HR_{rest}, HDL; *↓ SBP, FRS, GL EXCBT: **↓ BW, BMI; **↑ HR_{rest}; ↓ SBP, FRS, GL; *↑ HDL, TG CG: *↑ BW, HR_{rest}, GL, TG; *↓ HDL	EX: **↑ PF6, VO_2 est EXCBT: ↑ PF6; ≠ VO_2 est CG: ↓ PF6; ≠ VO_2 est
Delgado Floody et al., 2015a	W (n=9) M (n=1)	3 or 4 months Session: 60 min Warm-up: 10 min 3 series of 60 s, with 2 min rest STCH: 5 min	Until muscle failure	3 sessions	RT: forearm, trunk, pectorals, shoulder, knee, plantiflexors	Individualized and group educational sessions, 1 h before and/or exercise, about nutritional and psychological work (anxiety, depressive and self-image)	*↓ BW, BMI, FM%; ↓ WC; ↓ TCH, TG, LDL, GL, HDL	*↑ PF6
Delgado Floody et al., 2015b	W (n=10) M (n=4)						*↓ BW, BMI, FM%, WC, BGL	*↑ PF6; *↓ DP
Delgado Floody et al., 2015c	W (n=19)						*↓ BW, BMI, WC, FM%, GL	*↑ PF6
Delgado Floody et al., 2015d	W (n=25) M (n=3)					Not reported	*↓ BW, BMI, WC, HC	Not measured

*PreSET: Pre-Surgical Exercise Training; UC: usual care; TelePreSET: PreSET via telehealth; EX: exercise; EXCBT: exercise combined with cognitive-behavioural therapy; M: men; W: women; AE: aerobic exercise; SE: strength exercise; STCH: stretching; BS: Bariatric surgery; HRR: heart rate reserve; RPE: rate of perceived exertion; BW: body weight; BMI: body mass index; FM: fat mass; FM%: fat mass percentage; VF: visceral fat; FFM%: fat-free mass percentage; WC: waist circumference; HC: hip circumference; DP: depression; EM: emotions; EMBPA: embarrassment during physical activity; FI: fear of injury; QL: quality of life; reps: repetitions; SI: social interactions; SL: sexual life; SBP: systolic blood pressure; FRS: Framingham Risk Score; BGL: basal glycaemia; GL: glycaemia; HDL: high density lipoprotein; LDL: low density lipoprotein; TCH: total cholesterol; TG: triglycerides; ACT: arm curl test; HST: half-squat test; PF6: physical fitness by 6MWTD (6 minutes-walk test distance); VO_2 est: oxygen uptake estimated; VPA: vigorous physical activity; ≠: no change; * intragroup differences ($p < 0.05$); ** among intervention and control group differences ($p < 0.05$).*

Physical activity programs in patients after bariatric surgery.

BS is highly effective in reducing body weight and FM (Colquitt Jill, Pickett, Loveman, & Frampton Geoff, 2014), as well as T2DM (Warren et al., 2015). These effects are mainly observed during the first months after surgery and progress up to one year after surgery. Since that moment on, a weight regain tendency commonly appears (Herpertz et al., 2017). This phenomenon shows a great interindividual variability, with some individuals starting to regain weight 6 months after surgery, whilst in some other cases weight loss lasts for longer periods of time, even decades (Stewart & Avenell, 2016). Consequently, several guidelines recommend post-operative support, but do not advise for specific interventions (Stewart & Avenell, 2016).

In general, it is accepted that weight loss at 6 months after surgery seems to be caused directly by BS per se, and it is independent of any other intervention (Filou et al., 2017). Therefore, PAPs are considered to stabilize weight loss in the long-term after BS (Filou et al., 2017). Greater levels of aerobic physical activity (200 - 300 min·week^{-1}) are recommended to maintain weight loss or minimize weight regain in the long term after BS (Jensen et al., 2014). Some recent works also support this view but expand the effects of early delivery or PAPs after BS to physical condition-related outcomes, and not only to weight loss. For example, Hassannejad, Khalaj, Mansournia, Rajabian Tabesh and Alizadeh (2017), implemented a non-supervised PAP starting on the first month after surgery and extending for 12 weeks. Participants were asked to walk a total time of 150 to 200 min·week^{-1}, 3-5 days·week^{-1} and were educated about following a standard high-protein diet prepared/recommended by a trained nutritionist. Besides, a second intervention group was asked to carry out the same aerobic intervention combined with strength exercises using elastic bands. By the end of the intervention, patients in both groups showed a significant decrease of body weight, FM and FM%, and an increase in aerobic functional capacity, in comparison with a control group. However, lower extremity functionality measured with the sit-to-stand test improved similarly in the three groups after surgery, thus suggesting that at this early stage weight loss, rather than exercise, accounts for most of this effect. Similarly, Morana, Collignon and Nocca (2018), performed a functional rehabilitation program consisting in endurance training at the estimated maximal fat oxidation intensity, combined with strengthening and proprioception exercises, twice a week, for a total of 20 90-min sessions. PAP was delivered to BS patients two months after surgery. After the intervention, participants showed significant reductions in excess weight loss percentage, FM%, and waist and hip circumferences, as well as a significant increase in FFM% and in the self-reported physical activity level through the Baecke questionnaire. Likewise, Campanha-Versiani et al. (2017), implemented a twice weekly PAP during 36 weeks of combined weight-bearing and aerobic exercises (in this order of presentation) 1 month after BS. PAP caused significant reductions in anthropometric measurements, but as an unexpected result, a reduction of bone mineral density and bone mass was noticed. Our own observations support the idea that early introduction of PAP after surgery may reduce cardiovascular risk factors, improve glycaemic control and contribute to maintain FFM% (Hernández García et al., 2015a, 2015b; Hernández García, Aracil, García Valverde, Guillén García, & Moya-Ramón, 2016).

Given the fact that weight loss in the first semester after BS seems to be caused mainly by the surgical intervention per se, it seems interesting to know the effect of PAPs delivered by this time point. In this regard, the recent reports of Mundbjerg et al. (2018a & 2018b) have studied the effects of a supervised PAP delivered at 6 months after surgery. Participants were evaluated before the intervention as well as at 6, 12 and 24 months after surgery. The PAP combined aerobic exercise with resistance training, two weekly 40 min sessions each, during 26 consecutively weeks. Compared to the control group, the PAP did not improve anthropometry, abdominal fat, blood pressure, heart rate, glucose, insulin resistance and total cholesterol significantly, neither at the end of the intervention, nor at the retention measurement taken one year after (Mundbjerg et al., 2018b). In contrast, in the retention evaluation body weight and BMI were significantly lower in the intervention group (Mundbjerg et al., 2018a, 2018b). Additionally, glycated glucose tended to be lower in the intervention group at the retention measurement (Mundbjerg et al., 2018b). In addition, the PAP significantly improved VO_{2max}, hip adduction and the score at the stair climb test by the end of the intervention. However, these improvements were lost at the retention evaluation (Mundbjerg et al., 2018a).

Introduction of PAPs at later times after surgery also seem to impact weight control and physical function in BS patients. In the recent report by Herring et al. (2017), a PAP consisting in 3 weekly sessions, 60 min each, of aerobic exercise at moderate intensity and a 12-week resistance training, was combined with a standard, individual lifestyle advice session. Patients were recruited between 12 and 24 months after BS. Their results showed significant improvements in physical function, and reductions of body weight, FM, systolic blood pressure and heart rate at rest, in comparison with a control group that followed the usual follow-up care. The effects on anthropometric variables and systolic blood pressure persisted in a retention evaluation conducted 12 weeks after ending the intervention. In contrast, spontaneous moderate-to-vigorous physical activity and resting heart rate were not different among groups at the retention evaluation. A detailed summary of all these interventions may be found in table 2.

TABLE 2
Summary of the studies analyzed in this review in which a physical activity program after bariatric surgery is applied.

Ref.	Sample	Physical activity prescription				Time after BS	Multidisciplinary interventions	Results	
		Volume	Intensity	Frequency	Type			Anthropometry & health status	Fitness & quality of life
Hassannejad et al., 2017	AG ASG CG	12 weeks AE: 150-200 min per week SE: 20-30 min	AE: 12-14 RPE SE: green or blue for W and M	AE: 3-5 days SE: 3 sessions	Non-supervised sessions AE: walking SE: elastic band STCH: shoulder and hip (extension, flexion, abduction and adduction)	1 month	Education about having standard high-protein diet by a trained nutritionist	AG: *↓ BW, FM, FM% ASG: *↓ BW, FM, FM% CG: ↓ BW, FM, FM%	AG: *↑ 12MWRT; ↑ STST ASG: *↑ 12MWRT; ↑ STST CG: ↑ 12MWRT, STST
Morana et al., 2018	n = 23	20 sessions Session: 90 min AE: 20 min the first 6 sessions, 30 min the 7th to 10th, and 30 min the 11th to 20th changing machine each 15 min	AE: 60% HRmax estimated, assumed as Fatmax intensity SE: not reported	2 sessions	AE: circuit training SE: rower for the upper and lower limbs, and pulling an elastic band for core PE: single-leg stance with ball throws against a wall	2 months	Not applied	*↓ Excess weight loss %, waist and hip circumferences, HR_{rest}; FM%; *↑ FFM%	*↑ Physical activity level of the Baecke questionnaire

TABLE 2 (CONT.)

Ref.	Sample	Physical activity prescription				Time after BS	Multidisciplinary interventions	Results	
		Volume	Intensity	Frequency	Type			Anthropometry & health status	Fitness & quality of life
Campanha-Versiani et al., 2017	EG (n=18) CG (n=19)	36 weeks Session: 60 min SE: 8 exercises, 1-3 sets of 10-12 reps AE: 25 min	SE: 10RM, revaluated each 6 weeks AE: 70-80% HRmax	2 sessions	SE: bench press, posterior shoulder, seated leg curl and leg press AE: treadmill	1 month	Vitamin supplementation with Centrum®, and individualized dietary and nutrition advice to an appropriated calorie balance (60 g/protein/day)	EG: *↓ BMD and anthropometrics CG: *↓ BMD, greater than in EG; *↓ anthropometric	Not measured
Mundbjerg et al., 2018a	EG (n=32) CG (n=28)	26 weeks Session: 40 min AE: 15 min SE: 10 min, 20-10 reps AT optional: 15 min	AE: 50-70% VO_{2max} SE: 60-75% RM	2 sessions	AE: bike training SE: lateral raises, lateral pull-downs and chest press AE optional: stair climbing, rowing or treadmill	6 months	Not applied	Not measured	EG: **↑ VO2max, MS_{H-ADD}, SCT; ↑ MS_{H-ABD}, MS_{S-ADD}, MS_{S-ABD} CG: ≠
Mundbjerg et al., 2018b								EG: ↓** DBP, BMI, BW; **↑ HDL CG: ↓ BMI, BW	Not measured

TABLE 2 (CONT.)

Ref.	**Sample**	**Physical activity prescription**				**Time after BS**	**Multidisciplinary interventions**	**Results**	
		Volume	**Intensity**	**Frequency**	**Type**			**Anthropometry & health status**	**Fitness & quality of life**
Herring et al., 2017	EG (n=12) CG (n=12)	12 weeks Session: 60 min AE: 35-45 min SE: 2 exercises, 3 sets of 12 reps + 30-60 s rest	AE: 64-77% HRmax (12-14 RPE) SE: 60% RM	3 sessions	AE: personalised for each individual SE: leg press, abdominal twists, leg extensions	Between 12 and 24 months	A standard, individual lifestyle advice session (30-60') to discuss topics such as regular physical activity, diet information and goal settings.	EG: **↓ BW, FM, SBP, HRrest CG: ↓ BW, FM	EG: **↑ ISWT, STST CG: ↑ ISWT

*AG: aerobic group; ASG: aerobic and strength group; CG: control group; EG: experimental group; M: men; W: women; AE: aerobic exercise; SE: strength exercise; STCH: stretching; BS: Bariatric surgery; HR_{max}: maximal heart rate; RPE: rate of perceived exertion; BW: body weight; BMI: body mass index; FM: fat mass; FM%: fat mass percentage; FFM%: fat-free mass percentage; WC: waist circumference; HC: hip circumference; BMD: bone mineral density; SBP: systolic blood pressure; DBP: diastolic blood pressure; HDL: high density lipoprotein; HRR: heart rate reserve; VO_2 max: maximal oxygen uptake; 12MWRT: 12-min walk-run test; ISWT: incremental shuttle walk test; MS_{H-ABD}: maximal strength in hip adduction; MS_{S-ABD}; maximal strength in shoulder abduction; MS_{S-ADD}: maximal strength in shoulder adduction; PE: proprioception exercise; SCT: stair climb test; STST: sit-to-stand test; * intragroup differences (p <0 .05); ** among groups differences (p < 0.05).*

Psychosocial effects of physical activity programs applied to bariatric surgery patients

In addition to their effects on weight loss and physical function, PAPs in the context of BS may also produce psychological effects on severely obese individuals. For example, anxiety and depression are emotional states which derive in excess eating consumption in patients awaiting BS, so its presence should be taken into account during the development of PAPs. A systematic review by Jiménez-Loaisa, Beltrán-Carrillo, González-Cutre and Cervelló (2015) showed that BS usually has positive effects in health-related quality of life, depression and anxiety levels, psychiatric symptoms, self-esteem, body image and social relationships in patients that undergo this surgery. Postoperative weight loss reached, and the subsequent increased perceived physical functioning may account, at least partly, for the increased physical activity levels and social life. However, a lack of knowledge on physical activity prescription recommendations was identified to optimise its benefits (Jiménez-Loaisa et al., 2015). Similarly, Delgado Floody et al. (2015b) observed that a 12-week PAP in which resistance training was combined with nutritional and psychological advice sessions significantly decreased depression levels, without affecting anxiety levels. Similarly, in their review Filou et al. (2017) showed that patients undergoing BS had decreased depression and anxiety levels, and their quality of life increased after an aerobic exercise program.

