TESIS DOCTORAL

IMPACTO DE LA CIRUGÍA BARIÁTRICA SOBRE LA CONDICIÓN FÍSICA ASOCIADA A LA SALUD Y LA VARIABILIDAD DEL RITMO CARDIACO EN ADULTOS CON OBESIDAD SEVERA

IMPACT OF BARIATRIC SURGERY ON HEALTH-RELATED PHYSICAL FITNESS AND HEART RATE VARIABILITY IN ADULTS WITH SEVERE OBESITY

Paulina Ibacache Saavedra

Junio 2023

Director: Dr. Enrique García Artero

Programa de Doctorado en Ciencias Médicas

Escuela Internacional de Doctorado

Universidad de Almería

Toda naturaleza es un anhelo de servicio.
Sirve la nube, sirve el viento, sirve el surco.
Donde haya un árbol que plantar, plántalo tú;
Donde haya un error que enmendar, enmiéndalo tú;
Donde haya un esfuerzo que todos esquivan, acéptalo tú.
Sé el que aparta la piedra del camino, el odio entre los
corazones y las dificultades del problema.
Hay una alegría del ser sano y la de ser justo, pero hay,
sobre todo, la hermosa, la inmensa alegría de servir.
Que triste sería el mundo si todo estuviera hecho,
si no hubiera un rosal que plantar, una empresa que emprender.
Que no te llamen solamente los trabajos fáciles
¡Es tan bello hacer lo que otros esquivan!
Pero no caigas en el error de que sólo se hace mérito
con los grandes trabajos; hay pequeños servicios
que son buenos servicios: ordenar una mesa, ordenar
unos libros, peinar una niña.
Aquel que critica, éste es el que destruye, tu sé el que sirve.
El servir no es faena de seres inferiores.
Dios que da el fruto y la luz, sirve.
Pudiera llamarse así: "El que Sirve".
Y tiene sus ojos fijos en nuestras manos y nos
pregunta cada día: ¿Serviste hoy? ¿A quién?
¿Al árbol, a tu amigo, a tu madre?

El placer de servir, Gabriela Mistral

ÍNDICE DE CONTENIDOS

ABREVIATURAS 4

RESUMEN 5

ABSTRACT 7

INTRODUCCIÓN GENERAL

1. Obesidad: definición, epidemiología y morbimortalidad 10
2. Patogenia de la obesidad 13
3. Tratamiento de la obesidad 21
4. Condición física y obesidad 26
    4.1 Capacidad cardiorrespiratoria 27
    4.2 Fuerza muscular 32
5. Variabilidad del ritmo cardiaco y obesidad 35

OBJETIVOS 64

METODOLOGÍA 68

RESULTADOS Y DISCUSIÓN

Sección 1. Impacto de la cirugía bariátrica en la condición física asociada a la salud

Estudio 1. *Physical fitness and physical activity in women with obesity: short term effects of sleeve gastrectomy* 72
Estudio 2. *Effects of bariatric surgery on cardiorespiratory fitness: A systematic review and meta-analysis* 87
Estudio 3. *Effects of bariatric surgery on muscle strength and quality: A systematic review and meta-analysis* 129

Sección 2. Impacto de la cirugía bariátrica en la variabilidad del ritmo cardiaco

Estudio 4. *Improvements in heart rate variability in women with obesity: short-term effects of sleeve gastrectomy* 176

CONCLUSIONES GENERALES 199

OTRAS APORTACIONES CIENTÍFICAS DERIVADAS DE LA TESIS DOCTORAL 202

AGRADECIMIENTOS 203

ABREVIATURAS

Akt: protein kinase B
AMPK: AMP-activated protein kinase
ANS: autonomic nervous system
BAT: brown adipose tissue
BMI: body mass index
BS: bariatric surgery
CCK: Cholecystokinin
CI: confidence intervals
COPD: chronic obstructive pulmonary disease
CPET: cardiopulmonary exercise testing
CRF: cardiorespiratory fitness
CVD: cardiovascular disease
ES: effect size
ESRD: end-stage renal disease
FFM: fat-free mass
GLP-1: glucagon-like peptide-1
HF: high frequency power
HGS: handgrip strength
HR_{max}: maximum heart rate
HRV: heart rate variability
IGF-1: insulin-like growth factor 1
IL-6: interleukin-6
IMC: índice de masa corporal
LF: low frequency power
LM: lean mass
MET: metabolic equivalent of task
MQ: muscle quality
MS: muscle strength
mTOR: mammalian target of rapamycin
MVPA: moderate-to-vigorous physical activity
NHLBI: National Heart, Lung and Blood Institute
OAGB: one anastomosis gastric bypass
OMS: Organización Mundial de la Salud
PA: physical activity
PF: physical fitness
P13K: phosphatidylinositol 3-kinase
pNN50: percentage of consecutive RR intervals that differ by more than 50 ms
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PYY: Peptide YY
O_2pulse_{max}: maximal oxygen pulse
1RM: one-repetition maximum
RCT: randomized controlled trial
RMSSD: root mean square of successive differences in RR intervals
RYGB: Roux-en-Y gastric bypass
SAT: subcutaneous adipose tissue
SDNN: standard deviation of the average normal-to-normal interval
SampEn: sample entropy
SG: sleeve gastrectomy
TNF-α: tumor necrosis factor-alpha
VAT: visceral adipose tissue
VE_{max}: maximal minute ventilation
VLF: very low frequency power
$VO_{2max/peak}$: maximal/ peak oxygen consumption
WAT: white adipose tissue

RESUMEN

El incremento mundial en la prevalencia de obesidad observado en las últimas 5 décadas la ha llevado a alcanzar proporciones pandémicas. La obesidad se ha asociado consistentemente a múltiples morbilidades, a una disfunción autonómica, a un deterioro importante de la condición física y, en consecuencia, a una reducción de la expectativa de vida. Para enfrentar la obesidad, en particular, la obesidad severa, se han desarrollado e incrementado la realización de cirugías bariátricas (BS), las que han mostrado generar una reducción importante del peso corporal, que suele ser el principal indicador de éxito de los tratamientos de obesidad, y una mejora en las comorbilidades. Sin embargo, aún no existe claridad del impacto de las intervenciones bariátricas sobre la capacidad cardiorrespiratoria, la fuerza muscular y la variabilidad del ritmo cardiaco. Considerando que estos parámetros tienen un valor predictivo de salud, el propósito de esta tesis doctoral es determinar los cambios en la condición física y la variabilidad del ritmo cardiaco de adultos con obesidad, junto con analizar si las variaciones en estos indicadores de salud se encuentran asociados a la pérdida de peso corporal luego de una cirugía bariátrica. Para responder a este objetivo se realizaron dos revisiones sistemáticas y metaanálisis, además de un estudio de cohorte con mujeres que se sometieron a una gastrectomía vertical. En este último se evaluaron en el período preoperatorio y luego al mes y a los tres meses posteriores a la cirugía la fuerza de prensión manual y de extensores de rodilla (a través de dinamometría), la capacidad cardiorrespiratoria (por medio de ergoespirometría) y la variabilidad del ritmo cardiaco (mediante un registro corto con un monitor telemétrico del ritmo cardíaco). Se observó un aumento postquirúrgico de la variabilidad del ritmo cardiaco (parámetros espectrales, temporales y no lineales), al mismo tiempo que una reducción absoluta del consumo *peak* de oxígeno ($VO_{2peak)}$ y de la fuerza de prensión manual y de extensores de rodilla. Sin embargo, el VO_{2peak} y la fuerza de prensión manual relativos al peso corporal mostraron un incremento después de la cirugía bariátrica. Los cambios en el VO_{2peak} absoluto se relacionaron de manera directa con la pérdida de peso luego de la intervención quirúrgica. Asimismo, los metaanálisis y meta-regresiones mostraron que la cirugía bariátrica lleva a una reducción significativa de los valores absolutos del $VO_{2max/peak}$ y de la fuerza muscular de extremidades inferiores a corto plazo (hasta 12 meses postcirugía). Además, los sujetos que experimentaron una mayor reducción del índice de masa corporal (IMC) después de la cirugía, también sufrieron una mayor pérdida absoluta del

$VO_{2max/\textit{peak}}$ y de la fuerza. En conclusión, a pesar de la aparente recuperación de la función autonómica cardíaca, la BS parece afectar negativamente la capacidad cardiorrespiratoria y la fuerza muscular de las extremidades inferiores a corto plazo. Considerando que un bajo nivel de estos componentes de la condición física se asocia con un alto riesgo de morbimortalidad, independiente del nivel de IMC y que incluso pequeños incrementos en la capacidad cardiorrespiratoria o en la fuerza muscular pueden afectar el riesgo de morbimortalidad de manera clínicamente significativa, es que la reducción observada en la capacidad cardiorrespiratoria y en la fuerza posteriores a una cirugía bariátrica podría mitigarse prescribiendo un programa de ejercicio físico individualizado y supervisado como parte esencial del manejo de estos usuarios, tanto antes como después de la intervención quirúrgica. Son necesarios estudios con un seguimiento a largo plazo para confirmar el efecto adverso de la cirugía bariátrica sobre la condición física, así como estudiar las consecuencias de estos cambios en la salud de esta población. La combinación de evaluaciones de la composición corporal, la capacidad cardiorrespiratoria, la fuerza muscular y otros *outcomes* de salud, incluido un mayor tamaño muestral y múltiples evaluaciones de seguimiento postquirúrgicas, podría proporcionar una mejor comprensión del vínculo entre la pérdida de peso, los cambios en la masa muscular, la capacidad cardiorrespiratoria, la fuerza muscular y la salud en esta población.

ABSTRACT

The worldwide increase in the prevalence of obesity observed in the last five decades has led it to reach pandemic proportions. Obesity has consistently been associated with multiple morbidities, autonomic dysfunction, a significant deterioration in physical fitness and, consequently, a reduction in life expectancy. To treat obesity, particularly severe obesity, bariatric surgeries (BS) have been developed and increased, which have been shown to generate a significant reduction in body weight, which is usually the main indicator of success in obesity treatments, and an improvement in comorbidities. However, there is still no clarity on the impact of bariatric surgery on cardiorespiratory fitness, muscle strength, and heart rate variability. Considering that these parameters have a predictive value for health, the purpose of this doctoral thesis is to determine the changes in physical fitness and heart rate variability in adults with obesity, together with analyzing whether variations in these health indicators are associated to weight loss after bariatric surgery. To meet this objective, two systematic reviews and meta-analyses were conducted, as well as a cohort study with women who underwent sleeve gastrectomy. In the latter, handgrip strength and knee extensors (through dynamometry), cardiorespiratory fitness (through ergospirometry) and heart rate variability (by taking a short recording with a telemetric heart rate monitor) were evaluated in the preoperative period and then one month and three months after surgery. A post-surgical increase in heart rate variability (spectral, temporal, and nonlinear parameters) was observed, along with an absolute reduction in peak oxygen consumption (VO_{2peak}) and handgrip and knee extensor strength. However, VO_{2peak} and handgrip strength relative to body weight showed an increase after bariatric surgery. Changes in absolute VO_{2peak} were directly related to weight loss after surgery. Likewise, meta-analyses and meta-regressions showed that bariatric surgery leads to a significant reduction in the absolute values of $VO_{2max/peak}$ and lower-limb muscle strength in the short-term (up to 12 months post-surgery). In addition, subjects who experienced a higher reduction in body mass index (BMI) after surgery also suffered a higher absolute loss of $VO_{2max/peak}$ and strength. In conclusion, despite the apparent recovery of cardiac autonomic function, bariatric surgery seems to negatively affect cardiorespiratory fitness and lower-limb muscle strength in the short-term. Considering that a low level of these fitness components is associated with a high risk of morbidity and mortality, independent of BMI level, and that even small increases in cardiorespiratory fitness or muscle strength can affect the risk

of morbidity and mortality in clinically significant ways, is that the observed reduction in cardiorespiratory fitness and strength after bariatric surgery could be mitigated by prescribing an individualized and supervised physical exercise program as an essential part of the management of these subjects, both before and after surgery. More extended follow-up studies are needed to confirm the adverse effect of BS on physical fitness, as well as to study the consequences of these changes on the health of this population. Combining body composition, cardiorespiratory fitness, muscle strength, and other health outcomes assessments, including larger sample size and multiple time points, could provide a better understanding of the link between weight loss, changes in muscle mass, cardiorespiratory fitness, muscle strength, and health in this population.

Introducción General

INTRODUCCIÓN GENERAL

1. Obesidad: definición, epidemiología y morbimortalidad asociada

La obesidad, uno de los mayores problemas de salud pública a nivel mundial (Malik 2020), es definida como “una acumulación anormal o excesiva de grasa que puede ser perjudicial para la salud” (*World Health Organization* 2021; ICD-11 2023). Es considerada como una enfermedad desde hace más de 3 décadas debido a su fisiopatología particular, que da como resultado complejos mecanismos homeostáticos que dificultan la pérdida de peso y promueven un mayor aumento de éste (Blüher, 2019). El índice de masa corporal (IMC; peso corporal [kg]/estatura^2 [m]) es un indicador de adiposidad (American College of Cardiology 2013) altamente específico, pero con una sensibilidad de baja a moderada (Reilly JJ 2017), que se suele utilizar para identificar el sobrepeso (25,0-29,9 kg/m^2) y la obesidad (≥30,0 kg/m^2). De acuerdo con el nivel de IMC, se categoriza la obesidad en clase I (30,0–34,9 kg/m^2), clase II (35,0–39,9 kg/m^2) o clase III (≥40,0 kg/m^2) (WHO 2000; ICD-11 2023) y se habla de obesidad severa con un IMC ≥40 kg/m^2 o ≥35 kg/m^2 con comorbilidades (Kral 2012). Esta clasificación se basa en diferencias en el riesgo de salud implicado (Berrington 2010; Valenzuela 2023) y el tratamiento para cada nivel de exceso de peso (Kral, 1985; WHO, 1995; *National Institutes of Health*, 1998; Freedman et al., 2002). Sin embargo, existen grandes diferencias individuales en el porcentaje y distribución de la grasa corporal para un mismo valor de IMC, lo que puede atribuirse al sexo, la edad y la etnia (WHO, 2013; Lin 2021). Además, en algunas poblaciones los puntos de corte no son los mismos para definir el riesgo de salud (WHO, 2004; Dhawan 2020). Por otra parte, el exceso de depósito de grasa en la región abdominal- denominado obesidad abdominal o central- se asocia con mayores riesgos para la salud (Janssen 2004; Despress 2012; Dhawan 2020; Chait 2020; Lin 2021). Es por ello que se recomienda utilizar-además del IMC- la medición de la circunferencia de cintura (o la razón cintura/estatura), ya que se considera que es el mejor indicador antropométrico de la grasa visceral y un mejor predictor de trastornos metabólicos (Janssen 2004; Han 2006; Ashwell 2012; Cerhan 2014; Nazare et al., 2015). Asimismo, cuando se usa junto con el IMC, la circunferencia de cintura puede ser útil para distinguir el IMC elevado debido a la cantidad de masa muscular (McCafferty, 2020).

El incremento mundial en la prevalencia de obesidad observado en las últimas 5 décadas la ha llevado a alcanzar proporciones pandémicas (Blüher, 2019). Desde 1980, la prevalencia de obesidad se ha duplicado en más de 70 países (GBD 2015 Obesity Collaborators et al., 2017). Recientes informes han mostrado que más de un tercio de la población adulta mundial tiene exceso de peso corporal (obesidad o sobrepeso) (Chooi, 2019; Lobstain 2022). Si esta tendencia continúa, se estima que para el año 2030, esta cifra superará el 50% de la población adulta mundial (Mehrzad, 2020). Por su parte, la prevalencia mundial de obesidad en adultos se estima en alrededor de un 13%, siendo mayor en mujeres que en hombres (WHO 2021; Lobstain 2022; Ahmad 2016; Inoue, 2018; Williamson, 2020). Entre los años 1975 y 2014, la prevalencia de obesidad aumentó de 3,2% a 10,8% en adultos hombres y de 6,4% a 14,9% en mujeres adultas (NCD 2016). De acuerdo con estimaciones de *World Obesity Federation*, para el 2030 casi mil millones de personas en todo el mundo sufrirán obesidad, con al menos 111 millones de personas con un IMC ≥ 40 kg/m^2 (Lobstain 2022). Si bien la obesidad es un fenómeno global que está presente en todas las regiones del mundo, con excepción de algunos sectores de Asia, África y países como Indonesia, Sudán y Singapur (Lin 2021), muestra grandes diferencias en su prevalencia según el país, oscilando desde un 3,7% en Japón a un 38,2% en Estados Unidos (Blüher, 2019). Sin embargo, es importante considerar que es muy posible que la prevalencia de la obesidad se esté subestimando (Wong 2020), debido a que alrededor de la mitad de todos los adultos con exceso de grasa corporal son categorizados sin obesidad según el IMC (Okorodudu 2010; Valenzuela 2023).

La obesidad es uno de los factores de riesgo más importantes para las enfermedades no transmisibles, que corresponden a más del 70% de las muertes prematuras (aquellas ocurridas por debajo de los 70 años) en todo el mundo, representando la principal causa de discapacidad prematura y mortalidad (Blüher, 2019). Es así como la obesidad se asocia con numerosas comorbilidades metabólicas, inflamatorias, estructurales, degenerativas, neoplásicas y psicológicas [Ahmad 2016; Blüher, 2019], tales como diabetes mellitus tipo 2, dislipidemia, esteatosis hepática no alcohólica, osteoartritis, cáncer gastrointestinal y de mama [Williams, 2015; Sarma, 2021], apnea del sueño [Kuvat, 2020], síndrome de ovario poliquístico, infertilidad [Zeng, 2020], hipertensión, enfermedad coronaria [Manrique-Acevedo, 2020], Alzheimer y depresión. (Payne 2018; GBD, 2017; McCafferty 2020; Safaei 2021) Por otra parte, la obesidad y las enfermedades no transmisibles relacionadas se encuentran entre los principales predictores de la gravedad y mortalidad de enfermedad por coronavirus 2019 (COVID-19) (Aghili 2021; Stefan 2021). Adicionalmente, la esperanza de vida de las personas con obesidad se reduce en promedio de 5 a 20 años dependiendo de la gravedad de la condición y las comorbilidades presentes (Blüher, 2019).

Al mismo tiempo, la obesidad podría conducir a una disminución de la calidad de vida (Payne 2018; Bischoff 2017), desempleo y a una menor productividad y participación social (Blüher, 2019). Todo ello se suma a las implicancias económicas tanto para las personas que la padecen, como para sus empleadores (Loeppke 2009) y para el sector sanitario de los países afectados por esta pandemia (Wang et al., 2011; Cawley & Meyerhoefer, 2012; Lal et al., 2012; Lehnert et al., 2013; Dee et al., 2014; Frezza et al., 2014; de Oliveira et al., 2015; Cawley &Meyerhoefer, 2012; Cawley, 2015; Dee et al., 2014), generando un gasto en salud anual un 30-40% más alto que el requerido en personas con normopeso (Apovian, 2016; Lin 2021).

2. Patogenia de la obesidad

La obesidad es un proceso de enfermedad crónica complejo que resulta de un desequilibrio energético a largo plazo y la interacción de diversos factores, entre los que se encuentran la nutrición de alta densidad energética, la baja actividad física, el estrés, la susceptibilidad genética y los determinantes ambientales e individuales de la ingesta y el gasto energético (Bray 2017; Blüher 2019; Tsatsoulis 2020; Lin 2021).

De acuerdo con la Organización Mundial de la Salud (OMS), los principales impulsores potenciales de la pandemia de la obesidad han sido los cambios en los patrones dietéticos y de actividad física desarrollados desde la década de los 80 (Swinburn et al., 2011; Khan et al., 2012; WHO, 2021). La sociedad presenta entornos cada vez más obesogénicos que influyen profundamente en el comportamiento de las personas. Es así como se habla de una "occidentalización" de los estilos de vida (Blüher 2019), caracterizada por una reducción de la cocina casera y un incremento del consumo de productos de origen animal, cereales refinados y azúcar, debido a la mayor disponibilidad de productos procesados de bajo coste que son de baja calidad nutricional y alto contenido calórico (Malik 2020). Esto se aplica particularmente a la denominada comida basura, con un alto contenido de grasa y azúcar, diseñada específicamente para ser adictiva, ya que puede estimular los centros de recompensa del cerebro al igual que la cocaína, la heroína y otras drogas (Lin 2021). A ello se suma el cambio en los hábitos de actividad física, modificándose los patrones de movilización, trabajo y tiempo libre hacia actividades energéticamente menos demandantes (Popkin & Gordon-Larsen, 2004; Hill et al., 2012; Blüher 2019). Es así como se ha descrito un aumento de la inactividad física (no cumplir con las recomendaciones de actividad física para la salud) y del tiempo dedicado a actividades sedentarias como ver televisión, utilizar el teléfono móvil o estar sentado frente al ordenador (McCafferty 2020). La evidencia actual sugiere que los estilos de vida contemporáneos desencadenarían cambios epigenéticos, alterando el equilibrio energético y, por lo tanto, contribuyendo a la génesis de la obesidad (Obri 2019).

El tejido adiposo, más allá de su función de reserva energética, actúa también como un órgano endocrino que libera diversos péptidos, llamados adipocinas, que participan en la regulación del metabolismo sistémico (Jung 2014; Ghaben, 2019). Por ejemplo, la adiponectina es una hormona antiinflamatoria sensibilizadora de la insulina, que suprime la producción de glucosa hepática y reduce la fibrosis; la leptina actúa sobre los centros de saciedad del cerebro para suprimir la ingesta de alimentos y aumentar la actividad simpática para promover la lipólisis. Por otra parte, ciertas adipocinas son características del tejido adiposo metabólicamente disfuncional y pueden promover la inflamación sistémica como la interleukina 6 (IL-6), el factor de necrosis tumoral (TNF) y la angiotensina II (Ghaben, 2019).

Cuando se requiere el almacenamiento de calorías extra en el tejido adiposo, la expansión de éste puede generarse por el aumento del tamaño de los adipocitos (hipertrofia) o por la formación de nuevos adipocitos a partir de la diferenciación de precursores (preadipocitos) en el proceso de adipogénesis (hiperplasia). Se ha descrito que la expansión de los adipocitos a través de la adipogénesis podría compensar los efectos metabólicos negativos de la obesidad (Ghaben, 2019). Existen dos tipos principales de tejido adiposo, el tejido adiposo blanco (*WAT*, *White Adipose Tissue*), que es el más abundante en adultos humanos, y el tejido adiposo pardo (*BAT*, *Brown Adipose Tissue*), que representa una pequeña proporción (entre un 0,2 y un 3,0%) de la masa grasa total. El *WAT* a su vez se almacena en dos depósitos: el tejido adiposo subcutáneo (*SAT, Subcutaneous Adipose Tissue*; el que se encuentra directamente debajo de la piel) y el tejido adiposo visceral (*VAT*, *Visceral Adipose Tissue*, que está ubicado principalmente en la cavidad abdominal) (Ghaben, 2019; Valenzuela 2023).

El proceso de hiperplasia del tejido adiposo generalmente se considera "saludable" y adaptativo, porque el tejido es capaz de mantener una adecuada vascularización y los niveles de adiponectina (Ghaben, 2019). Se ha descrito que las personas con obesidad con un mayor número de adipocitos en el *SAT* poseen un perfil cardiometabólico más favorable que los que tienen un menor número de estos, incluyendo una mayor sensibilidad a la insulina y niveles de colesterol HDL y menores niveles plasmáticos de insulina y triglicéridos, independientemente de la masa grasa corporal total (Valenzuela 2023). En cambio, los adipocitos hipertróficos (es decir, que han ganado tamaño) pueden mostrar propiedades bioquímicas diferentes a las de los adipocitos más pequeños, incluyendo una lipólisis elevada, secreción aumentada de adipocinas proinflamatorias y reducida de adipocinas antiinflamatorias como la adiponectina, lo que favorece las alteraciones metabólicas asociadas a la obesidad (Ghaben, 2019).

La capacidad de aumentar el *SAT* a menudo se ve afectada en personas con obesidad, y cuando alcanza su límite de expansión, como lo reflejan los adipocitos hipertróficos, los lípidos comienzan a acumularse en el *VAT* y en otros tejidos y órganos, especialmente en el hígado, páncreas, músculo esquelético y corazón (Valenzuela 2023). Es importante considerar que existe una variabilidad individual en la capacidad máxima de expansión del *SAT*, determinada en parte por factores genéticos, lo que podría explicar por qué no todas las personas desarrollan complicaciones metabólicas con la misma cantidad de masa grasa total (Valenzuela 2023).

El *VAT* tiene propiedades únicas que hacen que se relacione mucho más con el riesgo cardiometabólico que el resto de los compartimentos del tejido adiposo, incluido que su expansión en la obesidad no se corresponde con un incremento paralelo en la angiogénesis. Ello sumado al incremento masivo del tamaño de los adipocitos generan un medio hipóxico que puede desencadenar estrés oxidativo y promover la fibrosis y necrosis de los adipocitos, provocando la infiltración de células inmunitarias y la inflamación del tejido (Reilly SM 2017; Valenzuela 2023). Los adipocitos, así como las células inmunitarias residentes, secretan numerosas moléculas proinflamatorias que se liberan a la circulación, lo que lleva a un estado de inflamación crónica sistémica de bajo grado (McCafferty 2020; Valenzuela 2023). Algunas de las citocinas proinflamatorias derivadas de los macrófagos pueden actuar sobre los adipocitos para activar la lipólisis y tanto los adipocitos como los macrófagos generan un círculo vicioso de respuestas inflamatorias durante el desarrollo de la obesidad. Estos factores se combinan para generar una disfunción del tejido adiposo, lo que conduce a niveles persistentemente elevados de nutrientes (carbohidratos y lípidos) en la sangre, provocando la deposición tóxica de lípidos (fenómeno denominado lipotoxicidad) en otros tejidos y contribuyendo a la aparición temprana de enfermedades metabólicas (Ghaben, 2019). La acumulación de lípidos en el hígado, esteatosis hepática, puede conducir a resistencia a la insulina hepática y al consiguiente aumento de la producción hepática de glucosa y triglicéridos. Por otro lado, la acumulación de lípidos en las células musculares puede causar resistencia a la insulina muscular. Además, el depósito de lípidos ectópicos en los islotes pancreáticos puede inducir disfunción de las células β y apoptosis, lo que en última instancia podría llevar al desarrollo de diabetes mellitus tipo 2 (Tsatsoulis 2020).

El incremento de *VAT* se caracteriza por un incremento en la producción y secreción de adipocinas, citocinas y otras moléculas, incluido el TNF, la resistina, la IL-6 y la leptina, que tienen varios efectos multisistémicos negativos, como una mayor inflamación, contribuyendo a incrementar el riesgo de padecer enfermedades no transmisibles (McCafferty 2020; Valenzuela 2023). La leptina y la resistina liberadas por el *VAT* inducen inflamación y disfunción de las células endoteliales que conducen a la vasoconstricción y contribuyen a la formación, vulnerabilidad y ruptura de las placas ateroscleróticas, al promover la polarización proinflamatoria de los macrófagos circulantes, la migración y proliferación de las células del músculo liso vascular y la degradación de la matriz extracelular. Además, la leptina aumenta la actividad nerviosa simpática renal y, en consecuencia, potencialmente el riesgo de hipertensión, al estimular la vía del receptor de melanocortina en el sistema nervioso central. Otro mecanismo que respalda que la presencia de un *VAT* excesivo es un factor de riesgo independiente para la hipertensión es la hiperactividad simpática, probablemente debido a una alteración del barorreflejo. Esta hiperactividad simpática, a su vez, podría conducir a la activación del sistema renina-angiotensina-aldosterona participando en la génesis de un cuadro hipertensivo (Valenzuela 2023).

La función termogénica del *BAT* también puede verse afectada en la obesidad. Es así como la prevalencia de *BAT* activa es menor en personas con obesidad que en individuos con normopeso (Valenzuela 2023). La obesidad está asociada a una reducción en la función oxidativa de *BAT* y una alteración de la capacidad del hipotálamo para estimular el gasto energético del *BAT*. El incremento de la síntesis de citocinas proinflamatorias en la obesidad, como el *TNF*, podría alterar la adipogénesis, la remodelación del *BAT* y desencadenar la conversión de adipocitos marrones en adipocitos de aspecto blanco. Adicionalmente, la obesidad también podría provocar un aumento de la apoptosis de los adipocitos marrones y contribuir a una disminución de la sensibilidad de estas células a los activadores del *BAT* (como la insulina, las catecolaminas o la exposición al frío), alterando el reclutamiento de adipocitos marrones y su actividad termogénica. Por lo tanto, el *BAT* disfuncional podría ser otro mecanismo a través del cual la obesidad se relaciona con un estado cardiometabólico deficiente, aunque la disfunción del *BAT* no siempre está presente en las personas con obesidad (Valenzuela 2023).

Por otra parte, es importante considerar el control hormonal de la homeostasis energética en la obesidad. Existen diversas hormonas del sistema digestivo que participan en la regulación del apetito y saciedad, tales como el péptido YY (*PYY, Peptide YY*) que se produce dentro de células intestinales en respuesta a la presencia de alimentos en el intestino delgado, siendo los lípidos los mayores responsables de su secreción (Steinert 2017). El *PYY* actúa a nivel neural y gastrointestinal para reducir la ingesta de alimentos, actuando en los centros de saciedad hipotalámicos al mismo tiempo que retrasa el vaciamiento gástrico. Los niveles de *PYY* se reducen en la obesidad tanto en el período de ayuno como en el período posprandial, lo que resulta en un control deficiente del apetito posprandial (Hanusch-Enserer et al., 2005; Steinert 2017). La colecistoquinina (*CCK*, *Cholecystokinin*) es otra hormona de la saciedad secretada principalmente por el intestino delgado en respuesta a la presencia de alimentos en este nivel, que, a diferencia del *PYY*, no se altera de manera importante por la obesidad. A través de mecanismos neurales y endocrinos, se cree que la *CCK* retrasa el vaciado gástrico, actuando sobre fibras vagales, y provoca saciedad centralmente, disminuyendo el apetito postprandial (Gibbons et al., 2016). El péptido similar al glucagón 1 (*GLP-1*, *glucagon-like peptide-1*) es secretado con *PYY* por las células del intestino delgado en respuesta a las comidas ricas en grasas y carbohidratos. El *GLP-1* induce la saciedad retrasando el vaciado gástrico al unirse a las células parietales y suprimiendo el apetito al actuar sobre los receptores dentro del tronco encefálico. Además, el *GLP-1* promueve la secreción de insulina y puede aumentar la sensibilidad a la glucosa. Se ha descrito que los niveles circulantes de *GLP-1* se reducen en la obesidad y se normalizan con la pérdida de peso (Guarino 2017). La insulina también está involucrada en la vía de la saciedad que actúa sobre el sistema nervioso central

(Guarino 2017). Los receptores de insulina se expresan en las neuronas del sistema nervioso central, especialmente en el núcleo arqueado y participan en el control de la ingesta de alimentos (Guarino 2017). La hiperinsulinemia crónica es una característica de la obesidad, cuyo objetivo es restablecer el equilibrio energético y limitar el aumento de peso de forma compensatoria. Sin embargo, puede actuar como un mecanismo de mala adaptación, induciendo hiperactividad simpática (Guarino 2017). Finalmente, la ghrelina es la única hormona orexígena conocida (estimulante del apetito). Esta se sintetiza predominantemente en el fondo gástrico (en las glándulas oxínticas) y sus receptores se encuentran en los centros de control del apetito del sistema nervioso central. Los niveles plasmáticos de ghrelina aumentan durante el ayuno y disminuyen tras la ingesta de alimentos (Müller, 2015), lo que contribuye a la dificultad de la dieta hipocalórica para perder peso. La supresión de la ghrelina después de una comida es fundamental para proporcionar una señal de retroalimentación al cerebro y detener la ingesta de alimentos (Guarino 2017). La supresión de ghrelina después de las comidas es inducida por varios factores que incluyen cambios en la insulina plasmática, la osmolaridad intestinal y la señalización neural entérica (Guarino 2017). Las personas con obesidad, aunque muestran niveles de ghrelina más bajos en ayunas que aquellos con normopeso (Raimondo et al., 2012), carecen de la supresión fisiológica de ghrelina en la fase posprandial (Guarino 2017; McCafferty 2020). Este fenómeno podría conducir a un mayor consumo de alimentos, favoreciendo la obesidad (English et al., 2002; Zigman et al., 2016; Guarino 2017).

Por su parte, el tejido adiposo produce leptina, un mediador a largo plazo de la saciedad, cuyos niveles en sangre se encuentran en proporción a la cantidad de grasa corporal. Por ello en las personas con una adiposidad incrementada se encuentran concentraciones plasmáticas de leptina elevadas (Izquierdo 2019; Obradovic 2021). La leptina actúa sobre el hipotálamo (núcleo arqueado) para suprimir el apetito, reducir el peso/grasa corporal y disminuir la glucosa (Guarino 2017; McCafferty 2020). El sistema nervioso simpático está involucrado en la regulación de la función secretora del *WAT*, especialmente en la producción de leptina (Guarino 2017), hormona que tiene efectos simpático-excitadores centrales y cumple un papel crucial en la regulación del gasto energético a través del sistema nervioso simpático. Es así como se ha demostrado que la leptina aumenta el gasto de energía actuando tanto en el sistema cardiovascular como en la termogénesis del *BAT* a través del hipotálamo (Guarino 2017). Sin embargo, se ha sugerido en la obesidad una "resistencia selectiva a la leptina", limitada a sus efectos metabólicos favorables (saciedad y pérdida de peso), mientras que se mantendrían sus efectos simpático-excitadores sobre el sistema cardiovascular (Guarino 2017; McCafferty 2020).

A su vez existe un control central del balance energético (regulación de la ingesta de alimentos y el gasto de energía), donde el hipotálamo tiene un papel fundamental (Obri 2019), ya que alberga el núcleo arqueado que posee dos poblaciones neuronales distintas que pueden detectar señales periféricas como la insulina, la leptina o la ghrelina. Por lo tanto, estas neuronas pueden monitorizar el estado energético de todo el organismo y son responsables de la estabilidad general del peso corporal a lo largo del tiempo (Guillemot-Legris, 2017). Estas neuronas comprenden dos conjuntos diferentes que ejercen efectos opuestos: las neuronas anorexígenas y las neuronas orexígenas (Obri 2019). Las personas con obesidad no pueden integrar adecuadamente la estimulación anorexígenas de la leptina, ya que poseen una resistencia hipotalámica a esta hormona. Esta desregulación en la señalización de leptina hipotalámica conduce aún más a un aumento del apetito, agravando la obesidad. La integración de señales periféricas y la subsiguiente respuesta de las neuronas del núcleo arqueado es delicada y puede alterarse fácilmente. Es así como se ha descrito el desarrollo de neuroinflamación hipotalámica como un proceso clave en el desarrollo de las enfermedades no transmisibles en la obesidad. Incluso se ha demostrado que esta neuroinflamación se desarrolla mucho antes de la aparición de la obesidad o la inflamación periférica (Guillemot-Legris, 2017).

A pesar de los numerosos mecanismos que vinculan la obesidad con las enfermedades no transmisibles, se debate si un subconjunto de personas con obesidad pudiera tener un estado "saludable", el que se ha denominado "obesidad metabólicamente saludable" (Valenzuela, 2023). Las personas con obesidad metabólicamente saludable parecen ser más activas físicamente, pasan menos tiempo en conductas sedentarias y tienen una mejor capacidad cardiorrespiratoria que sus pares con "obesidad metabólicamente no saludable" (Valenzuela, 2023).

3. Tratamiento de la obesidad

En aproximadamente el mismo período en que aumentó la prevalencia de la obesidad, también lo hizo la prevalencia mundial de los intentos de pérdida de peso corporal (Gaesser 2021). Según las recomendaciones del *American College of Cardiology*, *American Heart Association* y *Obesity Society*, son sugeridas en una primera instancia intervenciones integrales enfocadas en la modificación del estilo de vida, en particular en personas con un IMC ≥25 y <27 kg/m^2 (Jensen 2014). A estas se pueden sumar las intervenciones farmacológicas en personas con un IMC de ≥30 kg/m^2 o ≥27 kg/m^2 con comorbilidades relacionadas con la obesidad (Bray 2018; Lin 2021). En el caso de las personas con un IMC ≥40 o ≥35 kg/m^2 con comorbilidades, se puede evaluar la cirugía bariátrica como complemento de la intervención en el estilo de vida (Bray 2018; Lin 2021). Sin embargo, actualmente se ha sugerido considerar la cirugía bariátrica incluso para personas con un IMC ≥30 y <35 kg/m^2 con comorbilidades como la diabetes mellitus tipo 2 que no han logrado un control adecuado con el tratamiento médico (Bray 2016; Sinha et al., 2016; Nguyen 2017; Arterburn 2020).