Additionally, a significant decrease in the fear of injury and embarrassment during physical activity as well as improvements in perceived quality of life, emotions, social interactions and sexual life were observed after a PAP combining aerobic and strength exercises (Baillot et al., 2013). There was a non-significant change in confidence in athletic ability and in beliefs in exercise benefits (Baillot et al., 2013), although weekly, vigorous physical activity levels increased significantly (Baillot et al., 2016).

DISCUSSION AND CONCLUSIONS

This non-exhaustive review aimed to frame the current general knowledge on the effects of PAPs on BS patients. From our point of view, current knowledge on the effects of PAPs on BS patients is still limited but has increased progressively during the last years. However, as pointed out some years ago (Moya et al., 2014) heterogeneity in this field is still remarkably high and comes mainly from: a) study design; b) PAPs characteristics, including the timing for their implementation; and c) outcomes to be measured.

Regarding heterogeneity from study designs, most interventional studies were characterized by small sample sizes, with patients usually coming from a single centre. In the studies on patients awaiting BS, the absence of control groups is noticeable. Additionally, the surgical technique practiced by the enrolled participants is variable. Most of them underwent Roux-en-Y gastric bypass or sleeve gastrectomy, which influence weight loss through different biologic mechanisms. Consequently, due to the relative paucity of severe obese individuals selected for BS, one possibility to overcome these sources of heterogeneity could be to foster the development of collaborative multicentre studies in the future.

In practice, changing physical activity patterns of severe obese adults is challenging because of the barriers associated with excess body weight, which affects functional capacity and, consequently, their possibilities to reach the recommended daily level of physical activity (King & Bond, 2014). Thus, development of PAPs in this population should be supervised by expert exercise professionals, who are able to adjust the program characteristics to the evaluation and progression of the individuals, and to provide feedback to motivate and engage them. Given that after stopping PAPs their effects usually revert, it may be suggested that expert exercise professionals should be included in the multidisciplinary teams working with BS patients along the whole process, in order to stimulate the acquisition of healthy lifestyle which would let patients carry out their daily activities autonomously. However, several questions are still under discussion to optimize the effects of PAPs before and after BS.

Introduction of PAPs for each patient awaiting for surgery, i.e., not exclusively for BS candidates, is starting to be called "prehabilitation" (Fry, Hallway, & Englesbe, 2018). Weight loss before surgery by PAPs produces significant improvements in lung function and gas exchange, which can substantially reduce morbidity and mortality in individuals with severe obesity (Delgado Floody et al., 2015b). Additionally, having a physically active lifestyle before surgery could also contribute to maintaining FFM and basal metabolic rate, which are usually reduced after BS because of decreased energy intake conditions and have been shown to predict weight regain (Guida et al., 2018). To reach these objectives, aerobic exercise is the most common form of exercise recommended to patients awaiting BS due to its easier transfer capacity to daily life activities. However current interventional studies summarized in this review combined different type of exercises and workloads to improve functional capacity through weight loss and physical fitness improvements. Consequently, other modalities of exercise in the context of patients awaiting BS are gaining momentum. For instance, resistance training until muscle failure can contribute to maintaining FFM during intense weight-loss periods before BS (Delgado Floody, Jerez Mayorga, Caamaño Navarrete, Osorio Poblete, et al., 2015). Our preliminary data suggest that maintenance of FFM may, in turn, contribute to mitigate the reductions in basal metabolic rate caused by weight loss (Picó-Sirvent, Aracil, Sarabia-Marín, Pastor, & Moya-Ramón, 2018).

Concerning the optimal intensity for each exercise modality, there is still little information. Given the limited time for development of PAPs in patients awaiting BS, high-intensity interval training (HIIT) may be considered a suitable option. HIIT and moderate intensity continuous training have already been applied in obese individuals and have been associated with similar body fat reduction rates (Keating, Johnson, Mielke, & Coombes, 2017). However, in the context of severe obese adults awaiting BS, HIIT effects are mostly unknown because this modality of exercise is generally assumed as not suitable for patients with moderate-to-high cardiovascular risk (Al-Hazzaa, 2016). Consequently, more research in this field would be welcome. In addition to the above described effects of PAPs developed before surgery on body composition and physical condition, psycho-social outcomes such as improving adherence and beliefs related to physical activity benefits should be also taken into account, because they can affect the individual's motivation and self-confidence to practice autonomously.

The role of PAPs after BS has been studied more in the literature than the role of PAPs before BS. According to the recent review of Filou et al. (2017) weight loss in the months immediately after surgery is caused by the surgery per se, and seems to be independent of PAPs. However, the role of PAPs on other outcomes, such functional capacity and psycho-social well-being at these initial stages after surgery remains poorly studied. Latter introduction of PAPs after surgery (12-24 months) are effective for improving and/or maintaining the effects of BS, that tend to revert by that time. In a similar way to pre-surgery PAPs, aerobic exercise is commonly accepted as the indicated exercise modality after surgery, but interventional studies using different aerobic and strength exercise combinations have been carried out in the last years. Interestingly, most of them introduced resistance training at an intensity of 60-70% of one maximal repetition to maintain FFM, which seems to be related to basal metabolic rate, an independent predictor of future weight gain (Guida et al., 2018). Although physical activity before surgery has been suggested as a lifestyle intervention which could provide low surgical risk and a better recovery process (Sánchez Ortega et al., 2014), these claims seem to be insufficiently demonstrated in BS. To our knowledge, there is only one publication in which a PAP was applied preoperatively and its effects on spontaneous physical activity were measured one year after BS (Baillot et al., 2017a). Given that weight loss could be extended until 24 months after the surgical intervention (Schauer, Ikramuddin, Gourash, Ramanathan, & Luketich, 2000), prolonged follow-up periods are needed to demonstrated the effect of interventions developed before BS on postsurgical outcomes. In addition, we have not found any study that compares different effects related to physical activity depending on the type of surgical procedure.

Therefore, in order to obtain a clearer effect of the role of PAPs they should be accurately designed and be reproducible in any context. Relevant outcomes, that would allow mechanistic explanations, should be outlined, and measurement instruments and protocols should be standardized. Last, but not least, some disagreement can be found concerning the appropriate timing for introducing PAPs in the context of BS. On the one hand, Sánchez Ortega et al. (2014), proposed that the optimal timing for introducing PAPs could be before surgery for two reasons: 1) to gradually accustom patients to the changes that must be introduced in their lifestyle; and 2) to estimate their degree of motivation to strengthen the psychological treatment prior to surgery. On the other, Stewart and Avenell (2016), consider that the optimal time to initiate them could be by one year after surgery, when patients have adjusted to the physiological changes associated with BS and may be readier to incorporate lifestyle changes into their behaviour. Consequently, from a translational point of view, all these gaps have yet to be filled before PAPs could be definitely incorporated to the clinical standards of treatment of severe obese patients in the context of BS.

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ANNEXE 2

STUDY 2

Effects of a Combined High-Intensity Interval Training and Resistance Training Program in Patients Awaiting Bariatric Surgery: A Pilot Study.

Note. This article was published.

Picó-Sirvent I, Aracil-Marco A, Pastor D, Moya-Ramón M. Effects of a Combined High-Intensity Interval Training and Resistance Training Program in Patients Awaiting Bariatric Surgery: A Pilot Study. Sports (Basel). 2019 Mar 25;7(3):72. doi: 10.3390/sports7030072. PMID: 30934623; PMCID: PMC6473567.

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Effects of a Combined High-Intensity Interval Training and Resistance Training Program in Patients Awaiting Bariatric Surgery: A Pilot Study

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Received: 19 February 2019; Accepted: 21 March 2019; Published: 25 March 2019

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Abstract: Bariatric surgery (BS) is considered the most effective treatment for morbid obesity. Preoperative body weight is directly associated with a higher surgical morbimortality and physical activity could be effective in the preparation of patients. The aim of this study is to determine the effects of a six-month exercise training program (ETP), combining high-intensity interval training (HIIT) and resistance training in patients awaiting BS. Six candidates awaiting BS (38.78 ± 1.18 kg·m^{-2}; 38.17 ± 12.06 years) were distributed into two groups: the ETP group (experimental group (EG), n = 3) and a control group (CG, n = 3). Anthropometrical and blood pressure (BP), cardiorespiratory fitness and maximal strength were registered before and after the ETP. The EG participated in 93.25% of the sessions, showing reductions in body mass index (BMI) compared to the CG (34.61 ± 1.56 vs. 39.75 ± 0.65, $p = 0.006$, ANOVA). The inferential analysis showed larger effects on BMI, excess body weight percentage and fat mass, in addition to small to moderate effects in BP and the anthropometric measurements. Peak oxygen uptake normalized to fat-free mass showed likely positive effects with a probability of >95–99%. A six-month ETP seems to be a positive tool to improve body composition, cardiometabolic health, and fitness level in patients awaiting BS, but a larger sample size is needed to confirm these findings.

Keywords: morbid obesity; resistance training; HIIT; body composition; cardiometabolic risk

1. Introduction

Obesity is considered a worldwide epidemic, one of the greatest public health problems, and one of the primary death causes, both in the European Union and in the USA [1,2]; likewise, obesity is associated with cardiovascular disease risk factors, some types of cancer, type 2 diabetes mellitus, hypertension, hyperlipidemia, immune response affectation, greater morbidity and mortality state, and a considerable reduction of life expectancy [3,4]. In addition, the increase in the obesity rate and its associated diseases have been related to an increase in the variety of therapeutic interventions [5]. In cases of morbid obesity (body mass index (BMI) $\geq$ 40 kg/m^2), bariatric surgery (BS) has been demonstrated to be the most effective treatment for the loss and maintenance of body weight, as well as for the improvement of comorbidities and mortality associated with this pathology [6]. Nevertheless, even though physical activity is recommended to optimize BS results, nowadays the majority of candidates for BS are sedentary and do not increase their physical activity levels after surgery [7].

The influence of physical activity in maintaining long-term weight loss has been known for years, but its role in the preparation of patients awaiting surgery is not well-known. It has been suggested that it could reduce anesthetic risk and improve postoperative recovery [8]. The higher the preoperative weight is, the higher the risk of morbidity and mortality is. Currently, a low-calorie diet is recommended in short-term preoperative weight loss interventions, as these diets seem to be related to a decrease in the liver size and intraabdominal fat mass which reduce the surgical risk [9]. However, the loss of fat-free mass (FFM) associated with these interventions is an unintended consequence of BS and it is expected to cause a decrease in resting energy expenditure (REE) that could be related to weight regain after surgery [10]. Consequently, it is necessary to implement programs that improve the preoperative conditions and reduce the risk factors in patients awaiting BS. Experimental studies show that exercise training program (ETP) physical activity programs after BS provide benefits for health and fitness level in individuals with morbid obesity [11–13]. Moreover, after a physical activity program lasting six months prior to BS, there were increases in the practice of postoperative physical activity [14]. Other studies in which preoperative ETPs were conducted combining aerobic training with resistance training or only applying aerobic or resistance training have been shown to be effective in improving body weight, physical condition, quality of life related to health, and they also help to improve their willingness to practice physical activity in candidates awaiting BS [3,8,15–19]. However, methodologies to prescribe a training workload are not well-defined in this population.

Several studies have consistently found that high-intensity interval training (HIIT) is useful to increase aerobic capacity and muscle mass, the benefits of which are similar to those obtained with moderate-intensity continuous training (MICT) [20–24]. Nevertheless, HIIT is a time-efficient methodology that allows improvements in cardiorespiratory fitness and work capacity, mitochondrial muscle biogenesis and GLUT-4 levels, insulin sensitivity, fasting glucose, HbA1c and reduces several cardiometabolic risk factors in overweight/obese populations [25–27].

In addition, to our knowledge, there are no studies that analyze the effects of applying an ETP to increase or maintain muscle mass combining HIIT and resistance training with progressive loads. Although it has been amply demonstrated that resistance training with progressive resistance is safe, effective, and potentially more valid than aerobic exercise in many groups of patients [19], there is little scientific evidence to determine the exercise type, training loads to apply and results derived from ETP in patients with type III obesity awaiting BS.

The main purpose of this study was to determine the effects of a structured ETP, combining HIIT and resistance training with progressive workloads on the anthropometric profile, cardiometabolic risk factors (CRF), cardiorespiratory fitness and strength levels of patients with morbid obesity that are candidates for BS.

2. Materials and Methods

2.1. Participants

Six patients awaiting BS voluntarily took part in this study after being recommended to participate by the obesity surgery medical team both from the University Hospital of Vinalopó and the University General Hospital of Elche. They were divided, depending on their suitability possibilities to participate in a training program, into an experimental group (EG) or a control group (CG) that followed the usual medical care indications, see Table 1. Patients were eligible if they were awaiting BS and led a sedentary lifestyle (less than one hour of structured exercise weekly). The exclusion criteria were to suffer from: (a) any cardiovascular disease; (b) asthma or chronic obstructive pulmonary disease; (c) hypothyroidism or (d) functional limitations to perform an ETP. All participants were carefully informed about the risks associated with the study, and they were asked to sign an informed consent based on the Helsinki Declaration and approved by the University Ethical Committee.

Table 1. Baseline characteristics of participants before starting the exercise training program (ETP).

Variables	Total (n = 6)	EG (n = 3)	CG (n = 3)
Female (n)	5	2	3
Age (years)	38.17 ± 12.06	39.67 ± 10.21	36.67 ± 15.88
BMI ($Kg \cdot m^{-2}$)	38.78 ± 1.18	38.02 ± 1.16	39.54 ± 0.64
Weight (Kg)	111.83 ± 14.10	114.43 ± 19.11	109.23 ± 10.57
Fat mass (%)	46.40 ± 4.89	44.17 ± 6.21	48.63 ± 2.51
FFM (%)	53.60 ± 4.89	55.83 ± 6.21	51.37 ± 2.51
Visceral fat (%)	14.00 ± 3.88	15 ± 5.51	13.00 ± 2.08
$VO_{2peak\ abs}$ ($L \cdot min^{-1}$)	2.20 ± 0.86	2.62 ± 1.11	1.78 ± 0.29
$VO_{2peak\ abs/FFM}$ ($mL \cdot FFM^{-1} \cdot min^{-1}$)	35.77 ± 7.14	39.92 ± 8.01	31.61 ± 3.40
Systolic blood pressure (mmHg)	131.89 ± 27.39	144.22 ± 37.39	119.56 ± 4.53
Diastolic blood pressure (mmHg)	77.94 ± 13.48	83.22 ± 18.68	72.67 ± 4.63

Values are mean ± SD. ETP = exercise training program; EG = experimental group; CG = control group; Kg = kilograms; m = metres; BMI = body mass index; FFM = fat free mass; $VO_{2peak\ abs}$ = absolute peak oxygen uptake.

2.2. Procedure

All participants followed the usual presurgical care indications from their respective hospitals. The EG (n = 3) performed a six-month structured supervised ETP, in which the aerobic exercise they performed was carried out at high intensities and the resistance training was carried out with high workloads. The CG (n = 3) performed the same testing protocol, but without ETP.

The ETP was performed in the sports facilities of the University, under the direct supervision of sport sciences graduates. The weekly training frequency was established as two weekly sessions the first month up to four weekly sessions from the third month until the end of the program. The activities were individualized for each patient.

The EG and CG were tested a week before starting the ETP (E1), and six months after, at the end of the program (E3). In addition, the EG underwent an intermediate evaluation (E2) to check the evolution of the participants and to adapt the training loads. Body composition, cardiometabolic risk factors (CRF) and physical fitness were measured in a laboratory under controlled conditions.

2.3. Anthropometry, Body Composition and CRF Measurements

Patients visited the laboratory between 0700 and 0900 hours, after 12 h of overnight fasting, and with an empty bladder [28]. Caffeine or alcohol consumption and exercise were forbidden in the 48 h prior to the test. Total body weight and body composition were measured by bioimpedance analysis (Tanita BC-420MA, Tanita, Tokyo, Japan), and body mass index was calculated and expressed as $kg \cdot m^{-2}$. Blood pressure was measured according to established recommendations [29] using a digital sphygmomanometer (Microlife WatchBP Home, Heerbrugg, Switzerland). Both weight and the waist and hip circumferences were measured using the ISAK (International Society for the Advancement of Kinanthropometry) protocol [30].

2.4. Cardiorespiratory Fitness Measurement

A two-phase protocol on a cycle ergometer (Technogym Bike Med, Technogym, Gambettola, Italy), adapted from a previous study [31] was performed to determine the peak oxygen uptake (VO_{2peak}) and fat oxidation rates. Respiratory exchange was registered with an Oxycon Pro gas analysis system (Jaeger, Friedberg, Germany). Carbohydrate oxidation (CHO) and fat oxidation (FO) were calculated in the first phase, while the second phase was used to establish the VO_{2peak}. The first phase consisted of performing a 4-min warm-up at 40 watts (W), followed by increases of 20 W every 3 min, maintaining a cadence of 60 rotations per minute (rpm). The first phase ended if the respiratory exchange ratio (RER) reached 1.0 or cadence values reduced to under 60 rpm. At this point, the second phase, consisting of

20 W increments each minute until volitional fatigue, started. To calculate the VO_{2peak}, the average of the highest 30 s of peak oxygen was used and it was expressed in absolute values ($VO_{2peak\ abs}$).

2.5. Muscle Strength Measurements

Maximal dynamic and isometric strength (MDS and MIS, respectively) of the quadriceps and hamstrings were assessed by an isokinetic dynamometer (Biodex System 4; Biodex Medical Systems, New York, NY, USA). Participants performed a 5-min warm-up on a cycle ergometer (Technogym Bike Med, Technogym, Gambettola, Italy) at an intensity of 60% maximal heart rate (HR_{max}) before starting the test. After that, participants were seated on the dynamometer chair, with the chair back inclined at an angle of 85° between hip and back. Two Velcro straps were used to avoid pelvis and torso movements. The dynamometer rotation axis was aligned with the lateral femoral epicondyle, allowing movement in the sagittal plane. Three unilateral tests were performed with each limb, one isokinetic test and two isometric tests. The dominant limb was evaluated first, followed by the non-dominant limb, with a two-minute rest between tests and a three-minute rest between limbs.

MDS. Four sets of four concentric contractions (flexion-extension) of the knee were performed at an angular speed of 60°/s, with 90 s rest between repetitions. The knee motion range was 10°–105°. A first submaximal trial was performed to familiarize the participants with the protocol. The three following sets were performed at maximal individual effort, and participants were verbally encouraged to maintain their maximal effort in every contraction. The highest value of the last three sets was chosen to analyze the peak torque (N·m).

MIS. Participants completed a Maximum Voluntary Contraction (MVC) trial of four repetitions (the first set as a submaximal familiarization trial), with a fifteen-second rest between repetitions and were given verbal encouragement to perform at maximal effort for five seconds [32]. The angles used to assess the lower limbs were 105° for quadriceps and 75° for hamstrings.

2.6. Exercise Training Program (ETP)

A six-month ETP was performed by the EG, initially combining aerobic exercise at moderate intensities and resistance training to familiarise participants with physical exercise practice, see Table 2. The endurance training progressed from 60% to 95% VO_{2peak} intensities. The weekly frequency of the program was 2 days weekly (d/w) the first month, 3 d/w the second month, and 4 d/w from the third to the last month. The sessions lasted 60 minutes for the first two months and 70 minutes from the third to the last month. The endurance training days alternated MICT and HIIT. MICT sessions were performed from 60% to 85% HR_{peak}, while HIIT sessions were performed based on the percentage of VO_{2peak}. The HIIT programs were only performed on a cycle ergometer and consisted of intervals of 30 s of work interspersed by 30 s of active recovery at 30% VO_{2peak}. The MICT was carried out on a treadmill or on a cycle ergometer.

Resistance training was carried out after HIIT in the same session, prescribed based on the percentage of one repetition maximum (1RM), which was determined using the Brzycki formula [33]. The exercises (latissimus dorsi, pectorals, quadriceps, hamstrings, gastrocnemius, deltoids, triceps, and biceps brachial) were performed using guided machines with weights that ranged between 50% of 1RM and 75% of 1RM. All the sessions finished with five stretching exercises in standing (gastrocnemius, quadriceps, hamstrings, pectorals and latissimus dorsi).

To provide an internal load measure and to control the training process, each participant's rating of perceived exertion (RPE) was collected using the CR-10 Borg's scale [34]. RPE was taken 30 min after the end of each session, in order to prevent difficult or easy exercises near the end of the session that could influence the overall rating of the session [35].

Table 2. ETP schedule (EG).

	Month	1	2	3	4	5	6
MICT	Weekly frequency (sessions/week)	2	1	2	2	2	2
	Volume (min)	35	50	50	50	50	50
	Intensity (% HR_{peak})	60–70	65–75	70–80	70–85	70–85	70–85
HIIT	Weekly frequency (sessions/week)		2	2	2	2	2
	Volume (min)		20	20	20	20	20
	Intensity (% VO_{2peak})		60–70	70–80	75–85	80–90	80–95
Resistance training	Weekly frequency (sessions/week)	2	2	2	2	2	2
	Volume (series × exer. × rep.)	1 × 5 × 20	1 × 7 × 20	4 × 4 × 15	4 × 4 × 12	4 × 4 × 10	4 × 4 × 10
	Intensity (% 1RM)	55	60	65	70	75	75
Stretching training	Weekly frequency (sessions/week)	2	3	4	4	4	4
	Volume (series × exer.)	1 × 5	1 × 5	1 × 5	1 × 5	1 × 5	1 × 5
	Duration (min)	1	1	1	1	1	1

ETP = exercise training program; EG = experimental group; MICT= moderate-intensity continuous training; HIIT = high-intensity interval training; % HR_{peak} = peak heart rate percentage; min = minutes; % VO_{2peak} = peak oxygen uptake percentage; exer. x rep. = number of exercises performed and number of repetitions by exercise; % 1RM = percentage over a maximum repetition.

2.7. Statistical Analysis

The data are presented as mean (±SD). The normal distribution of all data series was verified by the Kolmogorov–Smirnov test. A one-factor ANOVA was used to check the changes produced in physical condition, body composition and cardiometabolic variables for each of the two testing moments (pre-program vs post-program). A t-test was performed for multiple within-group comparisons when ANOVA showed significant interaction effects among groups.

All data were log-transformed for the analysis to reduce bias arising from non-uniformity error and then they were analyzed for practical significance using magnitude-based inferences [36]. The effect size (ES) was calculated using Cohen's coefficient [37], which allowed the magnitude of the changes between the test and the post-test to be established based on the performance of the training session (i.e., ES of ≥ 0.2 = small; ≥ 0.5 = moderate; ≥ 0.8 = large magnitudes of change, respectively). Descriptors were used to interpret the probabilities of effects (clinical inferences based on threshold chances of harm and benefit of 0.5% and 25%) [38]. The probability that the true effects are harmful, trivial or beneficial was considered as the following: <1%, almost certainly not; 1–4%, very unlikely; 5–24%, unlikely or probably not; 25–74%, possibly or maybe; 75–94%, likely or probable; 95–99%, very likely; >99%, almost certainly [38]. Changes in mean were also included for each group (expressed in %) and their 90% confidence limits (CL).

Statistical analysis was performed with the SPSS package program (version 22, SPSS Inc., Chicago, IL, USA) and the null hypothesis was rejected at the 95% significance level ($p \leq 0.05$). For clarity, all results are presented as positive improvements, so that negative and positive differences can be viewed in the same direction.

3. Results

3.1. Description of the Dynamic Loads Performed by the Experimental Group

The EG participated in 93.25 ± 6.5% of the sessions, without any injury or adverse event experienced. Internal load values (calculated as the product of total session time duration and intensity), the monotony and the strain index during each week of ETP are shown in Figure 1.

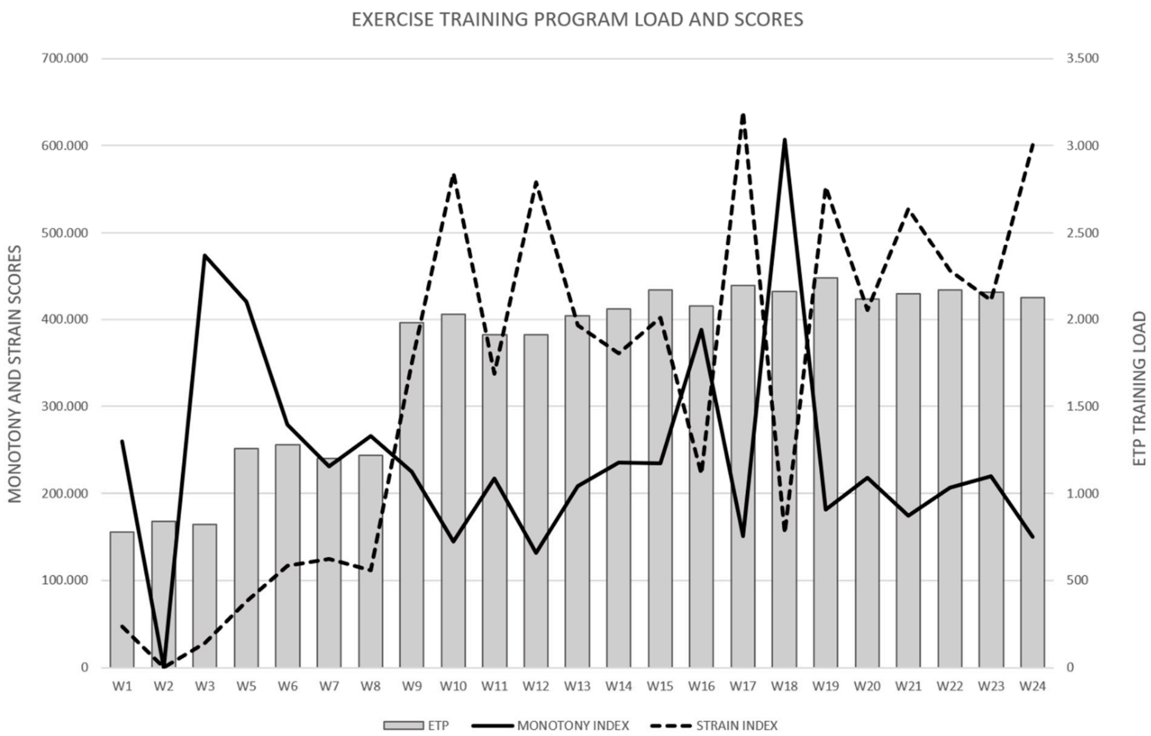


Figure 1. Load dynamics and scores during each week of ETP. W = week; ETP = exercise training program. * Week 4 does not show load values because 1RM tests were performed.