La piedra angular para el tratamiento de las personas con obesidad es una intervención de estilo de vida integral o de múltiples componentes. El término integral se refiere a la implementación simultánea de tres estrategias: estilo de vida o entrenamiento conductual, cambios en la dieta y un aumento en la actividad física (Bray 2016; Lin 2021). Se ha planteado, de acuerdo con *The Centers for Disease Control and Prevention*, enfocarse en 3 pasos para las modificaciones del comportamiento: reflexión, reemplazo y refuerzo (McCafferty, 2020). La evidencia respalda la eficacia de la intervención en el estilo de vida o modificación conductual (Bray 2016). Respecto a la elección de una dieta para bajar de peso, se recomienda considerar que debe aportar menos energía de la que se requiere para el mantenimiento diario y que permita que el usuario se adhiera y posiblemente proporcione otros beneficios para la salud (Bray 2016). Las diferentes dietas hipocalóricas (centradas en diferentes cantidades de grasas, proteínas o carbohidratos), al ser comparadas en algunos metaanálisis, no han mostrado diferencias entre ellas en la pérdida de peso corporal (Bray 2016). Por otra parte, las dietas de estilo mediterráneo se han asociado con una disminución significativa del peso corporal, de la hemoglobina A1c, la glucosa plasmática en ayunas, la insulina en ayunas y el riesgo de enfermedades cardiovasculares (Bray 2016). La comisión *EAT-Lancet* ha planteado también que existe un creciente interés mundial en las dietas que se basan principalmente en plantas, para beneficiar la salud humana y planetaria (Willett 2019), lo que podría ser una estrategia para combatir la obesidad y sus comorbilidades. Finalmente, el aumento de la actividad física es un componente esencial de la intervención integral del estilo de vida para el control de la obesidad (Bray 2016). La *American Heart Association* (Jensen 2014) y el American College of Sports Medicine (Donnelly 2009) recomiendan que las personas realicen 200-300 y 225-420 minutos de actividad física de intensidad moderada por semana respectivamente para promover la pérdida de peso. Por otra parte, la American College of Sports Medicine recomienda 200-300 min/semana de actividad física moderada para mantener el peso luego de una pérdida de peso corporal (Donnelly 2009). La realización de actividad física tiene beneficios para la salud general que son independientes de la pérdida de peso, la que puede ser más bien discreta en gran parte de los casos (Bray 2016). Por lo tanto, si bien el cambio en la alimentación al parecer es el componente fundamental para perder peso, la actividad física es la clave para mantener el peso perdido (McCafferty, 2020).

Es importante considerar que hay una mayor probabilidad de que se produzcan cambios conductuales (incluyendo la dieta y los patrones de actividad física) como resultado de cambios ambientales y sociales. Dichos cambios de comportamiento pueden resultar ineficaces en el contexto de la falta de políticas de apoyo en sectores como la salud, el transporte, la planificación urbana, la agricultura, el medio ambiente, la elaboración y comercialización de alimentos, la educación, entre otros. Por lo tanto, la OMS reconoce que la alimentación saludable y el aumento de la actividad física en la población deben ser promovidos por políticas y acciones implementadas desde las sociedades (Blüher 2019).

Por otra parte, los procedimientos quirúrgicos para tratar la obesidad, denominados cirugías bariátricas, se han establecido como una alternativa segura (Arterburn 2020) y cada vez más frecuente para las personas que sufren una obesidad severa (Bray 2016; Angrisani 2018; Welbourn, 2019; Angrisani 2021). Esto probablemente a causa de que hasta ahora el manejo no quirúrgico de la obesidad severa ha mostrado un éxito limitado en la reducción y mantención del peso corporal en el tiempo (Montesi, 2016). Por su parte, las cirugías bariátricas que apuntan a disminuir el peso corporal a través de la reducción de la capacidad gástrica y/o limitación de la absorción de los nutrientes y alimentos ingeridos (Khwaja et al., 2010; Buchwald et al., 2011; Nguyen 2017), han resultado ser el tratamiento con mayor costo-efectividad para estos usuarios (Alsumali, 2018; Lester, 2021). La cirugía bariátrica reduce la inflamación crónica relacionada con la obesidad (Lin 2021). Sus beneficios, además de la reducción del peso corporal, incluyen también la mejora y/o remisión de las comorbilidades de la obesidad, en particular de la diabetes mellitus tipo 2 (Abbatini et al., 2010; Schauer et al., 2012), pero también de otras afecciones como la esteatosis hepática no alcohólica (Lee 2019; Aminian 2021), la presión arterial (Kaul & Sharma, 2011; Kissler & Settmacher, 2013; Benaiges et al., 2016) y la dislipidemia (Puzziferri et al., 2014). A ello se suma un incremento en la calidad de vida y expectativa de vida de las personas (Mechanick, 2013; Sjöström, 2012; Nguyen 2017).

Se ha descrito que más del 70% de las cirugías bariátricas mundiales son realizadas en mujeres (Welbourn, 2019). La técnica quirúrgica más utilizada a nivel mundial es la gastrectomía vertical (*SG*; *sleeve gastrectomy*) (55,4%), seguida del bypass gástrico en Y de Roux (*RYGB*, *Roux-en-Y gastric bypass*) (29,3%) y del bypass gástrico de una anastomosis (*OAGB; one anastomosis gastric bypass*) (6,6%), que continúa aumentando su popularidad en todo el mundo (Angrisani 2021). La gastrectomía vertical es un procedimiento restrictivo, que consiste en una resección gástrica vertical parcial, por vía laparoscópica, de la curvatura mayor del estómago y del fondo gástrico, dejando un estómago tubular pequeño a lo largo de la curvatura menor del estómago, reduciendo así la capacidad gástrica y la producción de la hormona ghrelina (que se produce principalmente a nivel del fondo gástrico) (Karamanakos et al., 2008; Kissler & Settmacher, 2013; Nguyen 2017), a la vez que aumenta el *PYY* y el *GLP-1* (Karamanakos et al., 2008; Valderas et al., 2010; Meek et al., 2016), con la consecuente saciedad precoz y disminución del apetito (Kissler & Settmacher, 2013).

Por su parte, el *RYGB* consta de dos componentes. El componente restrictivo del procedimiento corresponde a la creación de una pequeña bolsa gástrica, de alrededor de 30-60 ml. Por lo tanto, la mayor parte del estómago está desconectada (aunque no extirpada) del flujo de los alimentos. A continuación, el extremo distal del intestino delgado se anastomosa a la bolsa gástrica recién construida. En consecuencia, existe poca o ninguna fase de digestión gástrica o duodenal, porque los alimentos nunca ingresan al cuerpo del estómago o al duodeno. Este constituye el componente malabsortivo (Nguyen 2017; Bray 2018). El *RYGB* funciona por varios mecanismos. La bolsa gástrica construida es considerablemente más pequeña que el estómago normal, lo que facilita el consumo de menos alimentos. Además, se produce una menor absorción de nutrientes. La exclusión del duodeno y el yeyuno proximal como resultado del bypass gástrico permite la presencia temprana de alimentos ingeridos que viajan al intestino delgado distal, estimulando la secreción de hormonas intestinales como el *GLP-1*, que conduce a la mejora de la sensibilidad a la insulina al aumentar la producción de insulina y/o disminuir la resistencia a la insulina (además de reducir el apetito). Se ha demostrado que esta mejora de la sensibilidad a la insulina es independiente de la pérdida de peso. Sin embargo, al evitar el duodeno, el *RYGB* tiene el potencial de causar deficiencias de vitaminas y minerales (Nguyen 2017). Es así como se han reportado algunos déficits nutricionales posteriores a la realización de una cirugía bariátrica, tales como una reducción de hierro (Ruz, et al., 2009), zinc (Ruz et al., 2011), calcio (Gletsu et al., 2013), ferritina (Salgado et al., 2014), vitamina B12, vitamina D, albúmina (Aarts et al., 2011) y hemoglobina (von Drygalski et al., 2011).

Al comparar los resultados obtenidos por el tipo de técnica quirúrgica, tanto el *RYGB* como la *SG* dan como resultado una pérdida de peso sostenida y un control de las comorbilidades a los 5 años, con un mayor porcentaje de pérdida de exceso de peso en usuarios sometidos a *RYGB* en comparación con *SG* (65,7% frente a 57,3%) (Sharples, 2020). *RYGB* también mostró mayores porcentajes de resolución de dislipidemia (Sharples, 2020). Por otra parte, tanto el *RYGB* como la *SG* parecen dar como resultado mejoras/remisiones duraderas en la diabetes y la hipertensión. La remisión o mejora de la diabetes tipo 2 se ha evidenciado muchas veces a pocos días después de la cirugía, por lo cual no puede ser explicada por la pérdida de peso (Madsbad et al., 2014), planteándose que se encontrarían involucrados péptidos intestinales, como *GLP-1*, cuya producción se ve aumentada tras el *RYGB* y la *SG* como se mencionó anteriormente (Laferrère et al., 2007; Jørgensen et al., 2013; Shah et al., 2014; Meek et al., 2016; Steinert 2017). Si bien el *RYGB* resultó en una tasa más alta de remisión de diabetes mellitus tipo 2 en comparación con la *SG* después de 1 año de la cirugía (Borgeraas 2020), las tasas de remisión de la diabetes no difirieron en los estudios con seguimiento de 2 a 5 años (Sharples, 2020; Borgeraas 2020). Aproximadamente dos tercios de las personas demostraron un mejor control de la diabetes a los 5 años y aproximadamente un tercio todavía estaban en remisión (Sharples, 2020).

A pesar del significativo aumento del número de procedimientos bariátricos realizados en los últimos años (Angrisani, 2018; Welbourn 2019; Angrisani 2021) y de sus positivos resultados en las morbilidades asociadas a la obesidad (Nguyen 2017), aún no hay acuerdo respecto al impacto de esta intervención sobre algunos componentes de la condición física que se encuentran alterados en los sujetos con obesidad, tales como la capacidad cardiorrespiratoria y la fuerza muscular, importantes por su valor predictivo de salud (Gulati et al., 2003; Lee et al., 2010; Lee et al., 2011; Artero et al., 2011; Artero et al., 2012; Lopez-Jaramillo et al., 2014; Volaklis et al., 2015; Laukkanen et al., 2015).

4. Condición física y obesidad

La condición física es un conjunto de atributos físicos, que tienen que ver con la capacidad de realizar un trabajo y que pueden o no estar relacionados a la salud. La condición física es un estado que puede modificarse de manera efectiva a través de la actividad física regular, pero que también depende de factores genéticos (Caspersen et al., 1985; Ross 2016). La condición física relacionada con la salud incluye distintas cualidades físicas: la capacidad cardiorrespiratoria, la fuerza muscular, la composición corporal y la flexibilidad (Caspersen et al., 1985; Vanhees et al., 2005).

Por otra parte, se ha demostrado que en las personas con obesidad existe un deterioro de los componentes de la condición física asociados a la salud, en particular de la fuerza muscular (*MS, muscle strength)* y de la capacidad cardiorrespiratoria (*CRF, cardiorespiratory fitness*) (Arena et al., 2014; Vilaça et al., 2014).

4.1. Capacidad cardiorrespiratoria

La *CRF* es un componente de la condición física que se ha posicionado como uno de los indicadores de salud y de expectativa de vida más importantes, tanto en individuos sanos, como en aquellos con morbilidades (Myers et al., 2002; Kurl et al., 2003; Kodama 2009; Lyerly et al., 2009; Lee et al., 2010; Gander et al., 2011; Lee et al., 2011). La creciente evidencia epidemiológica y clínica en las últimas décadas ha demostrado que los niveles bajos de *CRF* están asociados con un alto riesgo de enfermedades cardiovasculares y mortalidad por todas las causas, así como con mortalidad atribuible a varios tipos de cáncer, especialmente de tracto digestivo y de mama (Kodama 2009; Ross 2016). La *American Heart Association* recomienda que la *CRF* se mida en la práctica clínica como un signo vital (Ross et al., 2016), debido a que es un predictor de mortalidad potencialmente más fuerte que los factores de riesgo establecidos como el tabaquismo, la hipertensión, el colesterol alto y la diabetes mellitus tipo 2. Sin embargo, a diferencia de estos, la *CRF* no se evalúa de forma rutinaria en la práctica clínica (Ross 2016). Asimismo, la *CRF* es un marcador de la capacidad funcional de un individuo, es decir, la competencia que tiene para realizar las actividades de la vida diaria (Ross 2016).

Este elemento de la condición física es un reflejo de la capacidad integrada de transportar oxígeno de la atmósfera a las mitocondrias para realizar un trabajo físico (Ross 2016). Por lo tanto, depende de una cadena vinculada de procesos que incluyen ventilación y difusión pulmonar, función ventricular, acoplamiento ventrículo-arterial, la capacidad del sistema vascular para acomodar y transportar de manera eficiente la sangre desde el corazón para satisfacer los requisitos de oxígeno y la capacidad de las células musculares para recibir y utilizar el oxígeno y los nutrientes entregados por la sangre, así como para comunicar estas demandas metabólicas al centro de control cardiovascular (Ross 2016). En resumen, la *CRF* es dependiente de la salud y la función integrada de numerosos sistemas (principalmente del cardiovascular, respiratorio y músculo-esquelético) (Arena et al., 2010), y, por lo tanto, se considera un reflejo de la salud corporal total (Ross 2016).

La *CRF* es expresada habitualmente en términos del consumo máximo de oxígeno (VO_{2max}), que corresponde a la mayor cantidad de oxígeno que una persona puede consumir a partir del aire inspirado, durante la realización de un ejercicio dinámico que implique gran parte de la masa muscular total y representa la cantidad de oxígeno transportado y utilizado en el metabolismo celular (American Thoracic Society/American College of Chest Physicians, 2003). El VO_{2max} es considerado el *gold standard*, la mejor medida de la capacidad cardiorrespiratoria y de ejercicio físico (Arena et al., 2010). Este puede ser medido directamente, mediante el análisis de la ventilación y el intercambio de gases durante una prueba de ejercicio máximo, o estimado a partir de la tasa de trabajo máxima alcanzada en una cinta rodante, en un cicloergómetro o en una prueba de campo (Ross 2016). Si bien el VO_{2max} medido es más objetivo y preciso, el estimado suele ser más común, particularmente en estudios epidemiológicos que involucran grandes poblaciones, debido a que es más fácil de obtener. Por otra parte, numerosos estudios han informado que tanto la *CRF* medida como estimada predicen los resultados de salud mencionados previamente (Ross 2016). Es importante considerar que la evaluación del VO_{2max} requiere un esfuerzo de máxima intensidad por parte del sujeto (Bentley et al., 2007; Midgley et al., 2007), situación que puede no resultar aconsejable en usuarios que por sus patologías presentan un mayor riesgo de evento adverso (Mezzani et al., 2009). Es así como en personas con obesidad, gran parte de las evaluaciones de *CRF* son de carácter submáximo, no alcanzando la meseta del VO_2 (Poole 2017) y, por tanto, utilizando el término consumo de oxígeno *peak* (VO_{2peak}) que corresponde al consumo de oxígeno alcanzado en el momento de la detención de la prueba (Noonan et al., 2000; American Thoracic Society/American College of Chest Physicians, 2003; Forman et al., 2010; Arena et al., 2014). El consumo de oxígeno puede ser expresado en valores absolutos (Litros / minutos), relativos (mililitros / kilogramos / minutos) al peso corporal (Fletcher et al., 2013) o a la masa libre de grasa (*FFM, Fat-free mass*) / masa magra / masa musculoesquelética del sujeto, que es la forma menos usada en la clínica debido al coste implicado, pero la más recomendada en individuos con obesidad por su valor pronóstico (Osman 2000; Forman et al., 2010). Asimismo, una publicación reciente demostró que el VO_{2max} en ml/kg *FFM*/min resultó ser un predictor más fuerte de mortalidad por todas las causas que el VO_{2max} en ml/kg/min en un seguimiento de 19 años de alrededor de 3000 hombres y mujeres con y sin obesidad (Imboden et al., 2020).

Se considera que aproximadamente la mitad de la variación en la *CRF* es atribuible a factores genéticos (Ross 2016). De todas formas, la *CRF* puede mejorarse mediante el entrenamiento físico (American College of Sports

Medicine 1998; Santtila 2008; Ross 2016) y estos incrementos se han asociado consistentemente con una reducción del riesgo de mortalidad mayor que la pérdida de peso intencional (Gaesser 2021), incluso en la población con obesidad (Lee 2010). Además, la respuesta de la *CRF* a la actividad física también tiene una contribución entre un 45 y 50% aproximadamente de factores hereditarios (Bouchard 1986; Ross 2016). Cabe señalar que estas estimaciones de heredabilidad son similares en magnitud a otros factores de riesgo de enfermedades cardiovasculares, como la insulina, glucosa y presión arterial (Ross 2016).

Las personas con obesidad poseen distintos grados de disfunción cardiovascular, respiratoria y musculoesquelética, sumado a alteraciones biomecánicas, lo que compromete su capacidad para consumir el oxígeno adicional necesario durante el ejercicio dinámico, alterando su $VO_{2max/peak}$ y otras variables relevantes de la prueba de esfuerzo cardiopulmonar (*CPET, cardiopulmonary exercise testing*) (Li et al., 2001; Di Bello et al., 2006; Wong et al., 2007; Holloway et al., 2009; Duncan, 2010; Runhaar et al., 2011; Arena et al., 2014). Es así como se ha reportado en personas con obesidad una disfunción diastólica del ventrículo izquierdo (Willens et al., 2004; Di Bello et al., 2006; Russo 2011; Alpert 2016; Mandviwala 2016), lo que, de estar presente, provoca una limitación de la capacidad de incremento del gasto cardiaco durante el ejercicio físico (Arena et al., 2014). Asimismo, se ve restringida su capacidad para aumentar la ventilación / minuto por el exceso de masa corporal, lo que genera una alteración del patrón ventilatorio, necesitando mayores aumentos de la frecuencia respiratoria para compensar la disminución en la capacidad de incrementar el volumen corriente (Li et al., 2001; Littleton, 2012; Arena et al., 2014). A estas limitaciones, se suman alteraciones periféricas, tales como una disfunción endotelial (Koenen 2021) y, a nivel del músculo esquelético, una disfunción mitocondrial (Kim et al., 2000; Kelley et al., 2002; Ritov et al., 2005; Arena et al., 2014).

En concordancia con lo mencionado anteriormente, un estudio de más de 20.000 participantes mostró que el IMC se encontraba inversamente relacionado con la *CRF*, de manera que las mujeres y los hombres del quintil más alto de *CRF* tenían un IMC medio de 21,0 ± 2,1 y 25,3 ± 2,5 kg/m^2, respectivamente, mientras que las mujeres y los hombres del quintil más bajo de la *CRF* tenían un IMC medio de 27,5 ± 5,5 y 32,5 ± 5,7 kg/m^2, respectivamente (Lakoski et al., 2011); estos resultados concuerdan con otras investigaciones (Duncan, 2010; Dagan et al., 2013; Radovanović et al., 2014). Sin embargo, como se mencionó anteriormente una *CRF* más alta puede mitigar (Lee 2010; Barry et al., 2018) o incluso eliminar el mayor riesgo de muerte asociado a la obesidad (Barry et al., 2014). Es así como se ha reportado que una mejora ≥ a 1 *MET* (*Metabolic Equivalent of Task*; 3,5 ml de consumo de O_2/kg/min), que puede ser lograda después de 8 semanas de entrenamiento continuo de intensidad moderada o de intervalos de alta intensidad (sin pérdida de peso corporal), se asocia con un riesgo 14-29% menor de mortalidad por todas las causas y un riesgo 19% menor de mortalidad por enfermedades cardiovasculares (Gaesser 2021). En consecuencia, se ha descrito la paradoja "*fat but fit*", que consiste en que el poseer una buena condición física, particularmente de *CRF*, podría atenuar, al menos en parte, los efectos perjudiciales de la obesidad sobre la salud cardiometabólica (Valenzuela 2023), asociándose por ejemplo con una menor acumulación de grasa visceral (Tsatsoulis 2020). Asimismo, varios estudios han mostrado que las personas con obesidad y una *CRF* alta tienen un menor riesgo de enfermedades cardiovasculares y mortalidad que personas con normopeso y una *CRF* baja (Valenzuela 2023). Por lo que, una *CRF* baja es más peligrosa que un IMC alto (Barry 2014; Barry 2018). Toda esta evidencia hace plantearse si la pérdida de peso debiese ser el enfoque principal del tratamiento de la obesidad (Gaesser 2021).

Por otro lado, tras la cirugía bariátrica se han reportado resultados contradictorios de los cambios en la *CRF* expresada en términos absolutos (Stegen et al., 2011; Kanoupakis et al., 2001; Serés et al., 2006) y relativos al peso corporal (Stegen et al., 2011; Serés et al., 2006; Souza et al., 2010).

4.2 Fuerza muscular

La *MS* es otra importante cualidad de la condición física, ya que se asocia con una reducción del riesgo de enfermedades no transmisibles y mortalidad, y esta asociación es independiente del IMC (Carbone et al., 2020; Garcia-Hermoso et al., 2018; Kim et al., 2017; Saeidifard et al., 2019; Ruiz 2009; FitzGerald et al., 2004; Newman et al., 2006; Artero et al., 2011; Artero et al., 2012; Ortega et al., 2012; Lopez-Jaramillo et al., 2014; Volaklis et al., 2015). Esta reducción del riesgo de mortalidad se ha confirmado tanto en población sana (García-Hermoso 2018), como en aquella con morbilidades (Jochem 2019).

La *MS* de las extremidades superiores puede ser medida a través de la fuerza de prensión manual, la que ha sido relacionada con la expectativa de vida (Ortega et al., 2011; Kilgour et al., 2013; Bohannon 2015). Varios estudios han demostrado que la fuerza de prensión manual está relacionada de manera inversa con el riesgo de mortalidad por todas las causas, en adultos medios y mayores (Sasaki et al., 2007; Ling et al., 2010). Además, esta variable es un predictor relacionado con la salud en aspectos como la funcionalidad y la independencia en las actividades de la vida diaria (Norman et al., 2010; Marsh et al., 2011; Rijk 2016).

Existen múltiples definiciones de fuerza muscular en la literatura, entre ellas, se ha descrito como la tensión máxima o el torque desarrollado durante la contracción voluntaria máxima bajo un conjunto dado de condiciones (Sale 1991). La interacción entre la fuerza desarrollada por los músculos esqueléticos y las fuerzas externas presentadas por la masa corporal, la gravedad, los objetos deportivos (como la jabalina, pelota, disco) o los oponentes en deportes de contacto darán lugar a acciones musculares que producen contracciones estáticas (tradicionalmente descritas como isométricas, es decir, sin movimiento sobre las articulaciones relacionadas) o contracciones dinámicas (que implican movimiento con una disminución o un aumento en los ángulos de las articulaciones) (Komi 2008).

Las evaluaciones isocinéticas, que se realizan a una velocidad angular constante, se consideran el *gold standard* para evaluar la fuerza muscular; permiten condiciones mecánicas bien controladas para la contracción de los músculos evaluados y se aplican comúnmente en entornos de laboratorio (Verdijk 2009; Dvir 2020; Sizoo 2021). Sin embargo, los dinamómetros isocinéticos son costosos y generalmente solo evalúan un ejercicio muscular monoarticular. Por el contrario, las pruebas isométricas y de 1RM (*one-repetition máximum*) se utilizan principalmente para la evaluación de la fuerza en entornos clínicos (Dvir 2020). Las pruebas de fuerza isométrica, como la de prensión manual, son rentables y eficientes en cuanto al tiempo y están fuertemente correlacionadas con la fuerza dinámica máxima (Sizoo 2021; McGuigan 2010). Las pruebas de 1RM se aplican ampliamente porque son de bajo coste y permiten la evaluación de ejercicios que involucran múltiples articulaciones, reflejando acciones musculares dinámicas utilizadas en la vida diaria (Verdijk 2009).

Las personas con obesidad tienen una mayor masa y fuerza muscular absoluta (fuerza máxima isotónica, isométrica e isocinética) en comparación con las personas con normopeso, ya que se cree que el aumento de la adiposidad actuaría como un estímulo de sobrecarga crónica en los músculos antigravitatorios, aumentando así el tamaño muscular y la fuerza de estos (Tomlinson 2016). En cambio, generalmente no se han reportado diferencias en la fuerza de prensión manual entre personas con y sin obesidad (Cooper et al., 2014; Tomlinson 2016). Sin embargo, este aparente beneficio desaparece cuando la *MS* se normaliza por peso corporal, resultando en una fuerza relativa significativamente menor que en personas con normopeso (Maffiuletti et al., 2007; Tallis 2018). Esto mismo se observa generalmente cuando la *MS* se normaliza por *FFM* o masa muscular (Cooper et al., 2014; Tallis 2018), por lo que se considera que las personas con obesidad poseen una inferior calidad muscular (expresada habitualmente como la relación entre la fuerza muscular y la masa magra) (Tomlinson 2016; Valenzuela 2020). Asimismo, se ha evidenciado una relación inversa entre la masa grasa y la calidad muscular (Newman et al., 2003; Koster et al., 2011), como una mayor prevalencia e incidencia de obesidad en personas con niveles menores de fuerza muscular relativa al peso corporal (Jackson et al., 2010). Por otra parte, se ha demostrado que niveles más altos de fuerza muscular pueden mitigar el mayor riesgo de muerte asociado con la obesidad (Stenholm 2014).

La menor fuerza relativa de las personas con obesidad se ha intentado explicar por diversos mecanismos que se desarrollan en la obesidad mediados, en gran parte, por la inflamación sistémica crónica de bajo grado y que pueden afectar la función contráctil del músculo esquelético (Tomlinson 2016). Entre ellos se encuentran las alteraciones del ciclo del calcio (Tallis 2018), de la actividad de la *AMPK* (*AMP-activated protein kinase*) (Tallis 2018), de la actividad del factor de crecimiento similar a la insulina 1 (*IGF-1*, *insulin-like growth factor 1*) (Tomlinson 2016; Tallis 2018, Pellegrinelli 2015) y del reclutamiento de las células involucradas en la regeneración del músculo esquelético, generando un deterioro de la angiogénesis y la formación de miocitos, mientras se promueve la deposición de tejido fibrótico y adiposo (Tomlinson 2016). En consecuencia, se reduce la integridad estructural del músculo esquelético y su capacidad funcional (Tomlinson 2016).

En personas con obesidad sometidas a una pérdida de peso significativa como la resultante de una cirugía bariátrica, ha sido reportada una disminución de la masa grasa y de la *FFM* o masa magra (Carrasco et al., 2009; Zalesin et al., 2010; de Freitas et al., 2014). En concordancia con lo anterior, algunos estudios han mostrado una reducción de la fuerza muscular absoluta después de las intervenciones bariátricas (Stegen et al., 2011; Gil 2021). Sin embargo, otros estudios han reportado incrementos (Campanha-Versiani et al., 2017) así como ausencia de cambio en la fuerza absoluta posteriores a la cirugía (Otto et al. 2014).

5. Variabilidad del ritmo cardiaco y obesidad

La variabilidad del ritmo cardíaco (*HRV, heart rate variability*) corresponde al análisis estadístico matemático de la variación de los períodos de tiempo entre latidos cardiacos consecutivos, que entrega información acerca de la regulación autonómica cardiovascular y, al igual que los componentes de la condición física anteriormente descritos, es un predictor independiente de mortalidad (Kannel et al., 1987; Tsuji et al., 1994; Dekker et al., 1997; La Rovere et al., 1998; Bilchick et al., 2002; Mäkikallio et al., 2001 a; Mäkikallio et al., 2001 b; Tapanainen et al., 2002; Dewey et al., 2007; Oikawa et al., 2009; May et al., 2011; Sessa 2018). La *HRV* permite estimar el estado y balance de los componentes del sistema nervioso autónomo (simpático vs. parasimpático) y de sus influencias sobre el ritmo intrínseco del nódulo sinoauricular (Aubert et al., 2003), reflejando la capacidad del corazón para adaptarse a condiciones cambiantes, así como la salud cardíaca general (Acharya et al., 2006).

La *HRV* puede ser evaluada con electrocardiografía, *gold standard* para la medición de los intervalos R-R (*Task Force of the European Society of Cardiology and The North American Society of Pacing Electrophysiology*, 1996), así como mediante monitores telemétricos del ritmo cardiaco (tecnología validada para estos fines) (Gamelin et al., 2006; Nunan et al., 2009) e incluso en la actualidad con aplicaciones de relojes y teléfonos inteligentes (Dobbs 2019).

En las últimas décadas, la *HRV* no solo se ha empleado como una herramienta de evaluación de riesgos en entornos clínicos, sino que también se ha convertido en una herramienta útil para monitorizar el curso de las adaptaciones al entrenamiento y optimizar el rendimiento en los deportes y otras actividades físicas (Gavrilova 2015; Dong 2016). Además, se ha convertido en una herramienta valiosa para comprender la relación entre el sistema nervioso autónomo, los factores del estilo de vida y la salud en general (Coutts 2020). Una *HRV* más alta se ha asociado con una mejor salud y un menor riesgo de morbimortalidad, mientras que una *HRV* más baja se ha relacionado con resultados de salud deficientes, tales como las enfermedades cardiovasculares, diabetes, dislipidemia y depresión (Kamath 2012).

La *HRV* puede ser analizada de distintas formas, entre ellas en los dominios de tiempo y de frecuencia. El análisis de dominio de frecuencia describe las oscilaciones periódicas de las señales de la frecuencia cardíaca, que se componen de diferentes frecuencias y amplitudes y proporcionan información sobre su intensidad en la señal del ritmo sinusal del corazón (*Task Force of the European Society of Cardiology and The North American Society of Pacing Electrophysiology*, 1996). Este análisis emplea habitualmente una transformación algorítmica (Fourier) y para registros de corta duración (2 a 5 min), generalmente se identifican tres *peaks*: potencia de muy baja frecuencia (*VLF*, *very low frequency*), de baja frecuencia (LF, *low frequency*) y alta frecuencia (HF, *high frequency*). La *LF,* ubicada entre 0,04 a 0,15 Hz de variación de la frecuencia de cambio de los intervalos R-R, está posiblemente correlacionada con el tono simpático o el balance autonómico y generalmente refleja la actividad del barorreflejo en respuesta al tono vasomotor (Heathers

2014). La *HF*, entre 0,15 a 0,40 Hz de variación de la frecuencia de cambio de los intervalos R-R, es considerada un marcador de tono parasimpático (modulación vagal) y está mediada por la respiración. Por otra parte, la relación entre las potencias de baja y alta frecuencia (*LF/HF)*, corresponde a la interacción entre la actividad simpática y vagal (Xhyheri et al., 2012).

El análisis del dominio de tiempo se realiza mediante métodos descriptivos tradicionales y generalmente comprende la desviación estándar de todos los intervalos R-R (*SDNN, standard deviation of the average normal-to-normal interval*), es un índice global de *HRV* y se encuentra influenciada negativamente por el componente simpático del sistema nervioso autónomo (*Task Force of the European Society of Cardiology and The North American Society of Pacing Electrophysiology*, 1996; Xhyheri et al., 2012). Por su parte, la raíz cuadrada del promedio de las diferencias elevadas al cuadrado de intervalos R-R sucesivos (*RMSSD, root mean square of successive differences in RR intervals*) y el porcentaje de intervalos R-R sucesivos cuya diferencia es mayor a 50 milisegundos (*pNN50, percentage of consecutive RR intervals that differ by more than 50 ms*), corresponden a parámetros temporales que detectan las oscilaciones de alta frecuencia causadas por la actividad parasimpática (*Task Force of the European Society of Cardiology and The North American Society of Pacing Electrophysiology*, 1996; Xhyheri et al., 2012).

Por último, también en la *HRV* pueden analizarse variables no lineales, entre las cuales en el diagrama de Poincaré, que corresponde a una representación gráfica bidimensional donde cada intervalo R-R es graficado en función del intervalo R-R que lo precede, se pueden obtener las variables SD1 y SD2 (las desviaciones estándar de la distancia de cada uno de los puntos del gráfico respecto a los ejes en 45° y 135° respectivamente), las que entregan información relacionada a cambios rápidos y lentos en los intervalos R-R correspondientemente; además de la entropía de la muestra (*SampEn, Sample*

Entropy), que mide la complejidad de la señal y que se ha sugerido como un prometedor algoritmo de valor clínico (Lake 2020). Valores más altos en estas variables no lineales corresponden a una mayor variabilidad del ritmo cardiaco (Kleiger et al., 2005; Acharya et al., 2006).

Las personas con obesidad presentan una menor *HRV* que las personas con normopeso (Karason et al., 1999; Emdin et al., 2001; Sztajzel et al., 2009), lo que se explicaría por una sobreestimulación crónica del componente simpático del sistema nervioso autónomo (Lambert et al., 2010; Thorp 2015; Guarino 2017), así como por una reducción de la actividad parasimpática (Kamath 2016). Consecuentemente, en la obesidad se ha descrito una alteración del equilibrio simpático-vagal (Thayer et al., 2010), reflejada por un aumento de la relación *LF/HF* (Costa 2018). Asimismo, se cree que el sistema nervioso autónomo desempeña un papel en la fisiopatología de la obesidad y de sus complicaciones asociadas (Pal et al., 2012; Krishna et al., 2013; McCully et al., 2013; Guarino 2017). Es más, los cambios hormonales que sufren los sujetos con obesidad, tales como el incremento de la insulina y la leptina a nivel plasmático, han sido establecidos como factores implicados en la disfunción autonómica (Smith 2012; Russo 2021). Por su parte, la disfunción autonómica está relacionada con una mayor disfunción diastólica, hipertrofia ventricular y remodelado cardíaco (Bischoff 2017). Es así como ha sido descrito que los cambios que produce la obesidad en el sistema nervioso autónomo, como la reducción de la actividad parasimpática, tendrían un papel importante en el desarrollo y progresión de las complicaciones cardiovasculares en esta población (Thayer 2010; Kalil 2012; Guarino 2017)

Por otra parte, el ejercicio físico, un pilar fundamental del tratamiento de la obesidad, es capaz de mejorar la *HRV*, lo que indica una mejor función del sistema nervioso autónomo y salud cardiovascular (Singh 2018). El ejercicio físico provoca un cambio hacia el dominio parasimpático del sistema nervioso autónomo y un mejor equilibrio entre los sistemas simpático y parasimpático (Joyner 2009). Además, el ejercicio puede mejorar la capacidad cardiorrespiratoria y reducir la inflamación sistémica, lo que se ha asociado con una *HRV* más alta (Gerosa-Neto 2016; Toohey 2020). La *HRV* ha sido relacionada a su vez positivamente con la capacidad cardiorrespiratoria, tanto en sujetos sanos (Boutcher et al., 2013; Chen 2019) como en aquellos con obesidad (Kaikkonen et al., 2014). Sin embargo, una reciente revisión plantea que no parece haber consenso en la literatura acerca de la influencia del nivel de capacidad cardiovascular y el control autonómico cardíaco en personas sanas (Souza 2021).

Al momento de comenzar la presente tesis doctoral, las publicaciones acerca del impacto de la cirugía bariátrica en la *HRV* presentaban resultados contradictorios, tanto en los parámetros del dominio de tiempo, dominio de frecuencia, como en el análisis no lineal. Es así como existen reportes de aumentos en los parámetros del dominio de tiempo a los 3, 6 y 12 meses postquirúrgicos (Nault et al., 2007; Bobbioni-Harsch et al., 2009; Machado et al., 2009; Lips et al., 2013; Pontiroli et al., 2013), como otros estudios que no evidenciaron cambios en estas variables al mes y al año tras la cirugía (Alam et al. (2009) y Karason et al. (1999). Por otra parte, se ha descrito un incremento en los parámetros de dominio de frecuencia, tanto de *HF* como de *LF*, con un mantenimiento de la relación *LF/HF*, a los 3, 6 y 12 meses de la cirugía bariátrica (Nault et al., 2007; Kokkinos et al., 2013), mientras que otros estudios han evidenciado una reducción de la relación *LF/HF* a los 6 meses de la cirugía (Maser et al., 2013; Pontiroli et al., 2013). Por otro lado, se ha reportado que el incremento postcirugía de los parámetros de dominio de tiempo no se correlaciona con la pérdida de peso (Machado et al., 2009; Perugini et al., 2010), pero sí con los cambios en la circunferencia de cintura (Machado et al., 2009). Mientras que Bobbioni-Harsch et al. (2009) describieron una relación inversa entre *pNN50* y el IMC postquirúrgico y Karason et al. (1999) una asociación entre parámetros de dominio de frecuencia y el peso corporal postoperatorio.

Se debe considerar que parte de los estudios recién presentados incluyeron muestras muy pequeñas (12 sujetos o menos), sin explicitar un cálculo de tamaño muestral previo (Nault et al., 2007; Alam et al., 2009; Bobbioni-Harsch et al., 2009), o bien no realizaron una adecuada exposición de sus datos, omitiendo, por ejemplo, a qué tipo de logaritmo (natural o en base de 10) fueron transformados los resultados de los parámetros espectrales (Nault et al., 2007).

Por otra parte, una reciente revisión sistemática (Benjamim 2021) reportó que todos los estudios que analizaron (incluyendo Ibacache et al., 2019) coincidieron en que la cirugía bariátrica promueve un aumento de la variabilidad del ritmo cardíaco y una disminución de la frecuencia cardiaca. Sin embargo, hasta la fecha no hay metaanálisis disponibles de los cambios en la variabilidad del ritmo cardiaco después de esta intervención quirúrgica.

Referencias introducción

Malik VS, Willet WC, Hu FB. Nearly a decade on—trends, risk factors and policy implications in global obesity. Nature Reviews Endocrinology. 2020;16(11):615-6. https://doi.org/10.1038/s41574-020-00411-y

WHO. Obesity and overweight. 2021. https://www.who.int/news-room/fact-sheets/detail/obesity-and-overweight

ICD-11 for Mortality and Morbidity Statistics (Version: 01/2023) https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/149403041

Blüher M. Obesity: global epidemiology and pathogenesis. Nature Reviews Endocrinology. 2019;15(5):288-98.

American College of Cardiology/American Heart Association Task Force on Practice Guidelines, Obesity Expert Panel, 2013. Executive summary: Guidelines (2013) for the management of overweight and obesity in adults: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Obesity Society published by the Obesity Society and American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. Based on a systematic review from the The Obesity Expert Panel, 2013. Obesity (Silver Spring) 22(Suppl 2):S5-39, 2014.

Reilly JJ, El-Hamdouchi A, Diouf A, Monyeki A, Somda SA. Determining the worldwide prevalence of obesity. The Lancet. 2018;391(10132):1773-4.

WHO Consultation on Obesity (1999: Geneva, Switzerland) & World Health Organization. Obesity: Preventing and Managing the Global Epidemic. Report of a WHO Consultation. World Health Organ Tech Rep Ser (2000) 894:i–xii, 1-253.

Kral JG, Kava RA, Catalano PM, Moore BJ. Severe obesity: the neglected epidemic. Obesity facts. 2012;5(2):254-69.

Berrington de Gonzales A, Hartge P, Cerhan JR, et al. Body-mass index and mortality among 1.46 million white adults. N Engl J Med. 2010;363:2211–9.