3.2. Anthropometry and Body Composition

After performing the ETP, ANOVA showed no statistically significant differences in all the variables evaluated in the EG, except in BMI and excess body weight percentage (EBW%), which had higher significant reductions than the CG (34.61 ± 1.56% vs 39.75 ± 0.65%, p = 0.006, and 27.00 ± 4.06% vs 37.10 ± 1.02%, p = 0.014, respectively), as shown in Figure 2.

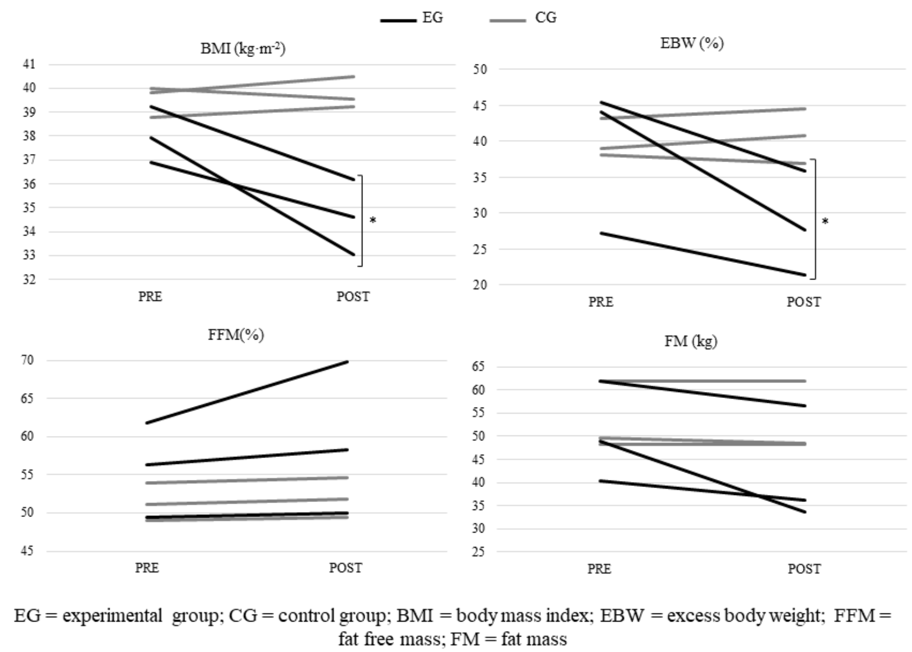
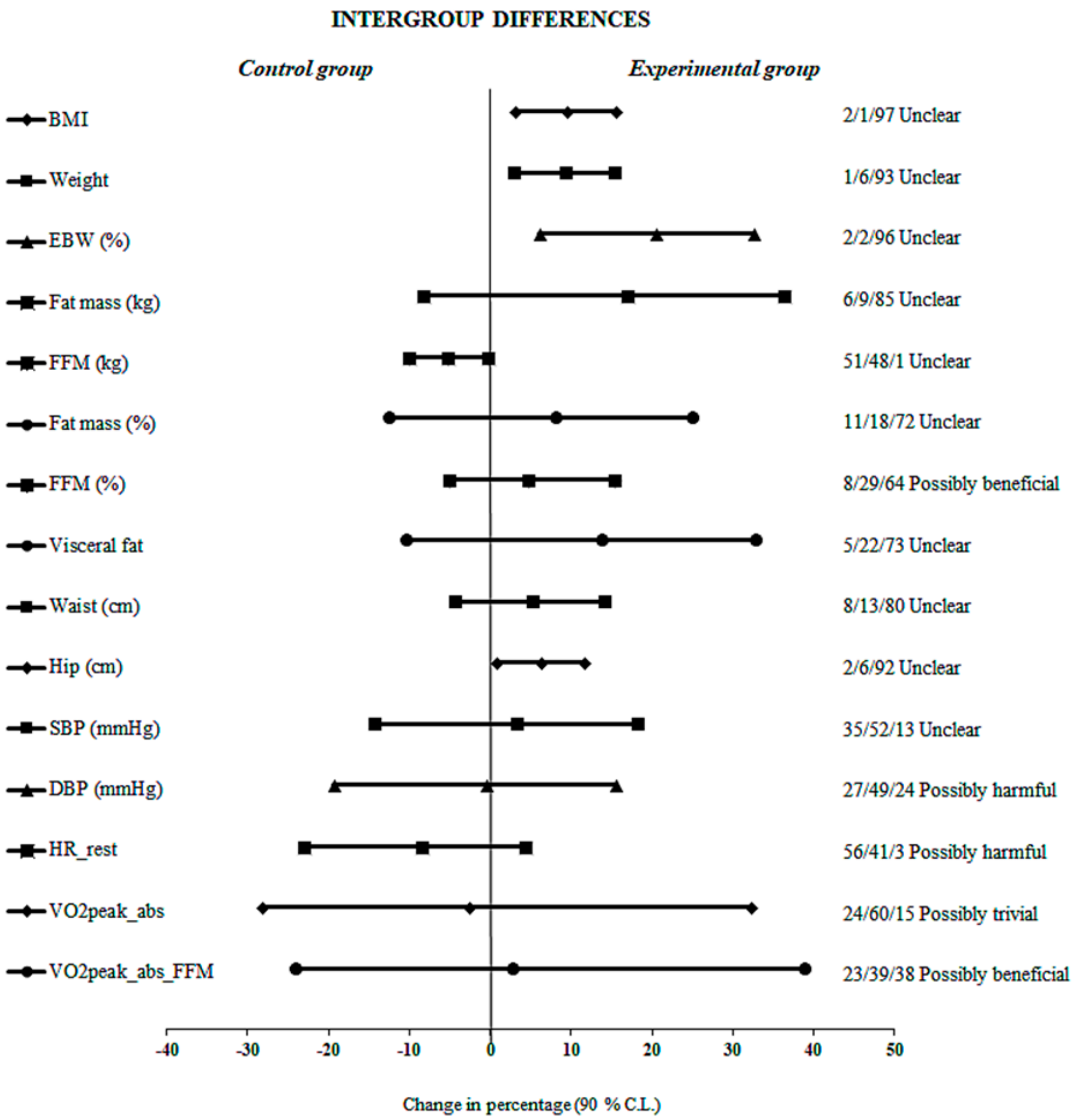


Figure 2. Changes in each participant in body composition variables after vs before ETP (* $p < 0.05$). There was no significant difference between the two groups for values observed before training.

T-test results are shown in Table 3 for the CG and EG, while among-group differences in the variables considered as the most relevant ones are represented in Figure 3. The EG shows a larger ES on BMI, EBW (kg, %) and fat mass (kg, %), which is not observed in the CG. In addition, all the anthropometric measurements showed small to moderate ES except FFM (kg) values. The inferential analysis showed unclear effects in BMI, EBW (kg, %), fat mass percentage (FM%) and visceral fat with a probability of ≥80–95%. However, likely positive effects with a probability of >95–99% were shown in the fat-free mass percentage (FFM%). Finally, two correlations between fat mass (kg) and FFM%, FM% and hip circumference were observed (r = −0.875 and r = 0.822, respectively). Qualitative inference and likelihood (%) of the effects being positive/trivial/negative for each of the groups could be consulted in Table S1.



CL = coefficient limits; BMI = body mass index; EBW = excess body weight; FFM = fat free mass; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR_{rest} = heart rate at rest; $VO_{2peak\ abs}$ = absolute peak oxygen uptake; $VO_{2peak\ abs/FFM}$ = absolute peak oxygen uptake normalized to FFM

Figure 3. Changes in anthropometric measurements, cardiometabolic risk factors and physical fitness variables among groups.

Table 3. Descriptive characteristics (mean ± SD) on anthropometric measurements before and after the ETP for each of the groups.

	EG (n = 3)			CG (n = 3)		
Variables	**Pre**	**Post**	**ES (d) (90% CL)**	**Pre**	**Post**	**ES (d) (90% CL)**
BMI (kg·m^{-2})	**38.02 ± 1.16**	**34.61 ± 1.56 ***	3.30 (1.05; 5.54)	39.54 ± 0.64	39.75 ± 0.65	**−0.19 (−1.03; 0.66)**
Weight (kg)	114.43 ± 19.11	103.87 ± 14.80	0.57 (0.18; 0.57)	109.23 ± 10.57	109.87 ± 11.43	−0.03 (−0.18; 0.11)
EBW (kg)	38.83 ± 10.14	28.27 ± 7.27	2.71 (0.79; 4.62)	40.09 ± 2.70	40.72 ± 3.74	−0.12 (−0.68; 0.43)
EBW (%)	**33.55 ± 3.89**	**27.00 ± 4.06 †**	4.42 (1.19; 7.65)	36.77 ± 1.04	37.10 ± 1.02	**−0.18 (−1.00; 0.63)**
Fat mass (kg)	50.48 ± 10.87	42.16 ± 12.52	0.81 (−0.30; 1.91)	53.25 ± 7.49	52.91 ± 7.91	0.03 (−0.08; 0.14)
Fat mass (%)	44.17 ± 6.21	40.63 ± 9.94	**−1.08 (−1.15; 3.31)**	**48.63 ± 2.51**	**48.03 ± 2.65 ***	0.14 (0.06; 0.21)
FFM (kg)	63.95 ± 13.83	61.71 ± 14.39	−0.32 (−0.70; 0.07)	55.98 ± 3.80	56.96 ± 4.40	0.14 (−0.05; 0.33)
FFM (%)	55.83 ± 6.21	59.37 ± 9.94	**0.66 (−0.48; 1.80)**	**51.37 ± 2.51**	**51.97 ± 2.65 ***	0.14 (0.08; 0.19)
Waist (cm)	120.27 ± 4.07	114.26 ± 5.68	0.37 (−0.31; 1.05)	115.62 ± 9.10	116.02 ± 8.18	−0.03 (−0.21; 0.16)
Hip (cm)	**130.57 ± 10.76**	**122.27 ± 13.63 †**	0.69 (0.12; 1.26)	134.04 ± 7.64	133.70 ± 8.72	0.03 (−0.14; 0.20)
WHR (cm)	0.93 ± 0.09	0.94 ± 0.06	−0.10 (−0.54; 0.35)	0.86 ± 0.08	0.87 ± 0.08	−0.04 (−0.10; 0.02)
Visceral fat (%)	14.67 ± 5.51	12 ± 2.65	**0.62 (−0.24; 1.47)**	12.67 ± 2.08	12.33 ± 1.53	0.08 (−0.16; 0.32)

PAP = physical activity program; EG = experimental group; CG = control group; CL = coefficient limits; BMI = body mass index; EBW = excess body weight; FFM = fat free mass; WHR = waist-to-hip ratio. * Statistical significant intragroup differences ($p < 0.05$, paired t-test). † ($p = 0.052$; $p = 0.059$, paired t-test).

Table 4. Descriptive characteristics (mean ± SD) on cardiometabolic risk factors and physical fitness variables before and after the PAP, for each of the groups.

	EG (n = 3)			CG (n = 3)		
Variables	**Pre**	**Post**	**ES (d) (90% CL)**	**Pre**	**Post**	**ES (d) (90% CL)**
SBP (mmHg)	144.22 ± 37.39	139.28 ± 28.76	0.41 (−2.02; 2.84)	119.56 ± 4.53	120.61 ± 8.92	−0.11 (−2.09; 1.86)
DBP (mmHg)	83.22 ± 18.68	79.83 ± 18.37	0.37 (−0.53; 1.28)	72.67 ± 4.63	69.39 ± 6.09	0.42 (−1.23; 2.06)
HR_{rest} (bpm)	56.33 ± 12.34	62.00 ± 11.53	−0.26 (−0.54; 0.03)	65.67 ± 13.58	66.67 ± 13.32	−0.04 (−0.32; 0.23)
$VO_{2peak\ abs}$ ($L \cdot min^{-1}$)	2.62 ± 1.11	2.69 ± 1.04	0.11 (−0.12; 0.35)	1.78 ± 0.29	1.89 ± 0.37	**0.21 (−0.85; 1.28)**
$VO_{2peak\ abs/FFM}$ ($mL^* \cdot FFM^{-1} \cdot min^{-1}$)	39.92 ± 8.01	42.58 ± 6.24	**0.38 (−0.23; 0.99)**	31.61 ± 3.40	33.07 ± 4.45	**0.23 (−1.29; 1.76)**
$MDS_{D\text{-}Q}$ (N·m)	151.84 ± 36.10	155.16 ± 43.38	0.05 (−0.36; 0.45)	144.12 ± 21.46	149.50 ± 18.35	**0.14 (−0.16; 0.45)**
$MDS_{D\text{-}H}$ (N·m)	86.53 ± 24.87	84.54 ± 17.37	−0.02 (−0.53; 0.48)	66.06 ± 18.67	59.93 ± 14.97	−0.17 (−0.40; 0.07)
$MDS_{ND\text{-}Q}$ (N·m)	149.88 ± 47.94	161.74 ± 54.86	**0.35 (0.13; 0.58)**	141.14 ± 15.73	142.03 ± 19.00	0.02 (−0.44; 0.49)
$MDS_{ND\text{-}H}$ (N·m)	75.81 ± 14.93	85.66 ± 21.93	**0.56 (−0.21; 1.32)**	57.03 ± 6.42	60.81 ± 6.69	**0.32 (0.06; 0.57)**
$MIS_{D\text{-}Q}$ (N·m)	141.90 ± 19.18	139.77 ± 21.19	−0.07 (−0.30; 0.16)	138.76 ± 19.35	130.11 ± 3.89	−0.24 (−1.02; 0.54)
$MIS_{D\text{-}H}$ (N·m)	95.83 ± 23.39	90.53 ± 12.71	−0.12 (−0.69; 0.45)	72.16 ± 15.02	62.48 ± 14.31	−0.37 (−1.20; 0.45)
$MIS_{ND\text{-}Q}$ (N·m)	147.50 ± 3.47	151.73 ± 16.01	0.11 (−0.48; 0.69)	133.61 ± 17.80	121.02 ± 8.40	−0.40 (−0.90; 0.10)
$MIS_{ND\text{-}H}$ (N·m)	90.30 ± 15.95	89.10 ± 15.30	−0.02 (−0.32; 0.28)	61.71 ± 19.85	61.18 ± 10.31	−0.03 (−0.52; 0.46)

PAP = physical activity program; EG = experimental group; CG = control group; CL = coefficient limits; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR_{rest} = heart rate at rest; $VO_{2peak\ abs}$ = absolute peak oxygen uptake; $VO_{2peak\ abs/FFM}$ = absolute peak oxygen uptake normalized to FFM; MDS = maximal dynamic strength; D = dominant; ND = non-dominant; Q = quadriceps; H = hamstrings; MIS = maximal isokinetic strength. * Statistical significant intragroup differences ($p < 0.05$).

3.3. Physical Fitness and Cardiometabolic Risk Factors

After performing the ETP, significant differences among groups were found in MDS normalized to FFM (MDSFFM) in the non-dominant (ND) limb hamstrings (EG = 138.34±3.29 N·m·FFM^{-1} vs CG = 106.68 ± 6.77 N·m·FFM^{-1}; p = 0.002), as well as in MIS in the ND hamstrings normalized to FFM (EG = 145.68 ± 8.41 N·m·FFM^{-1} vs CG = 106.98 ± 10.85 N·m·FFM^{-1}; p = 0.008) and in the ND quadriceps (EG = 151.73± 16.01 N·m vs CG = 121.02 ± 8.40 N·m; p = 0.042).

T-test results are shown in Table 4 for the CG and EG, respectively. Both the EG and the CG showed improvements in diastolic blood pressure (DBP), VO_{2peak} when it was normalized to FFM ($VO_{2peak\ abs}$/FFM) and ND hamstring MDS level, but only the EG improved hip circumference, systolic blood pressure (SBP) and MDS level in the ND quadriceps. However, the EG showed small and moderate effects on MDS in the ND lower limb both in quadriceps (dQ = 0.35, likely beneficial) and hamstrings (dH = 0.56, likely beneficial), while inferior results were found in the CG for the same variables (dQ = 0.02, possibly trivial; dH = 0.32, likely beneficial). Qualitative inference and likelihood (%) of the effects being positive/trivial/negative for each of the groups can be consulted in Table S1.

4. Discussion

Our pilot study suggests that a six-month ETP, combining long-term HIIT with resistance training from 55% to 75% 1RM seems to be a positive intervention to improve body composition, CRF and physical condition in patients awaiting BS. Despite the limitations associated with our small sample size, this pilot study could be useful as a starting point to design future research with similar physical activity interventions. The ETP could be feasible since subjects participated in >90% of the total supervised sessions proposed, which resulted in practical significant improvements in most of the anthropometrical variables, SBP, DBP, cardiorespiratory fitness and maximal strength level in the non-dominant lower limb. To our knowledge, this study is the first to examine the effects of an ETP combining endurance and resistance training with a programed and monitored workload in this population.

The results related to changes in FM observed in the EG could explain significant reductions in BMI and EBW% ($p < 0.05$). Participants in the EG showed FM and visceral fat reductions after the ETP, while FFM remained constant. Therefore, FFM% increased after the ETP. Conservative weight loss programs aim to lose from 5% to 10% body weight to be able to consider a reduction as clinically significant to decrease surgical risk [39]. In this pilot study, the EG showed a decrease close to 6% in EBW% (33.55 ± 3.89 vs 27.00 ± 4.06, p = 0.052). Consequently, our ETP seems to be a positive tool that could be analyzed and added to traditional weight loss programs to complement the effects associated with pharmacological, psychological and nutritional treatments in patients awaiting BS. In fact, a recent study showed that a twice-weekly low-intensity physical activity program encouraged individuals to adopt a more active lifestyle, both with and without the aid of support group therapy for lifestyle modification [40]. Therefore, multidisciplinary treatments that include physical activity could be the key to optimize not only weight loss parameters before surgery, but also the surgical risk and health status of patients, helping them to adopt more physically active lifestyles.

There are no standardized guidelines to establish recommendations of physical activity in obese patients awaiting BS. Previous studies [4,17,41] have performed aerobic exercise combined with resistance training which reported changes in body composition and anthropometrical variables. Our pilot study is characterized by programming and monitoring workloads over a six-month period, showing higher reductions in waist and hip circumferences, BMI, body weight, FM and visceral fat percentages than results reported by similar studies [8,17,42]. These results could be explained by two reasons: a) The longer duration of our program (84 training sessions in total), and b) the individualization of training prescription according to percentages of their VO_{2peak} and 1RM tests. In addition, none of these interventions compare their results with a CG that followed the usual care indications, so it is difficult to interpret the effect that is directly associated with physical activity. Only Baillot et al. [42] compared the effects of a 12-week intervention with a CG, the results of which did not present changes in body composition and CRF. Conversely, our data show differences with practical significance in body composition, among patients that performed a structured ETP or followed the usual medical care; therefore it can be guaranteed that changes are not a consequence of a traditional BS treatment preparation exclusively.

Small to moderate changes were observed in most of the CRF and physical condition variables after performing an ETP. Both the EG and the CG showed improvements in some maximal muscle strength variables. However, although the EG showed higher changes in $VO_{2peak\ abs}/FFM$, the CG improved $VO_{2peak\ abs}$ as well, so no influence of the previous experience of participants during E1 could be implied. Because severely obese adults often suffer from chronic knee pain, breathing arrhythmia and exercise intolerance [43], patients could be limited to performing a maximal test to prevent injuries or negative experiences. Thus, these results could be explained by the absence of learning sessions of both isokinetic and cardiorespiratory test protocols. Therefore, these sessions could be an alternative so that patients get to know each protocol, and consequently, to check that the results obtained are consistent and reliable.

Our results in MDS levels can be explained by excessive intra- and intermuscular fat accumulation which characterizes our population and influences both the force generation and the functional capacity of a skeletal muscle negatively. Although our ETP is related to FM% and fat visceral reductions, the electrical bioimpedance method cannot discriminate the body area in which greater FM has been reduced. A recent study [44] has suggested that FFM, mainly in the lower limbs, is crucial to increase the absolute MVC torques and, consequently, to prevent losses of muscle strength and functional limitations. Therefore, it could be because our participants did not show significant differences in MDS and MIS after performing an ETP as FFM remained constant and changes in FFM% were a direct consequence of body weight reduction due to FM decrease.

All participants were sedentary adults with no previous experience in practicing physical activity. This is particularly interesting since one of the most relevant practical problems for exercise professionals is the amount of physical activity required to reach specific outcomes without a negative impact. Although our ETP was performed with high workloads, no significant changes in training load were registered from the third to the sixth month of the ETP, see Figure 1. This could imply that patients with severe obesity likely need approximately eight weeks, see Figure 1, to adapt to the systematic practice of physical activity. In addition, the strain of training was well-controlled through interspersing combined high-intensity training sessions (HIIT and resistance training) with MICT sessions from the second to the sixth month, which could explain why no participants suffered any injury during the ETP.

5. Conclusions

In summary, our data suggest that a six-month ETP could be a positive and safe intervention to support traditional weight loss treatments for patients awaiting BS. However, this pilot study is not enough to establish specific guidelines. Future studies with a larger sample size are needed to confirm these benefits which are apparently associated with an ETP before BS. In addition, post-surgery data would be interesting to be able to assess the real effectivity to reduce surgical risk and improve the recovery process.

Supplementary Materials: The following are available online at http://www.mdpi.com/2075-4663/7/3/72/s1, Table S1: Changes (%) in all the variables evaluated. Qualitative inference and likelihood (%) of the effects being positive/trivial/negative for each of the groups.

Author Contributions: Conceptualization, I.P.-S. and M.M.-R.; methodology, I.P.-S. and M.M.-R.; formal analysis, I.P.-S. and M.M.-R.; investigation, I.P.-S.; resources, M.M.-R.; data curation, D.P., A.A.-M. and M.M.-R.; writing—original draft preparation, I.P.-S.; writing—review and editing, D.P., A.A.-M. and M.M.-R.; supervision, A.A.-M. and M.M.-R.; project administration, M.M.-R.

Funding: This research received no external funding.

Acknowledgments: We would like to thank the medical teams of the Vinalopó University Hospital and the Elche General University Hospital for their collaboration recommending our programme to patients awaiting bariatric surgery.

Conflicts of Interest: The authors declare no conflict of interest.

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SUPPLEMENTARY MATERIAL

Appendix I. Changes (%) in all the variables evaluated. Qualitative inference and likelihood (%) of the effects being positive/trivial/negative for each of the groups.

Variables	EG (n=3)					CG (n=3)				
	% Change (90% CL)	Chances that the true effects were substantial				% Change (90% CL)	Chances that the true effects were substantial			
		Harmful	Trivial	Beneficial	Qualitative inference		Harmful	Trivial	Beneficial	Qualitative inference
BMI (kg·m^{-2})	9.0 (3.0;14.6)	2	1	97	Unclear	-0.5 (-3.0;1.9)	48	36	16	**Possibly harmful**
Weight (kg)	9.0 (3.0;14.6)	1	4	95	Unclear	-0.5 (-3.0;1.9)	4	94	2	Likely trivial
EBW (kg)	26.9 (8.7;41.5)	2	1	97	Unclear	-1.4 (-8.2;4.9)	36	52	12	Possibly harmful
EBW (%)	19.7 (5.7;31.7)	3	0	97	Unclear	-0.9 (-5.1;3.1)	48	37	15	**Possibly harmful**
Fat mass (kg)	17.5 (-7.4;36.6)	6	7	87	Unclear	0.7 (-1.9;3.3)	1	96	2	Very likely trivial
Fat mass (%)	9.3 (-11.0;25.9)	12	7	82	**Unclear**	1.2 (0.6;1.9)	0	93	7	Likely trivial
FFM (Kg)	-3.7 (-8.1;0.9)	76	21	3	Unclear	1.7 (-0.5;4.0)	2	76	22	Likely trivial
FFM (%)	5.8 (-4.0;16.6)	8	10	82	**Likely beneficial**	1.2 (0.7;1.7)	0	96	4	Very likely trivial
Waist (cm)	5.0 (5.0;13.6)	7	20	73	Unclear	-0.4 (-3.0;2.2)	6	91	4	Likely trivial
Hip (cm)	6.5 (1.1;11.6)	2	4	93	Unclear	0.3 (-1.4;1.9)	3	92	5	Likely trivial
WHR (cm)	-1.6 (-9.2;5.5)	29	62	10	**Possibly harmful**	-0.7 (-1.7;0.3)	1	99	0	Very likely trivial
Visceral fat (%)	15.9 (-6.8;33.8)	5	9	86	**Unclear**	2.3 (-4.5;8.6)	4	82	14	Likely trivial
SBP (mmHg)	144.22±37.39	27	14	59	Unclear	-0.8 (-14.8;11.6)	45	20	34	Unclear
DBP (mmHg)	83.22±18.68	10	21	68	Unclear	4.6 (-15.0;20.9)	19	17	63	Unclear
HR_{rest} (bpm)	56.33±12.34	68	29	2	**Possibly harmful**	-1.7 (-13.3;8.7)	12	82	6	Likely trivial
$VO_{2peak\ abs}$ (L·min^{-1})	2.62±1.11	20	77	3	Likely trivial	6.1 (-21.3;43.0)	19	30	51	**Possibly beneficial**
$VO_{2peak\ abs/FFM}$ (mL*FFM^{-1}·min^{-1})	39.92±8.01	5	18	76	**Likely beneficial**	4.4 (-21.1;38.0)	25	23	52	**Possibly beneficial**
MDS_{D-Q} (N·m)	151.84±36.10	19	70	11	Possibly trivial	4.0 (-4.3;13.0)	4	64	32	**Possibly beneficial**
MDS_{D-H} (N·m)	86.53±24.87	21	63	16	Possibly trivial	-8.6 (-19.7;4.0)	36	62	2	Unclear
MDS_{ND-Q} (N·m)	149.88±47.94	1	8	91	**Likely beneficial**	0.4 (-8.5;10.3)	15	66	19	Possibly trivial
MDS_{ND-H} (N·m)	75.81±14.93	5	10	85	**Likely beneficial**	6.7 (1.3;12.3)	1	14	84	**Likely beneficial**
MIS_{D-Q} (N·m)	141.90±19.18	12	85	4	Likely trivial	-5.6 (-22.1;14.2)	55	33	12	Unclear
MIS_{D-H} (N·m)	95.83±23.39	35	52	12	Unclear	-13.5 (-37.2;19.2)	70	21	9	Unclear
MIS_{ND-Q} (N·m)	147.50±3.47	13	53	34	**Possibly beneficial**	-9.0 (-19.1;2.3)	82	14	4	Unclear
MIS_{ND-H} (N·m)	90.30±15.95	11	81	8	Likely trivial	-1.4 (-31.3;21.7)	20	64	16	Possibly trivial

PAP = Physical Activity Program; EG = experimental group; CL = coefficient limits; BMI = body mass index; EBW = excess body weight; FFM = fat free mass; WHR = waist-to-hip ratio; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR_{rest} = heart rate at rest; $VO_{2peak\ abs}$ = absolute peak oxygen uptake; $VO_{2peak\ abs/FFM}$ = absolute peak oxygen uptake normalized to FFM; MDS = maximal dynamic strength; D = dominant; ND = non-dominant; Q = quadriceps; H = hamstrings; MIS = maximal isokinetic strength.