Valenzuela PL, Carrera-Bastos P, Castillo-García A, Lieberman DE, Santos-Lozano A, Lucia A. Obesity and the risk of cardiometabolic diseases. Nature Reviews Cardiology. 2023 Mar 16:1-20.

Kral, J. G. (1985). Morbid obesity and related health risks. Annals of internal medicine, 103(6_Part_2), 1043-1047.

World Health Organization Expert Committee. (1995). Physical status: the use and interpretation of anthropometry. WHO technical report series, 854(121), 55.

National Institutes of Health. (1998). Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. Obesity research, 6 (Suppl 2), 51S– 209S.

Freedman, D. S., Khan, L. K., Serdula, M. K., Galuska, D. A., & Dietz, W. H. (2002). Trends and correlates of class 3 obesity in the United States from 1990 through 2000. JAMA, 288(14), 1758-1761.

World Health Organization. (2013). Obesity and overweight Fact sheet N 311. WHO Media Centre. Geneva, Switzerland.

Lin X, Li H. Obesity: epidemiology, pathophysiology, and therapeutics. Frontiers in endocrinology. 2021;12:706978.

World Health Organization, E. C. (2004). Appropriate body-mass index for Asian populations and its implications for policy and intervention strategies. Lancet, 363(9403), 157.

Janssen I, Katzmarzyk PT, Robert R. Waist circumference and not body mass index explains obesity-related health risk. Am J Clin Nutr. 2004;79:379–84.

Despress JP. Body fat distribution and risk of cardiovascular disease: an update. Circulation. 2012;126:1301–13.

Chait A, Den Hartigh LJ. Adipose tissue distribution, inflammation and its metabolic consequences, including diabetes and cardiovascular disease. Frontiers in cardiovascular medicine. 2020;7:22.

Dhawan D, Sharma S. Abdominal Obesity, Adipokines and Non-communicable Diseases. J Steroid Biochem Mol Biol. 2020;203:105737.

Han TS, Sattar N, Lean M. ABC of obesity. Assessment of obesity and its clinical implications. BMJ. 2006 Sep 30;333(7570):695-8.

Ashwell M, Gunn P, Gibson S. Waist-to-height ratio is a better screening tool than waist circumference and BMI for adult cardiometabolic risk factors: systematic review and meta-analysis. *Obes Rev* 2012; **13:** 275–86.

Cerhan JR, Moore SC, Jacobs EJ, et al. A pooled analysis of waist circumference and mortality in 650,000 adults. *Mayo Clin Proc* 2014; **89:** 335–45.

Nazare, J. A., Smith, J., Borel, A. L., Aschner, P., Barter, P., Van Gaal, L., et al. (2015). Usefulness of measuring both body mass index and waist circumference for the estimation of visceral adiposity and related cardiometabolic risk profile (from the INSPIRE ME IAA study). The American journal of cardiology, 115(3), 307-315.

McCafferty BJ, Hill JO, Gunn AJ. Obesity: scope, lifestyle interventions, and medical management. Techniques in vascular and interventional radiology. 2020;23(1):100653.

GBD 2015 Obesity Collaborators, Afshin A, Forouzanfar MH, et al. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med*. 2017;377:13–27.

Chooi YC, Ding C, Magkos F. The epidemiology of obesity. Metabolism. 2019;92:6-10.

Lobstain T, Brinsden H, Neveux M. *World Obesity Atlas 2022*.; 2022. www.worldobesity.org#worldobesityatlas

Mehrzad R. Definition and introduction to epidemiology of obesity. InObesity 2020 Jan 1 (pp. 1-6). Elsevier.

Ahmad NN, Butsch WS, Aidarous S. Clinical management of obesity in women: addressing a lifecycle of risk. Obstetrics and Gynecology Clinics. 2016;43(2):201-30. https://doi.org/10.1016/j.ogc.2016.01.007

Inoue Y, Qin B, Poti J, et al. Epidemiology of obesity in adults: latest trends. Curr Obes Rep. 2018;7(4):276–88. https://doi.org/10. 1007/s13679-018-0317-8

Williamson K, Nimegeer A, Lean M. Rising prevalence of BMI≥ 40 kg/m2: A high-demand epidemic needing better documentation. Obesity reviews. 2020 Apr;21(4):e12986. DOI: 10.1111/obr.12986

NCD Risk Factor Collaboration (NCD- RisC). Trends in adult body- mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population- based measurement studies with 19.2 million participants. *Lancet* **387**, 1377–1396 (2016).

NCD Risk Factor Collaboration (NCD- RisC). Worldwide trends in body- mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population- based measurement studies in 128.9 million children, adolescents, and adults. *Lancet* **390**, 2627–2642 (2017).

Wong MC, Huang J, Wang J, Chan PS, Lok V, Chen X, Leung C, Wang HH, Lao XQ, Zheng ZJ. Global, regional and time-trend prevalence of central obesity: a systematic review and meta-analysis of 13.2 million subjects. European journal of epidemiology. 2020;35:673-83.

Okorodudu DO, Jumean MF, Montori VM, et al. Diagnostic performance of body mass index to identify obesity as defined by body adiposity: a systematic review and meta-analysis. Int J Obes (Lond) 2010; 34: 791–99.

Williams EP, Mesidor M, Winters K, Dubbert PM, Wyatt SB. Overweight and obesity: prevalence, consequences, and causes of a growing public health problem. Curr Obes Rep. 2015;4(3):363–370.

Sarma S, Sockalingam S, Dash S. Obesity as a multisystem disease: Trends in obesity rates and obesity-related complications. Diabetes, Obesity and Metabolism. 2021 Feb;23:3-16.

Kuvat N, Tanriverdi H, Armutcu F. The relationship between obstructive sleep apnea syndrome and obesity: A new perspective on the pathogenesis in terms of organ crosstalk. The Clinical Respiratory Journal. 2020;14(7):595-604. https://doi.org/10.1111/crj.13175

Zeng X, Xie Y, Liu Y, Long S, Mo Z. Polycystic ovarian syndrome: Correlation between hyperandrogenism, insulin resistance and obesity. Clinica Chimica Acta. 2020;502:214-21. https://doi.org/10.1016/j.cca.2019.11.003

Manrique-Acevedo C, Chinnakotla B, Padilla J, Martinez-Lemus LA, Gozal D. Obesity and cardiovascular disease in women. International Journal of Obesity. 2020;44(6):1210-26. https://doi.org/10.1038/s41366-020-0548-0

Payne ME, Porter Starr KN, Orenduff M, et al. Quality of Life and Mental Health in Older Adults with Obesity and Frailty: Associations with a Weight Loss Intervention. *J Nutr Health Aging*. 2018;22(10):1259-1265. doi:10.1007/s12603-018-1127-0

Safaei M, Sundararajan EA, Driss M, Boulila W, Shapi'i A. A systematic literature review on obesity: Understanding the causes & consequences of obesity and reviewing various machine learning approaches used to predict obesity. *Comput Biol Med*. 2021;136. doi:10.1016/J.COMPBIOMED.2021.104754

Aghili SM, Ebrahimpur M, Arjmand B, Shadman Z, Pejman Sani M, Qorbani M, Larijani B, Payab M. Obesity in COVID-19 era, implications for mechanisms, comorbidities, and prognosis: a review and meta-analysis. International Journal of Obesity. 2021;45(5):998-1016.

Stefan N, Birkenfeld AL, Schulze MB. Global pandemics interconnected—obesity, impaired metabolic health and COVID-19. Nature Reviews Endocrinology. 2021;17(3):135-49.

Bischoff SC, Boirie Y, Cederholm T, Chourdakis M, Cuerda C, Delzenne NM, Deutz NE, Fouque D, Genton L, Gil C, Koletzko B. Towards a multidisciplinary approach to understand and manage obesity and related diseases. Clinical nutrition. 2017;36(4):917-38.

Loeppke R, Taitel M, Haufl e V, Parry T, Kessler RC, Jinnett K. Health and productivity as a business strategy: a multiemployer study. J Occup Environ Med 2009; 51: 411–28.

Wang, Y. C., McPherson, K., Marsh, T., Gortmaker, S. L., & Brown, M. (2011). Health and economic burden of the projected obesity trends in the USA and the UK. The Lancet, 378(9793), 815-825.

Cawley, J., &Meyerhoefer, C. (2012). The medical care costs of obesity:an instrumental variables approach. Journal of health economics, 31(1), 219-230.

Lal, A., Moodie, M., Ashton, T., Siahpush, M., & Swinburn, B. (2012). Health care and lost productivity costs of overweight and obesity in New Zealand. Australian and New Zealand journal of public health, 36(6), 550-556.

Lehnert, T., Sonntag, D., Konnopka, A., Riedel-Heller, S., & König, H. H. (2013). Economic costs of overweight and obesity. Best practice & research clinical endocrinology & metabolism, 27(2), 105-115.

Dee, A., Kearns, K., O¿Neill, C., Sharp, L., Staines, A., O¿Dwyer, V., et al. (2014). The direct and indirect costs of both overweight and obesity:a systematic review. BMC research notes, 7(1), 242.

Frezza, E. E., & Wacthel, M. S. (2014). Organizational Issues, Logistic and Economic Implications of Obesity. En Foletto, M., Rosenthal, R. (Eds.). The Globesity Challenge to General Surgery: A Guide to Strategy and Techniques (pp. 9-16). Milan, Italia: Springer Verlag.

de Oliveira, M. L., Santos, L. M. P., & da Silva, E. N. (2015). Direct healthcare cost of obesity in Brazil: An application of the cost-of-illness method from the perspective of the public health system in 2011. PLOS ONE, 10(4), e0121160.

Cawley, J. (2015). An economy of scales:A selective review of obesity's economic causes, consequences, and solutions. Journal of health economics, 43, 244-268.

Apovian, C. M. (2016). Obesity:definition, comorbidities, causes, and burden. Am J Manag Care, 22(7 Suppl), s176-85.

Bray GA, Kim KK, Wilding JPH, et al. Obesity: a chronic relapsing progressive disease process. A position statement of the world obesity Federation. Obes Rev 2017;18:715–23.

Tsatsoulis A, Paschou SA. Metabolically healthy obesity: criteria, epidemiology, controversies, and consequences. Current obesity reports. 2020;9:109-20.

Swinburn, B. A., Sacks, G., Hall, K. D., McPherson, K., Finegood, D. T., Moodie, M. L., & Gortmaker, S. L. (2011). The global obesity pandemic: shaped by global drivers and local environments. The Lancet, 378(9793), 804-814.

Khan, K. M., Thompson, A. M., Blair, S. N., Sallis, J. F., Powell, K. E., Bull, F. C., & Bauman, A. E. (2012). Sport and exercise as contributors to the health of nations. The Lancet, 380(9836), 59-64.

Popkin, B. M., & Gordon-Larsen, P. (2004). The nutrition transition: worldwide obesity dynamics and their determinants. International journal of obesity, 28, S2-S9.

Hill, J. O., Wyatt, H. R., & Peters, J. C. (2012). Energy balance and obesity. Circulation, 126(1), 126-132.

Obri A, Claret M. The role of epigenetics in hypothalamic energy balance control: implications for obesity. Cell stress. 2019;3(7):208.

Jung UJ, Choi MS. Obesity and its metabolic complications: the role of adipokines and the relationship between obesity, inflammation, insulin resistance, dyslipidemia and nonalcoholic fatty liver disease. International journal of molecular sciences. 2014;15(4):6184-223.

Ghaben AL, Scherer PE. Adipogenesis and metabolic health. Nature reviews Molecular cell biology. 2019 Apr;20(4):242-58.

Reilly SM, Saltiel AR. Adapting to obesity with adipose tissue inflammation. Nature Reviews Endocrinology. 2017;13(11):633-43.

Steinert RE, Feinle-Bisset C, Asarian L, Horowitz M, Beglinger C, Geary N. Ghrelin, CCK, GLP-1, and PYY (3–36): secretory controls and physiological roles in eating and glycemia in health, obesity, and after RYGB. Physiological reviews. 2017;97(1):411-63.

Hanusch-Enserer, U., & Roden, M. (2005). News in gut-brain communication: a role of peptide YY (PYY) in human obesity and following bariatric surgery? European journal of clinical investigation, 35(7), 425-430.

Gibbons, C., Finlayson, G., Caudwell, P., Webb, D. L., Hellström, P. M., Näslund, E., & Blundell, J. E. (2016). Postprandial profiles of CCK after high fat and high carbohydrate meals and the relationship to satiety in humans. Peptides, 77, 3-8.

Guarino D, Nannipieri M, Iervasi G, Taddei S, Bruno RM. The role of the autonomic nervous system in the pathophysiology of obesity. Frontiers in physiology. 2017;8:665.

Müller, T. D., Nogueiras, R., Andermann, M. L., Andrews, Z. B., Anker, S. D., Argente, J., et al. (2015). Ghrelin. Molecular metabolism, 4(6), 437-460.

Raimondo, S., Ronchi, G., Geuna, S., Pascal, D., Reano, S., Filigheddu, N., & Graziani, A. (2012). Ghrelin: a novel neuromuscular recovery promoting factor? International review of neurobiology, 108, 207-221.

English, P. J., Ghatei, M. A., Malik, I. A., Bloom, S. R., & Wilding, J. P. H. (2002). Food fails to suppress ghrelin levels in obese humans. The Journal of clinical endocrinology & metabolism, 87(6), 2984-2984.

Zigman, J. M., Bouret, S. G., & Andrews, Z. B. (2016). Obesity impairs the action of the neuroendocrine ghrelin system. Trends in endocrinology & metabolism, 27(1), 54-63.

Izquierdo AG, Crujeiras AB, Casanueva FF, Carreira MC. Leptin, obesity, and leptin resistance: where are we 25 years later?. Nutrients. 2019;11(11):2704.

Obradovic M, Sudar-Milovanovic E, Soskic S, Essack M, Arya S, Stewart AJ, Gojobori T, Isenovic ER. Leptin and obesity: role and clinical implication. Frontiers in Endocrinology. 2021;12:585887.

Guillemot-Legris O, Muccioli GG. Obesity-induced neuroinflammation: beyond the hypothalamus. Trends in Neurosciences. 2017;40(4):237-53.

Gaesser GA, Angadi SS. Obesity treatment: Weight loss versus increasing fitness and physical activity for reducing health risks. Iscience. 2021;24(10):102995.

Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation*. 2014;129(25 Suppl 2):S102-38.

Bray GA, Heisel WE, Afshin A, Jensen MD, Dietz WH, Long M, Kushner RF, Daniels SR, Wadden TA, Tsai AG, Hu FB. The science of obesity management: an endocrine society scientific statement. Endocrine reviews. 2018;39(2):79-132.

Sinha, A. C., Singh, P. M., & Bhat, S. (2016). Are we operating too late? Mortality Analysis and Stochastic Simulation of Costs Associated with Bariatric Surgery: Reconsidering the BMI Threshold. Obesity surgery, 26(1), 219-228.

Nguyen NT, Varela JE. Bariatric surgery for obesity and metabolic disorders: state of the art. Nature reviews Gastroenterology & hepatology. 2017;14(3):160-9.

Arterburn DE, Telem DA, Kushner RF, Courcoulas AP. Benefits and Risks of Bariatric Surgery in Adults: A Review. *JAMA - Journal of the American Medical Association*. 2020;324(9):879-887. doi:10.1001/jama.2020.12567

Bray GA, Frühbeck G, Ryan DH, Wilding JP. Management of obesity. The Lancet. 2016;387(10031):1947-56.

Willett, W. et al. Food in the Anthropocene: the EAT-Lancet Commission on healthy diets from sustainable food systems. Lancet 393, 447–492 (2019).

Donnelly JE, Blair SN, Jakicic JM, et al. American College of Sports Medicine Position Stand. Appropriate physical activity intervention strategies for weight loss and prevention of weight regain for adults. *Med Sci Sports Exerc*. 2009;41(2):459-71.

Angrisani L, Santonicola A, Iovino P, et al. IFSO Worldwide Survey 2016: primary, endoluminal, and revisional procedures. *Obes Surg*. 2018;28(12):3783–94.

Angrisani L, Santonicola A, Iovino P, Ramos A, Shikora S, Kow L. Bariatric surgery survey 2018: similarities and disparities among the 5 IFSO chapters. *Obes Surg*. 2021;31:1937-48.

Welbourn R, Hollyman M, Kinsman R, et al. Bariatric surgery worldwide: baseline demographic description and one-year outcomes from the fourth IFSO global registry report 2018. Obes surg. 2019;29(3):782-795.

Montesi L, El Ghoch M, Brodosi L, Calugi S, Marchesini G, Dalle Grave R. Long-term weight loss maintenance for obesity: a multidisciplinary approach. Diabetes Metab Syndr Obes. 2016;9:37–46.

Khwaja, H. A., & Bonanomi, G. (2010). Bariatric surgery: techniques, outcomes and complications. Current anaesthesia & critical care, 21(1), 31-38.

Buchwald, H., Ikramuddin, S., Dorman, R. B., Schone, J. L., & Dixon, J. B. (2011). Management of the metabolic/bariatric surgery patient. The American journal of medicine, 124(12), 1099-1105.

Alsumali A, Eguale T, Bairdain S, Samnaliev M. Cost-effectiveness analysis of bariatric surgery for morbid obesity. Obes surg. 2018;28(8):2203-14.

Lester EL, Padwal RS, Birch DW, et al. The real-world cost-effectiveness of bariatric surgery for the treatment of severe obesity: a cost–utility analysis. CMAJ open. 2021;9(2):E673-9. .

Abbatini, F., Rizzello, M., Casella, G., Alessandri, G., Capoccia, D., Leonetti, F., & Basso, N. (2010). Long-term effects of laparoscopic sleeve gastrectomy, gastric bypass, and adjustable gastric banding on type 2 diabetes. Surgical endoscopy, 24(5), 1005-1010.

Schauer, P. R., Kashyap, S. R., Wolski, K., Brethauer, S. A., Kirwan, J. P., Pothier, C. E., et al. (2012). Bariatric surgery versus intensive medical therapy in obese patients with diabetes. New England journal of medicine, 366(17), 1567-1576.

Lee Y, Doumouras AG, Yu J, Brar K, Banfield L, Gmora S, Anvari M, Hong D. Complete resolution of nonalcoholic fatty liver disease after bariatric surgery: a systematic review and meta-analysis. Clinical gastroenterology and Hepatology. 2019;17(6):1040-60.

Aminian A, Al-Kurd A, Wilson R, et al. Association of Bariatric Surgery With Major Adverse Liver and Cardiovascular Outcomes in Patients With Biopsy-Proven Nonalcoholic Steatohepatitis. *JAMA*. 2021;326(20):2031-42.

Kaul A, Sharma J. Impact of bariatric surgery on comorbidities. Surgical Clinics. 2011;91(6):1295-312.

Kissler HJ, Settmacher U. Bariatric surgery to treat obesity. In Seminars in nephrology 2013 Jan 1 (Vol. 33, No. 1, pp. 75-89). WB Saunders.

Benaiges D, Sagué M, Flores-Le Roux JA, Pedro-Botet J, Ramón JM, Villatoro M, Chillarón JJ, Pera M, Más A, Grande L, Goday A. Predictors of hypertension remission and recurrence after bariatric surgery. American Journal of Hypertension. 2016;29(5):653-9.

Puzziferri N, Roshek TB, Mayo HG, Gallagher R, Belle SH, Livingston EH. Long-term follow-up after bariatric surgery: a systematic review. Jama. 2014;312(9):934-42.

Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient 2013 update: cosponsored by American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery. Endocr Pract. 2013;19(2):337-372.

Sjöström L, Peltonen M, Jacobson P, Sjöström CD, Karason K, Wedel H, Ahlin S, Anveden Å, Bengtsson C, Bergmark G, Bouchard C. Bariatric surgery and long-term cardiovascular events. Jama. 2012;307(1):56-65.

Karamanakos SN, Vagenas K, Kalfarentzos F, Alexandrides TK. Weight loss, appetite suppression, and changes in fasting and postprandial ghrelin and peptide-YY levels after Roux-en-Y gastric bypass and sleeve gastrectomy: a prospective, double blind study. Annals of surgery. 2008;247(3):401-7.

Valderas JP, Irribarra V, Boza C, De La Cruz R, Liberona Y, Acosta AM, Yolito M, Maiz A. Medical and surgical treatments for obesity have opposite effects on peptide YY and appetite: a prospective study controlled for weight loss. The Journal of Clinical Endocrinology & Metabolism. 2010;95(3):1069-75.

Meek CL, Lewis HB, Reimann F, Gribble FM, Park AJ. The effect of bariatric surgery on gastrointestinal and pancreatic peptide hormones. Peptides. 2016;77:28-37.

Ruz M, Carrasco F, Rojas P, Codoceo J, Inostroza J, Rebolledo A, Basfi-fer K, Csendes A, Papapietro K, Pizarro F, Olivares M. Iron absorption and iron status are reduced after Roux-en-Y gastric bypass. The American journal of clinical nutrition. 2009;90(3):527-32.

Ruz M, Carrasco F, Rojas P, Codoceo J, Inostroza J, Basfi-fer K, Csendes A, Papapietro K, Pizarro F, Olivares M, Sian L. Zinc absorption and zinc status are reduced after Roux-en-Y gastric bypass: a randomized study using 2 supplements. The American journal of clinical nutrition. 2011;94(4):1004-11.

Gletsu-Miller N, Wright BN. Mineral malnutrition following bariatric surgery. Advances in Nutrition. 2013;4(5):506-17.

Salgado Jr W, Modotti C, Nonino CB, Ceneviva R. Anemia and iron deficiency before and after bariatric surgery. Surgery for Obesity and Related Diseases. 2014;10(1):49-54.

Aarts EO, Janssen IM, Berends FJ. The gastric sleeve: losing weight as fast as micronutrients?. Obesity surgery. 2011;21:207-11.

von Drygalski A, Andris DA, Nuttleman PR, Jackson S, Klein J, Wallace JR. Anemia after bariatric surgery cannot be explained by iron deficiency alone: results of a large cohort study. Surgery for Obesity and Related Diseases. 2011;7(2):151-6.

Sharples AJ, Mahawar K. Systematic review and meta-analysis of randomised controlled trials comparing long-term outcomes of Roux-en-Y gastric bypass and sleeve gastrectomy. Obesity surgery. 2020;30:664-72.

Madsbad S, Dirksen C, Holst JJ. Mechanisms of changes in glucose metabolism and bodyweight after bariatric surgery. The lancet Diabetes & endocrinology. 2014;2(2):152-64.

Laferrère B, Heshka S, Wang K, Khan Y, McGinty J, Teixeira J, Hart AB, Olivan B. Incretin levels and effect are markedly enhanced 1 month after Roux-en-Y gastric bypass surgery in obese patients with type 2 diabetes. Diabetes care. 2007;30(7):1709-16.

Jørgensen NB, Dirksen C, Bojsen-Møller KN, Jacobsen SH, Worm D, Hansen DL, Kristiansen VB, Naver L, Madsbad S, Holst JJ. Exaggerated glucagon-like peptide 1 response is important for improved β-cell function and glucose tolerance after Roux-en-Y gastric bypass in patients with type 2 diabetes. diabetes. 2013;62(9):3044-52.

Shah M, Law JH, Micheletto F, Sathananthan M, Dalla Man C, Cobelli C, Rizza RA, Camilleri M, Zinsmeister AR, Vella A. Contribution of endogenous glucagon-like peptide 1 to glucose metabolism after Roux-en-Y gastric bypass. Diabetes. 2014;63(2):483-93.

Borgeraas H, Hofsø D, Hertel JK, Hjelmesæth J. Comparison of the effect of Roux-en-Y gastric bypass and sleeve gastrectomy on remission of type 2 diabetes: A systematic review and meta-analysis of randomized controlled trials. Obesity Reviews. 2020;21(6):e13011.

Lee DC, Artero EG, Sui X, Blair SN. Mortality trends in the general population: the importance of cardiorespiratory fitness. Journal of psychopharmacology. 2010;24(4_suppl):27-35.

Lee DC, Sui X, Ortega FB, Kim YS, Church TS, Winett RA, Ekelund U, Katzmarzyk PT, Blair SN. Comparisons of leisure-time physical activity and cardiorespiratory fitness as predictors of all-cause mortality in men and women. British journal of sports medicine. 2011;45(6):504-10.

Artero EG, Lee DC, Ruiz JR, Sui X, Ortega FB, Church TS, Lavie CJ, Castillo MJ, Blair SN. A prospective study of muscular strength and all-cause mortality in men with hypertension. Journal of the American College of Cardiology. 2011;57(18):1831-7.

Artero EG, Lee DC, Lavie CJ, España-Romero V, Sui X, Church TS, Blair SN. Effects of muscular strength on cardiovascular risk factors and prognosis. Journal of cardiopulmonary rehabilitation and prevention. 2012;32(6):351.

Lopez-Jaramillo P, Cohen DD, Gómez-Arbeláez D, Bosch J, Dyal L, Yusuf S, Gerstein HC. Association of handgrip strength to cardiovascular mortality in pre-diabetic and diabetic patients: a subanalysis of the ORIGIN trial. International journal of cardiology. 2014;174(2):458-61.

Volaklis KA, Halle M, Meisinger C. Muscular strength as a strong predictor of mortality: a narrative review. European journal of internal medicine. 2015;26(5):303-10.

Laukkanen JA, Zaccardi F, Khan H, Kurl S, Rauramaa R. Long-term Change in Cardiorespiratory Fitness and All-cause Mortality: A Follow-up Study. Circulation. 2015;132(suppl_3):A19920- A19920.

Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public health reports. 1985;100(2):126.

Ross R, Blair SN, Arena R, Church TS, Després JP, Franklin BA, Haskell WL, Kaminsky LA, Levine BD, Lavie CJ, Myers J. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. Circulation. 2016;134(24):e653-99.

Vanhees L, Lefevre J, Philippaerts R, Martens M, Huygens W, Troosters T, Beunen G. How to assess physical activity? How to assess physical fitness?. European Journal of Preventive Cardiology. 2005;12(2):102-14.

Arena R, Cahalin LP. Evaluation of cardiorespiratory fitness and respiratory muscle function in the obese population. Progress in cardiovascular diseases. 2014;56(4):457-64.

Vilaça KH, Carneiro JA, Ferriolli E, da Costa Lima NK, de Paula FJ, Moriguti JC. Body composition, physical performance and muscle quality of active elderly women. Archives of gerontology and geriatrics. 2014;59(1):44-8.

Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. New England journal of medicine. 2002;346(11):793-801.

Kurl S, Laukkanen JA, Rauramaa R, Lakka TA, Sivenius J, Salonen JT. Cardiorespiratory fitness and the risk for stroke in men. Archives of internal medicine. 2003;163(14):1682-8.

Kodama S, Saito K, Tanaka S, Maki M, Yachi Y, Asumi M, Sugawara A, Totsuka K, Shimano H, Ohashi Y, Yamada N. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. Jama. 2009;301(19):2024-35.

Lyerly GW, Sui X, Lavie CJ, Church TS, Hand GA, Blair SN. The association between cardiorespiratory fitness and risk of all-cause mortality among women with impaired fasting glucose or undiagnosed diabetes mellitus. InMayo Clinic Proceedings 2009 (Vol. 84, No. 9, pp. 780-786). Elsevier.

Gander J, Lee DC, Sui X, Hébert JR, Hooker SP, Blair SN. Self-rated health status and cardiorespiratory fitness as predictors of mortality in men. British journal of sports medicine. 2011;45(14):1095-100.

Arena R, Myers J, Guazzi M. The future of aerobic exercise testing in clinical practice: is it the ultimate vital sign?. Future cardiology. 2010;6(3):325-42.

American Thoracic Society. ATS/ACCP statement on cardiopulmonary exercise testing. American journal of respiratory and critical care medicine. 2003;167(2):211-77.

Bentley DJ, Newell J, Bishop D. Incremental exercise test design and analysis: implications for performance diagnostics in endurance athletes. Sports medicine. 2007;37:575-86.

Midgley AW, McNaughton LR, Polman R, Marchant D. Criteria for determination of maximal oxygen uptake: a brief critique and recommendations for future research. Sports medicine. 2007;37:1019-28.

Mezzani A, Agostoni P, Cohen-Solal A, Corra U, Jegier A, Kouidi E, Mazic S, Meurin P, Piepoli M, Simon A, Laethem CV. Standards for the use of cardiopulmonary exercise testing for the functional evaluation of cardiac patients: a report from the Exercise Physiology Section of the European Association for Cardiovascular Prevention and Rehabilitation. European Journal of Preventive Cardiology. 2009;16(3):249-67.

Poole DC, Jones AM. Measurement of the maximum oxygen uptake Vo2max: Vo2peak is no longer acceptable. Journal of applied physiology. 2017;122(4):997-1002.

Noonan V, Dean E. Submaximal exercise testing: clinical application and interpretation. Physical therapy. 2000;80(8):782-807.

Forman DE, Myers J, Lavie CJ, Guazzi M, Celli B, Arena R. Cardiopulmonary exercise testing: relevant but underused. Postgraduate medicine. 2010;122(6):68-86.

Fletcher GF, Ades PA, Kligfield P, Arena R, Balady GJ, Bittner VA, Coke LA, Fleg JL, Forman DE, Gerber TC, Gulati M. Exercise standards for testing and training: a scientific statement from the American Heart Association. Circulation. 2013;128(8):873-934.

Osman AF, Mehra MR, Lavie CJ, Nunez E, Milani RV. The incremental prognostic importance of body fat adjusted peak oxygen consumption in chronic heart failure. Journal of the American College of Cardiology. 2000;36(7):2126-31.

Imboden MT, Kaminsky LA, Peterman JE, Hutzler HL, Whaley MH, Fleenor BS, Harber MP. Cardiorespiratory fitness normalized to fat-free mass and mortality risk. Medicine & Science in Sports & Exercise. 2020;52(7):1532-7.

American College of Sports Medicine. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness in healthy adults. American College of Sports Medicine position stand. Med Sci Sports Exerc. 1998; 30: 975-91.

Santtila M, Keijo H, Laura K, Heikki K. Changes in cardiovascular performance during an 8-week military basic training period combined with added endurance or strength training. Military medicine. 2008;173(12):1173-9.

Bouchard CL, Lesage RE, Lortie GI, Simoneau JA, Hamel PI, Boulay MR, Pérusse LO, Thériault GE, Leblanc CL. Aerobic performance in brothers, dizygotic and monozygotic twins. Medicine and science in sports and exercise. 1986;18(6):639-46.

Li J, Li S, Feuers RJ, Buffington CK, Jr GS. Influence of body fat distribution on oxygen uptake and pulmonary performance in morbidly obese females during exercise. Respirology. 2001;6(1):9-13.

Di Bello V, Santini F, Di Cori A, Pucci A, Palagi C, Delle Donne MG, Giannetti M, Talini E, Nardi C, Pedrizzetti G, Fierabracci P. Relationship between preclinical abnormalities of global and regional left ventricular function and insulin resistance in severe obesity: a Color Doppler Imaging Study. International journal of obesity. 2006;30(6):948-56.

Wong C, Marwick TH. Alterations in myocardial characteristics associated with obesity: detection, mechanisms, and implications. Trends in cardiovascular medicine. 2007;17(1):1-5.

Holloway GP, Bonen A, Spriet LL. Regulation of skeletal muscle mitochondrial fatty acid metabolism in lean and obese individuals. The American journal of clinical nutrition. 2009;89(1):455S-62S.

Duncan GE. The" fit but fat" concept revisited: population-based estimates using NHANES. International Journal of Behavioral Nutrition and Physical Activity. 2010;7:1-5.

Runhaar J, Koes BW, Clockaerts S, Bierma-Zeinstra SM. A systematic review on changed biomechanics of lower extremities in obese individuals: a possible role in development of osteoarthritis. Obesity reviews. 2011;12(12):1071-82.

Willens HJ, Chakko SC, Lowery MH, Byers P, Labrador E, Gallagher A, Castrillon JC, Myerburg RJ. Tissue Doppler imaging of the right and left ventricle in severe obesity (body mass index> 35 kg/m2). The American journal of cardiology. 2004;94(8):1087-90.

Russo C, Jin Z, Homma S, et al. Effect of obesity and overweight on left ventricular diastolic function: a community-based study in an elderly cohort. *J Am Coll Cardiol*. 2011;57(12):1368-74.

Alpert MA, Omran J, Bostick BP. Effects of Obesity on Cardiovascular Hemodynamics, Cardiac Morphology, and Ventricular Function. *Curr Obes Rep*. 2016;5(4):424-34.

Mandviwala T, Khalid U, Deswal A. Obesity and Cardiovascular Disease: a Risk Factor or a Risk Marker?. *Curr Atheroscler Rep*. 2016;18(5):21.

Littleton SW. Impact of obesity on respiratory function. Respirology. 2012;17(1):43-9.

Koenen M, Hill MA, Cohen P, Sowers JR. Obesity, Adipose Tissue and Vascular Dysfunction. *Circ Res*. 2021;128(7):951-68.

Kim JY, Hickner RC, Cortright RL, Dohm GL, Houmard JA. Lipid oxidation is reduced in obese human skeletal muscle. American Journal of Physiology-Endocrinology And Metabolism. 2000;279(5):E1039-44.

Kelley DE, He J, Menshikova EV, Ritov VB. Dysfunction of mitochondria in human skeletal muscle in type 2 diabetes. Diabetes. 2002;51(10):2944-50.

Ritov VB, Menshikova EV, He J, Ferrell RE, Goodpaster BH, Kelley DE. Deficiency of subsarcolemmal mitochondria in obesity and type 2 diabetes. Diabetes. 2005;54(1):8-14.

Lakoski SG, Barlow CE, Farrell SW, Berry JD, Morrow Jr JR, Haskell WL. Impact of body mass index, physical activity, and other clinical factors on cardiorespiratory fitness (from the Cooper Center longitudinal study). The American journal of cardiology. 2011;108(1):34-9.

Dagan SS, Segev S, Novikov I, Dankner R. Waist circumference vs body mass index in association with cardiorespiratory fitness in healthy men and women: a cross sectional analysis of 403 subjects. *Nutr J*. 2013;12:12.

Radovanović S, Kocić S, Gajović G, Radević S, Milosavljević M, Nićiforović J. The impact of body weight on aerobic capacity. *Med Glas (Zenica)*. 2014;11(1):204-9.

Barry VW, Caputo JL, Kang M. The Joint Association of Fitness and Fatness on Cardiovascular Disease Mortality: A Meta-Analysis. *Prog Cardiovasc Dis*. 2018;61(2):136-41.

Barry VW, Baruth M, Beets MW, Durstine JL, Liu J, Blair SN. Fitness vs. fatness on all-cause mortality: a meta-analysis. *Prog Cardiovasc Dis*. 2014;56(4):382-90.

Stegen S, Derave W, Calders P, Van Laethem C, Pattyn P. Physical fitness in morbidly obese patients: effect of gastric bypass surgery and exercise training. *Obes Surg*. 2011;21(1):61-70

Kanoupakis E, Michaloudis D, Fraidakis O, Parthenakis F, Vardas P, Melissas J. Left ventricular function and cardiopulmonary performance following surgical treatment of morbid obesity. *Obes Surg*. 2001;11(5):552-8.

Serés L, Lopez-Ayerbe J, Coll R, et al. Increased exercise capacity after surgically induced weight loss in morbid obesity. *Obesity (Silver Spring)*. 2006;14(2):273-9.

de Souza SA, Faintuch J, Sant'anna AF. Effect of weight loss on aerobic capacity in patients with severe obesity before and after bariatric surgery. *Obes Surg*. 2010;20(7):871-5.

Carbone S, Kirkman DL, Garten RS, et al. Muscular Strength and Cardiovascular Disease: AN UPDATED STATE-OF-THE-ART NARRATIVE REVIEW. *J Cardiopulm Rehabil Prev*. 2020;40(5):302-9.

García-Hermoso A, Cavero-Redondo I, Ramírez-Vélez R, et al. Muscular Strength as a Predictor of All-Cause Mortality in an Apparently Healthy Population: A Systematic Review and Meta-Analysis of Data From Approximately 2 Million Men and Women. *Arch Phys Med Rehabil*. 2018;99(10):2100-2113.e5.

Kim Y, Wijndaele K, Lee DC, Sharp SJ, Wareham N, Brage S. Independent and joint associations of grip strength and adiposity with all-cause and cardiovascular disease mortality in 403,199 adults: the UK Biobank study. *Am J Clin Nutr*. 2017;106(3):773-82.

Saeidifard F, Medina-Inojosa JR, West CP, et al. The association of resistance training with mortality: A systematic review and meta-analysis. *Eur J Prev Cardiol*. 2019;26(15):1647-65.

Ruiz JR, Sui X, Lobelo F, et al. Muscular strength and adiposity as predictors of adulthood cancer mortality in men. *Cancer Epidemiol Biomarkers Prev*. 2009;18(5):1468-76.

FitzGerald SJ, Barlow CE, Kampert JB, Morrow JR, Jackson AW, Blair SN. Muscular fitness and all-cause mortality: prospective observations. Journal of Physical Activity and Health. 2004;1(1):7-18.

Newman AB, Kupelian V, Visser M, et al. Strength, but not muscle mass, is associated with mortality in the health, aging and body composition study cohort. *J Gerontol A Biol Sci Med Sci*. 2006;61(1):72-7.

Ortega FB, Silventoinen K, Tynelius P, Rasmussen F. Muscular strength in male adolescents and premature death: cohort study of one million participants. *BMJ*. 2012;345:e7279.

Jochem C, Leitzmann M, Volaklis K, Aune D, Strasser B. Association between muscular strength and mortality in clinical populations: a systematic review and meta-analysis. Journal of the American Medical Directors Association. 2019;20(10):1213-23.

Kilgour RD, Vigano A, Trutschnigg B, Lucar E, Borod M, Morais JA. Handgrip strength predicts survival and is associated with markers of clinical and functional outcomes in advanced cancer patients. *Support Care Cancer*. 2013;21(12):3261-70.

Bohannon RW. Muscle strength: clinical and prognostic value of hand-grip dynamometry. Curr Opin Clin Nutr Metab Care. 2015;18(5):465-70.