ANNEXE 3

STUDY 3

A Combination of Aerobic Exercise at Fatmax and Low Resistance Training Increases Fat Oxidation and Maintains Muscle Mass, in Women Waiting for Bariatric Surgery.

Note. This article was published.

Picó-Sirvent I, Manresa-Rocamora A, Aracil-Marco A, Moya-Ramón M. A Combination of Aerobic Exercise at Fatmax and Low Resistance Training Increases Fat Oxidation and Maintains Muscle Mass, in Women Waiting for Bariatric Surgery. Obes Surg. 2022 Apr;32(4):1130-1140. doi: 10.1007/s11695-022-05897-1. Epub 2022 Jan 20. PMID: 35048250; PMCID: PMC8933381.

Obesity Surgery
https://doi.org/10.1007/s11695-022-05897-1

ORIGINAL CONTRIBUTIONS

A Combination of Aerobic Exercise at Fatmax and Low Resistance Training Increases Fat Oxidation and Maintains Muscle Mass, in Women Waiting for Bariatric Surgery

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Received: 13 October 2021 / Revised: 3 January 2022 / Accepted: 11 January 2022

Abstract

Purpose There is no consensus on the best exercise recommendation for women affected by severe obesity while they are waiting for bariatric surgery. For this reason, the effects of a combination of aerobic exercise performed at the intensity at which maximal fat oxidation is reached (Fatmax) with low-intensity resistance training were studied.

Materials and Methods Twenty sedentary middle-aged Caucasian women (43.2 ± 7.5 years, BMI = 46.5 ± 5.9 kg·m^{-2}) were allocated to a control group (CG, $n = 10$) that followed solely the conventional preoperative care or to an experimental group (EG, $n = 10$) that, in addition, performed a 12-week individualized and supervised physical activity program (PAP) that combined aerobic training at Fatmax with low-intensity resistance training.

Results After the PAP, maximal fat oxidation during exercise increased in the EG (0.187 ± 0.068 vs 0.239 ± 0.080 g·min^{-1}, $p = 0.025$, pre *vs.* post, respectively), but resting fat oxidation did not (0.088 ± 0.034 vs 0.092 ± 0.029 g·min^{-1}, $p = 0.685$, pre *vs.* post, respectively). Additionally, the resting metabolic rate in the EG was also unchanged (1869 ± 406 *vs.* 1894 ± 336 kcal; $p = 0.827$, pre *vs.* post, respectively), probably because of the effects of resistance training on the maintenance of fat-free mass. No significant changes were observed in the CG.

Conclusion A PAP that combines aerobic exercise at Fatmax with low resistance training may counteract some of the deleterious side effects of the standard presurgical care of women waiting for bariatric surgery and increase maximal fat oxidation during exercise.

Key Points

- Aerobic training at the intensity at which maximal fat oxidation is reached (Fatmax) plus low resistance training may act synergistically.
- Twenty Caucasian women (BMI 46.5 ± 5.9 kg·m^{-2}) participated in this study.
- The combined training program increased lipid oxidation during exercise.
- Resting metabolic rate was preserved by the program.

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Published online: 20 January 2022

Introduction

The existing obesity pandemic we live with today continues to increase and represents a serious public health challenge worldwide, especially due to the huge growth of class II and III obesity during these last years [1]. The concomitant coincidence of cardiometabolic risk factors with extreme obesity worsens the patient's prognosis, and in these cases bariatric surgery (BS) is commonly recommended with the aim to quickly reduce the associated morbidity and mortality [2].

Although BS candidates are usually encouraged to increase their physical activity before the surgery, the effects of exercise programs delivered pre-operatively are still under discussion. Two recent meta-analyses [3, 4] coincide in that the very limited number of published works in which pre-operative exercise programs were prescribed to BS candidates makes almost impossible to clearly conclude their effects and their clinical relevance. Additionally, the heterogeneity between studies seems to be another major problem and it has been claimed that more evidence is needed to recommend specific training programs in terms of volume, intensity, frequency, and type of exercise in BS candidates [5]. Combining aerobic exercise with resistance training could be the best choice for the management of persons with obesity, given the summation of their effects on weight and fat loss with lean mass preservation, increased muscle strength, and cardiorespiratory fitness and prevention of additional comorbidities [6, 7]. In agreement with that, recent studies have shown that concurrent training, i.e., in which high intensity interval training (HIIT) and resistance training were combined during the same session, improves maximal oxygen uptake (VO_2max), reduces fat mass (FM), increases fat-free mass (FFM), and reduces cardiometabolic risk factors in BS candidates [8, 9]. These positive effects may have also been extended to a better blood pressure control, a lower insulin resistance, and lower intrahepatic fat deposits [10].

Obesity is commonly considered a consequence of an energy imbalance that negatively affects energetic substrate metabolism, since the increase of body fat leads to changes in the physiologic function [11]. For example, energy expenditure is reduced in adults with severe obesity (BMI $\geq$ 35 kg·m^{-2}) during rest and low-intensity exercise (i.e., performed at an intensity of 25 W) compared to patients with class I obesity or normal weight adults [12]. Similarly, obesity seems to be associated with metabolic inflexibility during exercise, which is characterized by reduced fat oxidation by the skeletal muscle in fasting conditions as well as by a reduced capacity to oxidize carbohydrates in response to food intake or in hyperinsulinemic state [13]. However, although obesity could imply lower fat oxidation rates, most of the previously published studies do not provide information in that regard during exercise. Moreover, there is a lack of knowledge regarding if physical activity or exercise could influence the metabolic rate and/or fat oxidation at rest in the specific context of BS.

The maximal quantity of fat that the organism can oxidize to obtain energy is called maximal fat oxidation (MFO) and the exercise intensity at which it occurs (typically medium intensities located around 45–55% VO_2max in obese sedentary adults [14, 15]) is known as Fatmax. In overweight middle-aged women, training at Fatmax has shown improvements in body composition related to fat mass, blood lipid profile, cardiovascular function, and whole-body fitness after 10 weeks of intervention [16, 17]. In addition, a similar intervention in a recent study in overweight older women showed improvements in body composition and functional capacity compared to a control group [18]. Another study in which Fatmax training was combined with a low-fat diet showed weight loss in obese adults who followed a 1-year intervention compared to non-interventional controls [19]. However, to the best of our knowledge, isolated Fatmax training in patients with class II and class III obesity has only been performed in men, showing improvements in cardiorespiratory fitness and fat oxidation rates during exercise [20].

Given the fact that most of the BS candidates are women [21], and that their fat oxidation response to exercise is unknown, in the present work, we have measured the effect of a 12-week physical activity program that combined aerobic training at Fatmax with low-intensity resistance training on body composition, cardiorespiratory fitness, and substrate oxidation (both at rest and during exercise), in middle-aged women awaiting BS. We hypothesized that training at Fatmax would increase maximal fat oxidation during exercise.

Materials and Methods

Participants

After excluding patients due to functional limitations to perform a physical activity program, or the presence of asthma, chronic obstructive pulmonary disease, hypothyroidism or cardiovascular diseases, 20 non-physically active women awaiting BS (BMI $\geq$ 45 kg·m^{-2}; obesity class IV) voluntarily enrolled in the study (Fig. 1). Volunteers were recruited from two University Hospitals of an urban area serving ≈ 230,000 inhabitants.

Depending on their possibilities to attend the training program regularly, they were allocated to an experimental group (EG, $n = 10$) or a control group (CG, $n = 10$) (Table 1). Volunteers from both hospitals were distributed among both groups in order to have the most

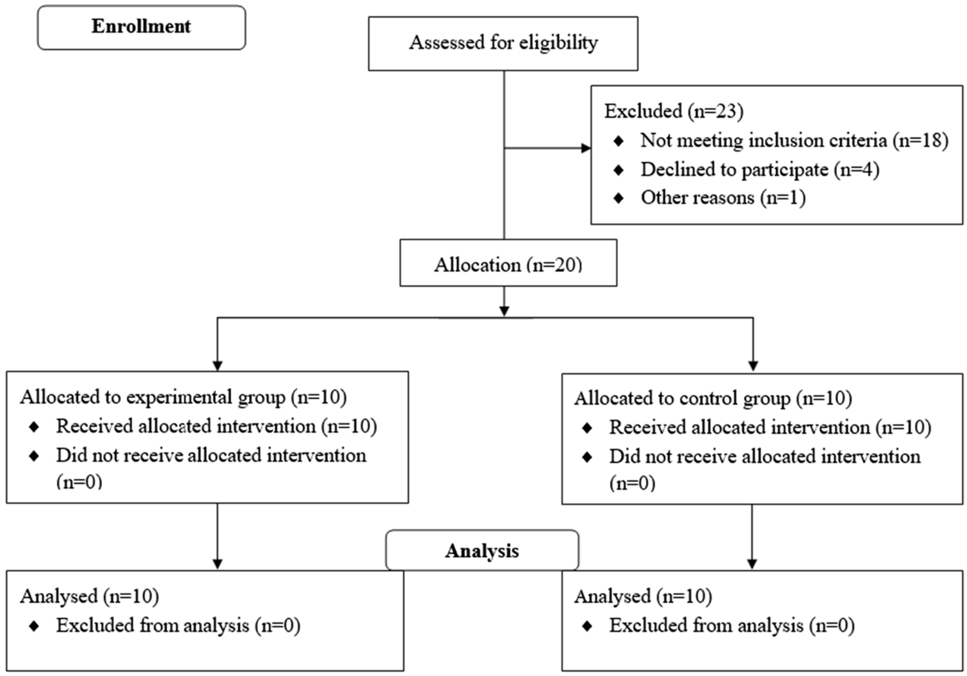

Fig. 1 Study flowchart (adapted from CONSORT 2010 Flow Diagram)

balanced group composition (EG: 6:4; CG: 5:5; hospital-1:hospital-2 ratio; 2 postmenopausal women per group).

Intervention

Both groups followed the presurgical care indications from their corresponding medical team. Additionally, the EG performed a 12-week structured physical activity program (Table 2) at the University sports facilities under the supervision of Sport Sciences Graduates. Participants in the EG trained together, and the PAP alternated continuous aerobic exercise at individual Fatmax intensity with resistance training performed at low workloads. First, participants combined continuous aerobic training (CAT) at individual Fatmax intensity on a cycle ergometer and resistance training in a single session to familiarize themselves with regular physical exercise. During the 12 weeks of the training program, frequency progressed from 2 days/week (d/w) during the first month to 3 d/w during the second month, and then to 4 d/w until the end of the physical activity program (PAP). The sessions lasted 60 min for the first 2 months and 70 min for the third month. The single sessions of CAT at Fatmax started on the second month and progressed from 50 to 60 min. Intensity was monitored throughout the session by means of a pulsometer (POLAR H7 Bluetooth Smart, Polar Electro, Kempele, Finland). The actual time of the session that the subject spent at Fatmax was estimated from heart rate (HR) recordings. Resistance training (RT) was prescribed based on the percentage of one repetition maximum (1RM), which was determined using the Brzycki formula [22]. The exercises (quadriceps, hamstrings, latissimus dorsi, pectoral, deltoids, gastrocnemius, triceps, and biceps brachii) were performed using guided machines with a weight that ranged between 20% 1RM and 30% 1RM. The single RT sessions started on the second month with 1 d/w and progressed to 2 d/w the third month. Every session finished with five stretching exercises in standing position (quadriceps, hamstrings, pectoral, latissimus dorsi, and gastrocnemius).

Table 1 Baseline participant characteristics

	EG (*n* = 10)	CG (*n* = 10)	*p*
Age (years)	43 ± 5	42 ± 9	0.725
Weight (kg)	125.3 ± 13.9	115.8 ± 15.1	0.161
Postmenopausal (yes)	2 (20)	2 (20)	0.999
Medication (yes)	5 (50)	4 (40)	0.653
Diabetes (yes)	3 (30)	2 (20)	0.606
Smoker (yes)	1 (10)	1 (10)	0.166

Data are shown as number of cases (percentage) or mean ± *SD*. *p* values refer to differences between groups. *EG* experimental group, *CG* control group

Measurements

Both groups were tested 1 week before the EG started the PAP and when the PAP ended (respectively PRE and POST). At both time points, anthropometry, resting metabolic rate, substrate oxidation during exercise, and physical fitness were measured. All the laboratory measurements were taken at ~ 80 m above sea, under controlled conditions (temperature 22–24 °C and relative air humidity 45–60%).

Table 2 Physical activity program schedule

Type of exercise		Month		
		1	2	3
CAT at Fatmax	Weekly frequency (sessions/week)	2	2	2
	Volume (min)	40	50	60
	Intensity (W)	Fatmax	Fatmax	Fatmax
Resistance training	Weekly frequency (sessions/week)	2	1	2
	Volume (series × exer. × rep.)	2 × 5 × 20	3 × 8 × 30	4 × 8 × 30
	Volume (min)	20	50	60
	Intensity (%1RM)	20	25	30
Stretching training	Weekly frequency (sessions/week)	2	3	4
	Volume (series × exer.)	1 × 5	1 × 5	1 × 5
	Duration (min)	1	1	1

CAT continuous aerobic training, *Fatmax* intensity at which maximal fat oxidation is registered, *min* minutes, *W* watts, *exer.* × *rep.* number of exercises performed and number of repetitions per exercise, *%1RM* percentage over a maximum repetition

Anthropometry and Body Composition

Anthropometric measurements were taken between 7:00 and 9:00 A.M., after 12 h of overnight fasting, with an empty bladder [23], and a restriction of caffeine or alcohol intake and physical exercise during the previous 48 h. The ISAK protocol was used to measure both body weight (BW) and waist and hip circumferences [24], and BMI was calculated and expressed as kilograms per square·meter. Excess body weight both in kilogram (EBW) and in percentage (EBW%) were also calculated and expressed as raw or normalized values [25]. Visceral fat percentage (VF%), and fat mass and fat-free mass—both in kilogram and in percentage (FM and FFM vs FM% and FFM%, respectively)—were estimated by bioimpedance analysis [9] (Tanita BC-420MA, Tanita, Tokyo, Japan; tetra-polar, 50 kHz, 90 µA, 150-1200Ω, accuracy = ±2%).

Resting Metabolic Rate and Substrate Oxidation

An indirect calorimetry was performed immediately after the anthropometric measurements to estimate the resting metabolic rate (RMR) and the resting energetic substrate oxidation (fat oxidation (RFO) and carbohydrate oxidation (RCHO)) [26, 27]. Raw RMR and RFO values were also normalized both to body weight (RMR_{BW}; RFO_{BW}) and fat-free mass (RMR_{FFM}; RFO_{FFM}) for each participant.

Briefly, the participants rested in supine position for 30 min, while their respiratory gases were continuously analyzed (Oxycon Pro, Jaeger, Friedberg, Germany). Data of the last 10 min were used to calculate the RMR according to Weir's equation [26], and substrate oxidation was calculated from non-protein respiratory quotient [27], using the following equations:

$$RMR = [\left(3.94 \times VO_2\right) + \left(1.106 \times VCO_2\right)] \times 1440$$
$$RFO = (1.695 \times VO_2) - (1.701 \times VO_2)$$
$$RCHO : (4.585 \times VO_2) - (3.226 \times VO_2)$$

Cardiorespiratory Fitness Measurements and Determination of Fatmax

The participants performed two ergoespirometric incremental tests up to exhaustion on a cycle ergometer (Technogym Bike Med, Technogym, Gambettola, Italy) under continuous respiratory gas analysis (Oxycon Pro, Jaeger, Friedberg, Germany), separated by 48 h.

The first test was carried out immediately after the indirect calorimetry described above and it aimed to determine the peak oxygen uptake (VO_2peak), the peak power output (PO_{peak}), the peak heart rate (HR_{peak}), and both ventilatory thresholds (VT1 and VT2). Participants performed a 5-min warm-up at 40 W with a controlled cadence at 60 revolutions per minute (rpm). Then, participants kept a voluntary cadence between 60 and 80 rpm while the power output (PO) increased 20 W every minute until volitional fatigue [24]. When inability to maintain a minimum of 60 rpm as a cadence occurred despite providing verbal encouragement, a 5-min active cool-down period started, in which participants pedaled at the cadence of the warm-up instructions. After that, a verification test was performed at a constant power of 100% of the maximal power registered during the incremental test. Participants were asked to maintain their previously voluntary cadence and pedal for as long as possible during the verification test until volitional fatigue, while verbal encouragement was provided. Lastly, a 5-min cool-down period was performed at 25 W. Verification test ≥ 60 s were used for analysis [28]. VO_2peak was calculated as the average of the highest 30 s of VO_2 and expressed in absolute values (VO_2peak abs).

The MFO and Fatmax were determined in a second ergoespirometric test. This test was carried out in a fasting state. Participants started a 10-min warm-up at 20% of their PO_{peak} reached during the previous test, and then, in a first phase the PO increased by 10% PO_{peak} every 5 min until reaching 70% PO_{peak}, or until respiratory exchange ratio (RER) reached 1.0. Then, a second phase started, and PO increased by 15 W every minute until exhaustion [24]. Participants were asked to maintain a cadence of 60 rpm during the warm-up and the first phase, while in the second phase they could modify it voluntarily from 60 to 80 rpm. Heart rate (HR) at Fatmax was registered and used to control the intensity of the aerobic exercise during the intervention (see below). An intermediate test was carried out in the EG on the sixth week of the PAP, solely to adapt the training loads depending on individual Fatmax changes.

Mean values of VO_2 and VCO_2 for the last 60 s in each 5-min step were needed to prescribe CAT at Fatmax intensity for each participant. First, fat oxidation (FO) rates were calculated according to Frayn's equations [27], with the assumption that the urinary nitrogen excretion rate was negligible. Then, the identification of the maximal fat oxidation value measured in the second ergoespirometric test and its corresponding intensity in W were estimated using a third polynomial equation (P3 model) [29]. For these calculations, mean values for the last 60 s in each 5 min step were used.

HR values related to FO rates were also calculated for each participant to control the intensity during the intervention. The P3 model was used to construct another standard fitting curve for HR and FO values. HR at which Fatmax occurred was registered for each participant and used during sessions to ensure training at individual Fatmax intensity.

Statistical Analysis

Continuous and categorical variables are presented as mean ± standard deviation (SD) and number of cases (percentage), respectively. The normal distribution of the continuous data was verified by the Shapiro–Wilk test, box plot, and Q-Q graphs. Student's independent *t*-test, Mann–Whitney *U* test, and Fisher's exact test were used for between-group comparisons at pre-intervention in normally distributed continuous variables, non-normally distributed continuous variables, and categorical variables, respectively. A two-way analysis of variance (ANOVA) of repeated measures with group (i.e., experimental vs. control) as between-subjects factor and time (i.e., pre- vs. post-intervention) as within-subjects factor was used to test the interaction between both factors. Skewed data were transformed before performing the ANOVA. Nonetheless, pre- and post-intervention values are shown in the original scale to facilitate their interpretation. All analyses were considered statistically significant at critical level of $p \leq 0.05$. Moreover, partial eta squared (η^2) was used as effect size index. The η^2 magnitude was classified as trivial (< 10%), small (10–24%), medium (25–37%), and large (> 37%), respectively. In case of interaction between both factors (i.e., $p \leq 0.05$ and/or $\eta^2 \geq 10\%$), simple effects with Sidak correction for multiple comparisons were estimated for studying within-group changes. Standardized mean difference (*d*) was used as effect size index for pairwise comparisons. The *d* magnitude was classified as trivial (< 0.50), small (0.50–1.24), moderate (1.25–1.9), and large (≥ 2.00). All analyses were performed with the SPSS package program (version 25, SPSS Inc., Chicago, IL, USA).

Results

Anthropometry and Body Composition

Pre- and post-intervention values, as well as changes at follow-up based on the allocated groups and training effect in anthropometry and body composition, are shown in Table 3. Our findings showed that FM% at baseline was higher in the EG compared to the CG ($p < 0.05$, Student's *t* test), while FFM% at baseline was lower in the EG compared to the CG ($p < 0.05$, Mann–Whitney test). No differences at baseline were noticed for the remaining analyzed variables. After the intervention, the results showed that FM% was reduced and FFM% increased only in the EG, and no changes at follow-up were found in the CG for any of the analyzed variables. However, compared with the CG, none of the analyzed variables at the 12-week follow-up changed in the EG.

Resting Metabolic Rate and Substrate Oxidation

Pre- and post-intervention values, within-group changes at follow-up, and training effect in RMR and substrate oxidation are shown in Table 4. The results showed that RMR_{FFM} was higher in the EG compared to the CG ($p < 0.05$, Student's *t* test), while no differences were found for the remaining variables at baseline. After the intervention, it was observed that RCHO increased in the CG, while no changes at follow-up or training effect were found in the EG for any of the analyzed variables. More specifically, RFO was unaffected by the intervention (Table 4, Fig. 2A, B).

Cardiorespiratory Fitness Measurements and Substrate Oxidation During Exercise

Pre- and post-intervention values, changes at follow-up based on the allocated groups, and training effect

Table 3 Effect of the intervention on anthropometric measurements

Variables	Experimental ($n=10$) Pre	Experimental ($n=10$) Post	Change p	Change d	Control ($n=10$) Pre	Control ($n=10$) Post	Change p	Change d	ANOVA (interaction) F	ANOVA (interaction) p	ANOVA (interaction) η^2 (%)
BMI (kg·m^{-2})$^{\&}$	48.7 ± 5.5	47.8 ± 5.9	0.071	−0.86	44.2 ± 5.7	43.9 ± 5.2	0.540	−0.28	0.837	0.372	4.4
Weight (kg)	125.3 ± 13.9	123.1 ± 14.8	0.078	−0.84	115.8 ± 15.1	114.9 ± 13.9	0.497	−0.31	0.690	0.417	3.7
EBW (kg)	60.9 ± 13.6	58.6 ± 14.4	0.078	−0.84	50.2 ± 14.4	49.4 ± 13.2	0.497	−0.31	0.690	0.417	3.7
EBW (%)	48.1 ± 5.8	47.1 ± 6.2	0.060	−0.90	42.7 ± 6.8	42.4 ± 6.4	0.565	−0.26	1.010	0.328	5.3
Fat mass (kg)$^{\&}$	66.3 ± 8.3	63.8 ± 8.5	0.006*	−1.37	58.9 ± 8.8	58.6 ± 8.6	0.718	−0.16	3.729	0.069	17.2
Fat mass (%)	52.9 ± 1.8	51.8 ± 2.2	0.015*	−1.20	50.8 ± 2.4	50.8 ± 2.5	0.839	0.09	4.160	0.056	18.8
FFM (kg)	58.9 ± 6.3	59.2 ± 7.2	0.782	0.13	56.9 ± 7.5	56.3 ± 6.3	0.491	−0.31	0.484	0.496	2.6
FFM (%)	47.1 ± 1.8&	48.1 ± 2.2	0.015*	1.20	49.2 ± 2.4	49.1 ± 2.5	0.839	−0.09	4.160	0.056	18.8
Waist (cm)$^{\&}$	142 ± 14	140 ± 15	0.334	−0.44	134 ± 16	134 ± 15	0.719	−0.16	0.197	0.663	1.1
Hip (cm)	147 ± 11	146 ± 14	0.410	−0.38	140 ± 14	139 ± 13	0.633	−0.22	0.064	0.803	0.4
WHR (cm)^{a}	0.9 ± 0.1	0.9 ± 0.1	0.721	−0.16	0.9 ± 0.1	0.9 ± 0.1	0.929	−0.04	0.037	0.850	0.2
Visceral fat (%)$^{\&}$	17.8 c 2.5	17.2 ± 2.5	0.013*	−1.23	15.6 ± 2.9	15.3 ± 2.7	0.189	−0.61	0.944	0.344	0.5

BMI body mass index, *EBW* excess body weight, *FFM* fat-free mass, *WHR* waist-to-hip ratio. Data at pre- and post-intervention are delivered as mean ± SD

$^{\&}$Data were log-transformed before performing the ANOVA

^{a}Non-normally distributed data

in cardiorespiratory fitness and substrate oxidation are reported in Table 5. The findings showed that VO_2peak abs/BW at baseline was higher in the CG compared to the EG ($p < 0.05$, Student's t test), and no differences were found between the EG and the CG at baseline for the remaining cardiorespiratory and substrate oxidation variables.

Regarding cardiorespiratory fitness, it was observed that Fatmax, VT2, PO at Fatmax, and PO_{peak} significantly increased only in the EG. Similarly, MFO during exercise only increased in the EG (Table 5, Fig. 2C, D).

Conclusion

This study aimed to describe the effects of a training program that combined aerobic exercise at Fatmax and low-intensity resistance training in middle-aged women affected by class IV obesity while they were awaiting BS. To the best of our knowledge, this is the first study in which the effects of an individualized and supervised PAP of these characteristics has been carried out on this population. As expected, the results showed that in the EG, the body composition and the physical fitness improved.