Sasaki H, Kasagi F, Yamada M, Fujita S. Grip strength predicts cause-specific mortality in middle-aged and elderly persons. *Am J Med*. 2007;120(4):337-42.

Ling CH, Taekema D, de Craen AJ, Gussekloo J, Westendorp RG, Maier AB. Handgrip strength and mortality in the oldest old population: the Leiden 85-plus study. *CMAJ*. 2010;182(5):429-35.

Norman K, Stobäus N, Smoliner C, et al. Determinants of hand grip strength, knee extension strength and functional status in cancer patients. *Clin Nutr*. 2010;29(5):586-91.

Marsh AP, Rejeski WJ, Espeland MA, et al. Muscle strength and BMI as predictors of major mobility disability in the Lifestyle Interventions and Independence for Elders pilot (LIFE-P). *J Gerontol A Biol Sci Med Sci*. 2011;66(12):1376-83.

Rijk JM, Roos PR, Deckx L, van den Akker M, Buntinx F. Prognostic value of handgrip strength in people aged 60 years and older: a systematic review and meta-analysis. Geriatrics & gerontology international. 2016;16(1):5-20.

Sale DG. Testing strength and power. In: MacDougal JD, Wenger HA, Green HJ, editors. Physiological testing of the high performance athlete. Champaign (IL): Human Kinetics, 1991: 21-7.

Komi P, editor. Strength and power in sport. John Wiley & Sons; 2008.

Verdijk LB, Van Loon L, Meijer K, Savelberg HH. One-repetition maximum strength test represents a valid means to assess leg strength in vivo in humans. J Sports Sci. 2009;27(1):59-68.

Dvir Z, Müller S. Multiple-joint isokinetic dynamometry: a critical review. J Strength Cond Res. 2020;34(2):587-601.

Sizoo D, de Heide LJ, Emous M, van Zutphen T, Navis G, van Beek AP. Measuring muscle mass and strength in obesity: a review of various methods. Obes Surg. 2021;31 (1):384-93.

McGuigan MR, Newton MJ, Winchester JB, Nelson AG. Relationship between isometric and dynamic strength in recreationally trained men. J Strength Cond Res. 2010;24(9):2570-3.

Tomlinson DJ, Erskine RM, Morse CI, Winwood K, Onambélé-Pearson G. The impact of obesity on skeletal muscle strength and structure through adolescence to old age. *Biogerontology*. 2016;17(3):467-83.

Cooper R, Hardy R, Bann D, et al. Body mass index from age 15 years onwards and muscle mass, strength, and quality in early old age: findings from the MRC National Survey of Health and Development. *J Gerontol A Biol Sci Med Sci*. 2014;69(10):1253-9.

Maffiuletti NA, Jubeau M, Munzinger U, et al. Differences in quadriceps muscle strength and fatigue between lean and obese subjects. *Eur J Appl Physiol*. 2007;101(1):51-9.

Tallis J, James RS, Seebacher F. The effects of obesity on skeletal muscle contractile function. *J Exp Biol*. 2018;221(13):jeb163840.

Valenzuela PL, Maffiuletti NA, Tringali G, De Col A, Sartorio A. Obesity-associated poor muscle quality: prevalence and association with age, sex, and body mass index. *BMC Musculoskelet Disord*. 2020;21(1):200.

Newman AB, Haggerty CL, Goodpaster B, et al. Strength and muscle quality in a well-functioning cohort of older adults: the Health, Aging and Body Composition Study. *J Am Geriatr Soc*. 2003;51(3):323-30.

Koster A, Ding J, Stenholm S, et al. Does the amount of fat mass predict age-related loss of lean mass, muscle strength, and muscle quality in older adults?. *J Gerontol A Biol Sci Med Sci*. 2011;66(8):888-95.

Jackson AW, Lee DC, Sui X, et al. Muscular strength is inversely related to prevalence and incidence of obesity in adult men. *Obesity (Silver Spring)*. 2010;18(10):1988-1995.

Stenholm S, Mehta NK, Elo IT, Heliövaara M, Koskinen S, Aromaa A. Obesity and muscle strength as long-term determinants of all-cause mortality—a 33-year follow-up of the Mini-Finland Health Examination Survey. Int J Obes. 2014;38(8):1126-32.

Pellegrinelli V, Rouault C, Rodriguez-Cuenca S, et al. Human adipocytes induce inflammation and atrophy in muscle cells during obesity. *Diabetes*. 2015;64(9):3121-34.

Carrasco F, Ruz M, Rojas P, et al. Changes in bone mineral density, body composition and adiponectin levels in morbidly obese patients after bariatric surgery. *Obes Surg*. 2009;19(1):41-6.

Zalesin KC, Franklin BA, Lillystone MA, et al. Differential loss of fat and lean mass in the morbidly obese after bariatric surgery. *Metab Syndr Relat Disord*. 2010;8(1):15-20. doi:10.1089/met.2009.0012

de Freitas Junior WR, Ilias EJ, Kassab P, et al. Assessment of the body composition and the loss of fat-free mass through bioelectric impedance analysis in patients who underwent open gastric bypass. *ScientificWorldJournal*. 2014;2014:843253.

Gil S, Kirwan JP, Murai IH, et al. A randomized clinical trial on the effects of exercise on muscle remodelling following bariatric surgery. *J Cachexia Sarcopenia Muscle*. 2021;12(6):1440-55.

Campanha-Versiani L, Pereira DA, Ribeiro-Samora GA, et al. The effect of a muscle weight-bearing and aerobic exercise program on the body composition, muscular strength, biochemical markers, and bone mass of obese patients who have undergone gastric bypass surgery. *Obes Surg*. 2017;27:2129-37.

Otto M, Kautt S, Kremer M, Kienle P, Post S, Hasenberg T. Handgrip strength as a predictor

for post bariatric body composition. *Obes Surg*. 2014;24:2082-8.

Kannel WB, Kannel C, Paffenbarger RS Jr, Cupples LA. Heart rate and cardiovascular mortality: the Framingham Study. *Am Heart J*. 1987;113(6):1489-1494.

Tsuji H, Venditti FJ Jr, Manders ES, et al. Reduced heart rate variability and mortality risk in an elderly cohort. The Framingham Heart Study. *Circulation*. 1994;90(2):878-883.

Dekker JM, Schouten EG, Klootwijk P, Pool J, Swenne CA, Kromhout D. Heart rate variability from short electrocardiographic recordings predicts mortality from all causes in middle-aged and elderly men. The Zutphen Study. *Am J Epidemiol*. 1997;145(10):899-908.

La Rovere MT, Bigger JT Jr, Marcus FI, Mortara A, Schwartz PJ. Baroreflex sensitivity and heart-rate variability in prediction of total cardiac mortality after myocardial infarction. ATRAMI (Autonomic Tone and Reflexes After Myocardial Infarction) Investigators. *Lancet*. 1998;351(9101):478-84.

Bilchick KC, Fetics B, Djoukeng R, et al. Prognostic value of heart rate variability in chronic congestive heart failure (Veterans Affairs' Survival Trial of Antiarrhythmic Therapy in Congestive Heart Failure). *Am J Cardiol*. 2002;90(1):24-28.

Mäkikallio TH, Huikuri HV, Hintze U, et al. Fractal analysis and time- and frequency-domain measures of heart rate variability as predictors of mortality in patients with heart failure. *Am J Cardiol*. 2001;87(2):178-82.

Mäkikallio TH, Huikuri HV, Mäkikallio A, et al. Prediction of sudden cardiac death by fractal analysis of heart rate variability in elderly subjects. *J Am Coll Cardiol*. 2001;37(5):1395-1402.

Tapanainen JM, Thomsen PE, Køber L, et al. Fractal analysis of heart rate variability and mortality after an acute myocardial infarction. *Am J Cardiol*. 2002;90(4):347-352.

Dewey FE, Freeman JV, Engel G, et al. Novel predictor of prognosis from exercise stress testing: heart rate variability response to the exercise treadmill test. *Am Heart J*. 2007;153(2):281-8.

Oikawa K, Ishihara R, Maeda T, et al. Prognostic value of heart rate variability in patients with renal failure on hemodialysis. *Int J Cardiol*. 2009;131(3):370-7.

May O, Arildsen H. Long-term predictive power of heart rate variability on all-cause mortality in the diabetic population. *Acta Diabetol*. 2011;48(1):55-9.

Sessa F, Anna V, Messina G, Cibelli G, Monda V, Marsala G, Ruberto M, Biondi A, Cascio O, Bertozzi G, Pisanelli D. Heart rate variability as predictive factor for sudden cardiac death. Aging (Albany NY). 2018;10(2):166.

Aubert AE, Seps B, Beckers F. Heart rate variability in athletes. *Sports Med*. 2003;33(12):889-919.

Rajendra Acharya U, Paul Joseph K, Kannathal N, Lim CM, Suri JS. Heart rate variability: a review. *Med Biol Eng Comput*. 2006;44(12):1031-51.

Heart rate variability. Standards of measurement, physiological interpretation, and clinical use. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. *Eur Heart J*. 1996;17(3):354-81.

Gamelin FX, Berthoin S, Bosquet L. Validity of the polar S810 heart rate monitor to measure R-R intervals at rest. *Med Sci Sports Exerc*. 2006;38(5):887-93.

Nunan D, Donovan G, Jakovljevic DG, Hodges LD, Sandercock GR, Brodie DA. Validity and reliability of short-term heart-rate variability from the Polar S810. *Med Sci Sports Exerc*. 2009;41(1):243-50.

Dobbs WC, Fedewa MV, MacDonald HV, Holmes CJ, Cicone ZS, Plews DJ, Esco MR. The accuracy of acquiring heart rate variability from portable devices: a systematic review and meta-analysis. Sports Medicine. 2019;49:417-35.

Gavrilova EA. Heart rate variability and sports. Human physiology. 2016;42(5):571-8.

Dong JG. The role of heart rate variability in sports physiology. Experimental and therapeutic medicine. 2016;11(5):1531-6.

Coutts L V., Plans D, Brown AW, Collomosse J. Deep learning with wearable based heart rate variability for prediction of mental and general health. *J Biomed Inform*. 2020;112.

Kamath MV, Watanabe M, Upton A, editors. Heart rate variability (HRV) signal analysis: clinical applications. Taylor & Francis; 2012. Accessed May 13, 2023. https://books.google.es/books?hl=es&lr=&id=72HSBQAAQBAJ&oi=fnd&pg=PP1&ots=2Gux_1Lzch&sig=imHVVl6rC6Kvzst-LvtibcdGniE#v=onepage&q&f=false

Heathers JA. Everything Hertz: methodological issues in short-term frequency-domain HRV. *Front Physiol*. 2014;5:177.

Xhyheri B, Manfrini O, Mazzolini M, Pizzi C, Bugiardini R. Heart rate variability today. *Prog Cardiovasc Dis*. 2012;55(3):321-31.

Lake DE, Richman JS, Griffin MP, et al. Sample entropy analysis of neonatal heart rate variability. 2020;22908:789-97.

Kleiger RE, Stein PK, Bigger JT Jr. Heart rate variability: measurement and clinical utility. *Ann Noninvasive Electrocardiol*. 2005;10(1):88-101.

Karason K, Mølgaard H, Wikstrand J, Sjöström L. Heart rate variability in obesity and the effect of weight loss. *Am J Cardiol*. 1999;83(8):1242-7.

Emdin M, Gastaldelli A, Muscelli E, et al. Hyperinsulinemia and autonomic nervous system dysfunction in obesity: effects of weight loss. *Circulation*. 2001;103(4):513-9.

Sztajzel J, Golay A, Makoundou V, et al. Impact of body fat mass extent on cardiac autonomic alterations in women. *Eur J Clin Invest*. 2009;39(8):649-56.

Thorp AA, Schlaich MP. Relevance of sympathetic nervous system activation in obesity and metabolic syndrome. Journal of diabetes research. 2015;2015.

Thayer JF, Yamamoto SS, Brosschot JF. The relationship of autonomic imbalance, heart rate variability and cardiovascular disease risk factors. International journal of cardiology. 2010;141(2):122-31.

Costa J, Moreira A, Moreira P, Delgado L, Silva D. Effects of weight changes in the autonomic nervous system: A systematic review and meta-analysis. Clinical nutrition. 2019;38(1):110-26.

Pal GK, Chandrasekaran A, Hariharan AP, et al. Body mass index contributes to sympathovagal imbalance in prehypertensives. *BMC Cardiovasc Disord*. 2012;12:54.

Krishna P, Rao D, Navekar VV. Cardiac autonomic activity in overweight and underweight young adults. *Indian J Physiol Pharmacol*. 2013;57(2):146-152.

McCully BH, Hasan W, Streiff CT, et al. Sympathetic cardiac hyperinnervation and atrial autonomic imbalance in diet-induced obesity promote cardiac arrhythmias. *Am J Physiol Heart Circ Physiol*. 2013;305(10):H1530-H1537.

Smith MM, Minson CT. Obesity and adipokines: effects on sympathetic overactivity. The Journal of physiology. 2012;590(8):1787-801.

Russo B, Menduni M, Borboni P, Picconi F, Frontoni S. Autonomic nervous system in obesity and insulin-resistance—The complex interplay between leptin and central nervous system. International Journal of Molecular Sciences. 2021;22(10):5187.

Kalil GZ, Haynes WG. Sympathetic nervous system in obesity-related hypertension: mechanisms and clinical implications. Hypertension Research. 2012;35(1):4-16.

Singh N, Moneghetti KJ, Christle JW, Hadley D, Plews D, Froelicher V. Heart Rate Variability: An Old Metric with New Meaning in the Era of using mHealth Technologies for Health and Exercise Training Guidance. Part One: Physiology and Methods. *Arrhythm Electrophysiol Rev*. 2018;7(3):193-8.

Joyner MJ, Green DJ. Exercise protects the cardiovascular system: effects beyond traditional risk factors. *J Physiol*. 2009;587(23):5551-8.

Gerosa-Neto J, Antunes BMM, Campos EZ, et al. Impact of long-term high-intensity interval and moderate-intensity continuous training on subclinical inflammation in overweight/obese adults. *J Exerc Rehabil*. 2016;12(6):575-80.

Toohey K, Pumpa K, Mckune A, et al. The impact of high-intensity interval training exercise on breast cancer survivors: a pilot study to explore fitness, cardiac regulation and biomarkers of the stress systems. *BMC Cancer*. 2020;20(787):1-11.

Boutcher SH, Park Y, Dunn SL, Boutcher YN. The relationship between cardiac autonomic function and maximal oxygen uptake response to high-intensity intermittent-exercise training. *J Sports Sci*. 2013;31(9):1024-9.

Kaikkonen KM, Korpelainen RI, Tulppo MP, et al. Physical activity and aerobic fitness are positively associated with heart rate variability in obese adults. *J Phys Act Health*. 2014;11(8):1614-21.

Chen LY, Zmora R, Duval S, Chow LS, Lloyd-Jones DM, Schreiner PJ. Cardiorespiratory Fitness, Adiposity, and Heart Rate Variability: The Coronary Artery Risk Development in Young Adults Study. *Med Sci Sports Exerc*. 2019;51(3):509-14.

Souza HC, Philbois SV, Veiga AC, Aguilar BA. Heart rate variability and cardiovascular fitness: what we know so far. Vascular Health and Risk Management. 2021:701-11.

Nault I, Nadreau E, Paquet C, et al. Impact of bariatric surgery--induced weight loss on heart rate variability. *Metabolism*. 2007;56(10):1425-30.

Bobbioni-Harsch E, Sztajzel J, Barthassat V, et al. Independent evolution of heart autonomic function and insulin sensitivity during weight loss. *Obesity (Silver Spring)*. 2009;17(2):247-53.

Machado MB, Velasco IT, Scalabrini-Neto A. Gastric bypass and cardiac autonomic activity: influence of gender and age. *Obes Surg*. 2009;19(3):332-8.

Lips MA, de Groot GH, De Kam M, et al. Autonomic nervous system activity in diabetic and healthy obese female subjects and the effect of distinct weight loss strategies. *Eur J Endocrinol*. 2013;169(4):383-90.

Pontiroli AE, Merlotti C, Veronelli A, Lombardi F. Effect of weight loss on sympatho-vagal balance in subjects with grade-3 obesity: restrictive surgery versus hypocaloric diet. *Acta Diabetol*. 2013;50(6):843-50.

Alam I, Lewis MJ, Lewis KE, Stephens JW, Baxter JN. Influence of bariatric surgery on indices of cardiac autonomic control. *Auton Neurosci*. 2009;151(2):168-73.

Kokkinos A, Alexiadou K, Liaskos C, Argyrakopoulou G, Balla I, Tentolouris N et al. Improvement in cardiovascular indices after roux-en-y gastric bypass or sleeve gastrectomy for morbid obesity. Obes Surg. 2013;23(1):31-8.

Maser RE, Lenhard MJ, Peters MB, Irgau I, Wynn GM. Effects of surgically induced weight loss by Roux-en-Y gastric bypass on cardiovascular autonomic nerve function. *Surg Obes Relat Dis*. 2013;9(2):221-6.

Perugini RA, Li Y, Rosenthal L, Gallagher-Dorval K, Kelly JJ, Czerniach DR. Reduced heart rate variability correlates with insulin resistance but not with measures of obesity in population undergoing laparoscopic Roux-en-Y gastric bypass. *Surg Obes Relat Dis*. 2010;6(3):237-41.

Benjamim CJ, Pontes YM, de Sousa Junior FW, Porto AA, Júnior CR, da Silva AA, Cavalcante TC, Garner DM, Valenti VE. Does bariatric surgery improve cardiac autonomic modulation assessed by heart rate variability? A systematic review. Surgery for Obesity and Related Diseases. 2021;17(8):1497-509.

Ibacache P, Cárcamo P, Miranda C, Bottinelli A, Guzmán J, Martínez-Rosales E, Artero EG, Cano-Cappellacci M. Improvements in heart rate variability in women with obesity: short-term effects of sleeve gastrectomy. Obesity Surgery. 2020 (10):4038-45.

Objetivos

OBJETIVOS

Objetivo general

Determinar los cambios en la condición física asociada a la salud y la variabilidad del ritmo cardiaco posteriores a una cirugía bariátrica y su relación con la pérdida de peso corporal.

Objetivos específicos

Sección 1. Impacto de la cirugía bariátrica en la condición física asociada a la salud

Objetivo específico 1. Describir los cambios en la fuerza muscular y la capacidad cardiorrespiratoria posteriores a la gastrectomía vertical.

Objetivo específico 2. Describir la relación entre la pérdida de peso corporal, posterior a la gastrectomía vertical, y los cambios en la capacidad cardiorrespiratoria.

Objetivo específico 3. Reunir y analizar la evidencia sobre cambios en el nivel de capacidad cardiorrespiratoria en personas con obesidad tras someterse a una cirugía bariátrica y su relación con la pérdida de peso corporal.

Objetivo específico 4. Reunir y analizar la evidencia sobre cambios en la fuerza y calidad muscular en personas con obesidad tras someterse a una cirugía bariátrica y su relación con la pérdida de peso corporal.

Sección 2. Impacto de la cirugía bariátrica en la variabilidad del ritmo cardiaco

Objetivo específico 5. Describir los cambios en la variabilidad del ritmo cardiaco posteriores a la gastrectomía vertical.

Objetivo específico 6. Describir la relación entre la pérdida de peso corporal, posterior a la gastrectomía vertical, y los cambios en la variabilidad del ritmo cardiaco.

Metodología

Tabla 1. Resumen de metodología utilizada en los estudios incorporados en la presente tesis doctoral

Estudio	Diseño	Participantes	Variables estudiadas	Evaluaciones realizadas	Tiempo de seguimiento postquirúrgico
Physical fitness and physical activity in women with obesity: short term effects of sleeve gastrectomy	Estudio observacional de cohorte	N: 23 (mujeres); edad: 36.1 ± 11.1 años; IMC: 35.1 ± 3.4 kg/m^2	Fuerza de prensión manual y de extensores de rodilla; capacidad cardiorrespiratoria (VO$_{2peak}$); actividad física; variables antropométricas	Dinamometría; ergoespirometría en cicloergómetro; acelerometría triaxial;	3 meses (evaluaciones 1 y 3 meses)
Effects of bariatric surgery on cardiorespiratory fitness: a systematic review and meta-analysis	Revisión sistemática y metaanálisis	17 estudios en revisión sistemática (3624 participantes: 81% mujeres, 36,1-48,2 años, IMC de 35,1-49,4 kg/m^2); 11 estudios en metaanálisis (312 participantes)	Capacidad cardiorrespiratoria (VO$_{2max/peak}$ absoluto y relativo al peso corporal/masa libre de grasa), frecuencia cardiaca máxima, ventilación minuto máxima, pulso máximo de oxígeno, tiempo hasta el agotamiento	Ergoespirometría (treadmill y cicloergómetro)/ test indirectos (en metaanálisis sólo ergoespirometría)	1-28 meses (11 estudios realizaron sus evaluaciones dentro de los primeros 12 meses).
Effects of bariatric surgery on muscle strength and quality: a systematic review and meta-analysis	Revisión sistemática y metaanálisis	28 estudios en revisión sistemática (697 participantes: 78% mujeres, 33-49 años, IMC de 35,1-53,0 kg/m^2);	Fuerza muscular absoluta y relativa al peso corporal/masa magra; composición muscular	Dinamometría isométrica/ isocinética/ 1RM; tomografía computarizada/biopsia muscular/ultrasonido	1 mes-9 años (26 estudios realizaron sus evaluaciones dentro de los primeros 12 meses)

		16 en metaanálisis (421 participantes).			
Improvements in heart rate variability in women with obesity: short-term effects of sleeve gastrectomy	Estudio observacional de cohorte	N: 23 (mujeres); edad: 36.1 ± 11.1 años; IMC: 35.1 ± 3.4 kg/m^2	Variabilidad del ritmo cardiaco (análisis temporal, espectral y no lineal); variables antropométricas	Monitor telemétrico de la frecuencia cardiaca (registro corto)	3 meses (evaluaciones 1 y 3 meses)

Resultados y discusión

Impacto de la cirugía bariátrica en la condición física asociada a la salud

Estudios 1-3

SECCIÓN 1

Sección 1

Estudio 1

Physical fitness and physical activity in women with obesity: short term effects of sleeve gastrectomy

Nutrición Hospitalaria (2019)

http://dx.doi.org/10.20960/nh.02515

Paulina Ibacache, Marcelo Cano-Cappellacci, Claudia Miranda, Juan Rojas, Pablo Maldonado, Andrés Bottinelli

ABSTRACT

Introduction: the increase on prevalence of obesity has been linked to a higher number of bariatric surgeries, being sleeve gastrectomy (SG) the most frequent bariatric procedures in the world. However, there are few studies that determine the impact of SG on health’s determinants such as physical fitness (PF) and physical activity (PA).

Objectives: to describe the changes in PF and PA of patients after SG.

Methods: twenty-three women with obesity (mean 36.1 ± 11.1 years old and body mass index [BMI] of 35.1 ± 3.4 kg/m^2) were evaluated preoperatively to SG and at one and three months after surgery. An assessment of PF was conducted, including handgrip (HGS) and quadriceps muscle strength (QMS) with dynamometers and cardiorespiratory fitness (CRF) with an ergospirometer. PA was assessed with a three-axis accelerometer.

Results: the absolute VO_2 peak decreased after the first and third month ($p< 0.001$) post SG. The VO_2 peak relative to body weight showed an increase from baseline after the SG ($p = 0.002$). After SG, there was a reduction in absolute values for HGS and QMS ($p < 0.001$) and an increase in relative HGS after three months post-surgery compared to preoperative ($p = 0.011$), without changes in relative QMS ($p = 0.596$). No changes in PA were observed.

Conclusions: after SG, there is a short term decline on PF when it is expressed on absolute values. However, when it is expressed in relative terms to body weight, some components of PF improve, while others showed no change. There was no modification in PA levels of the participants.

Key words: Obesity. Bariatric surgery. Cardiorespiratory fitness. Muscle strength. Physical activity.

INTRODUCTION

Physical inactivity and high-calorie foods have increased the prevalence of obesity worldwide above 13% (15% in women) (1). Obesity is a greater risk factor for cardiovascular disease for women than men (2) and it has been associated with multiple comorbidities (3) and adverse effects on physical fitness (4). Frequently, therapeutic strategies are insufficient, since they fail to prevent weight regain (5). Thus, surgical treatments are often adopted for morbid obesity or obesity in the presence of comorbidities (6).

The increase in obesity cases (7) has led to a parallel increase in the number of bariatric surgeries, particularly laparoscopic sleeve gastrectomy (SG), which is currently the most frequent bariatric surgical procedure in the world (8). Although the surgical treatment of obesity has been demonstrated as an effective intervention for weight loss, as well as for remission or improvement of obesity-associated comorbidities (6,9), the impact on some components of physical fitness (PF), such as cardiorespiratory fitness (CRF) and muscle strength (MS), is unclear. These physical factors are important for their predictive health value (10,11). Moreover, so far there is few information about the impact of SG in objectively assessed physical activity (PA) (12).

Cardiorespiratory fitness and muscle strength are strong determinants of morbidity and mortality (10,11,13) and the inclusion of serial CRF testing should be considered in the obese population when an intervention is applied (4). However, there is contradictory information regarding the impact of bariatric surgery on CRF (14-16) and MS (14,17,18). The vicious cycle between physical inactivity, obesity and poor physical fitness is well known (19). People with obesity perform less PA compared to eutrophic people (20), but there is contradictory information about changes in physical activity after bariatric surgery (12,18,21,22). Research into physical activity patterns of bariatric patients has primarily relied on self-report questionnaires (18,22), with only one study (n = 4) assessing the impact of sleeve gastrectomy on objectively assessed PA of subjects undergoing this surgery (12).

Considering that physical inactivity is associated with noncommunicable diseases (23) and has been considered by the

World Health Organization (WHO) as the fourth risk factor for global mortality, and that cardiorespiratory fitness and muscle strength are indicators of health and life expectancy (10,11,13), the purpose of this study is to describe the changes in physical fitness and physical activity in patients with obesity after undergoing sleeve gastrectomy.

MATERIALS AND METHODS

Subjects

In this observational study, 23 females with obesity who underwent SG were included. Two patients did not receive the second evaluation (one month after surgery). Exclusion criteria were severe cardiovascular diseases, chronic renal insufficiency and exercise-limiting comorbidities such as musculoskeletal impairments. In addition, patients with smoking habits, postmenopausal women and patients with previous bariatric surgery were excluded. Inclusion criteria for adult women patients were a BMI equal to or greater than 30 kg/m^2 who were scheduled for sleeve gastrectomy.

Participants were recruited during the years 2015 and 2016, from different clinics in the region of Valparaiso, Chile. Subjects were required at least three hours of fasting, using comfortable clothes and to refrain from drinking coffee and alcoholic beverages and performing intense physical exercise at least 24 hours before each evaluation. Time was given for the familiarization of the participants with the laboratory and each one of the tests. The evaluations were performed in the morning, to avoid variations in circadian rhythm at the Laboratory of Exercise Physiology of Universidad Andres Bello, Vina del Mar, Chile.

Prior to surgery, and at one month and three months thereafter, an assessment of anthropometrics measures, physical fitness and physical activity was conducted.

All procedures performed in studies involving human participants were in accordance with the standards of the Ethic Committee for Research in Human Beings of the Faculty of Medicine of Universidad de Chile (registered number 149-2014) and with the Declaration of Helsinki of 1964 and its later amendments or comparable ethical standards. Informed consent was approved by the corresponding ethic committee and was obtained from all individual participants included in the study.

Anthropometrics

Anthropometrics were taken using standardized protocols (24). Body mass index (BMI) and waist circumference (at iliac crests level) were determined using a Detecto 439 balance scale and a Rosscraft anthropometric tape, respectively. Weight loss was expressed as percentage excess weight loss (%EWL) (25).

Muscle strength assessment

Static MS was evaluated by measuring the handgrip strength (HGS) with a Dynatron handgrip dynamometer (Dynatronics Corporation, Salt Lake City, USA). Patients stood in the anatomical position, with the elbow extended. The participants were verbally told to produce their maximal force and strongly encouraged to maintain it for five seconds.

Isometric quadriceps MS was assessed with the subjects seated with the hip angle fixed at 100° and knee angle set at 90° of flexion. A padded cuff was secured above the ankle malleolus and attached to the load cell artOficio FMON-1 (artOficio, Santiago, Chile). The subjects were fixed to chair and told verbally to produce their maximal force for five seconds.

For HGS and quadriceps MS, three trials were done (left and right side were alternated) with a pause of about two minutes between trials. The best score was registered and the average strength between both sides was calculated.

Cardiorespiratory fitness assessment

Patients performed a submaximal cardiopulmonary bicycle test on a cycloergometer Monark 915 E (Monark Exercise AB, Vansbro, Sweden). A gradual protocol was used, starting at 0.5 Watts/kg of body weight with gradual increase of 20 W/2 minutes, with the subjects cycling at 60 rpm, until the stopping criteria (respiratory quotient ≥ 1.1 or modified Borg scale of perceived exertion > 7/10 points). After the patients reached their VO_2 peak, determined as the highest attained VO_2 over 30 seconds during the test, as previously recommended (4), subjects cycled during three minutes for active recovery with no load.

During the test, gas exchange was measured using an ergospirometry system Cortex MetalyzerR 3B (Cortex Biophysik, Leipzig, Germany) and heart rate was monitored with a Polar H7 telemetry heart rate monitor (Polar Electro Oy, Kempele, Finland).

Physical activity assessment

Physical activity was measured using the Actigraph wGT3X monitor (ActiGraph, Pensacola, USA) and magnitude vector activity counts were analyzed. The interval of recorded time (epoch) was set at 60 seconds, shown as valid for measuring PA in adults (26). Participants were asked to wear the monitor on the dominant side, at waist level, during all waking hours for seven consecutive days and to remove it only for water activities. All women with ≥ 10 h/day of monitor wear time for ≥ 3 days at both the pre- and post-surgery assessments were included in the analysis. Non-wear time was defined as 60 minutes or more of consecutive zero counts (26).

Data were analyzed with Actilife 6 software (ActiGraph, Pensacola, USA), and the results were expressed as a percentage of light, moderate and vigorous PA using the cutoff points of Freedson for adults (27).

Statistical analysis

For data distribution, the Shapiro-Wilk normality test was used. Data for all variables were normally distributed, except for PA parameters. The changes in CRF and MS were evaluated using a repeated-measures ANOVA with the Bonferroni post-hoc analysis. To compare PA non-parametric tests were applied due to their non-normal distribution. Wilcoxon tests were used in cases where Friedman tests found differences in PA between values from the three evaluations. The statistical analysis was performed using SPSS 21.0 software (SPSS Inc, Chicago, IL, USA). A p-value of < 0.05 was considered as statistically significant.

RESULTS

Twenty-three female patients were included in this study. Two patients had a diagnosis of controlled arterial hypertension, seven had controlled hypothyroidism and 14 had hepatic steatosis. All patients underwent laparoscopic SG. The mean age of these patients was 36.1 ± 11.1 years at admission.

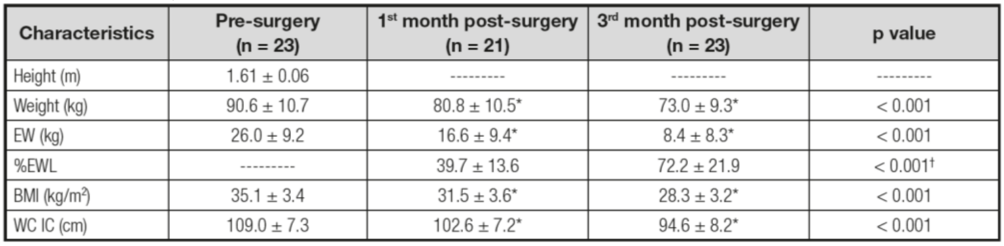
Anthropometric characteristics

After SG, body weight, excess weight, BMI and waist circumference decreased significantly ($p < 0.001$) (Table I).

Muscle strength

Patients had a decrease in absolute quadriceps strength one month ($p = 0.045$) and three months ($p = 0.001$) after surgery. Patients lost 19% of their quadriceps strength after three months. However, quadriceps strength relative to body weight did not change ($p = 0.596$) (Fig. 1).

Table I. Anthropometric characteristics in the three moments of assessment



Characteristics	Pre-surgery (n = 23)	1st month post-surgery (n = 21)	3rd month post-surgery (n = 23)	p value
Height (m)	1.61 ± 0.06	---------	---------	---------
Weight (kg)	90.6 ± 10.7	80.8 ± 10.5*	73.0 ± 9.3*	< 0.001
EW (kg)	26.0 ± 9.2	16.6 ± 9.4*	8.4 ± 8.3*	< 0.001
%EWL	---------	39.7 ± 13.6	72.2 ± 21.9	< 0.001†
BMI (kg/m^2)	35.1 ± 3.4	31.5 ± 3.6*	28.3 ± 3.2*	< 0.001
WC IC (cm)	109.0 ± 7.3	102.6 ± 7.2*	94.6 ± 8.2*	< 0.001

OB: obesity; EW: excess weight; %EWL: percentage excess weight loss; WC IC: waist circumference at the level of iliac crests. Data are presented as means ± SD.
*ANOVA p value. *p < 0.001 compared with the preoperative values. †t-test p value*

.

Absolute handgrip strength decreased after both one and three months post SG ($p < 0.001$). There was also a reduction in absolute handgrip strength after three months post-surgery compared to the first postoperative month ($p = 0.003$) (Fig. 1). When expressing handgrip strength in proportion to body weight, there was an increase in handgrip strength after three months postsurgery compared to preoperative ($p = 0.011$) (Table II).

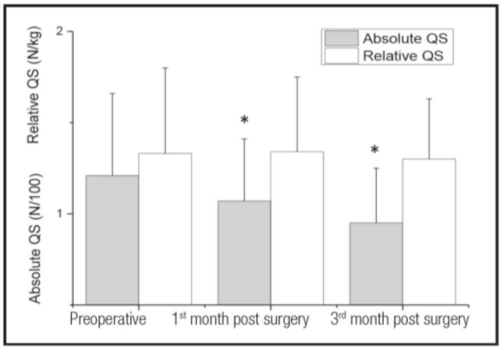


Figure 1. Comparison of quadriceps strength (QS) between the three moments of assessment.
*$p < 0.05$ compared with the preoperative values.

Cardiorespiratory fitness

The absolute VO_2 peak significantly decreased by the first and third month ($p < 0.001$) post-surgery with respect to the preoperative assessment, without changes between the two postoperative assessments. The VO_2 peak relative to body weight showed an increase from baseline at third months ($p = 0.005$) after SG (Table II).

Physical activity

The average number of valid days of PA assessed was six. No significant differences were observed between the three assessment periods for the percentages of light ($p = 0.056$), moderate ($p = 0.151$), and moderate-vigorous ($p = 0.056$) PA. Percent vigorous physical activity decreased only at the first postoperative month compared with baseline ($p = 0.022$) (Table III).

DISCUSSION

The present study indicates that sleeve gastrectomy results in a considerable decrease in absolute MS in the short term after surgery. This data concurs with another study which found absolute MS decreased four months after gastric bypass surgery (14). It is important to consider that these results were obtained in the periods of greater post-surgical caloric restriction, which may influence the loss of MS (28). However, a reduction of absolute MS in both upper and lower limbs one year after biliopancreatic diversion (17) and gastric bypass was also reported (29). These results are likely a consequence of the decrease in muscle mass that has been previously described (30). A decrease in ghrelin, hormone that has a protective effect against loss of muscle mass after bariatric surgery, could have a role in those changes (31). On the other hand, Otto et al. (32) showed no changes on absolute HGS at six, 12 and 18 weeks after a SG or gastric bypass, and Neunhaeuserer et al. (18) showed no changes in absolute HGS and in quadriceps MS in patients six months after SG.

As a palliative approach, exercise training after bariatric surgery could preserve absolute muscle strength and even increase it (14,33).

In the present study, when expressing HGS according to body weight, an increase in HGS three months post-surgery was observed when compared to preoperative HGS. These observations concur with previous studies evaluating one year after bariatric intervention (17,29). The most plausible explanation is the effect of the magnitude of the reduction in post-surgical body weight patients, thus, overestimating muscle strength by expressing it relative to body weight.

Regarding the evaluation of CRF, our research group suggest the use of cycloergometer instead of treadmill or walking test (i.e., six minutes walking test or shuttle walking test) in the evaluation of obese patients, where the impact of body weight is less relevant.

The VO2 peak results in this study from the preoperative assessment are similar to those reported by Wilms et al. (34) and are associated with a high risk of mortality from any cause (35).

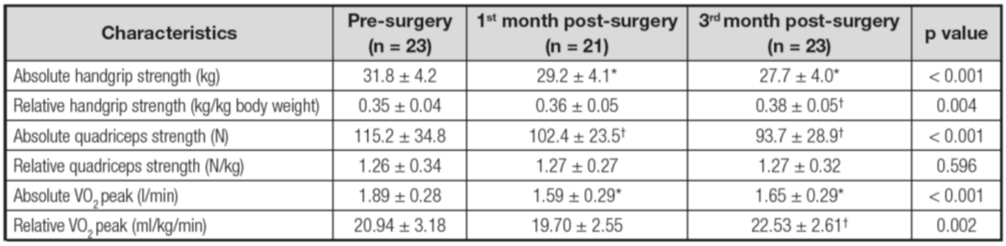
Some studies report maintained (14,15) or decreased (18) CRF when expressed in absolute values after bariatric surgery. These results could be explained by considering the significant loss of post-surgical muscle mass (30). Additionally, the reduction of ghrelin (31) could be a factor that would negatively influence myocardial contractility and cardiac output (36).

The results of this study showed an improvement in CRF relative to body weight after surgery, which agrees with those reported from other studies (14,15,18) and differ regarding the lack of changes in CRF related to body weight reported by De Souza et al. (16). The studies that presented VO2 peak related to lean mass did not find changes after surgery (14,15).

On the other hand, bariatric patients should begin the exercise intervention before surgery (37) and continue it as soon as possible after the procedure (33). In addition, it is interesting to note that low values in preoperative VO_2 peak have been associated with an increase in short-term complications after bariatric surgery. So it has been suggested that CRF should be improved prior to intervention to potentially reduce postoperative complications (38).

Additionally, the results of this study show that SG does not affect patients' lifestyles, regarding their PA habits. The same has been described by studies of gastric bypass patients who did not change their level of PA, objectively measured, at six (21) and nine months postoperatively (39). However, when PA was subjectively assessed through questionnaires, an improvement in PA behavior was reported (18,21,22).

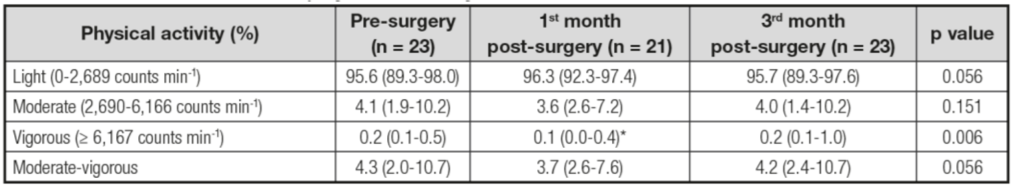
Table II. Physical fitness in the three moments of assessment



Characteristics	Pre-surgery (n = 23)	1st month post-surgery (n = 21)	3rd month post-surgery (n = 23)	p value
Absolute handgrip strength (kg)	31.8 ± 4.2	29.2 ± 4.1*	27.7 ± 4.0*	< 0.001
Relative handgrip strength (kg/kg body weight)	0.35 ± 0.04	0.36 ± 0.05	0.38 ± 0.05†	0.004
Absolute quadriceps strength (N)	115.2 ± 34.8	102.4 ± 23.5†	93.7 ± 28.9†	< 0.001
Relative quadriceps strength (N/kg)	1.26 ± 0.34	1.27 ± 0.27	1.27 ± 0.32	0.596
Absolute VO$_2$ peak (l/min)	1.89 ± 0.28	1.59 ± 0.29*	1.65 ± 0.29*	< 0.001
Relative VO$_2$ peak (ml/kg/min)	20.94 ± 3.18	19.70 ± 2.55	22.53 ± 2.61†	0.002

*VO$_2$ peak: peak oxygen uptake; N: Newtons. Data are presented as means ± SD. ANOVA p value. *$p < 0.001$ compared with the preoperative values. †$p < 0.05$ compared with the preoperative values.*

Table III. Percent physical activity in the three moments of assessment



Physical activity (%)	Pre-surgery (n = 23)	1st month post-surgery (n = 21)	3rd month post-surgery (n = 23)	p value
Light (0-2,689 counts min^{-1})	95.6 (89.3-98.0)	96.3 (92.3-97.4)	95.7 (89.3-97.6)	0.056
Moderate (2,690-6,166 counts min^{-1})	4.1 (1.9-10.2)	3.6 (2.6-7.2)	4.0 (1.4-10.2)	0.151
Vigorous (≥ 6,167 counts min^{-1})	0.2 (0.1-0.5)	0.1 (0.0-0.4)*	0.2 (0.1-1.0)	0.006
Moderate-vigorous	4.3 (2.0-10.7)	3.7 (2.6-7.6)	4.2 (2.4-10.7)	0.056

*Data are presented as median values (min-max). Friedman p value. *$p < 0.05$ compared with the preoperative values.*

Given the importance of moderate-to-vigorous physical activity (MVPA) for health outcomes and surgical success, there is a need of using more valid methods for objectively measuring PA. Considering that the objectively measured amount of MVPA of obese subjects is below WHO recommendations for adults aged between 18 and 64 years, the maintenance of physical inactivity following bariatric surgery could mean an increased risk of regaining body weight lost with surgery. Further, there may also be an increased risk of developing non-communicable diseases (23).

For future studies, it is advisable to conduct a body composition evaluation through DEXA in order to express the variables of physical fitness not only in relation to body weight, but also to lean mass, as previously recommended (4).

Considering the fact that MS and CRF do not improve by weight loss only, we suggest adding physical fitness assessments before and after surgery to design personalized specific exercise programs for these patients and also implement PA counselling about the importance of changing their lifestyle (40).

In conclusion, large-scale weight loss through SG results in a decrease in absolute muscle strength. Despite a large decline in quadriceps strength, when it was expressed relative to body weight, its ratio remained unchanged. Also, regarding muscle strength, we observed an improvement in the handgrip strength/body weight ratio. In addition, patients with obesity have very low CRF, which decreases after SG. However, when peak oxygen consumption was expressed as a ratio to body weight, improvement was observed. Finally, no significant differences were observed in objectively measured PA with respect to the preoperative assessment.

REFERENCES

1. World Health Organization (WHO). Obesity and overweight. Geneva: WHO; 2018. Cited: Jan 17th, 2019. Available from: www.who.int/mediacentre/factsheets/fs311/en

2. Garcia M, Mulvagh SL, Merz CN, Buring JE, Manson JE. Cardiovascular disease in women: clinical perspectives. Circ Res 2016;118(8):1273-93. DOI: 10.1161/CIRCRESAHA.116.307547

3. Ahmad NN, Butsch WS, Aidarous S. Clinical management of obesity in women: addressing a lifecycle of risk. Obstet Gynecol Clin North Am 2016;43(2):201-30. DOI: 10.1016/j.ogc.2016.01.007.

4. Arena R, Cahalin LP. Evaluation of cardiorespiratory fitness and respiratory muscle function in the obese population. Prog Cardiovasc Dis 2014;56(4):457-64. DOI: 10.1016/j.pcad.2013.08.001

5. Kouvelioti R, Vagenas G, Langley-Evans S. Effects of exercise and diet on weight loss maintenance in overweight and obese adults: a systematic review. J Sports Med Phys Fitness 2014;54(4):456-74.

6. Nguyen NT, Varela JE. Bariatric surgery for obesity and metabolic disorders: state of the art. Nat Rev Gastroenterol Hepatol 2017;14(3):160-9. DOI: 10.1038/nrgastro.2016

7. Ng M, Fleming T, Robinson M, Thomson B, Graetz N, Margono C, et al. Global, regional, and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014;384(9945):766-81. DOI: 10.1016/S0140-6736(14)60460-8

8. Angrisani L, Santonicola A, Iovino P, Vitiello A, Zundel N, Buchwald H, et al. Bariatric surgery and endoluminal procedures: IFSO

Worldwide Survey 2014. Obes Surg 2017;27(9):2279-89. DOI: 10.1007/s11695-017-2666-x

9. Benaiges D, Sague M, Flores-Le Roux JA, Pedro-Botet J, Ramon JM, Villatoro M, et al. Predictors of hypertension remission and recurrence after bariatric surgery. Am J Hypertens 2016;29(5):653-9. DOI: 10.1093/ajh/hpv153

10. Laukkanen JA, Zaccardi F, Khan H, Kurl S, Jae SY, Rauramaa R. Long-term change in cardiorespiratory fitness and all-cause mortality: a populationbased follow-up study. Mayo Clin Proc 2016;91(9):1183-8. DOI: 10.1016/j.mayocp.2016.05.014

11. Volaklis KA, Halle M, Meisinger C. Muscular strength as a strong predictor of mortality: a narrative review. Eur J Intern Med 2015;26(5):303-10. DOI: 10.1016/j.ejim.2015.04.013

12. Afshar S, Seymour K, Kelly SB, Woodcock S, Van Hees VT, Mathers JC. Changes in physical activity after bariatric surgery: using objective and selfreported measures. Surg Obes Relat Dis 2017;13(3):474-83. DOI: 10.1016/j.soard.2016.09.012

13. Artero EG, Lee DC, Lavie CJ, Espana-Romero V, Sui XM, Church TS, et al. Effects of muscular strength on cardiovascular risk factors and prognosis. J Cardiopulm Rehabil 2012;32(6):351-8. DOI: 10.1097/HCR.0b013e3182642688

14. Stegen S, Derave W, Calders P, Van Laethem C, Pattyn P. Physical fitness in morbidly obese patients: effect of gastric bypass surgery and exercise training. Obes Surg 2011;21(1):61-70. DOI: 10.1007/s11695-009-0045-y

15. Seres L, Lopez-Ayerbe J, Coll R, Rodriguez O, Vila J, Formiguera X, et al. Increased exercise capacity after surgically induced weight loss in morbid obesity. Obesity (Silver Spring) 2006;14(2):273-9.

16. De Souza SAF, Faintuch J, Sant’Anna AF. Effect of weight loss on aerobic capacity in patients with severe obesity before and after bariatric surgery. Obes Surg 2010;20(7):871-5. DOI: 10.1007/s11695-010-0109-z

17. Hue O, Berrigan F, Simoneau M, Marcotte J, Marceau P, Marceau S, et al. Muscle force and force control after weight loss in obese and morbidly obese men. Obes Surg 2008;18(9):1112-8. DOI: 10.1007/s11695-008-9597-5

18. Neunhaeuserer D, Gasperetti A, Savalla F, Gobbo S, Bullo V, Bergamin M, et al. Functional evaluation in obese patients before and after sleeve gastrectomy. Obes

Surg 2017;27(12):3230-9. DOI: 10.1007/s11695-017-2763-x

19. Pietilainen KH, Kaprio J, Borg P, Plasqui G, Yki-Jarvinen H, Kujala UM, et al. Physical inactivity and obesity: a vicious circle. Obesity (Silver Spring) 2008;16(2):409-14. DOI: 10.1038/oby.2007.72

20. Tudor-Locke C, Brashear MM, Johnson WD, Katzmarzyk PT. Accelerometer profiles of physical activity and inactivity in normal weight, overweight, and obese US men and women. Int J Behav Nutr Phys Act 2010;7:60. DOI: 10.1186/1479-5868-7-60

21. Bond DS, Jakicic JM, Unick JL, Vithiananthan S, Pohl D, Roye GD, et al. Preto postoperative physical activity changes in bariatric surgery patients: selfreport vs. objective measures. Obesity (Silver Spring) 2010;18(12):2395-7. DOI: 10.1038/oby.2010.88

22. Gallart-Aragon T, Fernandez-Lao C, Castro-Martin E, Cantarero-Villanueva I, Cozar-Ibanez A, Arroyo-Morales M. Health-related fitness improvements in morbid obese patients after laparoscopic sleeve gastrectomy: a cohort study. Obes Surg 2017;27(5):1182-8. DOI: 10.1007/s11695-016-2427-2

23. Booth FW, Roberts CK, Thyfault JP, Ruegsegger GN, Toedebusch RG. Role of inactivity in chronic diseases: evolutionary insight and pathophysiological mechanisms. Physiol Rev 2017;97(4):1351-402. DOI: 10.1152/physrev.00019.2016

24. Redberg RF, Benjamin EJ, Bittner V, Braun LT, Goff DC Jr, Havas S, et al. AHA/ACCF (corrected) 2009 performance measures for primary prevention of cardiovascular disease in adults: a report of the American College of Cardiology Foundation/American Heart Association task force on performance measures. Circulation 2009;120(13):1296-336. DOI: 10.1161/CIRCULATIONAHA.109.192617

25. Van de Laar AW. Algorithm for weight loss after gastric bypass surgery considering body mass index, gender, and age from the Bariatric Outcome Longitudinal Database (BOLD). Surg Obes Relat Dis 2014;10(1):55-61. DOI: 10.1016/j.soard.2013.05.008

26. Van Dyck D, Cerin E, De Bourdeaudhuij I, Hinckson E, Reis RS, Davey R, et al. International study of objectively measured physical activity and sedentary time with body mass index and obesity: IPEN adult study. Int J Obes 2015;39(2):199-207. DOI: 10.1038/ijo.2014.115

27. Sasaki JE, John D, Freedson PS. Validation and comparison of ActiGraph activity monitors. J Sci Med Sport 2011;14(5):411-6. DOI: 10.1016/j.jsams.2011.04.003

28. Racette SB, Rochon J, Uhrich ML, Villareal DT, Das S, Fontana L, et al. Effects of two years of calorie restriction on aerobic capacity and muscle strength. Med Sci Sports Exerc 2017;49(11):2240-9. DOI:

10.1249/MSS.0000000000001353

29. Miller GD, Nicklas BJ, You T, Fernandez A. Physical function improvements after laparoscopic Roux-en-Y gastric bypass surgery. Surg Obes Relat Dis 2009;5(5):530-7. DOI: 10.1016/j.soard.2008.11.003

30. Schneider J, Peterli R, Gass M, Slawik M, Peters T, Wolnerhanssen BK. Laparoscopic sleeve gastrectomy and Roux-en-Y gastric bypass lead to equal changes in body composition and energy metabolism 17 months postoperatively: a prospective randomized trial. Surg Obes Relat Dis 2016;12(3):563-70. DOI: 10.1016/j.soard.2015.07.002

31. Karamanakos SN, Vagenas K, Kalfarentzos F, Alexandrides TK. Weight loss, appetite suppression, and changes in fasting and postprandial ghrelin and peptide-YY levels after Roux-en-Y gastric bypass and sleeve gastrectomy: a prospective, double blind study. Ann Surg 2008;247(3):401-7. DOI: 10.1097/SLA.0b013e318156f012

32. Otto M, Kautt S, Kremer M, Kienle P, Post S, Hasenberg T. Handgrip strength as a predictor for post bariatric body composition. Obes Surg 2014;24(12):2082-8. DOI: 10.1007/s11695-014-1299-6

33. Coen PM, Goodpaster BH. A role for exercise after bariatric surgery? Diabetes Obes Metab 2016;18(1):16-23. DOI: 10.1111/dom.12545

34. Wilms B, Ernst B, Thurnheer M, Weisser B, Schultes B. Differential changes in exercise performance after massive weight loss induced by bariatric surgery. Obes Surg 2013;23(3):365-71. DOI: 10.1007/s11695-012-0795-9

35. Blair SN, Kohl HW III, Paffenbarger RS Jr, Clark DG, Cooper KH, Gibbons LW. Physical fitness and all-cause mortality. A prospective study of healthy men and women. JAMA 1989;262(17):2395-401.

36. Muller TD, Nogueiras R, Andermann ML, Andrews ZB, Anker SD, Argente J, et al. Ghrelin. Mol Metab 2015;4(6):437-60. DOI: 10.1016/j.molmet.2015.03.005

37. Delgado Floody P, Caamano Navarrete F, Jerez Mayorga D, Campos Jara C, Ramirez Campillo R, Osorio Poblete A, et al. Efectos de un programa de tratamiento multidisciplinar en obesos morbidos y obesos con comorbilidades candidatos a cirugia bariatrica. Nutr Hosp 2015;31(5):2011-6. DOI: 10.3305/nh.2015.31.5.8569.

38. McCullough PA, Gallagher MJ, Dejong AT, Sandberg KR, Trivax JE, Alexander D, et al. Cardiorespiratory fitness and short-term complications after bariatric surgery. Chest 2006;130(2):517-25.

39. Berglind D, Willmer M, Eriksson U, Thorell A, Sundbom M, Udden J, et al. Longitudinal assessment of physical activity in women undergoing Roux-en-Y gastric bypass. Obes Surg 2015;25(1):119-25. DOI: 10.1007/s11695-014-1331-x

40. Creel DB, Schuh LM, Reed CA, Gomez AR, Hurst LA, Stote J, et al. A randomized trial comparing two interventions to increase physical activity among patients undergoing bariatric surgery. Obesity (Silver Spring) 2016;24:1660-8. DOI: 10.1002/oby.2154816

Effects of bariatric surgery on cardiorespiratory fitness: A systematic review and meta-analysis

Obesity Reviews (2021)

https://doi.org/10.1111/obr.13408

Paulina Ibacache-Saavedra, Daniel Jerez-Mayorga, Alejandro Carretero-Ruiz, Claudia Miranda-Fuentes, Marcelo Cano-Cappellacci, Enrique G. Artero

SUMMARY

Although bariatric surgery (BS) is recognized as an effective strategy for body weight loss and comorbidities, its impact on cardiorespiratory fitness (CRF) is still unclear. We aimed to examine postoperative changes in CRF ($VO_{2max/peak}$) and its relationship with weight loss among adults undergoing BS. We systematically searched the WoS, PubMed, MEDLINE, and Scopus databases. Observational and intervention studies were selected reporting the pre- and post-surgery CRF, measured by breath-by-breath VO_2 or its estimation. This meta-analysis, which included eleven articles (312 patients), revealed that BS leads to a reduction in absolute $VO_{2max/peak}$ in the short-term in adults with obesity (ES= -0.539; 95%CI= -0.708, -0.369; $p<0.001$), and those patients who suffered a more significant decrease in body mass index after BS also had a greater loss of absolute $VO_{2max/peak}$. However, $VO_{2max/peak}$ relative to body weight increased after surgery (ES= 0.658; 95%CI= 0.473, 0.842; $p<0.001$). An insufficient number of studies were found investigating medium and long-term changes in CRF after BS. This study provides moderate-quality evidence that the weight loss induced by BS can reduce CRF in the short term, which represent a therapeutic target to optimize BS outcomes. More high-quality studies are needed to evaluate the impact of BS on $VO_{2max/peak}$ in the short, medium, and long-term including normalized values for fat-free mass, as previously recommended.

Keywords

Obesity, bariatric surgery, physical fitness, weight loss.

1. INTRODUCTION

Obesity is a growing worldwide public health crisis that affects over 600 million people[1-3] and has been associated with several comorbidities such as dyslipidemia, diabetes, osteoarthritis, some cancers,[4] sleep apnea,[5] hypertension and coronary heart disease.[6-9] Consequently, the average life expectancy of people with class II obesity is reduced by two to four years and by eight to ten years in those with class III obesity.[10-12]

Moreover, obesity is associated with impaired physical fitness.[13,14] Physical fitness is a major health indicator[15] and includes various dimensions such as cardiorespiratory fitness (CRF), muscular fitness, and flexibility.[16] Maximal oxygen consumption (VO_{2max}) is usually considered the gold standard to assess CRF.[15] CRF is not only an objective measure of the ability to perform physical activity, but also a useful diagnostic and prognostic health indicator for patients in clinical settings.[17] It is recognized as a strong determinant of morbidity and mortality,[18] with low CRF being a significant risk factor for all-cause mortality and cardiovascular events, including in the obese population.[19,20] People with obesity have varying degrees of cardiovascular, pulmonary, and musculoskeletal dysfunction that affect VO_{2max} and other relevant variables of cardiopulmonary exercise testing (CPET).[13] Furthermore, a higher CRF may mitigate the increased risk of death associated with obesity.[17] Likewise, CRF is a marker of functional capacity and the ability to perform daily living tasks.[15]

Conventional obesity treatment has shown to have limited success in reducing body weight over time.[21] Bariatric surgery (BS) is the most cost-effective treatment in patients with class II and III obesity [22,23] as it induces marked weight loss, improves obesity-related comorbidities, and reduces mortality.[24,25] Therefore, it has been widely used in the last decades to overcome obesity, with an increased number of bariatric procedures performed in recent years.[26,27]

Despite the previously described efficacy of BS,[28-31] its impact on CRF remains unclear, with contradictory results reported in the literature.[32-36] Considering that CRF is so relevant for its predictive health value[18] and that low CRF has been associated with increased short-term postoperative complications of BS,[37] a description of the impact of BS on this health marker is needed for making the best clinical decisions.[15]

The present systematic review and meta-analysis aims to bring together and adequately analyze the evidence on postoperative changes in CRF ($VO_{2max/peak}$) and its relationship with weight loss among adults with obesity undergoing BS. Furthermore, other factors have also been examined, such as pre-surgery body mass index (BMI), type of exercise test used (cycle vs. treadmill), surgical technique, and some CPET variables.

2. METHODS

2.1 Study reporting and protocol registration

This systematic review and meta-analysis was registered in PROSPERO (ID CRD42020155961). The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement and checklist[38] (Supplementary Table S1), together with the Cochrane Handbook for Systematic Reviews of Interventions,[39] have been strictly followed in the design and implementation of this study.

2.2 Data sources and searches

A systematic electronic search was conducted for articles published in the Web of Science, PubMed, MEDLINE, and Scopus databases with a deadline of November 26, 2020.

The search strategy consisted of two blocks of search terms (Table 1). In addition to searching databases, the reference lists of all included papers and relevant review articles were scanned for further eligible studies.[40]

TABLE 1. Search strategy

Bariatric surgery		Cardiorespiratory fitness
"bariatric surgery" OR "gastric bypass" OR "gastroplasty" OR "metabolic surgery" OR "obesity surgery" OR "roux-en-y" OR "sleeve gastrectomy" OR "gastric banding" OR "one anastomosis gastric bypass" OR "minigastric bypass" OR "gastric band" OR "biliopancreatic diversion"	AND	"cardiorespiratory fitness" OR "aerobic capacity" OR "maximal oxygen consumption" OR "maximal oxygen uptake" OR "peak oxygen uptake" OR "VO_2max" OR "peak oxygen consumption" OR "VO_2peak"

VO_{2max}: maximal oxygen consumption; VO_{2peak}: peak oxygen consumption.

2.3 Study selection and screening criteria

The systematic review was independently and simultaneously performed by the research team: titles and abstracts of studies retrieved using the search strategy were assessed and screened by four reviewers (DJ-M, AC-R, MC-C, and PI-S) to identify studies that potentially met the selection criteria. The full text of these potentially eligible studies was assessed for eligibility by five members of the review team (DJ-M, AC-R, CM-F, MC-C, and PI-S).

They discussed and resolved any disagreement on the studies' eligibility with another reviewer (EGA).

We included published reports of both observational and intervention studies (randomized and non-randomized controlled trials). Studies in adults with obesity describing the effect of BS on CRF, measured by breath-by-breath VO_2 or its estimation by indirect testing, were included (the meta-analysis only included studies measuring breath-by-breath VO_2). There were no restrictions on the duration of post-surgical follow-up or the number of post-surgical follow-up measurements performed.

The exclusion criteria for this systematic review were: a) studies that did not report the outcome CRF before and after the surgery; b) reports not written in English, French, or Spanish; c) studies in which the population sample studied were animals; d) studies where participants were under the age of 18 years old; e) retracted studies; f) duplicate studies; g) reports published more than ten years ago (due to the evolution of surgical techniques); h) non-selectable publications, as in the case of reviews, guidelines, interviews, comments, case studies, or conference presentations.

2.4 Data selection

The data extraction was conducted independently by two reviewers (PI-S and CM-F) using a standardized data extraction form and any discrepancies were resolved by mutual consensus in consultation with a third reviewer (MC-C). The following data were extracted from each of the selected studies: a) first author last name; b) year of the study; c) country; d) study design; e) BS technique; f) participants' characteristics, number, gender distribution, and age; g) pre- and post-surgery anthropometric characteristics, BMI, excess weight, and waist circumference; h) pre- and post-surgery CRF; i) methodology used for the evaluation of CRF; j) pre- and post-surgery of other CPET variables: maximum heart rate (HR_{max}), maximal minute ventilation (VE_{max}), maximal oxygen pulse (O_2pulse_{max}), and time to exhaustion; k) mean follow-up. As necessary, we attempted to contact the authors of included studies to clarify any relevant information or request additional data.

2.5 Evaluation of the quality of the reports

The PEDro scale, based on the Delphi scale, was used to assess the quality of the selected intervention studies.[41] This scale considers 11 items answered "yes" or "no": eligibility criteria, random allocation, concealed allocation, similarity groups' baseline, blinding subjects, blinding therapist/trainers, blinding assessors, measured more than 85% of subjects, intention to treat and point measure. From these 11 items, the first one (eligibility criteria) was not considered when calculating total scores, meaning that the quality of each article was scored from 0 to 10.[42] The selected articles were then categorized according to the quality of their methodology, to wit, poor (with< 4 points), fair (4-5 points), good (6-8 points), or excellent (9-10 points).[42,43]

The reporting quality of observational studies was assessed through the Newcastle-Ottawa Scale (NOS), whose content validity and inter-rater reliability have been established.[44] The NOS for cohort studies is comprised of eight items divided into three categories: selection of study groups, comparability of study groups, and ascertainment of outcome of interest. Studies were awarded one star for each fulfilled item and the overall NOS scores could range from 0 to 9 stars, where more stars meaning a higher study quality.[44]

Two investigators (MC-C and DJ-M) independently conducted the quality assessment of selected studies (both intervention and observational). Any disagreement on the ratings of the selected studies was discussed with a third reviewer (AC-R).

2.6 Statistical analysis

The comprehensive MetaAnalysis 2.0 software was used to perform the principal statistical and sensitivity analysis. The analysis variables (primary outcomes) were absolute $VO_{2max/peak}$ and $VO_{2max/peak}$ relative to body weight. The secondary outcomes were other CPET variables (HR_{max}, VE_{max}, O_2pulse_{max}, and time to exhaustion). The effect size (ES) was calculated using the standardized mean difference of the change in the mentioned variables (pre- to post-surgery) and the Cohen's D estimator, interpreted conventionally as small (0.2), medium (0.5), and large (0.8) ES.[45] Random-effects meta-analysis using the DerSimonian-Laird method was used, and the 95% confidence intervals were also calculated (95% CI).[46] Two-sided $p \leq 0.05$ was calculated as the significance level.

The I^2 statistic was used to assess heterogeneity between the studies included in the forest plots.[47] To assess the publication bias, Funnel plots and the Egger test were performed,[48] using $p \leq 0.1$ as the significance level for the Egger test.[49] A sensitivity analysis was performed, recalculating all analyses by removing each selected study one by one.

Data were extracted from each study by applying the following criteria: I) if two or more studies used an identical database, only the data from the main study were used; II) outcome data were collected by measurements before and after surgery, where no more than six months had elapsed between surgery and measurement; III) in those studies that presented two or more measurements between surgery and the subsequent six months, the data closest to the surgery was analyzed; IV) those studies that only estimated CRF were not included in the meta-analysis.

Subgroups analyses were carried out considering the influence of the type of exercise test used (cycle vs. treadmill) on the magnitude of CRF changes.

Finally, through a random-effects regression model for meta-analysis,[50] we investigated: I) the influence of preoperative obesity level (BMI) on the magnitude of CRF changes; II) the impact of pre- to post-surgery BMI change on the magnitude of CRF changes.

3. RESULTS

The search identified 181 records (Web of Science 72, PubMed 31, MEDLINE 40, and Scopus 38). After eliminating duplicates, 85 records remained. On November 26, 2020, we performed an updated search in the same databases (only papers published in 2019 and 2020). The updated search identified 72 records (Web of Science 22, PubMed 18, MEDLINE 17, and Scopus 15). After eliminating duplicates, 28 records remained (Figure 1). The searches were performed by four of the authors (PI-S, DJ-M, CM-F, and MC-C).

Searches identified a total of 113 unique references. After initial screening based on titles and abstracts, 32 articles remained for further evaluation. Of these, 15 were excluded in the subsequent detailed assessments. Seventeen publications met the selection criteria for the systematic review (Figure 1).

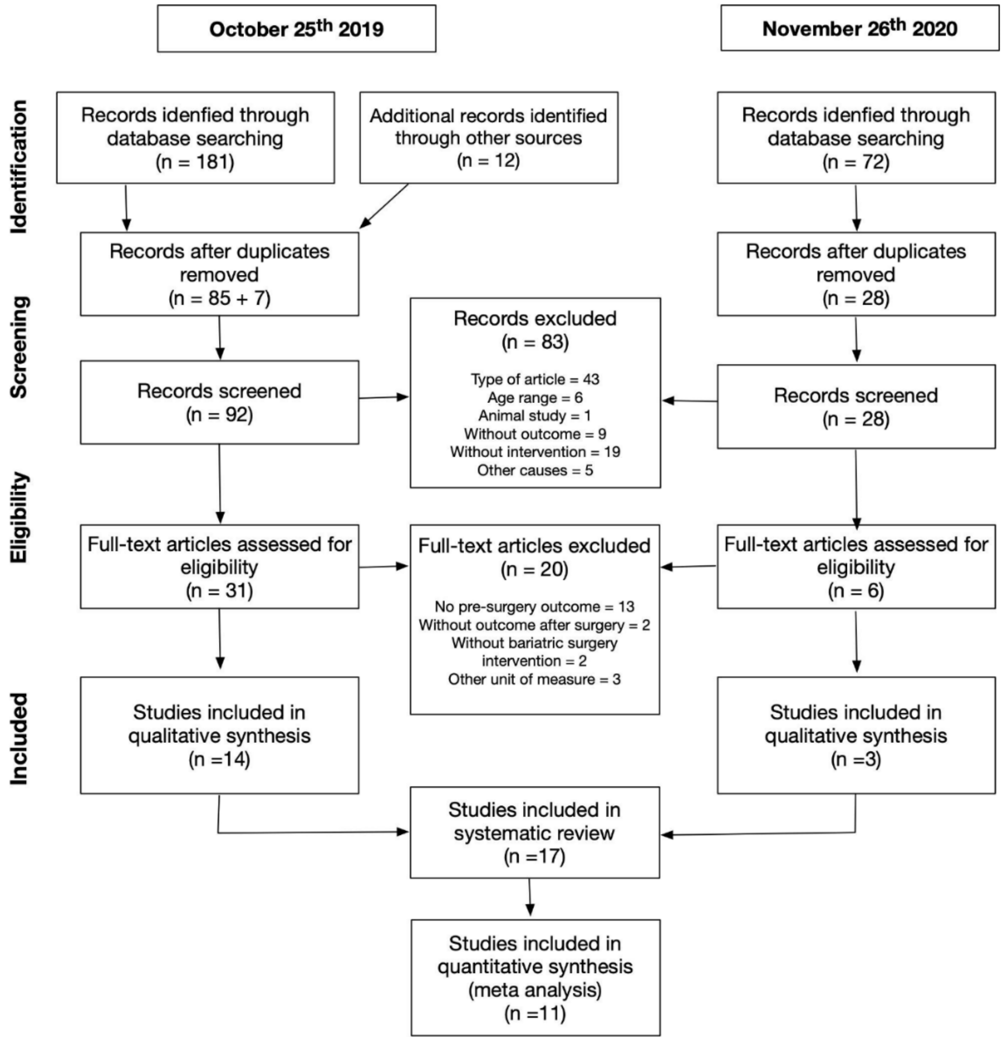


FIGURE 1. Flow diagram of study selection as per the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[38]

Two studies were not included in the meta-analysis from the 17 selected for the systematic review because $VO_{2max/peak}$ was only estimated.[51,52] In addition, one more study was also excluded from the meta-analysis because the postoperative assessment of $VO_{2max/peak}$ was performed in a wide range of time.[53]

Because only outcome data collected no later than six months after surgery were considered for statistical analysis, two studies were not incorporated into the meta-analysis. Dereppe et al.[54] carried out the post-surgical assessment one year after surgery, while Neunhaeuserer et al.[55] is a longer-term follow-up of the same cohort included in Neunhaeuserer et al.[36] Although Lund et al.[56] indicated that an assessment was carried out four months after the surgery, it was excluded from the meta-analysis because they did not show the exact values of $VO_{2max/peak}$ from this evaluation.

Three studies followed participants with two postoperative assessments within the first six months.[57-59] In these cases, except for Ibacache et al.[58] (the evaluation of the first postoperative month was not considered), the statistical analysis considered the data closest to the surgery for CRF evaluation.

On the other hand, as in two of the studies authors performed more than one preoperative $VO_{2max/peak}$ evaluation,[56,60] only the assessment closest to surgery was considered.

Analyses of the changes in CRF in the medium or long term[61] or a sub-analysis according to surgical technique was not possible as there were not enough studies that considered these factors.

3.1 Study characteristics

Study characteristics are summarized in Table 2. The systematic review includes 13 observational studies [one study[62] performed a subgroup analysis of participants from a randomized controlled trial)], two randomized controlled trials, and two non-randomized controlled trials, comprising a total of 3624 patients. Participants' mean age ranged from 36.1 to 48.2 years, and most were female (81%).

The BS technique varied between studies, being Roux-en-Y gastric bypass (8 studies[32,34,35,52,56,60,62,63]) and sleeve gastrectomy (3 studies[36,55,58]) the most frequent. Besides, five studies used either gastric bypass or sleeve gastrectomy[51,53,54,57,64] and one study used biliopancreatic diversion with duodenal switch or sleeve gastrectomy.[59]

All the studies used BMI to assess obesity and its evolution after surgery. Only four studies additionally used waist circumference to measure central obesity.[35,57-59] All studies reported an average preoperative BMI corresponding to class III obesity (BMI ≥ 40 kg/m^2), except for one study in class II obesity (35.1 kg/m^2).[58]

TABLE 2. Characteristics of studies included in the systematic review

Author, year	Design	Country	Sample size (male/female)	Age (years)	BS technique	Follow-up time-point (months)	Type of evaluation	Ergometer
Auclair et al. (2020)[59]	RCT	Canada	17 (NR)	42 ± 12	BPD/DS or SG (10/7)	3 and 6	Indirect calorimetry	Cycle ergometer
Bellicha et al. (2019)[62]	OS	France	41 (0/41)	43.0 (38.0–51.0)	RYGB	6	Indirect calorimetry	Cycle ergometer
Browning et al. (2017)[34]	OS	USA	9 (0/9)	37.4 ± 9.8	RYGB	3	Indirect calorimetry	Treadmill
Dereppe et al. (2019)[54]	OS	Belgium	42 (0/42)	42 ± 13	RYGB or SG (24/18)	12	Indirect calorimetry	Cycle ergometer
De Souza et al. (2010)[32]	OS	Brazil	61 (NR)	40.4 ± 8.4	RYGB	6 and 12	Indirect calorimetry	Treadmill
Ibacache et al. (2019)[58]	OS	Chile	23 (0/23)	36.1 ± 11.1	SG	1 and 3	Indirect calorimetry	Cycle ergometer
Lund et al. (2015)[56]	OS	Denmark	33 (9/24)	40 ± 2	RYGB	4 and 18	Indirect calorimetry	Cycle ergometer
Mundbjerg et al. (2018)[52]	RCT	Denmark	60 (18/42)	42.3 ± 9.1	RYGB	6, 12 and 24	Estimated through the Åstrand test	Cycle ergometer
Nedeljkovic et al. (2019)[63]	OS	Serbia	66 (15/51)	38.8 ± 10.1	RYGB	6	Indirect calorimetry	Treadmill
Neunhaeuserer et al. (2017)[36]	OS	Italy	26 (8/18)	48.2 ± 9.0	SG	6	Indirect calorimetry	Treadmill
Neunhaeuserer et al. (2020)[55]	OS	Italy	24 (10/14)	47.0 ± 9.0	SG	16	Indirect calorimetry	Treadmill
Onofre et al. (2017)[57]	NRCT	Brazil	6 (0/6)	39.5 ± 7.2	RYGB or SG (1/5)	3 and 6	Indirect calorimetry	Treadmill
Remígio et al. (2018)[64]	OS	Brazil	24 (4/20)	20–43	RYGB or SG (14/10)	4	Indirect calorimetry	Treadmill
Stegen et al. (2011)[35]	NRCT	Belgium	7 (3/4)	43.1 ± 5.6	RYGB	4	Indirect calorimetry	Cycle ergometer
Tettero et al. (2018)[51]	OS	Holland	3,159 (NR)	43.2 ± 10.7	RYGB or SG (NR)	9, 15, and 24	Estimated through the Åstrand test	Cycle ergometer
Wilms et al. (2013)[53]	OS	Switzerland	18 (7/11)	42.5 ± 2.5	RYGB or SG (16/2)	27.7 ± 2.5 (15–45)	Indirect calorimetry	Cycle ergometer
Wimmelmann et al. (2016)[60]	OS	Denmark	32 (NR)	39.5 ± 8.9	RYGB	4 and 18	Indirect calorimetry	Cycle ergometer

Note: Data are presented as means ± SD except for Wilms [mean±SE], Bellicha [median (25th–75th percentile)], and Remígio [range]. In RCTs, data from the control group is shown.
BS, bariatric surgery, RCT, randomized controlled trial; NRCT, non-randomized controlled trial; OS, observational study; BPD/DS, biliopancreatic diversion with duodenal switch; SG, sleeve gastrectomy; RYGB, roux-en-Y Gastric Bypass; NR, not reported.

3.2 CRF outcomes

Most of the studies reported $VO_{2max/peak}$ in absolute terms (L/min) and relative to body weight (ml/kg/min), except for two that did not report absolute values[32,60] and two articles that estimated $VO_{2max/peak}$, and did not show values relative to body weight.[51,52] Only four studies reported $VO_{2max/peak}$ relative to fat-free mass (FFM),[34,35,51,62] and one presented VO_2 values indexed to mid-thigh muscle area.[59]

Ten studies (60%) measured CRF on a cycle ergometer,[35,51-54,56,58-60,62] while seven (40%) used a treadmill. Most of the studies (15, 88%) used breath-by-breath measurements to obtain max/peak oxygen consumption. The follow-up periods after surgery ranged from one to 24 months: nine studies reported follow-ups between one and six months;[34-36,57-59,62-64] two studies until one year;[32,54] and six studies carried out follow-ups beyond the year after the surgery.[51-53,55,56,60]

Twelve studies used indirect calorimetry for CRF assessments and reported changes in $VO_{2max/peak}$ in absolute terms (L/min): eight of them (67%) showed a significant decrease in CRF after the surgery,[36,54,56,58,59,62-64] while the other four (33%) reported no change.[34,35,53,57] Otherwise, the two studies estimating $VO_{2max/peak}$ reported an increase[51] or maintenance[52] of CRF after BS (Table 3).