Table 4 Effect of the intervention on resting metabolic rate and substrate oxidation

Variables	Experimental ($n=10$) Pre	Experimental ($n=10$) Post	Change p	Change d	Control ($n=10$) Pre	Control ($n=10$) Post	Change p	Change d	ANOVA (interaction) F	ANOVA (interaction) p	ANOVA (interaction) η^2 (%)
RCHO (g·min^{-1})$^{\&}$	0.121 ± 0.06	0.122 ± 0.05	0.851	0.09	0.102 ± 0.08	0.143 ± 0.08	0.008*	1.35	3.969	0.062	18.1
RCHO (g·day^{-1})$^{\&}$	173.3 ± 81.4	175.0 ± 67.7	0.826	0.10	146.1 ± 119.1	206.7 ± 110.5	0.006*	1.38	4.098	0.058	18.5
RCHO (%)	53.2 ± 20.9	53.7 ± 14.4	0.932	0.04	51.6 ± 26.3	62.7 ± 18.5	0.067	0.87	1.738	0.204	8.8
RFO (g·min^{-1})	0.088 ± 0.03	0.092 ± 0.03	0.685	0.18	0.070 ± 0.033	0.065 ± 0.03	0.612	−0.23	0.432	0.520	2.3
RFO (%)	46.7 ± 20.9	46.3 ± 14.4	0.932	−0.04	48.3 ± 26.3	37.2 ± 18.5	0.067	−0.87	1.738	0.204	8.8
RFO_{BW}	0.710 ± 0.26	0.731 ± 0.19	0.804	0.11	0.622 ± 0.28	0.630 ± 0.20	0.924	0.04	0.012	0.913	0.1
RFO_{FFM}	1.5 ± 0.5	1.5 ± 0.3	0.964	0.02	1.2 ± 0.5	1.2 ± 0.3	0.852	0.08	0.010	0.921	0.1
RFO (g·day^{-1})	128.6 ± 49.6	130.5 ± 40.1	0.895	0.06	98.3 ± 49.1	97.0 ± 41.1	0.928	−0.04	0.025	0.875	0.1
RMR (kcal)	1869 ± 406	1894 ± 336	0.827	0.10	1480 ± 474	1695 ± 270	0.073	0.85	1.414	0.250	7.3
RMR_{BW} (kcal)	14.8 ± 2.5	15.3 ± 2.0	0.582	0.25	12.42 ± 3.2	14.4 ± 1.8	0.040*	0.99	1.359	0.259	7.0
RMR_{FFM} (kcal)	31.7 ± 6.1	32.0 ± 4.6	0.859	0.08	24.6 ± 5.4	29.2 ± 3.7	0.029*	1.06	2.407	0.138	11.8

RCHO resting carbohydrate oxidation, *RFO* resting fat oxidation, *RMR* resting metabolic rate, *BW* body weight, *FFM* fat-free mass. Data at pre- and post-intervention are delivered as mean ± SD

$^{\&}$Data were log-transformed before performing the ANOVA

^{a}Non-normally distributed data

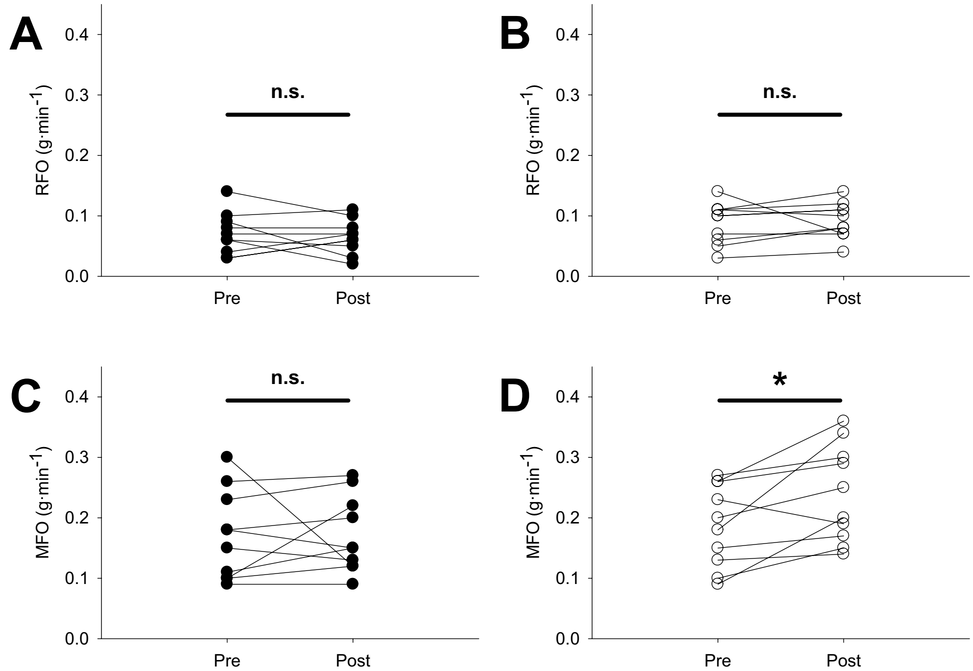

Fig. 2 Individual data values of resting fat oxidation (RFO; **A** and **B**), and maximal fat oxidation at exercise (MFO; **C** and **D**). Left panels (filled circles) correspond to the control group. Right panels (open circles) correspond to the experimental group. Pre- and post- indicate that the measurement was taken before or after the intervention, respectively. The clear trend of increasing MFO specifically in the experimental group (**D**) can be seen. N.S: non-significant differences; $*p<0.05$. For the mean and SD values, please see Tables 4 and 5

Interestingly, in addition to that, an increase in fat oxidation specifically during exercise, but not at rest, was also found in this group and not in the control group.

Previous studies in which exclusively aerobic exercise at Fatmax was prescribed to overweight and obese women have shown reductions of both FM and FFM [16–18], although resistance training was not included in these studies. The results of the current study suggest that including resistance training prevents FFM reduction. This finding could be of clinical interest, since achieving a stable or improved FFM has been associated to better weight loss and prevention of weight regain [6, 8, 9] in the specific context of BS. This can be related to the increased RMR associated to the FFM maintenance that has been previously described in BS patients [30, 31]. The observations in the specific population that participated in the present study reinforce this idea, and suggest that FFM maintenance in patients waiting for BS is important to counteract the deleterious effects on resting VO_2 and energy expenditure that have been associated with the severe diet-induced weight loss commonly prescribed to these patients [12].

As mentioned earlier, one of the most remarkable findings was the increase of fat oxidation during exercise. This observation agrees with previously published data in middle-aged overweight women [17], therefore suggesting that fat oxidation during exercise may be sensitive to exercise-based interventions, independently of the obesity level. The increase of either MFO and Fatmax, in response to exercise training, is currently considered an indicator of metabolic flexibility [32]. After the intervention, MFO increased in the EG. Work capacity also increased. Taken together, these results may reflect a higher work efficiency after the PAP. Previous works have suggested that this finding could be only observed associated to body weight reductions and low levels of muscle work [12, 33]. However, given the fact that in our results these responses were not associated to weight changes, this finding may be interpreted as that the PAP described here was able to restore the impaired metabolic flexibility that has been suggested is associated to obesity [13]. The confirmation of this hypothesis, as well as the identification of its explanatory mechanisms at the molecular or cellular level, needs further experimentation. In this regard, acute-phase reactants like serum amyloid A [34] and adipokines like leptin [35, 36] are potential targets that merit future investigation.

Some limitations should be considered in this research. First, the small size of the sample and the short period of the intervention make the generalization of these findings difficult, especially due to the absence of a retention test. These circumstances are highly common in patients awaiting BS since they follow several medical controls which directly affect their possibilities to participate regularly in long interventional trials carried out in ecological environments. Second, cycling was considered the best choice to prevent knee pain instead of a treadmill due to the BMI of the participants, but it caused discomfort in some of the participants when performing CAT for more than 30 min. Although the intervention allowed 1-min breaks in the middle of the Fatmax sessions, it was not enough to avoid this problem in all cases as severely obese adults often suffer from exercise intolerance [37]. Third, training sessions were carefully programmed and controlled but the measurements

Table 5 Effect of the intervention on cardiorespiratory fitness and substrate oxidation during exercise

Variables	Experimental ($n=10$)		Change		Control ($n=10$)		Change		ANOVA (interaction)		
	Pre	Post	*p*	*d*	Pre	Post	*p*	*d*	*F*	*p*	η^2 (%)
$VO_{2peak\ abs}$ ($L \cdot min^{-1}$)	1.8 ± 0.4	1.9 ± 0.4	0.073	0.85	1.7 ± 0.2	1.8 ± 0.2	0.265	0.51	0.281	0.602	1.5
$VO_{2peak\ abs/BW}$ ($mL*BW^{-1} \cdot min^{-1}$)	14.6 ± 3.2	15.7 ± 2.8	0.166	0.65	21.6 ± 8.4	22.6 ± 8.7	0.204	0.59	0.008	0.931	0.0
$VO_{2peak\ abs/FFM}$ ($mL*FFM^{-1} \cdot min^{-1}$)	31.1 ± 6.5	32.7 ± 5.4	0.119	0.73	25.2 ± 9.4	26.3 ± 9.7	0.262	0.52	0.114	0.739	0.6
PO_{peak} (W)	127 ± 41	148 ± 46	< 0.001*	2.36	146 ± 23	148 ± 25	0.621	0.22	11.400	0.003*	38.8
VT2 (W)[a]	104.4 ± 24.1	128.6 ± 39.6	0.001*	1.82	98.5 ± 17.1	114.0 ± 18.9	0.018*	1.17	1.013	0.328	5.6
$VO_{2peak\ abs/BW}$ at VT2 ($L \cdot min^{-1}$)	12.5 ± 2.7	13.8 ± 3.7	0.064	0.93	11.8 ± 1.9	13.6 ± 1.1	0.011*	1.27	0.270	0.610	1.6
MFO ($g \cdot min^{-1}$)	0.187 ± 0.068	0.239 ± 0.080	0.025*	1.10	0.170 ± 0.074	0.171 ± 0.063	0.963	0.02	2.888	0.106	13.8
MFO_{BW} ($mg \cdot kg^{-1} \cdot min^{-1}$)	1.4 ± 0.4	1.9 ± 0.6	0.020*	1.14	1.4 ± 0.6	1.4 ± 0.4	0.922	−0.04	3.522	0.077	16.4
MFO_{FFM} ($mg \cdot kg^{-1} \cdot min^{-1}$)	3.1 ± 0.9	4.0 ± 1.2	0.044*	1.21	2.9 ± 1.1	2.9 ± 0.9	0.790	0.14	2.867	0.108	13.7
Fatmax (W)[a]	37.1 ± 10.2	49.2 ± 12.7	< 0.001*	2.15	42.2 ± 9.3	38.7 ± 9.5	0.181	−0.62	19.223	< 0.001*	51.6
PO at Fatmax (%)	23.5 ± 5.3	31.6 ± 7.0	< 0.001*	2.40	26.1 ± 5.6	24.6 ± 5.5	0.320	−0.46	20.440	< 0.001*	53.2
VO_{2peak} at Fatmax (%)[a]	54.9 ± 8.8	55.9 ± 7.2	0.679	0.19	50.9 ± 8.0	50.9 ± 9.1	0.955	−0.03	0.114	0.739	0.6
HR at Fatmax (%)	77.1 ± 7.9	79.6 ± 6.8	0.347	0.43	71.9 ± 12.7	71.8 ± 7.5	0.967	−0.02	0.508	0.485	2.7

VO_2 oxygen uptake, *PO* power output, *MFO* maximal fat oxidation, *Fatmax* intensity at which maximal fat oxidation was reached, *HR* heart rate, *BW* body weight, *FFM* fat-free mass, *VT2* second ventilatory threshold. Data at pre- and post-intervention are delivered as mean ± SD

[&]Data were log-transformed before performing the ANOVA

[a]Non-normally distributed data

were not sufficient to evaluate molecular changes in muscle tissue related to substrate oxidation. This fact is highly relevant as skeletal muscle contributes to VO_2, energy expenditure, and FO, so knowing oxidative enzyme content could be useful to design future interventions to stimulate non-aggressive and progressive weight loss in patients awaiting BS. In addition, MFO and Fatmax depend on several key factors such as training status, sex, or chronic nutritional status [14], so these findings should be analyzed carefully since no similar studies are available nowadays in middle-aged women awaiting BS. Therefore, future studies could propose similar interventions for this population in which other training modalities may be performed and accurately controlled to solve these limitations. Last, but not the least, although the bioimpedance system that we have used in this and in previous works with this population [9, 38] has been validated and is sensitive to body composition changes [39], more precise methods to measure body composition would be preferred in future studies. In addition, the potential effect of some covariables—such as age, menopausal state, and medications—should be also analyzed.

Despite these limitations, our work adds some novelties and strengths to previous published research. First, the protocol used to determine the Fatmax and MFO has been applied only in men with lower BMI than those recorded in our sample [24]. Second, we included a verification step at the end of the protocol to ensure its maximality [28]. This is especially relevant in a population with very low tolerance to exercise, such the one described here. Third, ergoespirometry were performed to every participant, therefore allowing for individual measurement of Fatmax, W, and HR based on which the exercise intensity was individually prescribed. Other previous works, for example, have extrapolated the target HR to reach during the exercise session by the whole sample, simply by measuring a subset of participants and estimating the mean value [40]. In addition to that, in our experimental design, the ergoespirometries were performed in a clycoergometer, which provided a greater transfer of the obtained values to the PAP. Therefore, our experimental design was able to overcome some limitations of previous studies. Finally, we consider that similarly to other previous works [9, 38], the individualized approach that we followed with every participant was a key factor to reach the high adherence to the PAP during the 3 months of the intervention. This is particularly noticeable for a population like this one, with very low intrinsic motivation to exercise as well as multiple socioeconomic and sociocultural limiting factors to be physically active.

Albeit this is a first description of the effects of combining aerobic exercise at Fatmax with low-intensity resistance training, these results may be of clinical relevance, since patients awaiting BS are typically requested to lose from 5 to 10% body weight before the intervention to decrease the associated surgical risk [41]. To reach this reduction, highly restrictive dietary protocols are usually prescribed aimed to change the patient's metabolism [41]. So, if an individualized and supervised PAP such the one described here might be able to stimulate higher fat oxidation rates during exercise, while maintaining FFM and RMR in the long term, its implementation before surgery may counteract some of the unwanted side effects of the highly restrictive dietary interventions usually seen in this population [42].

Acknowledgements We would like to thank to our laboratory colleagues Dr. José Manuel Sarabia Marín, PhD, and Dr. Diego Pastor Campos, PhD, for their comments and suggestions on the P3 model for maximal fat oxidation estimation. The cooperation of the medical teams of both hospitals is also acknowledged.

Funding Open Access funding provided thanks to the CRUE-CSIC agreement with Springer Nature. This work has been carried out under the agreement for scientific cooperation among the Hospital Vinalopó, the Hospital General Universitario de Elche, and the Universidad Miguel Hernández de Elche (FISABIO3.15X), and has been funded by the following research projects: "Physical and psychological effects of an exercise program in bariatric patients"(UEM2.11X; Escuela de Estudios Universitarios Real Madrid-Universidad Europea de Madrid) and "Physiological and psychological effects of a physical activity program on bariatric patients" (Fundación MAPFRE).

Declarations

Ethical Approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed Consent Participants were carefully informed about the risks related to the research, and informed consent was obtained from all individual participants included in the study. The intervention was as approved by the University Ethical Committee (DPS.MMR.01.15).

Conflict of Interest The authors declare no competing interests.

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