On the other hand, 11 of the 14 studies (79%) that reported changes in $VO_{2max/peak}$ relative to body weight showed an increase in CRF after the surgery,[32,35,36,53-56,59,60,63,64] while the other three studies did not show any change (Table 3).[34,57,62]

$VO_{2max/peak}$ relative to FFM showed different results, reporting either an increase,[51,59] or no changes (Table 3).[34,35,62]

HR_{max} did not change after surgery in any of the studies that reported this parameter. VE_{max} did not change in most studies, decreasing in only two studies (Table 3).[36,63]

BS reduced oxygen pulse at maximal workload in most studies that reported it.[36,54,59,63] In contrast, most studies reported an increase in time to exhaustion, except for two studies that reported no change after the surgery (Table 3).[53,57]

3.3 Methodological quality

The methodological quality of the studies evaluated with the PEDro scale was between good and fair (Supplementary Table S2). The scores ranged between four and seven, with an average score of 5.5. Deficiencies on the PEDro scale were primarily observed in the lack of blinding of subjects, therapists who administered the therapy, and assessors who measured at least one key outcome. However, it is not possible to blind patients or therapists due to the type of intervention.

The average score using the Newcastle-Ottawa Scale for observational studies was 6, ranging between 5 and 9 out of a possible maximum of 9 (Supplementary Table S3). Because observational studies of bariatric surgery typically use a single exposed cohort design, the two NOS items pertaining to non-exposed study groups were the main deficiencies.

3.4 Meta-analyses

Meta-analyses showed a significant decrease in absolute $VO_{2max/peak}$ after BS with a medium effect size (ES=-0.539; 95% CI=-0.708,-0.369; $p < 0.001$) (Figure 2a). On the other hand, the same analysis revealed a significant increase in $VO_{2max/peak}$ relative to body weight with a medium effect size (ES= 0.658; 95% CI= 0.473, 0.842; $p < 0.001$) (Figure

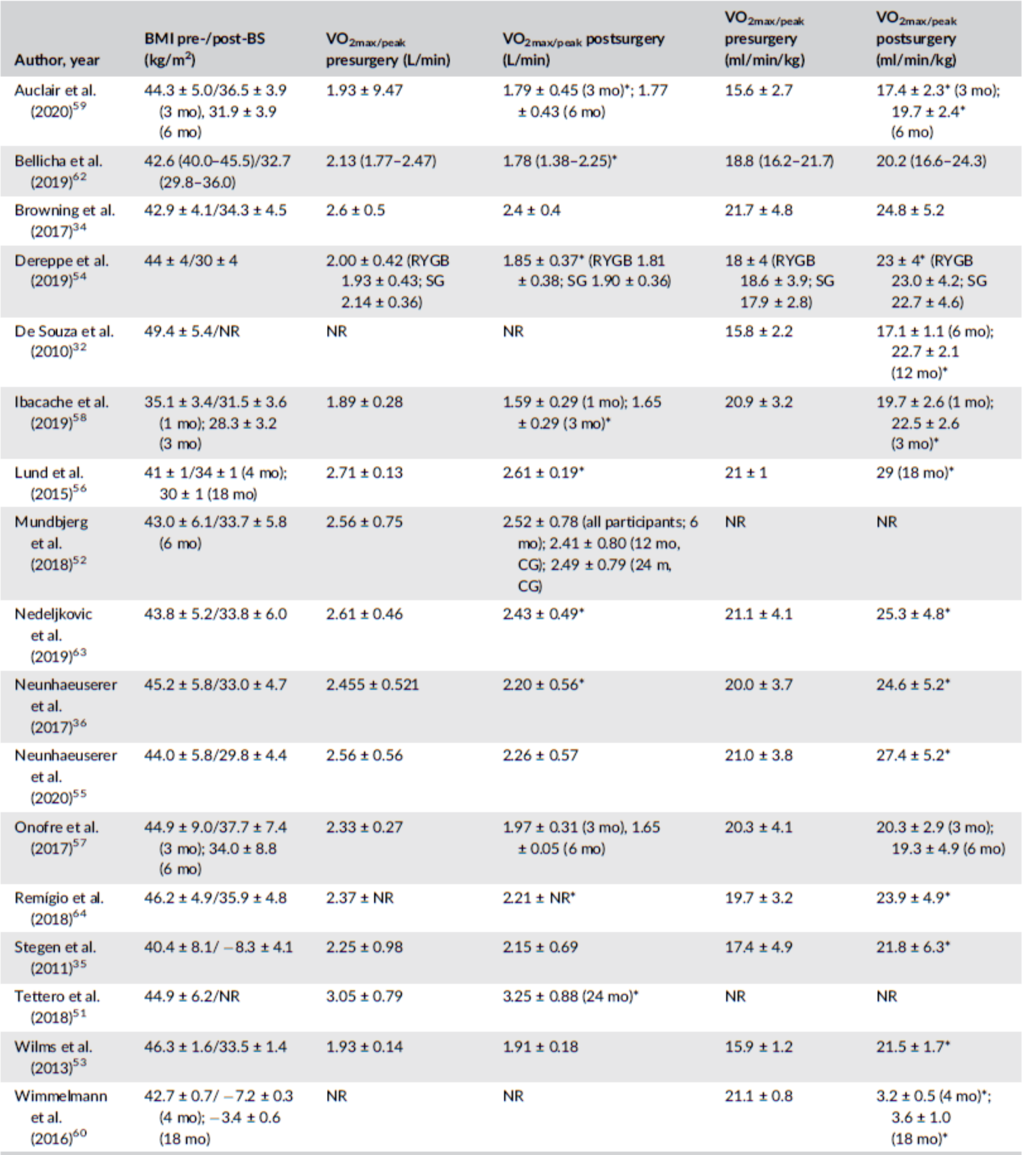
2b). Non-important and moderate heterogeneity was observed across studies, with $I^2 = 42\%$ ($p = 0.682$, Figure 2a) in the absolute $VO_{2max/peak}$ and $I^2 = 0\%$ in the relative $VO_{2max/peak}$ ($p = 0.794$; Figure 2b).

In relation to the other variables of the CPET, meta-analyses showed a significant decrease in VE_{max} (ES=-0.261; 95% CI= -0.506, -0.016; $p = 0.037$) and in O_2pulse_{max} (ES= -0.426; 95% CI= -0.654, -0.198; $p < 0.001$) after BS with a small effect size. In contrast, the time to exhaustion increased after surgery with a medium effect size (ES= 0.694; 95% CI= 0.403, 0.985; $p < 0.001$). Finally, HR_{max} did not change after BS (ES= 0.014; 95% CI= -0.284, 0.312; $p = 0.926$).

3.5 Subgroups analyses

The subgroups analyses (Supplementary Table S4) confirmed the significant decrease in absolute $VO_{2max/peak}$ after bariatric surgery regardless of the type of ergometer, although with a larger effect size when using a cycle ergometer (ES= -0.613; 95% CI= -0.886,-0.341; $p < 0.001$) compared to a treadmill (ES=-0.491; 95% CI=-0.708, -0.275; $p < 0.001$). When analyzing $VO_{2max/peak}$ relative to body weight, the significant increase was also confirmed regardless of the type of ergometer, but in this case, the effect size was larger when a treadmill was used (ES= 0.831; 95% CI= 0.549, 1.114; $p < 0.001$) compared to a cycle ergometer (ES= 0.528; 95% CI= 0.283, 0.772; $p < 0.001$).

TABLE 3. Summary of main findings of studies on the effect of bariatric surgery on cardiorespiratory fitness



Author, year	BMI pre-/post-BS (kg/m^2)	$VO_{2max/peak}$ presurgery (L/min)	$VO_{2max/peak}$ postsurgery (L/min)	$VO_{2max/peak}$ presurgery (ml/min/kg)	$VO_{2max/peak}$ postsurgery (ml/min/kg)
Auclair et al. (2020)[59]	44.3 ± 5.0/36.5 ± 3.9 (3 mo), 31.9 ± 3.9 (6 mo)	1.93 ± 9.47	1.79 ± 0.45 (3 mo)*; 1.77 ± 0.43 (6 mo)	15.6 ± 2.7	17.4 ± 2.3* (3 mo); 19.7 ± 2.4* (6 mo)
Bellicha et al. (2019)[62]	42.6 (40.0–45.5)/32.7 (29.8–36.0)	2.13 (1.77–2.47)	1.78 (1.38–2.25)*	18.8 (16.2–21.7)	20.2 (16.6–24.3)
Browning et al. (2017)[34]	42.9 ± 4.1/34.3 ± 4.5	2.6 ± 0.5	2.4 ± 0.4	21.7 ± 4.8	24.8 ± 5.2
Dereppe et al. (2019)[54]	44 ± 4/30 ± 4	2.00 ± 0.42 (RYGB 1.93 ± 0.43; SG 2.14 ± 0.36)	1.85 ± 0.37* (RYGB 1.81 ± 0.38; SG 1.90 ± 0.36)	18 ± 4 (RYGB 18.6 ± 3.9; SG 17.9 ± 2.8)	23 ± 4* (RYGB 23.0 ± 4.2; SG 22.7 ± 4.6)
De Souza et al. (2010)[32]	49.4 ± 5.4/NR	NR	NR	15.8 ± 2.2	17.1 ± 1.1 (6 mo); 22.7 ± 2.1 (12 mo)*
Ibacache et al. (2019)[58]	35.1 ± 3.4/31.5 ± 3.6 (1 mo); 28.3 ± 3.2 (3 mo)	1.89 ± 0.28	1.59 ± 0.29 (1 mo); 1.65 ± 0.29 (3 mo)*	20.9 ± 3.2	19.7 ± 2.6 (1 mo); 22.5 ± 2.6 (3 mo)*
Lund et al. (2015)[56]	41 ± 1/34 ± 1 (4 mo); 30 ± 1 (18 mo)	2.71 ± 0.13	2.61 ± 0.19*	21 ± 1	29 (18 mo)*
Mundbjerg et al. (2018)[52]	43.0 ± 6.1/33.7 ± 5.8 (6 mo)	2.56 ± 0.75	2.52 ± 0.78 (all participants; 6 mo); 2.41 ± 0.80 (12 mo, CG); 2.49 ± 0.79 (24 m, CG)	NR	NR
Nedeljkovic et al. (2019)[63]	43.8 ± 5.2/33.8 ± 6.0	2.61 ± 0.46	2.43 ± 0.49*	21.1 ± 4.1	25.3 ± 4.8*
Neunhaeuserer et al. (2017)[36]	45.2 ± 5.8/33.0 ± 4.7	2.455 ± 0.521	2.20 ± 0.56*	20.0 ± 3.7	24.6 ± 5.2*
Neunhaeuserer et al. (2020)[55]	44.0 ± 5.8/29.8 ± 4.4	2.56 ± 0.56	2.26 ± 0.57	21.0 ± 3.8	27.4 ± 5.2*
Onofre et al. (2017)[57]	44.9 ± 9.0/37.7 ± 7.4 (3 mo); 34.0 ± 8.8 (6 mo)	2.33 ± 0.27	1.97 ± 0.31 (3 mo), 1.65 ± 0.05 (6 mo)	20.3 ± 4.1	20.3 ± 2.9 (3 mo); 19.3 ± 4.9 (6 mo)
Remígio et al. (2018)[64]	46.2 ± 4.9/35.9 ± 4.8	2.37 ± NR	2.21 ± NR*	19.7 ± 3.2	23.9 ± 4.9*
Stegen et al. (2011)[35]	40.4 ± 8.1/ −8.3 ± 4.1	2.25 ± 0.98	2.15 ± 0.69	17.4 ± 4.9	21.8 ± 6.3*
Tettero et al. (2018)[51]	44.9 ± 6.2/NR	3.05 ± 0.79	3.25 ± 0.88 (24 mo)*	NR	NR
Wilms et al. (2013)[53]	46.3 ± 1.6/33.5 ± 1.4	1.93 ± 0.14	1.91 ± 0.18	15.9 ± 1.2	21.5 ± 1.7*
Wimmelmann et al. (2016)[60]	42.7 ± 0.7/ −7.2 ± 0.3 (4 mo); −3.4 ± 0.6 (18 mo)	NR	NR	21.1 ± 0.8	3.2 ± 0.5 (4 mo)*; 3.6 ± 1.0 (18 mo)*

Note: Data are presented as means ± SD except for Wimmelmann, Wilms [mean ± SE] and Bellicha [median (25th–75th percentile)]. Some changes are presented as mean change ± SD [BMI in Stegen] and mean change ± SE [Wimmelmann]. In RCTs, data from the control group is shown.

Abbreviations: BS, bariatric surgery; BMI, body mass index; BM, body mass; $VO_{2max/peak}$, maximal/peak oxygen consumption; HR_{max}, maximum heart rate; O_2pulse_{max}, maximal oxygen pulse; VE_{max}, maximal minute ventilation; FFM, fat-free mass; mo, months; CG, control group; NR, not reported.

[a] Indexed values to mid-thigh muscle area (mLO$_2$/cm^2/min)

*$p < 0.05$ compared with preoperative values.

TABLE 3 (Continued)

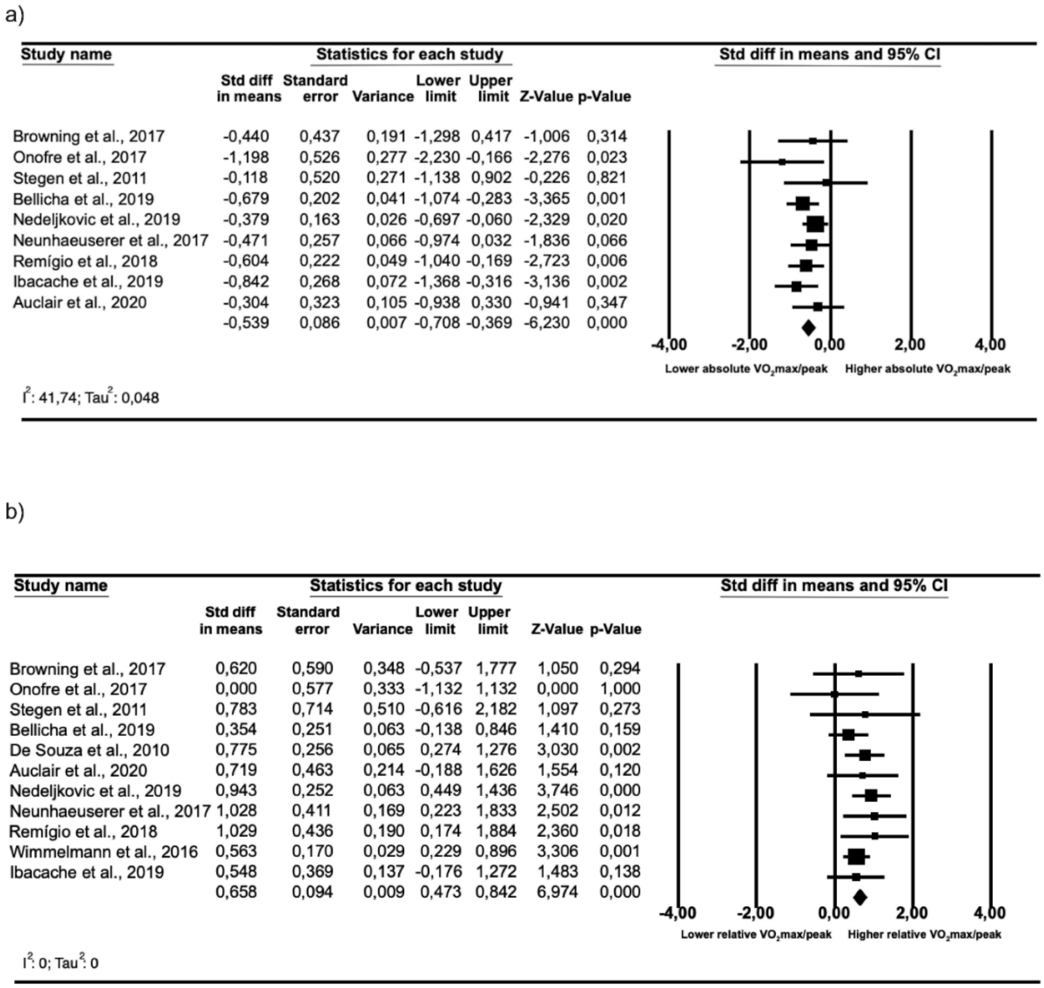
Author, year	BMI pre-/post-BS (kg/m^2)	VO$_{2max/peak}$ presurgery (L/min)	VO$_{2max/peak}$ postsurgery (L/min)	VO$_{2max/peak}$ presurgery (ml/min/kg)	VO$_{2max/peak}$ postsurgery (ml/min/kg)
Auclair et al. (2020)[59]	44.3 ± 5.0/36.5 ± 3.9 (3 mo), 31.9 ± 3.9 (6 mo)	1.93 ± 9.47	1.79 ± 0.45 (3 mo)*; 1.77 ± 0.43 (6 mo)	15.6 ± 2.7	17.4 ± 2.3* (3 mo); 19.7 ± 2.4* (6 mo)
Bellicha et al. (2019)[62]	42.6 (40.0–45.5)/32.7 (29.8–36.0)	2.13 (1.77–2.47)	1.78 (1.38–2.25)*	18.8 (16.2–21.7)	20.2 (16.6–24.3)
Browning et al. (2017)[34]	42.9 ± 4.1/34.3 ± 4.5	2.6 ± 0.5	2.4 ± 0.4	21.7 ± 4.8	24.8 ± 5.2
Dereppe et al. (2019)[54]	44 ± 4/30 ± 4	2.00 ± 0.42 (RYGB 1.93 ± 0.43; SG 2.14 ± 0.36)	1.85 ± 0.37* (RYGB 1.81 ± 0.38; SG 1.90 ± 0.36)	18 ± 4 (RYGB 18.6 ± 3.9; SG 17.9 ± 2.8)	23 ± 4* (RYGB 23.0 ± 4.2; SG 22.7 ± 4.6)
De Souza et al. (2010)[32]	49.4 ± 5.4/NR	NR	NR	15.8 ± 2.2	17.1 ± 1.1 (6 mo); 22.7 ± 2.1 (12 mo)*
Ibacache et al. (2019)[58]	35.1 ± 3.4/31.5 ± 3.6 (1 mo); 28.3 ± 3.2 (3 mo)	1.89 ± 0.28	1.59 ± 0.29 (1 mo); 1.65 ± 0.29 (3 mo)*	20.9 ± 3.2	19.7 ± 2.6 (1 mo); 22.5 ± 2.6 (3 mo)*
Lund et al. (2015)[56]	41 ± 1/34 ± 1 (4 mo); 30 ± 1 (18 mo)	2.71 ± 0.13	2.61 ± 0.19*	21 ± 1	29 (18 mo)*
Mundbjerg et al. (2018)[52]	43.0 ± 6.1/33.7 ± 5.8 (6 mo)	2.56 ± 0.75	2.52 ± 0.78 (all participants; 6 mo); 2.41 ± 0.80 (12 mo, CG); 2.49 ± 0.79 (24 m, CG)	NR	NR
Nedeljkovic et al. (2019)[63]	43.8 ± 5.2/33.8 ± 6.0	2.61 ± 0.46	2.43 ± 0.49*	21.1 ± 4.1	25.3 ± 4.8*
Neunhaeuserer et al. (2017)[36]	45.2 ± 5.8/33.0 ± 4.7	2.455 ± 0.521	2.20 ± 0.56*	20.0 ± 3.7	24.6 ± 5.2*
Neunhaeuserer et al. (2020)[55]	44.0 ± 5.8/29.8 ± 4.4	2.56 ± 0.56	2.26 ± 0.57	21.0 ± 3.8	27.4 ± 5.2*
Onofre et al. (2017)[57]	44.9 ± 9.0/37.7 ± 7.4 (3 mo); 34.0 ± 8.8 (6 mo)	2.33 ± 0.27	1.97 ± 0.31 (3 mo), 1.65 ± 0.05 (6 mo)	20.3 ± 4.1	20.3 ± 2.9 (3 mo); 19.3 ± 4.9 (6 mo)
Remígio et al. (2018)[64]	46.2 ± 4.9/35.9 ± 4.8	2.37 ± NR	2.21 ± NR*	19.7 ± 3.2	23.9 ± 4.9*
Stegen et al. (2011)[35]	40.4 ± 8.1/ −8.3 ± 4.1	2.25 ± 0.98	2.15 ± 0.69	17.4 ± 4.9	21.8 ± 6.3*
Tettero et al. (2018)[51]	44.9 ± 6.2/NR	3.05 ± 0.79	3.25 ± 0.88 (24 mo)*	NR	NR
Wilms et al. (2013)[53]	46.3 ± 1.6/33.5 ± 1.4	1.93 ± 0.14	1.91 ± 0.18	15.9 ± 1.2	21.5 ± 1.7*
Wimmelmann et al. (2016)[60]	42.7 ± 0.7/ −7.2 ± 0.3 (4 mo); −3.4 ± 0.6 (18 mo)	NR	NR	21.1 ± 0.8	3.2 ± 0.5 (4 mo)*; 3.6 ± 1.0 (18 mo)*

Note: Data are presented as means ± SD except for Wimmelmann, Wilms [mean ± SE] and Bellicha [median (25th–75th percentile)]. Some changes are presented as mean change ± SD [BMI in Stegen] and mean change ± SE [Wimmelmann]. In RCTs, data from the control group is shown.

Abbreviations: BS, bariatric surgery; BMI, body mass index; BM, body mass; VO$_{2max/peak}$, maximal/peak oxygen consumption; HR$_{max}$, maximum heart rate; O$_2$pulse$_{max}$, maximal oxygen pulse; VE$_{max}$, maximal minute ventilation; FFM, fat-free mass; mo, months; CG, control group; NR, not reported.

[a] Indexed values to mid-thigh muscle area (mLO$_2$/cm^2/min)

*p < 0.05 compared with preoperative values.



a)

Study name	Statistics for each study							Std diff in means and 95% CI
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
Browning et al., 2017	-0,440	0,437	0,191	-1,298	0,417	-1,006	0,314	
Onofre et al., 2017	-1,198	0,526	0,277	-2,230	-0,166	-2,276	0,023	
Stegen et al., 2011	-0,118	0,520	0,271	-1,138	0,902	-0,226	0,821	
Bellicha et al., 2019	-0,679	0,202	0,041	-1,074	-0,283	-3,365	0,001	
Nedeljkovic et al., 2019	-0,379	0,163	0,026	-0,697	-0,060	-2,329	0,020	
Neunhaeuserer et al., 2017	-0,471	0,257	0,066	-0,974	0,032	-1,836	0,066	
Remígio et al., 2018	-0,604	0,222	0,049	-1,040	-0,169	-2,723	0,006	
Ibacache et al., 2019	-0,842	0,268	0,072	-1,368	-0,316	-3,136	0,002	
Auclair et al., 2020	-0,304	0,323	0,105	-0,938	0,330	-0,941	0,347	
	-0,539	0,086	0,007	-0,708	-0,369	-6,230	0,000	

I^2: 41,74; Tau^2: 0,048

b)

Study name	Statistics for each study							Std diff in means and 95% CI
	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value	
Browning et al., 2017	0,620	0,590	0,348	-0,537	1,777	1,050	0,294	
Onofre et al., 2017	0,000	0,577	0,333	-1,132	1,132	0,000	1,000	
Stegen et al., 2011	0,783	0,714	0,510	-0,616	2,182	1,097	0,273	
Bellicha et al., 2019	0,354	0,251	0,063	-0,138	0,846	1,410	0,159	
De Souza et al., 2010	0,775	0,256	0,065	0,274	1,276	3,030	0,002	
Auclair et al., 2020	0,719	0,463	0,214	-0,188	1,626	1,554	0,120	
Nedeljkovic et al., 2019	0,943	0,252	0,063	0,449	1,436	3,746	0,000	
Neunhaeuserer et al., 2017	1,028	0,411	0,169	0,223	1,833	2,502	0,012	
Remígio et al., 2018	1,029	0,436	0,190	0,174	1,884	2,360	0,018	
Wimmelmann et al., 2016	0,563	0,170	0,029	0,229	0,896	3,306	0,001	
Ibacache et al., 2019	0,548	0,369	0,137	-0,176	1,272	1,483	0,138	
	0,658	0,094	0,009	0,473	0,842	6,974	0,000	

I^2: 0; Tau^2: 0

FIGURE 2. Forest plot of absolute (a) and relative (b) $VO_{2max/peak}$ after bariatric surgery.

3.6 Meta-Regressions

According to the data obtained, those patients who suffered a more significant decrease in BMI after the surgery also had a greater loss of absolute $VO_{2max/peak}$ (correlation coefficient= 0.0537; $p< 0.001$). On the other hand, patients with higher BMI before BS had a more significant decrease in absolute $VO_{2max/peak}$ (correlation coefficient=-0.0123; $p< 0.001$).

Regarding $VO_{2max/peak}$ relative to body weight, the opposite occurred: those patients who showed most significant decrease in their BMI after bariatric surgery also showed a greater increase in $VO_{2max/peak}$ relative to body weight (correlation coefficient= -0.0742; $p< 0.001$). Similarly, patients with a higher BMI prior to BS shown a greater increase in $VO_{2max/peak}$ after surgery (correlation coefficient= 0.015; $p< 0.001$).

3.7 Sensitivity analysis and publication bias

No differences were observed in ES, the direction of effect, or *p*-values when each study was individually eliminated, and all analyses recalculated ($p< 0.001$ in all cases).

Furthermore, all studies were symmetrically located within the limits of the funnel plots, and no significance was observed in any case in the Egger test, suggesting no publication bias.

4. DISCUSSION

This systematic review and meta-analysis, examining the changes in CRF level in patients with obesity undergoing BS, provides a comprehensive qualitative and quantitative summary of the evidence to date, including in 17 studies (11 in the meta-analysis) comprising 3624 participants (312 in the meta-analysis). We did not find a sufficient number of studies investigating the medium and long-term changes in CRF level after BS. At the short term (up to 6 months), absolute $VO_{2max/peak}$ was reduced after surgery (ES=-0.539; 95%CI=-0.708, -0.369; $p< 0.001$), but increased when corrected for body weight (ES= 0.658; 95%CI= 0.473, 0.842; $p< 0.001$), being these changes related to the magnitude of weight loss.

Since CRF depends on the integrated function of the cardiovascular, pulmonary, and skeletal muscle systems,[65] the reduction in absolute $VO_{2max/peak}$ may be due to several factors. Many studies have previously reported that loss of lean body mass occurs with fat mass loss after BS.[34, 35, 66-70] This is especially true in the initial postsurgical period, where the decrease in body weight mainly corresponds to FFM loss, with a low effect on total adiposity.[71] That could explain the result observed in the meta-regression, suggesting that the more significant decrease in BMI, the greater reduction in postoperative $VO_{2max/peak}$. However, this postoperative reduction in muscle mass does not seem to affect mitochondrial function since $VO_{2max/peak}$ relative to FFM was maintained after BS in all studies that used indirect calorimetry, except for one in which it was increased.[59] Furthermore, an improvement in mitochondrial function has been described after BS.[72, 73]

It is essential to consider that postoperative loss of muscle mass leads to a reduction in energy expenditure. This loss of muscle mass, together with the substantial caloric restriction after BS (mainly in the first months), produces a global reduction in sympathetic activity,[74, 75] with implications regarding energy expenditure at rest as an adaptive response.[75, 76] This could limit exercise capacity by affecting the VO_2 achieved in a test. Furthermore, the positive impact that physical training after BS has shown on FFM and CRF[59, 77, 78] supports the idea that muscle mass decrease largely explains the reduction in absolute $VO_{2max/peak}$ observed after BS. Likewise, considering that physical activity is a main determinant of CRF,[17] the described lack of improvement in level of physical activity after bariatric surgery in the first 6 months,[79] could contribute to the observed reduction in absolute $VO_{2max/peak}$.

Also of note, in individuals with obesity the ability to increase minute ventilation during exercise is limited by excess body mass and increased mechanical load on the thorax, originating an altered ventilatory pattern where the respiratory rate is higher than expected to offset a diminished ability to increase tidal volume.[13] Meta-analyses showed a significant decrease in VE_{max} after BS, and in the two studies that showed an upward trend, this increase was achieved at a lower maximal workload, indicating a reduction in respiratory efficiency.

In addition, some studies have reported a reduction in hemoglobin after BS.[54, 80, 81] However, a decrease in absolute $VO_{2max/peak}$ was observed after BS even when participants had normal hemoglobin levels that did not change after BS.[36] Besides, it has been suggested that changes in hemoglobin explain only a small percentage of the variation in VO_{2max} in healthy subjects.[82] In contraposition, there are postoperative cardiovascular factors that could favor $VO_{2max/peak}$, such as an improvement in left ventricular systolic and diastolic function,[83, 84] and the consequently increase in ejection fraction,[85, 86] which could, in turn, improve the limited capacity to increase the cardiac output of subjects with obesity when performing physical exercise.[13] Additionally, GLP-1, a peptide that increases after bariatric intervention,[87-90] improves myocardial contractility,[91,92] which could influence the increase in stroke volume and thus oxygen transport and consumption during exercise testing. These physiological factors could counteract the adverse effects of a potential decrease in postoperative hemoglobin.

Meanwhile, O_2pulse_{max}, an index of stroke volume associated with oxygen extraction, was significantly reduced after BS. Therefore, considering the improvements in postsurgical cardiac function, it is likely that this reduction is more closely related to a peripheral muscle limitation. In addition, it has been reported that the postoperative reduction in the O_2 pulse disappears after it is adjusted for FFM.[33.] However, O_2 pulse adjusted for FFM was only reported in one of the studies of our review.[34]

Psychological factors could also, at least partially, explain our results.[93-95] Given that a $VO_{2max/peak}$ assessment is a performance test, after the surgery, the patients may be anxious or fearful to perform at the same intensity as they did previously, affecting the predominant energy system for ATP resynthesis during the test and consequently its respiratory quotient and $VO_{2max/peak}$.

Time to exhaustion, an indicator commonly used to assess exercise performance, significantly increased after BS. Therefore, it appears that these improvements in physical functioning are due more to a mechanical phenomenon attributable primarily to the weight loss achieved than to real improvements in CRF.

Unlike the absolute values, significant increase was observed when $VO_{2max/peak}$ was reported in relation to body weight. A recent systematic review and meta-analysis confirmed these results, showing additional improvement with postsurgical physical exercise, although the changes in absolute $VO_{2max/peak}$ were not reported.[96]

In the studies analyzed in the present review, patients' mean

$VO_{2max/peak}$ related to body weight before the BS was in the lower quintiles of CRF, which, in addition to the increased risk of death from any cause,[97] has also been linked to an increase in short-term complications after BS.[98] For this reason, an increase in CRF has been suggested before the intervention to reduce postoperative complications.[37] However, several decades ago, it was shown that the correction of the $VO_{2max/peak}$ per body weight is only valid in normal healthy adults, but a drift will be introduced in any deviating situation.[99] It may also be misleading when $VO_{2max/peak}$ is compared in particular situations where body weight changes occur due to factors such as diet, surgery, growth, training, or sickness. The increased $VO_{2max/peak}$ related to body weight observed after BS in the reviewed studies largely depends on body mass loss after surgery. Therefore, the composition of weight loss could be relevant in this context. As previously mentioned, after BS there is a significant loss of FFM. Although historically $VO_{2max/peak}$ has been adjusted according to body weight, it has been shown that the major influence of body weight on $VO_{2max/peak}$ is explained by FFM, leading to the recommendation that $VO_{2max/peak}$ should be expressed relative to FFM.[100]

Furthermore, adipose tissue consumes a relatively smaller amount of O_2 than muscle during exercise.[101] Moreover, previous research indicates that $VO_{2max/peak}$ normalized to lean body mass may improve prognostic.[13, 101] Unfortunately, we did not find sufficient studies that assessed body composition alongside CRF to perform the corresponding corrections. Thus, while we agree with the recommendation to report CRF in absolute and relative values (at least to body weight, but ideally to FFM),[13] caution is needed when interpreting the normalized values to body weight.

It is important to mention that different protocols and ergometers were used to assess $VO_{2max/peak}$, which should be considered when comparing results. The use of cycle ergometer has been usually suggested for CRF assessment in people with obesity,[101] but due to the use of a lower amount of muscle mass, the $VO_{2max/peak}$ measured with a cycle ergometer tends to be between 10% and 20% lower than that obtained on a treadmill.[101] However, since the pre- and post-surgical assessments are performed with the same ergometer, they do not influence the change in CRF. The subgroup analysis confirmed the decrease in absolute $VO_{2max/peak}$ and the increase in $VO_{2max/peak}$ relative to body weight after bariatric surgery regardless of the type of ergometer used.

We believe that this systematic review is the most comprehensive analysis of changes in $VO_{2max/peak}$ after BS. Some strengths of this study include: 1) the use of a pre-specified protocol registered on PROSPERO; 2) no restriction on populations, settings, or age among adults; 3) sensitive search strategy of the literature using multiple electronic databases with supplementary hand searching, following the PRISMA recommendations; 4) the use of the PEDro scale[42] and the scale by Newcastle-Ottawa Scale[44] to assess the quality of the selected studies; and 5) subgroups analyses on the type of exercise test used (cycle vs. treadmill) and meta-regression to investigate the effect of changes in BMI.

However, the following limitations should be considered. Firstly, we only know the impact of BS on CRF in the short-term. Four studies performed a medium-term follow-up (1–5 years), but only two of them reported absolute $VO_{2max/peak}$. No studies were found in the long term (5–10 years). Second, it was impossible to perform a subgroup analysis by BS technique, as some studies reported the results of the different surgical techniques together, and we could not contact the authors. Thirdly, most of the included studies did not provide assessments of body composition, which preclude any analysis of changes in FFM and its effect on $VO_{2max/peak}$.

Other weaknesses of the present review are the following: observational studies were included, as the main aim was to investigate the natural course of CRF after bariatric surgery; the methodological quality of the reviewed studies ranged between good and fair; most of the studies had sample sizes < 50 participants, some even below 10; finally, a potentially eligible study had to be excluded from the meta-analysis,[56] as the authors did not report the assessment of $VO_{2max/peak}$ at four months after surgery.

5. CONCLUSION

In conclusion, although BS has been shown to have many health benefits, in the short term, it appears to affect CRF negatively. This adverse effect could be mitigated by prescribing individualized and supervised exercise as a therapeutic complement, both before and after the surgery. Longer follow-up studies are necessary to confirm $VO_{2max/peak}$ adverse effect of BS. The combination of body composition and CRF assessments, including a higher number of participants and multiple time points, could provide a better understanding of the link between weight loss and changes in muscle mass and $VO_{2max/peak}$ in these patients.

ACKNOWLEDGMENTS

This work is part of a research project supported by the Spanish Ministry of Economy and Competitiveness (MINECO), Plan Nacional de I+D+i calls RETOS 2016 (reference DEP2016-74926-R). This

paper will be part of PhD thesis of Paulina Ibacache-Saavedra performed in the Medical Science Program of the University of Almería.

CONFLICT OF INTEREST

No conflict of interest statement.

AUTHOR CONTRIBUTION

All authors had full access to all of the data in the study and can take responsibility for its integrity and the accuracy of the data analysis. The study was conceived and designed by PI-S, EGA, MC-C, and DJ-M. PI-S drafted the manuscript with the support of EGA, MC-C, and AC-R. PI-S and CM-F extracted the data. MC-C, DJ-M, and AC-R assessed bias. DJ-M and AC-R performed the statistical analysis. All authors conducted a critical revision of the manuscript for important intellectual content.

SUPPORTING INFORMATION

CÓDIGO QR

REFERENCES

1. World Health Organization. Obesity and overweight, 2020. www.who.int/mediacentre/factsheets/fs311/en/. Accessed October 11, 2021.

2. Di Cesare M, Bentham J, Stevens GA, et al. Trends in adult body-mass index in 200 countries from 1975 to 2014: a pooled analysis of 1698 population-based measurement studies with 19·2 million participants. Lancet. 2016;387:1377–1396.

3. Finucane MM, Stevens GA, Cowan MJ, et al. National, regional, and global trends

in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9·1 million participants. Lancet. 2011;377:557–567.

4. Williams EP, Mesidor M, Winters K, Dubbert PM, Wyatt SB. Overweight and obesity: prevalence, consequences, and causes of a growing public health problem. Curr Obes Rep. 2015;4(3):363–370.
5. Schwartz AR, Patil SP, Laffan AM, Polotsky V, Schneider H, Smith PL. Obesity and obstructive sleep apnea: pathogenic mechanisms and therapeutic approaches. Proc Am Thorac Soc. 2008;5(2):185-192.
6. Mandviwala T, Khalid U, Deswal A. Obesity and cardiovascular disease: a risk factor or a risk marker? Curr Atheroscler Rep. 2016;18(5):21.
7. Pareek M, Bhatt DL, Schiavon CA, Schauer PR. Metabolic surgery for hypertension in patients with obesity. Circ Res. 2019;124(7): 1009–1024.
8. GBD 2015 Obesity Collaborators, Afshin A, Forouzanfar MH, et al. Health effects of overweight and obesity in 195 countries over 25 years. N Engl J Med. 2017;377:13–27.
9. Lavie CJ, De Schutter A, Parto P, et al. Obesity and prevalence of cardiovascular diseases and prognosis—the obesity paradox updated. Prog Cardiovasc Dis. 2016;58(5):537–547.

10. MacMahon S, Baigent C, Duffy S, et al. Body-mass index and cause-specific mortality in 900 000 adults: Collaborative analyses of 57 prospective studies. The Lancet. 2009;373(9669):1083-1096.

11. Fontaine K, Redden D, Wang C, et al. Years of life lost due to obesity. JAMA. 2003;289:187–193.

12. Kitahara CM, Flint AJ, Berrington de Gonzalez A, et al. Association between class III obesity (BMI of 40-59 kg/m^2) and mortality: a pooled analysis of 20 prospective studies. PLoS Med. 2014;11:e1001673.

13. Arena R, Cahalin LP. Evaluation of cardiorespiratory fitness and respiratory muscle function in the obese population. Prog Cardiovasc Dis 2014;56(4):457-464.

14. Tomlinson DJ, Erskine RM, Morse CI, Winwood K, Onambélé-Pearson G. The impact of obesity on skeletal muscle strength and structure through adolescence to old age. Biogerontology. 2016;17(3):467-483.

15. Ross R, Blair SN, Arena R, et al. Importance of assessing cardiorespiratory fitness in clinical practice: a case for fitness as a clinical vital sign: a scientific statement from the American Heart Association. Circulation. 2016;134(24):e653-99.

16. Caspersen CJ, Powell KE, Christenson GM. Physical activity, exercise, and physical fitness: definitions and distinctions for health-related research. Public Health Rep. 1985;100(2):126-131.

17. Lee DC, Artero EG, Sui X, Blair SN. Mortality trends in the general population: the importance of cardiorespiratory fitness. J Psychopharmacol. 2010;24(4_suppl):27-35.

18. Laukkanen JA, Zaccardi F, Khan H, Kurl S, Jae SY, Rauramaa R. Longterm change in cardiorespiratory fitness and all-cause mortality: a population- based follow-up study. Mayo Clin Proc. 2016;91(9):1183-1188.

19. Kodama S, Saito K, Tanaka S, et al. Cardiorespiratory fitness as a quantitative predictor of all-cause mortality and cardiovascular events in healthy men and women: a meta-analysis. JAMA. 2009;301(19):2024–2035.

20. Fogelholm M. Physical activity, fitness and fatness: relations to mortality, morbidity and disease risk factors. A systematic review. Obes Rev. 2010;11(3):202–221.

21. Montesi L, El Ghoch M, Brodosi L, Calugi S, Marchesini G, Dalle Grave R. Long-term weight loss maintenance for obesity: a multidisciplinary approach. Diabetes Metab Syndr Obes. 2016;9:37–46.

22. Lester EL, Padwal RS, Birch DW, et al. The real-world cost-effectiveness of bariatric surgery for the treatment of severe obesity: a cost–utility analysis. CMAJ open. 2021;9(2):E673-9. .

23. Alsumali A, Eguale T, Bairdain S, Samnaliev M. Cost-effectiveness analysis of bariatric surgery for morbid obesity. Obes surg. 2018;28(8):2203-14.

24. Mechanick JI, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient 2013 update: cosponsored by American Association of Clinical Endocrinologists, The Obesity Society, and American Society for Metabolic & Bariatric Surgery. Endocr Pract. 2013;19(2):337-372.

25. Sjöström L, Peltonen M, Jacobson P, et al. Bariatric surgery and long-term cardiovascular events. JAMA. 2012;307(1):56-65.

26. Angrisani L, Santonicola A, Iovino P, et al. IFSO Worldwide Survey 2016: primary, endoluminal, and revisional procedures. Obes Surg. 2018;28(12):3783–3794.

27. Welbourn R, Hollyman M, Kinsman R, et al. Bariatric surgery worldwide: baseline demographic description and one-year outcomes from the fourth IFSO global registry report 2018. Obes surg. 2019;29(3):782-795.

28. Jakobsen GS, Småstuen MC, Sandbu R, et al. Association of bariatric surgery vs medical obesity treatment with long-term medical complications and obesity-related comorbidities. JAMA. 2018;319(3):291–301.

29. Nguyen NT, Varela JE. Bariatric surgery for obesity and metabolic disorders: state of the art. Nat Rev Gastroenterol Hepatol. 2017;14(3):160–169.

30. Yu J, Zhou X, Li L, et al. The long-term effects of bariatric surgery for type 2

diabetes: systematic review and meta-analysis of randomized and non-randomized evidence. Obes Surg. 2015;25(1):143–158.

31. Bower G, Toma T, Harling L, et al. Bariatric surgery and nonalcoholic fatty liver disease: a systematic review of liver biochemistry and histology. Obes Surg. 2015;25(12):2280–2289.

32. De Souza SA, Faintuch J, Sant'Anna AF. Effect of weight loss on aerobic capacity in patients with severe obesity before and after bariatric surgery. Obes Surg. 2010;20(7):871-875.

33. Serés L, Lopez-Ayerbe J, Coll R, et al. Increased exercise capacity after surgically induced weight loss in morbid obesity. Obesity. 2006;14(2):273-279.

34. Browning MG, Franco RL, Herrick JE, Arrowood JA, Evans RK. Assessment of cardiopulmonary responses to treadmill walking following gastric bypass surgery. Obes Surg. 2017;27(1):96-101.

35. Stegen S, Derave W, Calders P, Van Laethem C, Pattyn P. Physical fitness in morbidly obese patients: effect of gastric bypass surgery and exercise training. Obes Surg. 2011;21(1):61-70.

36. Neunhaeuserer D, Gasperetti A, Savalla F, et al. Functional evaluation in obese patients before and after sleeve gastrectomy. Obes Surg. 2017;27(12):3230-3239.

37. McCullough PA, GallagherMJ, Dejong AT, et

al. Cardiorespiratory fitness and short-term complications after bariatric surgery. Chest. 2006;130(2):517–525.

38. Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Int J Surg. 2010;8(5):336-341.

39. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Cochrane. 2011.

40. Horsley T, Dingwall O, Sampson M. Checking reference lists to find additional studies for systematic reviews. Cochrane Database of Systematic Reviews. 2011(8).

41. Verhagen A, De Vet H, De Bie RA, et al. The Delphi list: A criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. J Clin Epidemiol. 1998;51(12):1235-1241.

42. de Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. Aust J Physiother. 2009;55:129–133.

43. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. Phys Ther. 2003;83(8):713-721.

44. Wells G, Shea B, O'Connell D, et al. The Newcastle-Ottawa scale (NOS) for assessing the quality of nonrandomised studies in meta-analysis.

http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed October 11, 2021.

45. Cohen J. A power primer. Psychological bulletin. 1992;112(1):155.
46. DerSimonian R, Laird N. Meta-analysis in clinical trials. Controlled clinical trials. 1986;7(3):177-188.
47. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ. 2011;343(7829).
48. Irwig L, Macaskill P, Berry G, Glasziou P. Bias in meta-analysis detected by a simple, graphical test. Graphical test is itself biased. BMJ. 1998;316(7129):1-11.
49. Sterne JAC, Gavaghan D, Egger M. Publication and related bias in meta-analysis: Power of statistical tests and prevalence in the literature. J Clin Epidemiol. 2000;53(11):1119-1129.
50. Berkey CS, Hoaglin DC, Mosteller F, Colditz GA. A random-effects regression model for meta-analysis. Statistics in medicine. 1995;14(4):395-411.
51. Tettero OM, Aronson T, Wolf RJ, Nuijten MA, Hopman MT, Janssen IM. Increase in physical activity after bariatric surgery demonstrates improvement in weight loss and cardiorespiratory fitness. Obes Surg. 2018;28(12):3950-3957.
52. Mundbjerg LH, Stolberg CR, Bladbjerg EM, Funch-Jensen P, Juhl CB, Gram B. Effects of 6 months supervised physical training on muscle strength and aerobic capacity in

patients undergoing Roux-en-Y gastric bypass surgery: a randomized controlled trial. Clin Obes. 2018;8(4):227-235.

53. Wilms B, Ernst B, Thurnheer M, Weisser B, Schultes B. Differential changes in exercise performance after massive weight loss induced by bariatric surgery. Obes Surg. 2013;23(3):365-371.
54. Dereppe H, Forton K, Pauwen NY, Faoro V. Impact of bariatric surgery on women aerobic exercise capacity. Obes Surg. 2019;29(10):3316-3323.
55. Neunhaeuserer D, Francesco S, Andrea G, et al. Cardiorespiratory function and VO2 kinetics after sleeve gastrectomy: a follow-up analysis. Intern Emerg Med. 2020;15(7):1201-1205.
56. Lund MT, Hansen M, Wimmelmann CL, et al Increased post-operative cardiopulmonary fitness in gastric bypass patients is explained by weight loss. Scand J Med Sci Sports. 2016;26(12):1428-1434.
57. Onofre T, Carlos R, Oliver N, et al. Effects of a physical activity program on cardiorespiratory fitness and pulmonary function in obese women after bariatric surgery: a pilot study. Obes Surg. 2017;27(8):2026-2033.
58. Ibacache P, Cano-Cappellacci MA, Fuentes CM, Montero JR, Pinuer PM, Mercadino AB. Physical fitness and physical activity in women with obesity: short term effects of sleeve gastrectomy. Nutr Hosp. 2019;36(4):840-845.

59. Auclair A, Harvey J, Leclerc J, et al. Determinants of Cardiorespiratory Fitness After Bariatric Surgery: Insights From a Randomised Controlled Trial of a Supervised Training Program. Can J Cardiol. 2021;37(2):251-259.

60. Wimmelmann CL, Lund MT, Hansen M, Dela F, Mortensen EL. The effect of preoperative type 2 diabetes and physical fitness on mental health and health-related quality of life after Roux-en-Y gastric bypass. J Obes. 2016;2016.

61. Mahawar KK. Defining short-term, medium-term, long-term, and very long-term follow-up after bariatric surgery. Obes Surg. 2018;28(5):1425-1426.

62. Bellicha A, Ciangura C, Roda C, Torcivia A, Portero P, Oppert JM. Changes in cardiorespiratory fitness after gastric bypass: relations with accelerometry-assessed physical activity. Obes Surg. 2019;29(9):2936-2941.

63. Nedeljkovic-Arsenovic O, Banovic M, Radenkovic D, et al. The amount of weight loss six months after bariatric surgery: It makes a difference. Obes Facts. 2019;12(3):281-290.

64. Remígio MI, Santa Cruz F, Ferraz Á, et al. The impact of bariatric surgery on cardiopulmonary function: analyzing VO2 recovery kinetics. Obes Surg. 2018;28(12):4039-4044.

65. Arena R, Myers J, Guazzi M. The future of aerobic exercise testing in clinical practice: is it the ultimate

vital sign?. Future Cardiol. 2010;6(3):325-342.

66. Chaston TB, Dixon JB, O'Brien PE. Changes in fat-free mass during significant weight loss: a systematic review. Int J Obes. 2007;31(5):743-750.
67. Carnero EA, Dubis GS, Hames KC, et al. Randomized trial reveals that physical activity and energy expenditure are associated with weight and body composition after RYGB. Obesity. 2017;25(7):1206–1216.
68. Zalesin KC, Franklin BA, Lillystone MA, et al. Differential loss of fat and lean mass in the morbidly obese after bariatric surgery. Metab Syndr Relat Disord. 2010;8(1):15-20.
69. Santarpia L, Contaldo F, Pasanisi F. Body composition changes after weight-loss interventions for overweight and obesity. Clinical Nutrition. 2013;32(2):157-161.
70. Ciangura C, Bouillot JL, Lloret-Linares C, et al. Dynamics of change in total and regional body composition after gastric bypass in obese patients. Obesity. 2010;18(4):760-765.
71. Frühbeck G. Bariatric and metabolic surgery: a shift in eligibility and success criteria. Nat Rev Endocrinol. 2015;11(8):465.
72. Vijgen GH, Bouvy ND, Hoeks J, Wijers S, Schrauwen P, van Marken Lichtenbelt WD. Impaired skeletal muscle mitochondrial function in morbidly obese patients is normalized one year after bariatric surgery. Surg

Obes Relat Dis. 2013;9(6):936-941.

73. Nijhawan S, Richards W, O'Hea MF, Audia JP, Alvarez DF. Bariatric surgery rapidly improves mitochondrial respiration in morbidly obese patients. Surg Endosc. 2013;27(12):4569-4573.
74. Straznicky NE, Lambert EA, Lambert GW, et al. Effects of dietary weight loss on sympathetic activity and cardiac risk factors associated with the metabolic syndrome. J Clin Endocrinol Metab. 2005;90(11):5998–6005.
75. Rosenbaum M, Hirsch J, Murphy E, et al. Effects of changes in body weight on carbohydratemetabolism, catecholamine excretion, and thyroid function. Am J Clin Nutr. 2000;71(6):1421–1432.
76. Bettini S, Bordigato E, Fabris R, et al. Modifications of resting energy expenditure after sleeve gastrectomy. Obes Surg. 2018;28(8):2481–2486.
77. Shah M, Snell PG, Rao S, et al. High-volume exercise program in obese bariatric surgery patients: a randomized, controlled trial. Obesity. 2011;19(9):1826-1834.
78. Hassannejad A, Khalaj A, Mansournia MA, Tabesh MR, Alizadeh Z. The effect of aerobic or aerobic-strength exercise on body composition and functional capacity in patients with BMI≥ 35 after bariatric surgery: a randomized control trial. Obes Surg. 2017;27(11):2792-2801.
79. Adil MT, Jain V, Rashid F, et al. Meta-analysis of the

effect of bariatric surgery on physical activity. Surg Obes Relat Dis. 2019;15(9):1620-31.

80. Aarts, E. O., Janssen, I. M., & Berends, F. J. (2011). The gastric sleeve: losing weight as fast as micronutrients? Obes Surg. 21(2), 207-211.

81. von Drygalski A, Andris DA, Nuttleman PR, Jackson S, Klein J, Wallace JR. Anemia after bariatric surgery cannot be explained by iron deficiency alone: results of a large cohort study. Surg Obes Relat Dis. 2011;7(2):151-156.

82. Saunders PU, Garvican-Lewis LA, Schmidt WF, Gore CJ. Relationship between changes in haemoglobin mass and maximal oxygen uptake after hypoxic exposure. Br J Sports Med. 2013;47(Suppl 1):i26-30.

83. Leung M, Xie M, Durmush E, et al. Weight loss with sleeve gastrectomy in obese type 2 diabetes mellitus: impact on cardiac function. Obes Surg. 2016;26(2):321–326.

84. Kanoupakis E, Michaloudis D, Fraidakis O, Parthenakis F, Vardas P, Melissas J. Left ventricular function and cardiopulmonary performance following surgical treatment of morbid obesity. Obes Surg. 2001;11(5):552-558.

85. Valezi AC, Machado VH. Morphofunctional evaluation of the heart of obese patients before and after bariatric surgery. Obes Surg. 2011;21(11):1693-1697.

86. Kokkinos A, Alexiadou K, Liaskos C, et al. Improvement in cardiovascular indices after Roux-en-Y gastric bypass or

sleeve gastrectomy for morbid obesity. Obes Surg. 2013;23(1):31-38.

87. Laferrère B, Heshka S, Wang K, et al. Incretin levels and effect are markedly enhanced 1 month after Roux-en-Y gastric bypass surgery in obese patients with type 2 diabetes. Diabetes care. 2007;30(7):1709-1716.

88. Jørgensen NB, Dirksen C, Bojsen-Møller KN, et al. Exaggerated glucagon-like peptide 1 response is important for improved β-cell function and glucose tolerance after Roux-en-Y gastric bypass in patients with type 2 diabetes. Diabetes. 2013;62(9):3044-3052.

89. Shah M, Law JH, Micheletto F, et al. Contribution of endogenous glucagon-like peptide 1 to glucose metabolism after Roux-en-Y gastric bypass. Diabetes. 2014;63(2):483-493.

90. Meek CL, Lewis HB, Reimann F, Gribble FM, Park AJ. The effect of bariatric surgery on gastrointestinal and pancreatic peptide hormones. Peptides. 2016;77:28-37.

91. Poornima I, Brown SB, Bhashyam S, Parikh P, Bolukoglu H, Shannon RP. Chronic glucagon-like peptide-1 infusion sustains left ventricular systolic function and prolongs survival in the spontaneously hypertensive, heart failure–prone rat. Circ Heart Fail. 2008;1(3):153-160.

92. Fields AV, Patterson B, Karnik AA, Shannon RP. Glucagon-like peptide-1 and myocardial protection:

more than glycemic control. Clin Cardiol. 2009;32(5):236-243.

93. De Zwaan M, Enderle J, Wagner S, et al. Anxiety and depression in bariatric surgery patients: a prospective, follow-up study using structured clinical interviews. J Affect Disord. 2011;133(1-2):61-68.

94. Smits JA, Tart CD, Presnell K, Rosenfield D, Otto MW. Identifying potential barriers to physical activity adherence: Anxiety sensitivity and body mass as predictors of fear during exercise. Cogn Behav Ther. 2010;39(1):28-36.

95. Kalarchian MA, Marcus MD, Levine MD, et al. Psychiatric disorders among bariatric surgery candidates: relationship to obesity and functional health status. Am J Psychiatry. 2007;164(2):328-334.

96. Bellicha A, van Baak MA, Battista F, et al. Effect of exercise training before and after bariatric surgery: A systematic review and meta-analysis. Obes Rev. 2021:e13296.

97. Myers J, Prakash M, Froelicher V, Do D, Partington S, Atwood JE. Exercise capacity and mortality among men referred for exercise testing. N Engl J Med. 2002;346(11):793-801.

98. Balady GJ, Arena R, Sietsema K, et al. Clinician's guide to cardiopulmonary exercise testing in adults: a scientific statement from the American Heart Association. Circulation. 2010;122(2):191-225.

99. Tanner JM. Fallacy of per-weight and per-surface

area standards, and their relation to spurious correlation. J Appl Physiol. 1949;2(1):1-5.

100. Goran M, Fields DA, Hunter GR, Herd SL, Weinsier RL. Total body fat does not influence maximal aerobic capacity. International journal of obesity. 2000;24(7):841-848.

101. Forman DE, Myers J, Lavie CJ, Guazzi M, Celli B, Arena R. Cardiopulmonary exercise testing: relevant but underused. Postgrad Med. 2010;122(6):68-86.

Sección 1

Estudio 4

Effects of bariatric surgery on muscle strength and quality: A systematic review and meta-analysis

Draft

Paulina Ibacache-Saavedra, Elena Martínez-Rosales, Daniel Jerez-Mayorga, Claudia Miranda-Fuentes, Enrique G. Artero, Marcelo Cano-Cappellacci

SUMMARY

The increasing prevalence of obesity is a major health burden worldwide. Although bariatric surgery (BS) is recognized as an effective strategy for weight loss and comorbidities improvement, its impact on muscle strength (MS) and quality (MQ) is still unclear. We aimed to examine postoperative changes in MS and MQ and their relationship with body mass index (BMI) changes among adults undergoing BS. To this end, we systematically searched the WoS, PubMed, EBSCO, and Scopus databases. The meta-analyses, which included 16 articles with a total of 421 participants (observational and intervention studies), showed that BS reduces absolute lower-limb isometric strength in the short-term (ES=-0.599; 95% CI=0.972, -0.226; p=0.002). Moreover, subjects who experienced a more significant reduction in BMI after BS also suffered a higher loss of absolute MS. However, MS relative to body weight did not change significantly after surgery. We found insufficient studies investigating medium- and long-term changes in MS/MQ after BS. This study provides moderate-quality evidence that BS-induced weight loss can reduce the strength of the antigravity muscles in the short-term, which should be addressed in managing these subjects. More high-quality studies are needed to evaluate the impact of BS on MS and the different dimensions of MQ in the short-, medium- and long-term. This review was registered on PROSPERO (CRD42022332581).

1. INTRODUCTION

The increasing prevalence of obesity is a major health burden worldwide,[1] as it has been associated with several diseases such as type 2 diabetes mellitus, fatty liver disease, musculoskeletal disorders, sleep apnea, depression, some cancers, and cardiovascular diseases.[2,3] Consequently, the life expectancy of people with obesity is reduced, on average, between 5 and 20 years, depending on the severity of the condition and comorbidities.[3]

A greater amount of adipose tissue is often accompanied by sarcopenia (low skeletal muscle mass/function), a condition known as sarcopenic obesity, the prevalence of which is rapidly increasing among adults worldwide.[4] Furthermore, a link between visceral obesity and loss of skeletal muscle mass has been reported.[5] Thus, obesity and sarcopenia can act in a synergic way, and sarcopenic obesity may further increase the risk of metabolic disorders, cardiovascular disease, and mortality than obesity alone.[4]

In contrast, higher muscle strength (MS) levels may mitigate the increased risk of death associated with obesity.[6] MS is an important component of health-related fitness, as it is recognized as a strong determinant of morbidity and mortality.[7,8] However, muscle quality (MQ) is a broader concept that involves aspects such as anatomic structure, metabolic, and mechanical performance of the muscles,[9] including dimensions like muscle composition and ultrastructure.[10] As the generation of MS is the most prominent feature within the various functions of skeletal muscle,[11] MQ has been habitually expressed as MS per unit of muscle mass ratio,[12] determined, among others, by magnetic resonance imaging, dual-energy x-ray absorptiometry, or computed tomography.[9,10] Traditionally, the focus for improving MS has been on increasing muscle mass; however, a recent review has highlighted the need to consider muscle quality to improve its function.[12]

MQ is a valuable functional assessment, as two individuals with similar muscle mass may not be able to produce equivalent levels of MS. In fact, adults with obesity may have greater muscle mass and absolute MS levels than people with normal weight, nevertheless they are less effective in producing strength relative to their muscle mass; that is, they have lower MQ.[13,14]

Bariatric surgery (BS) is the most cost-effective treatment for subjects with class II and III obesity.[15] It induces more significant weight loss than non-surgical management,[16] improves obesity-related comorbidities and reduces mortality.[17]

Despite the previously described efficacy of BS,[17] its impact on MS-MQ remains unclear, with contradictory results published.[18-20] Considering that both MS and MQ are relevant for their predictive value for health and life expectancy,[6-8,21,22] and that low MS-MQ may increase short-term postoperative complications of BS,[23-25] a description of the impact of BS on these health markers is relevant for achieving the best clinical decisions.[26,27]

This systematic review and meta-analysis aims to analyze the evidence of postoperative changes in MS and MQ (and their relationship with body mass index [BMI] changes) among adults with obesity undergoing BS, according to different muscle groups and MS/MQ tests used.

2. METHODS

2.1 Study reporting and protocol registration

This systematic review and meta-analysis was registered in PROSPERO (ID CRD42022332581). The PRISMA statement and checklist,[28] (Table S1), together with the Cochrane Handbook for Systematic Reviews of Interventions,[29] were strictly followed in the design and implementation of this study.

2.2 Data sources and searches

A systematic electronic search was conducted for articles published in the Web of Science, PubMed, EBSCO, and Scopus databases with a deadline of May 31, 2022. The search strategy consisted of two blocks of search terms (Table 1). The Rayyan software program was used to remove duplicate references before the screening.[30]

2.3 Study selection and screening criteria

The systematic search was performed by two of the authors (DJ-M and PI-S). The titles and abstracts of studies retrieved using the search strategy were subsequently assessed and screened independently and simultaneously by four reviewers (CM-F, EM-R, MC-C, and PI-S) to identify studies that potentially met the selection criteria. The full text of these potentially eligible studies was assessed for eligibility by two review team members (PI-S and EM-R). Disagreements were resolved by a third reviewer (MC-C).

Studies in adults with obesity describing the effect of BS on MS and/or MQ in upper and/or lower limbs were included. There were no restrictions on the - post-surgical follow-up duration or the number of -follow-up measurements performed. Both observational and intervention studies (randomized and nonrandomized controlled trials) were included. Studies were excluded if: (a) did not report the MS / MQ outcome before and after surgery; (b) were not written in English or Spanish; (c) study participants were animals; (d) participants were under 18 years of age or over 65; (e) used non-laparoscopic bariatric surgeries; (f) more than 30% of the sample corresponded to revisional bariatric surgeries; (g) included participants with serious illnesses such as heart failure, COPD or ESRD; (h) retracted; (i) duplicates; and (j) not eligible publications (i.e., reviews, guidelines, or case studies).

Table 1. Search strategy.

Bariatric Surgery		Strength / muscle quality
"bariatric surgery" OR "gastric bypass" OR "gastroplasty" OR "metabolic surgery" OR "obesity surgery" OR "roux-en-y" OR "sleeve gastrectomy" OR "gastric banding" OR "one anastomosis gastric bypass" OR "minigastric bypass" OR "gastric band" OR "biliopancreatic diversion"	AND	"muscle strength" OR "relative strength" OR “muscle force” OR "relative force" OR “muscle power" OR "strength" OR "muscle quality" OR "skeletal muscle quality" OR "muscle quality index" OR "muscle function" OR "muscular strength" OR "muscular force" OR "muscular power" OR "muscular quality" OR "muscle architecture" OR "muscle composition" OR "myosteatosis"

2.4 Data selection

Two authors (PI-S and MC-C) independently performed data extraction using a standardized data extraction form, and discrepancies were resolved by discussion with a third author (EGA). The following data were extracted: (a) author; (b) year; (c) country; (d) study design; (e) BS technique; (f) participants' characteristics; (g) pre- and post-surgery anthropometric characteristics; (h) pre- and post-surgery MS and/or MQ; (i) assessment technique of MS and/or MQ; (j) muscle group(s) tested; and (k) follow-up time-point. As necessary, we contacted the authors of included studies to clarify any relevant information or request additional data.

2.5 Quality assessment

The PEDro scale, based on the Delphi scale, was used to assess the quality of the selected RCT.[31] This scale comprises 11 items answered “yes” or “no” (item 1 is not considered when calculating total scores), meaning that each article was scored from 0 to 10.[32] The selected articles were then categorized as poor (< 4 points), fair (4–5 points), good (6–8 points), or excellent (9–10 points).[32,33]

The reporting quality of the remaining studies was assessed using the “Quality Assessment Tool for Before-After (Pre-Post) Studies with No Control Group”, developed by NHLBI. This tool has 12 items that can be answered with “yes”, “no” or “other” (cannot be determined, not applicable, or not reported). These comprise the risk for different types of bias, such as selection, reporting, or observer bias.[34]

Two investigators (CM-F and EM-R) independently assessed the selected studies' quality. Disagreements were resolved through discussion with a third author (MC-C).

2.6 Statistical analysis

The comprehensive Meta-Analysis 2.0 software (Biostat Inc., USA) was used to perform the principal statistical analysis as well as all sensitivity analyses. The analyzed variables were absolute upper-limb isometric strength (handgrip), absolute upper-limb dynamic strength (one-repetition maximum [1RM]), absolute lower-limb isometric strength, relative (to body weight) lower-limb isometric strength, and absolute lower-limb dynamic strength (1RM). The effect size (ES) was calculated using the standardized mean difference of the change in the mentioned variables (pre-to post-surgery) and the Cohen's D estimator, interpreted as small (0.2), medium (0.5), and large (0.8) ES.[35] Random-effects meta-analysis using the DerSimonian–Laird method was used, and the 95% confidence intervals were also calculated (95% CI).[36] Two-sided p≤ 0.05 was set as the significance level.

The I^2 statistic assessed heterogeneity between the studies included in the forest plots.[37] Funnel plots and the Egger test were performed to assess publication bias.[38] In the case of the Egger test, p≤ 0.1 was used as the significance level.[39] A sensitivity analysis was performed, recalculating all analyses by removing each selected study one by one.

Finally, through a random-effects regression model for meta-analysis,[40] we investigated: (I) the influence of preoperative obesity level (BMI) on the magnitude of MS/MQ changes; and (II) the impact of pre-to post-surgery BMI change on the magnitude of MS/MQ changes.

3. RESULTS

A total of 1706 records were initially identified (Web of Science 358, PubMed 329, EBSCO 572, and Scopus 447). After eliminating duplicates, 663 records remained. Initial screening based on titles and abstracts excluded 580 articles, while 83 remained for further evaluation. Of these, 55 were excluded in the subsequent detailed assessments, and 28 finally met the selection criteria for the systematic review (Figure 1).

From the studies selected for the systematic review, seven were not included in the meta-analysis due to: (i) incomplete data (n=3),[41-43] (ii) expressed in measures were either not reported or could not be converted to mean and standard deviation (n=2),[44,45] (iii) a later postoperative assessment of handgrip strength (n=1),[46] (iv) and the only study using isokinetic testing (n=1).[47] Furthermore, the five studies that reported muscle composition were not incorporated into the meta-analysis due to the heterogeneity in the assessment methodologies used.[48-52]

For 16 of the selected studies, the authors were contacted to clarify relevant information or to provide additional data. Answers were obtained in 63% of the cases.[18,20,45,50-56]

Most of the selected studies performed short-term post-surgical evaluations (i.e., between one and 12 months after BS), except for two publications that followed participants up to two[56] and nine years[57] post-surgery. Therefore, analyses of the changes in MS/ MQ in the medium or long term[58] were not possible as there were insufficient studies.

3.1 Study characteristics

The systematic review included 13 observational studies, eight nonrandomized controlled trials, and seven RCTs (one study[47] performed a subgroup analysis of participants from an RCT), comprising 697 subjects. Participants' mean age ranged from 33 to 49 years; most were female (77.5%) (Table 2).

The studies covered various BS techniques: Roux-en-Y gastric bypass (13 studies[18,20,42,44,46,49,50,52,54,56,57,59,60]) and sleeve gastrectomy (four studies[45,61-63]), the most frequently used. Besides, seven studies presented results covering either gastric bypass or sleeve gastrectomy,[19,43,47,55,64-66] while the remainder used biliopancreatic diversion or duodenal switch.[41,48,51,53]

All the included studies used BMI to assess obesity and its evolution after surgery, with nine studies additionally using waist circumference to measure central obesity.[41,46-48,53,59,60,62,66]

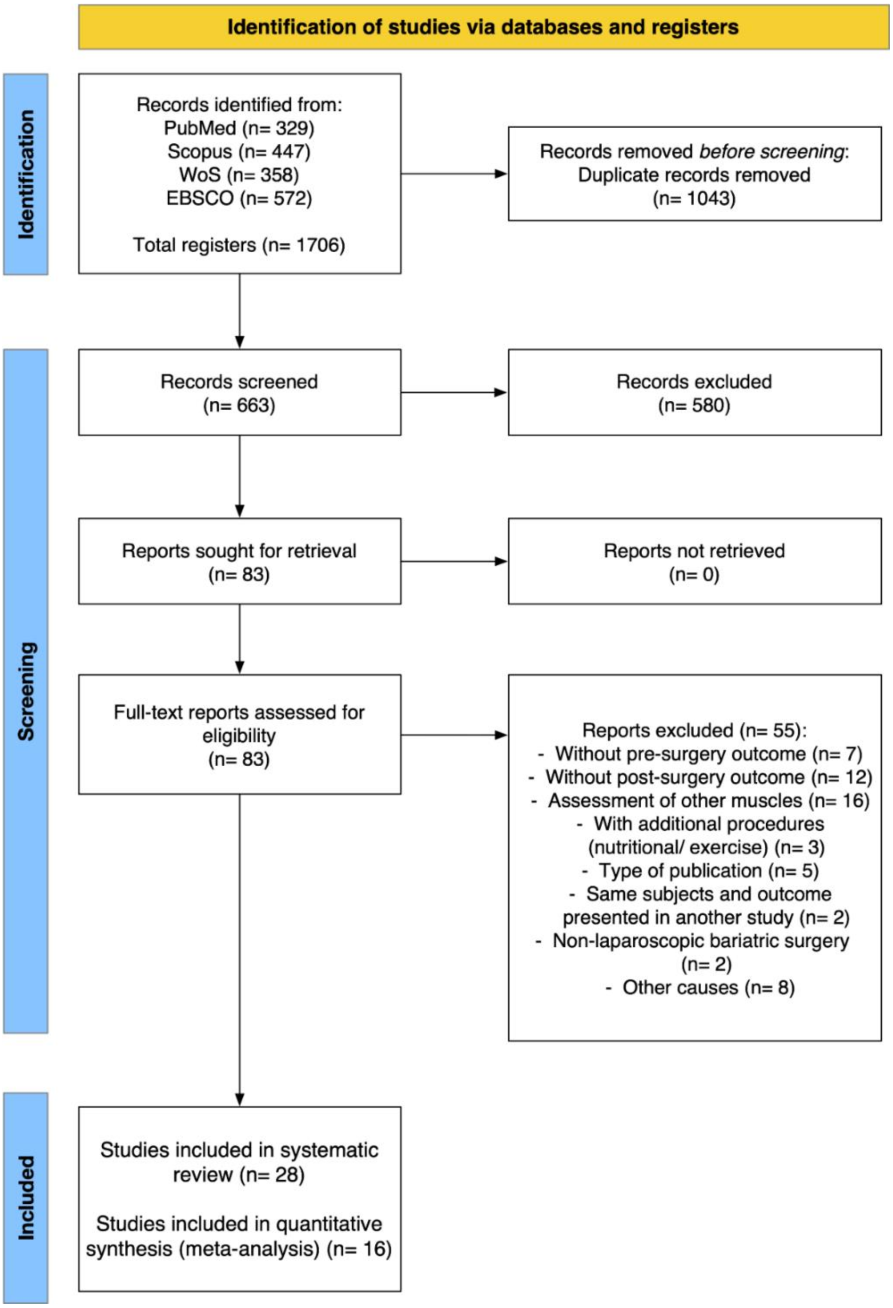


Figure 1. Flow diagram of study selection according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement[30]

3.2 Muscle strength/ quality outcomes

Most studies reported absolute handgrip strength (14 studies, 50%), followed by absolute isometric lower-limb strength (seven studies, 25%) and absolute dynamic lower-limb strength (six studies, 21%). Indeed, the most commonly used assessments were dynamometry and 1RM. The most reported dimension of muscle quality was MS relative to body weight (eight studies),[20,41,44,47,53,54,59,62] followed by muscle composition (five studies),[48-52] while only three articles presented MS relative to lean mass (LM).[42,44,66] Computed tomography scans were principally used to assess muscle composition.[49,51,52]

The absolute upper-limb isometric strength showed different results, reporting a decrease[42-45,53,56,57,60,62] or no changes.[19,46,56,61,63-66] In contrast, six of the seven studies that showed absolute lower-limb isometric strength reported a decrease after surgery,[41,53,54,56,59,62] while the other study did not show any change[66] (Table 3).

Absolute dynamic muscular strength showed mixed results. In upper limbs, it decreased[44,60] or did not change[18,55] after BS; similarly, in lower limbs, most studies reported a decreased,[20,44,47,60] followed by two studies showing no change after surgery.[60,63] Only one study reported an increase in absolute dynamic strength after BS in upper (bench press 12 months post-BS) and lower limbs (angle leg press and seat leg curls 12 months post-BS)[18] (Table 3).

The studies that reported strength relative to body weight showed an increase after surgery in all studies that performed isometric[53,62] or dynamic testing[44] of the upper limbs. Lower-limb strength relative to body weight presented different results when an isometric evaluation was carried out, showing an increase[41,53,54] or no changes after BS.[54,59,62] When a dynamic strength test was performed, lower-limb strength relative to body weight increased[44,47] or decreased[20] (Table 3).

The isometric strength of the upper and lower limbs increased after surgery when expressing MS in relation to LM.[42,66] In contrast, dynamic upper- and lower-limb strength relative to LM showed no change in the only study that reported it[44] (Table 3).

Regarding muscle composition, reductions in absolute muscle fat content were reported after surgery in all studies that evaluated it.[48-52] In contrast, lipid concentration in skeletal muscle increased after BS in all studies,[50-52] except for Auclair et al. at 12 months after the surgery[51] (Table S2).

On the other hand, five studies assessed lower-limb functional capacity through the sit-to-stand test,[50,55,56,59,60] showing a significant improvement after surgery in three of them.[55,56,59]

Finally, the only study that evaluated changes in muscle ultrastructure after BS showed that the cross-sectional area of type I and type II fibers and the type I muscle fiber myonuclei content were reduced after BS.[20]

3.3 Methodological quality

The methodological quality of the RCT evaluated with the PEDro scale ranged between excellent and fair. Scores ranged from 4 to 9, with an average score of 5.9. Deficiencies were mainly observed in the lack of blinding of participants, therapists, and assessors who measured at least one key outcome (Table S3). It must be acknowledged that in these types of intervention (surgery/exercise), it is not possible to blind participants or therapists.

The average score of the NHLBI scale used in the remaining studies was 5.9, ranging between 3 and 9. More than half of the studies evaluated met at least 55% of the criteria. The most frequent deficiencies observed using the NHLBI scale were the lack of blinding of participants' exposures/interventions and that the participants were not representative of those who would be eligible for the intervention in the clinical population of interest (Table S4).

3.4 Meta-analyses

Meta-analysis showed a significant decrease in absolute lower-limb isometric strength at 3-12 months after BS with a medium ES (ES= -0.599; 95% CI= 0.972, -0.226; p= 0.002) (Figure 2B). Similarly, absolute lower-limb dynamic strength at 2-6 months showed a significant decrease, although with a small ES (ES= -0.255; 95% CI= -0.476,-0.035; p= 0.023) (Figure 3B). High and significant heterogeneity was observed across studies, with I^2= 74% (p= 0.002) in the absolute lower-limb isometric strength (Figure 2B) and I^2= 81% (p= 0.571) in the absolute lower-limb dynamic strength (Figure 3B).

In contrast, absolute handgrip strength at 3-6 months (ES=-0.220; 95% CI= -0.480, 0.041; p= 0.098) (Figure 2A), absolute upper-limb dynamic strength at 2-4 months (ES=-0.272; 95% CI=-0.738, 0.194; p= 0.252) (Figure 3A), and relative (to body weight) lower-limb isometric strength at 3-12 months (ES= 0.221; 95% CI=-0.020, 0.463; p= 0.073) (Figure 2C) did not show significant change after BS.

Table 2. Characteristics of studies included in the systematic review (n=28).

Author, year	Country	Study design	Sample size (male/ female)	Age±SD (years)	BS technique	Follow-up time-point (months)	Strength or dimension(s) of muscle quality	Type(s) of evaluation
Alba et al., 2019[42]	USA	OS	47 (10/37)	45±12	RYGB	6 and 12	Absolute and relative muscle strength (to BMI and appendicular LM).	Isometric strength: handgrip dynamometry. DXA.
Auclair et al., 2020[51]	Canada	NRCT	40 (10/30)	44±11	BPD/DS	6 and 12	Muscle composition.	Computed tomography scan in midthigh: low-density muscle (fat-infiltrated muscle) and normal-density muscle areas.
Campanha-Versiani et al., 2017[18]	Brazil	NRCT	19 (5/14)	35.7±12.5	RYGB	2, 9 and 12	Absolute muscle strength.	Dynamic strength: 10RM test (leg press, seat leg curls, bench press, and posterior shoulders).
Cole et al., 2017[57]	USA	OS	5 (0/5)	47.2±10.9	RYGB	1.5, 6 and 12 mo. 9 yr	Absolute muscle strength.	Isometric strength: handgrip dynamometry.
Coral et al., 2021[19]	Brazil	OS	62 (10/52)	38.4±10.8	SG/RYGB	6	Absolute muscle strength.	Isometric strength: handgrip dynamometry.
Diniz-Sousa et al., 2021[47]	Portugal	RCT	15 (3/12)	45.1±10.6	SG/RYGB	6	Absolute and relative muscle strength (to body weight).	Dynamic strength: Isokinetic dynamometry [60 degrees/s] (knee extension)

Gallart-Aragón et al., 2017[61]	Spain	OS	72 (25/47)	45.4±9.4	SG	1 and 6	Absolute muscle strength.	Isometric strength: handgrip dynamometry.
Gil et al., 2021[20]	Brazil	RCT	40 (0/40)	42±8	RYGB	3 and 9	Absolute and relative muscle strength (to body weight). Muscle ultrastructure. Lower-limb functional capacity.	Dynamic strength: 1RM (leg-press and bench-press). Muscle biopsies (vastus lateralis). Timed-stands test.
Greco et al., 2002[48]	Italy	NRCT	8 (NR)	39±12	BPD	6	Muscle composition.	Muscle biopsies: Perivascular, interfibrillar and intramyocellular fat by quantitative histochemistry (quadriceps).
Handrigan et al., 2010[41]	Canada	NRCT	10 (10/0)	46±9	DS	3 and 12	Absolute and relative muscle strength (to body weight).	Isometric strength: load cell (knee extension).
Hassannejad et al., 2017[55]	Iran	RCT	20 (4/16)	36.7±6.2	SG/RYGB	3	Absolute muscle strength. Lower-limb functional capacity.	Dynamic strength: 1RM (Pectoral muscle). Sit-to-stand test 60 s.
Hue et al., 2008[53]	Canada	NRCT	10 (10/0)	43.8±9.0	DS	12	Absolute and relative muscle strength (to body weight).	Isometric strength: load cells (quadriceps and thumb opposition).

Ibacache et al., 2019[62]	Chile	OS	23 (0/23)	36.1±11.1	SG	1 and 3	Absolute and relative muscle strength (to body weight).	Isometric strength: handgrip dynamometry and quadriceps strength with load cell.
In et al., 2021[43]	Turkey	NRCT	17 (5/12)	41.0±13.0 (total sample)	SG/RYGB	1 and 3	Absolute muscle strength.	Isometric strength: handgrip dynamometry.
Lyytinen et al., 2013[50]	Finland	OS	16 (3/13)	45.1±9.5	RYGB	9	Muscle composition. Lower-limb functional capacity.	Ultrasound (lower-limb). Five times sit-to-stand.
Miller et al., 2009[54]	USA	OS	16 (NR)	43.5 (27.1-59.1)[#]	RYGB	3 wk and 3, 6, and 12 mo	Absolute and relative muscle strength (to body weight).	Isometric strength: quadriceps dynamometry.
Miller et al., 2011[49]	USA	OS	18 (0/18)	46.0±9.0	RYGB	12	Muscle composition.	Computed tomography scans (thigh).
Mundbjerg et al., 2018[56]	Denmark	RCT	28 (7/21)	42.4±9.0	RYGB	6, 12 and 24	Absolute muscle strength. Lower-limb functional capacity.	Isometric strength: shoulder and hip dynamometry. Sit-to-stand test: number of reps in 30 s.
Nachit et al., 2021[52]	Belgium	NRCT	24 (9/15)	41±6 (total sample)	RYGB	12	Muscle composition.	Computed tomography scans (psoas): skeletal muscle fat index (SMFIPsoas) = 100 * [psoas area (cm^2)/psoas density (HU)].
Neunhaeuserer et al., 2017[63]	Italy	OS	26 (8/18)	48.2±9.0	SG	6	Absolute muscle strength.	Isometric strength (handgrip dynamometry) and dynamic

								strength (estimated 1RM of lower-limb).
Noack-Segovia et al., 2019[45]	Chile	RCT	22 (NR)	33±6.9 (total sample)	SG	1 and 6	Absolute muscle strength.	Isometric strength: handgrip dynamometry.
Oppert et al., 2018[44]	France	RCT	22 (0/22)	43.9±10.7	RYGB	6	Absolute and relative muscle strength (to body weight and LM).	Isometric strength (handgrip dynamometry) and dynamic strength (1RM of lower and upper limbs).
Otto et al., 2014[64]	Germany	OS	25 (9/16)	NR (F 36.8±11.7 yr and M 46.7±9.0 yr)	RYGB/SG	6, 12 and 18 wk	Absolute muscle strength.	Isometric strength: handgrip dynamometry.
Reinmann et al., 2021[59]	Switzerland	OS	33 (8/25)	43.6±10.6	RYGB	3	Absolute and relative muscle strength (to body weight). Lower-limb functional capacity.	Isometric strength: quadriceps dynamometry. 5 times sit-to-stand test.
Schollenberger et al., 2016[65]	Germany	RCT	10 (2/8)	47.0±11.9	SG/RYGB	1, 3 and 6	Absolute muscle strength.	Isometric strength: handgrip dynamometry.

Stegen et al., 2011[60]	Belgium	NRCT	7 (3/4)	43.1±5.6	RYGB	4	Absolute muscle strength. Lower-limb functional capacity.	Dynamic strength: 1RM (biceps, triceps, quadriceps, and hamstrings). Isometric strength: handgrip dynamometry. Sit-to-stand test 30 s.
Wiklund et al., 2014[46]	Sweden	OS	37 (0/37)	41.2±9.6	RYGB	12	Absolute muscle strength.	Isometric strength: handgrip dynamometry.
Zhou et al., 2022[66]	Belgium	OS	13 (6/7)	49±14	SG/RYGB	6	Absolute and relative muscle strength (to lower/upper-limb LM).	Isometric strength: quadriceps and handgrip dynamometry.

Note: In RCTs and NRCTs, data from the group receiving only bariatric surgery is shown. Abbreviations: NRCT, nonrandomized controlled trial; OS, observational study; RCT, randomized controlled trial; BS, bariatric surgery; RYGB, roux-en-Y Gastric Bypass; SG, sleeve gastrectomy; BPD, biliopancreatic diversion; DS, duodenal switch; wk, week(s); mo, month(s); yr, year(s); BMI, body mass index; LM: lean mass; RM, repetition maximum; HU, Hounsfield unit; DXA, dual-energy X-ray absorptiometry; F, females; M, males; NR, not reported. [#]Age range.

Table 3. Summary of main findings of studies on absolute and relative muscle strength changes post-bariatric surgery (n=23).

Author, year	BMI pre-/post-BS (kg/m^2)	WC pre-/post-BS (cm)	Absolute strength pre-surgery	Absolute strength post-surgery	Relative strength pre-surgery	Relative strength post-surgery
Alba et al., 2019[42]	44±7/ NR	120±14/ NR	Handgrip men (kg): 42.9 Handgrip women (kg): 26.5	-11.9 (-6.3,-17.5)%** [6 mo], -8.8 (-3.4,-14.1)%** [12 mo]	Handgrip/BMI: NR	17.8 (10.2, 15.5)%** [6 mo], 31.9 (24.3, 39.6)%** [12 mo]
					Handgrip/LM: NR	2.5 (-4.3, 9.2)% [6 mo], 9.2 (2.8, 15.7)%** [12 mo]
Campanha-Versiani et al., 2017[18]	43.0±4.2/ 36.5±4.1 [3 mo], 30.9±2.9 [9 mo], 28.1±2.7 [12 mo]	NR	Angle leg press (kg): 26.58±18.93	25.14±14.36 [2 mo], 45.79±19.53** [12 mo]	NR	NR
			Seat leg curls (kg): 20.79±13.97	20.86±10.42 [2 mo], 32.63±12.29** [12 mo]		
			Bench press (kg): 13.42 ± 8.98	13.51±7.88 [2 mo], 21.32±10.39** [12 mo]		
			Posterior shoulder (kg): 11.58±6.88	12.97±7.02 [2 mo], 13.68±6.63 [12 mo]		
Cole et al., 2017[57]	48.8±9.7/ 43.9±9.0 [1.5 mo], 35.3±9.2 [6 mo], 32.6±9.7 [12 mo], 34.9±8.8 [9 yr]	NR	Handgrip (kg): 31.9±6.1	29.3±5.8 [1.5 mo], 29.1±5.2 [6 mo], 29.2±5.5 [12 mo], 26.2±4.5 [9 yr]**	NR	NR

Coral et al., 2021[19]	42.2±5.4/ 30.7±3.93	NR	Handgrip (kg): 25.7±9.5	25.4±7.9	NR	NR
Diniz-Sousa et al., 2021[47]	46.7±4.8/ 33.7±3.9	122.7±13.3/ 99.9±10.4	Knee extension (Nm): 141.8±48.8	115.2±35.1**	Knee extension (Nm/kg body weight): 1.25±0.42	1.43±0.49**
Gallart-Aragón et al., 2017[61]	46.5±5.6/ 41.1±5.0 [1 mo], 36.5±4.6 [6 mo]	NR	Handgrip dominant hand (kg): 31.12±11.48	31.41±13.37 [1 mo], 32.72±11.41 [6 mo]	NR	NR
			Handgrip non-dominant hand (kg): 29.53±9.98	28.51±10.49 [1 mo], 31.41±9.97 [6 mo]		
Gil et al., 2021[20]	47.4±7.6/ 36.2±5.0 [3 mo], 31.7±5.7 [9 mo]	NR	Leg press (kg): 190±60	130.4±49.0 [3 mo], 120.4±47.4* [9 mo]	Leg press (kg/kg body weight): 1.5±0.49	1.38±0.57 [3 mo], 1.49±0.63* [9 mo]
			Bench press (kg): 36±8	26.9±7.3 [3 mo], 24.8±5.6* [9 mo]	Bench-press (kg/kg body weight): 0.3±0.1	0.28±0.08 [3 mo], 0.31±0.08 [9 mo]
Handrigan et al., 2010[41]	49.1±6.5/ 38.3±6.3 [3 mo], 27.3±5.5 [12 mo]	151.1±12.6/ 128.4±17.2 [3 mo], 101.3±17.6 [12 mo]	Knee extension (kg): NR	-15.5 kg (-6.0,-25.1) [3 mo] and of-23.9 kg (-12.1,-35.8)** [12 mo]	Knee extension (kg/kg body weight): NR	0.005 (-0.07, 0.06) [3 mo] and 0.11 (0.03, 0.19)** [12 mo]
Hassannejad et al., 2017[55]	46.6±7.1/ 38.1±7.4	NR	Pectoral (kg): 12.5±6.7	11.9±7.0	NR	NR
Hue et al., 2008[53]	50.2±6.9/ 27.0±5.4	152.4±13.9/ 99.5±17.7	Lower limb (N): 742.8±131.3	493.9±84.3**	Lower limb (N/kg body weight): 0.5±0.54	0.61±0.58**

			Upper limb (N): 71.4±18.6	61.2±19.6**	Upper limb (N/kg body weight): 0.047±0.08	0.08±0.13**
Ibacache et al., 2019[62]	35.1±3.4/ 31.5±3.6 [1 mo], 28.3±3.2 [3 mo]	109.0±7.3/ 102.6±7.2 [1 mo], 94.6±8.2 [3 mo]	Handgrip (kg): 31.8±4.2	29.2±4.1** [1 mo], 27.7±4.0** [3 mo]	Handgrip (kg/kg body weight): 0.35±0.04	0.36±0.05 [1 mo], 0.38±0.05* [3 mo]
			Quadriceps (N): 115.2±34.8	102.4±23.5* [1 mo], 93.7±28.9* [3 mo]	Quadriceps (N/kg body weight): 1.26±0.34	1.27±0.27 [1 mo], 1.27±0.32 [3 mo]
In et al., 2021[43]	41.4±6.1/ 37.0±5.9 [1 mo], 33.3±5.0 [3 mo]	NR	Handgrip: NR	NR (a statistically significant decrease was observed in the hand grip strength)*	NR	NR
Miller et al., 2009[54]	53.0±8.47/ 34.8±6.88 [12 mo]	NR	Quadriceps (Nm): 126.3±9.52	113.2±43.9 [3 wk], 108.5±37.6 [3 mo], 111.7±48.7* [6 mo], 97.7±41.8* [12 mo]	Quadriceps (Nm/kg body weight): 0.87±0.28	0.87±0.28 [3 wk], 0.93±0.28 [3 mo], 1.06±0.32* [6 mo], 1.03±0.32 [12 mo]
Mundbjerg et al., 2018[56]	42.8±5.5/ 34.1±5.4 [6 mo], 31.8±5.0 [12 mo], 32.6±5.2 [24 mo]	NR	Shoulder adduction (N): 210.6±76.7	196.9±67.1 [6 mo], 193.3±77.5* [12 mo], 195.9±73.3* [24 mo]	NR	NR
			Shoulder abduction (N): 177.0±60.0	160.1±54.9** [6 mo], 166.1±65.9 [12 mo], 171.7±67.6 [24 mo]		
			Hip extension (N): 213.6±70.2	198.7±60.0* [6 mo], 196.0±58.8** [12 mo], 193.6±60.5 [24 mo]		

			Hip adduction (N): 151.8±56.9	137.1±46.3** [6 mo], 132.2±47.5** [12 mo], 142.7±55.8 [24 mo]		
			Hip abduction (N): 151.2±41.6	137.2±37.5** [6 mo], 133.5±38.9** [12 mo], 139.4±43.1 [24 mo]		
Neunhaeuserer et al., 2017[63]	45.2±5.8/ 33.0±4.7	NR	Leg extension (kg): 68.18±22.58	75.41±23.68	NR	NR
			Handgrip right (kg): 32.0±9.3	32.7±10.1		
			Handgrip left (kg): 29.4±10.6	29.4±10.8		
Noack-Segovia et al., 2019[45]	36.7±3.3/ 31.4±3.8 [1 mo], 24.3±3.2 [6 mo]	NR	Handgrip (kg): 34.2±8.9	32.9±5.4 [1 mo], 31.9±9.1 [6 mo]	NR	NR
Oppert et al., 2018[44]	43.6±6.2/ -10.5 (-11.4,-9.6)	NR	Handgrip (kg): 30.6±5.7	-21.0 (-43.1, 1.1)**	Lower-limb (kg/kg body weight): 1.58±0.59	+0.12 (-0.14, 0.38)**
			Lower-limb (kg): 175.7±53.1	-30.4 (-55.8,-5.0)*	Lower-limb (kg/kg LM): 9.41±3.69	-0.08 (-1.53, 1.38)
			Upper-limb (kg): 31.4±6.9	-6.2 (-9.9,-2.6)**	Upper-limb (kg/kg body weight): 0.27±0.05	+0.02 (-0.02, 0.06)**
					Upper-limb (kg/kg LM): 7.56±2.03	-1.0 (-2.0,-0.1)

Otto et al., 2014[64]	47.4±6.3/ 42.2±5.3 [6 wk], 39.4±4.6 [12 wk], 37.4±4.4 [18 wk]	NR	Handgrip dominant hand (kg): 31.2±7.0	33.3±7.9 [6 wk], 33.7±8.8 [12 wk], 34.1±9.3 [18 wk]	NR	NR
			Handgrip nondominant hand (kg): 29.3±6.6	29.0±7.0 [6 wk], 29.8±7.8 [12 wk], 29.9±8.5 [18 wk]		
Reinmann et al., 2021[59]	45.4±7.9/ 36.9±7.8	130.2±17.6/ 115.8±17.6	Quadriceps (N): 282.0±105.3	234.0±73.6**	Quadriceps (N/kg body weight): 2.22±0.74	2.29±0.75
Schollenberger et al., 2016[65]	49.0±5.1/ 44.7±5.1 [1 mo], 41.7±4.7 [3 mo], 38.7±4.3 [6 mo]	NR	Handgrip (pounds): 66.1±10.8	64.3±7.8 [6 mo]	NR	NR
Stegen et al., 2011[60]	40.4±8.1/ -8.3±4.1	129.7±20.1/-20.3±11.6	Quadriceps (kg): 57.3±28.2	45.9±25.1*	NR	NR
			Hamstrings (kg): 39.0±35.0	35.3±27.8		
			Biceps (kg): 27.3±9.6	20.8±8.8**		
			Triceps (kg): 30.1±10.5	22.0 ± 6.6*		
			Handgrip (kg): 95.9±24.9	78.7±22.2*		
Wiklund et al., 2014[46]	42.0±6.5/ 30.5±5.8	119.9±11.7/ 96.0±14.2	Handgrip right hand (N): 298±102	287±62	NR	NR
			Handgrip left hand (N): 295±92	276±60		

Zhou et al., 2022[66]	39.5±3.5/ 30.7±3.4	127±9/ 106±10	Quadriceps (kg): 53±15	51±13	Quadriceps (kg/kg LM): 5.0±1.1	5.5±0.8*
			Handgrip (kg): 36±9	37±9	Handgrip (kg/kg LM): 11.4±2.0	13.7±3.0**

Note: Data are presented as means ± SD except for Noack-Segovia (median ± SD), Alba (mean percentage changes from baseline (95% confidence intervals)), Oppert and Handrigan (Mean changes from baseline (95% confidence intervals)). In RCTs and NRCTs, data from the group receiving only bariatric surgery is shown. Muscle groups and units of measurement are mentioned only in the preoperative values.

Abbreviations: BS, bariatric surgery; BMI, body mass index; Nm, Newton-meters; LM, lean mass; WC, waist circumference; wk, week(s); mo, month(s); yr, year(s); NR, not reported.

*Significantly different from baseline measure (P <0.05); **significantly different from baseline measure (P <0.01).

3.5 Meta-regressions

A meta-regression was performed to evaluate the possible effect of change in BMI on muscle strength after BS. According to the data, those subjects who suffered a higher decrease in BMI after the surgery also had a higher loss of absolute lower-limb isometric strength (correlation coefficient= 0.0722; p= 0.02). However, pre-surgery BMI was not associated with the change in absolute lower-limb isometric strength after the surgery (correlation coefficient= -0.0270; p= 0.435).

3.6 Sensitivity analysis and publication bias

No differences were observed in ES, the direction of effect, or p-values when each study was individually eliminated, and all analyses were recalculated (p< 0.001 in all cases).

Furthermore, all studies were symmetrically located within the limits of the funnel plots, and no significance was observed in any case in the Egger test, suggesting no publication bias.

4. DISCUSSION

This systematic review and meta-analysis, that examined the changes in MS and MQ levels in subjects with obesity undergoing BS, provides a comprehensive qualitative and quantitative summary of the evidence to date, including 28 studies (16 in the meta-analyses) comprising 697 participants (421 in the meta-analyses). There was evidence of a significant decrease in absolute lower-limb isometric strength after BS, related to the magnitude of BMI changes. Absolute lower-limb dynamic strength also showed a significant decrease. However, no changes in the rest of the outcomes were observed.

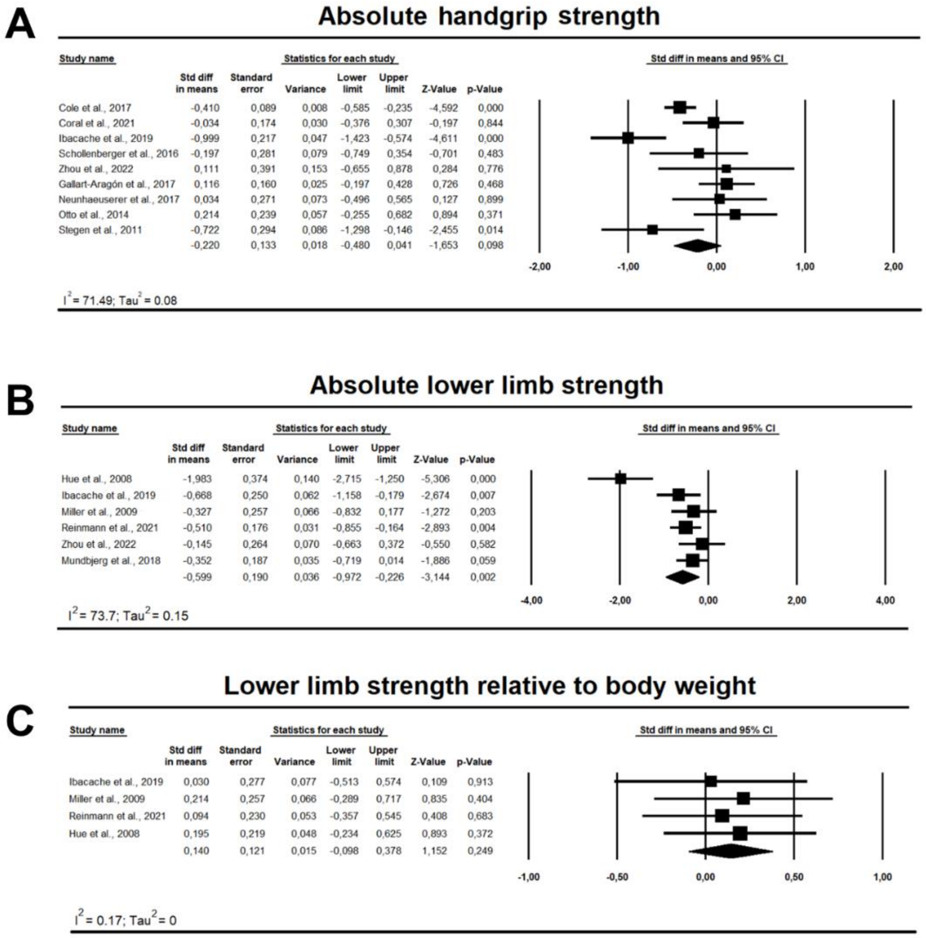
The reduction in absolute lower limbs strength after surgery was specifically in weight-bearing muscles, whereas absolute handgrip strength only showed a tendency to reduce. Similar results were reported in a meta-analysis about the effect of diet-induced weight loss on upper and lower limb strength.[67] Likewise, Herring et al.[68] published a meta-analysis reporting a reduction in absolute MS after BS; however, they combined the results of studies that evaluated MS with different tests and muscle groups.[68] People with obesity normally have greater absolute MS values compared to lean people since it is believed that increased adiposity would act as a chronic overload stimulus on the antigravity muscles, thus increasing their muscle size and strength, without affecting handgrip strength.[13] However, this apparent benefit disappears when MS is normalized to body mass, resulting in significantly lower relative strength than lean individuals.[69] The same is generally observed when MS is normalized to fat-free mass (FFM) or muscle mass.[69]

People with obesity present a lower relative MS due partly to the low-grade systemic inflammation related to obesity, with elevated levels of several proinflammatory cytokines, such as IL-6 and TNF-α.[13] These have been associated with lower muscle mass and strength, possibly through stimulating catabolism and inhibiting muscle protein synthesis, with one of the key mechanisms being their inhibitory effects on insulin-like growth factor 1 (IGF-1).[13,69,70] Decreases in IGF-1 inhibit muscle growth signaling pathway (IGF-1→ P13K→ Akt→ mTOR), which can prevent the muscle from adequately adapting to mechanical stimuli.[69,71] Furthermore, increased myostatin levels in obesity, a potent inhibitor of skeletal muscle growth, can also contribute to impaired muscle growth.[71,72]

These obesity-related metabolic complications can conduce to inadequate recruitment of the cells involved in the regeneration of skeletal muscle, which leads to impaired angiogenesis and myocyte formation while promoting the deposition of fibrotic and adipose tissue, reducing muscle structural integrity and its functional capacity.[13] In addition, obesity can impair muscle contractile function through a variety of signaling pathways, among others calcium cycling and AMPK activity.[69]

After undergoing BS, evidence suggests that IGF-1 levels increase proportionately to the amount of weight loss,[13,73,74] which could favor the muscle growth signaling pathway and lead to further adaptations to resistance training. Additionally, studies have shown a decrease in muscle myostatin expression after BS.[72,75] However, the abrupt weight loss after BS can reduce the training stimulus on skeletal muscle, resulting in a reduction of muscle mass and strength due to the extra loss of body mass.

Many studies have previously reported that loss of LM occurs together with fat mass loss after BS,[76,77] especially in the initial post-surgical period, where the decrease in body weight largely corresponds to FFM loss.[78] These results can be explained partly because current clinical guidelines do not consider physical exercise[79] or indicate that resistance exercise should only begin in the sixth week post-BS,[80] promoting muscle unloading in the first weeks, which is known to generate a reduction in muscle mass and strength. Likewise, considering that physical activity / exercise is the primary determinant of MS,[81] the lack of improvement described in the level of physical activity after BS in the short-term[82] could contribute to the observed reduction in MS.



Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Cole et al., 2017	-0,410	0,089	0,008	-0,585	-0,235	-4,592	0,000
Coral et al., 2021	-0,034	0,174	0,030	-0,376	0,307	-0,197	0,844
Ibacache et al., 2019	-0,999	0,217	0,047	-1,423	-0,574	-4,611	0,000
Schollenberger et al., 2016	-0,197	0,281	0,079	-0,749	0,354	-0,701	0,483
Zhou et al., 2022	0,111	0,391	0,153	-0,655	0,878	0,284	0,776
Gallart-Aragón et al., 2017	0,116	0,160	0,025	-0,197	0,428	0,726	0,468
Neunhaeuserer et al., 2017	0,034	0,271	0,073	-0,496	0,565	0,127	0,899
Otto et al., 2014	0,214	0,239	0,057	-0,255	0,682	0,894	0,371
Stegen et al., 2011	-0,722	0,294	0,086	-1,298	-0,146	-2,455	0,014
	-0,220	0,133	0,018	-0,480	0,041	-1,653	0,098

$I^2 = 71.49$; $Tau^2 = 0.08$

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Hue et al., 2008	-1,983	0,374	0,140	-2,715	-1,250	-5,306	0,000
Ibacache et al., 2019	-0,668	0,250	0,062	-1,158	-0,179	-2,674	0,007
Miller et al., 2009	-0,327	0,257	0,066	-0,832	0,177	-1,272	0,203
Reinmann et al., 2021	-0,510	0,176	0,031	-0,855	-0,164	-2,893	0,004
Zhou et al., 2022	-0,145	0,264	0,070	-0,663	0,372	-0,550	0,582
Mundbjerg et al., 2018	-0,352	0,187	0,035	-0,719	0,014	-1,886	0,059
	-0,599	0,190	0,036	-0,972	-0,226	-3,144	0,002

$I^2 = 73.7$; $Tau^2 = 0.15$

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Ibacache et al., 2019	0,030	0,277	0,077	-0,513	0,574	0,109	0,913
Miller et al., 2009	0,214	0,257	0,066	-0,289	0,717	0,835	0,404
Reinmann et al., 2021	0,094	0,230	0,053	-0,357	0,545	0,408	0,683
Hue et al., 2008	0,195	0,219	0,048	-0,234	0,625	0,893	0,372
	0,140	0,121	0,015	-0,098	0,378	1,152	0,249

$I^2 = 0.17$; $Tau^2 = 0$

Figure 2. Forest plots of changes in isometric muscle strength after bariatric surgery according to the dynamometry

Moreover, it has been described that in periods of reduced caloric and protein intake, such as the first postoperative months, unused muscle tissue breaks down to compensate for caloric restriction and acquire amino acids for other processes.[83] This could explain the results observed in this meta-regression, suggesting that a higher decrease in BMI implies a more significant reduction in FFM and, consequently, a higher reduction in postoperative absolute MS.

A significant decrease in FFM reduces the resting metabolic rate.[84-86] The loss of muscle mass described, together with the substantial caloric restriction after BS (mainly in the first months), produces a global reduction in sympathetic activity,[86,87] improving the heart rate variability[88] but with deleterious implications regarding energy expenditure at rest as an adaptive response.[85,87,89] This could slow down the rate of weight loss and predispose to regain it, facilitating fat accumulation,[84,90,91] a mechanism that could explain why people after BS are considered at high risk for the development of sarcopenic obesity,[25,83] with the consequent increased risk of frailty, functional disability, cardiometabolic diseases, and mortality.[4] On the other hand, the positive results that exercise has shown after BS on FFM and MS[92-94] support the idea that the decrease in muscle mass largely explains the reduction in absolute MS observed after BS.

Unlike the absolute values, a tendency to increase MS after BS was observed when lower-limb strength relative to body weight was analyzed. However, interpretation of relative MS values when body weight changes due to factors such as diet, surgery, growth, exercise, or sickness, can be challenging. Caution is needed when interpreting the MS results normalized to body weight after BS, as they are likely to be highly dependent on body mass loss after surgery. On the other hand, it was not possible to perform a meta-analysis of changes in MS relative to LM due to insufficient studies, showing both an increasing (isometric strength) and decreasing trend (dynamic strength) after BS.

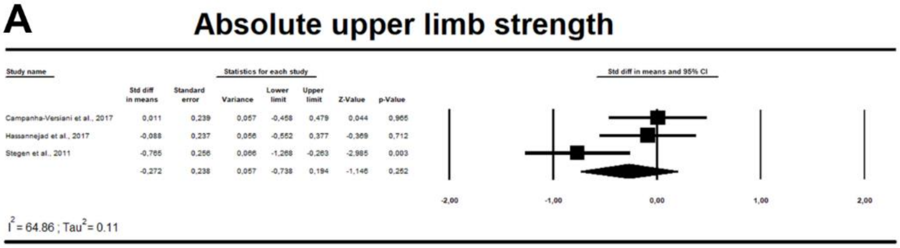
Although it is known that MS depends to a large extent on muscle mass,[10,95] this is not the only determining factor. As an example, the longitudinal declines in knee extensor strength observed in an aging study were ∼3 times greater than the reductions observed in in lower-limb LM.[96] Furthermore, obesity can affect the association between muscle mass and MS due to muscle deconditioning, inflammation, and accumulation of lipids within the muscle.[97,98]

Muscle composition, a dimension of MQ, showed a short-term reduction in absolute fat-infiltration muscle content after BS in all studies that evaluated it.[48-52] However, a meta-analysis could not be performed due to the heterogeneity of the assessment methodologies used. Although the absolute fat content within the muscle decreased after BS, in most studies included in this systematic review the fat concentration in skeletal muscle (or myosteatosis) increased after BS (i.e., reduced muscle density) in the same postoperative period.[50-52] This could be explained by a reduction in skeletal muscle mass in a greater proportion than the decrease in lipids stored within the muscle.

It is important to mention that different protocols, equipment, and muscle groups were used to assess MS and MQ, which was considered when analyzing the results. Isokinetic dynamometers, used only in one of the reviewed studies, are the gold standard for determining MS and are commonly applied in laboratory environments.[99-101] However, isokinetic devices are expensive and generally only assess a monoarticular muscle exercise.[100] Conversely, isometric and 1RM tests are mainly used for MS assessment in clinical settings. Isometric strength tests, such as the handgrip test, are cost- and time-efficient and strongly correlated with maximum dynamic strength.[101,102] The 1RM testing are widely applied because they are cost-effective and allow the evaluation of exercises involving multiple joints, reflecting dynamic muscle actions used in daily life.[99]

This review has also some limitations to acknowledge. First, our data were limited to the short-term impact of BS on MS and MQ. Only one study performed a medium-term follow-up (>1 ≤5 years) and another study a long-term follow-up (>5 ≤10 years). Second, most of the included studies did not provide body composition parameters, which precludes drawing any conclusions about changes in MS relative to muscle/lean mass. Finally, observational studies were included (as the main aim was to investigate the natural course of MS/MQ after BS), the methodological quality of the reviewed studies ranged from excellent to fair, and most of the studies had small sample sizes (<30 participants).

To the best of our knowledge, this is the first study to systematically review the changes in MS and MQ following BS and perform a separate meta-analysis for studies that used different muscle groups and MS tests. The strengths of this review include (1) the use of a prespecified protocol registered on PROSPERO; (2) no restriction on populations, settings, or year of publication; (3) sensitive search strategy of the literature using multiple electronic databases following the PRISMA recommendations; (4) the use of the PEDro scale[32] and the scale by NHLBI[34] to assess the quality of the selected studies; and (5) meta-regression to investigate the effect of changes in BMI on changes in MS after BS.

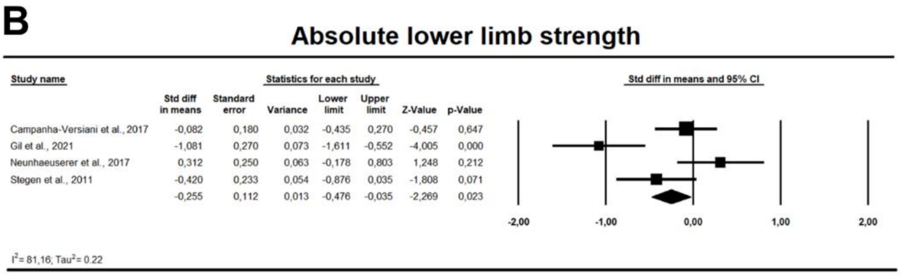


A

Absolute upper limb strength

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Campanha-Versiani et al., 2017	0,011	0,239	0,057	-0,458	0,479	0,044	0,965
Hassannejad et al., 2017	-0,088	0,237	0,056	-0,552	0,377	-0,369	0,712
Stegen et al., 2011	-0,765	0,256	0,066	-1,268	-0,263	-2,985	0,003
	-0,272	0,238	0,057	-0,738	0,194	-1,146	0,252

$I^2 = 64.86$; $Tau^2 = 0.11$



B

Absolute lower limb strength

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Campanha-Versiani et al., 2017	-0,082	0,180	0,032	-0,435	0,270	-0,457	0,647
Gil et al., 2021	-1,081	0,270	0,073	-1,611	-0,552	-4,005	0,000
Neunhaeuserer et al., 2017	0,312	0,250	0,063	-0,178	0,803	1,248	0,212
Stegen et al., 2011	-0,420	0,233	0,054	-0,876	0,035	-1,808	0,071
	-0,255	0,112	0,013	-0,476	-0,035	-2,269	0,023

$I^2 = 81,16$; $Tau^2 = 0.22$

Figure 3. Forest plots of changes in dynamic muscle strength after bariatric surgery according to the maximum repetition test

5. CONCLUSION

In conclusion, although BS has shown to provide many health benefits, in the short-term, it seems to negatively affect the strength of the antigravity muscles and the lower-limb MQ in its dimension of muscle composition. Considering that low MS is more strongly and significantly associated with all-cause mortality than low muscle mass and that even small changes in MS can affect the mortality risk, strength reduction could be mitigated by prescribing individualized and supervised resistance or concurrent exercise as a therapeutic adjunct, both before and after the surgical intervention. More extended follow-up studies are needed to confirm the adverse effect of BS on MS and MQ and to study its health consequences in this population. Combining body composition, MS, and other health outcomes assessments, including larger sample size and multiple time points, could provide a better understanding of the link between health, weight loss, and changes in muscle mass and muscle strength/quality in these subjects.

Acknowledgments

This work is part of a research project supported by the Spanish Ministry of Economy and Competitiveness (MINECO), Plan Nacional de I+D+i calls RETOS 2016 (reference DEP2016-74926-R). EM-R was supported by the Spanish Ministry of Universities (FPU18/01107). DJ-M was supported by the program "Recualificación del Profesorado Universitario. Modalidad Margarita Salas", Universidad de Granada/ Ministerio de Universidades y Fondos Next Generation de la Unión Europea. This article is part of the PhD Thesis by PI-S performed in the Medical Sciences Doctoral

Program of the University of Almería.

Conflicts of interest

The authors declare that they have no competing interests.

SUPPORTING INFORMATION

CÓDIGO QR

REFERENCES

1. Malik VS, Willet WC, Hu FB. Nearly a decade on—trends, risk factors and policy implications in global obesity. *Nat Rev Endocrinol*. 2020;16(11):615-6.
2. GBD 2015 Obesity Collaborators, Afshin A, Forouzanfar MH, et al. Health effects of overweight and obesity in 195 countries over 25 years. *N Engl J Med*. 2017;377:13–27.
3. Blüher M. Obesity: global epidemiology and pathogenesis. *Nat Rev Endocrinol*. 2019;15(5):288-98.
4. Roh E, Choi KM. Health consequences of sarcopenic obesity: a narrative review. *Front Endocrinol*. 2020 May 21;11:332.
5. Kim TN, Park MS, Ryu JY, et al. Impact of visceral fat on skeletal muscle mass and vice versa in a prospective cohort study: the Korean Sarcopenic Obesity Study (KSOS). *PloS One*. 2014;9(12):e115407.
6. Stenholm S, Mehta NK, Elo IT, Heliövaara M, Koskinen S, Aromaa A. Obesity and muscle strength as long-term determinants of all-cause mortality—a 33-year follow-up of the Mini-Finland Health Examination Survey. *Int J Obes*. 2014;38(8):1126-32.
7. Artero EG, Lee DC, Lavie CJ, et al. Effects of muscular strength on cardiovascular risk factors and prognosis. *J Cardiopulm Rehabil Prev.* 2012; 32(6): 351-8.
8. Volaklis KA, Halle M, Meisinger C. Muscular

strength as a strong predictor of mortality: A narrative review. *Eur J Intern Med.* 2015; 26(5): 303-10.

9. Heymsfield SB, Gonzalez MC, Lu J, Jia G, Zheng J. Skeletal muscle mass and quality: evolution of modern measurement concepts in the context of sarcopenia. *Proc Nutr Soc.* 2015; 74(4): 355-66.

10. Fragala MS, Kenny AM, Kuchel GA. Muscle quality in aging: a multi-dimensional approach to muscle functioning with applications for treatment. *Sports Med.* 2015;45:641-58.

11. Correa-de-Araujo R, Harris-Love MO, Miljkovic I, Fragala MS, Anthony BW, Manini TM. The need for standardized assessment of muscle quality in skeletal muscle function deficit and other aging-related muscle dysfunctions: a symposium report. *Front Physiol.* 2017;8:87.

12. Naimo MA, Varanoske AN, Hughes JM, Pasiakos SM. Skeletal muscle quality: a biomarker for assessing physical performance capabilities in young populations. *Front Physiol.* 2021;12:706699.

13. Tomlinson DJ, Erskine RM, Morse CI, Winwood K, Onambélé-Pearson G. The impact of obesity on skeletal muscle strength and structure through adolescence to old age. *Biogerontology*. 2016;17(3):467-483.

14. Valenzuela PL, Maffiuletti NA, Tringali G, De Col A, Sartorio A. Obesity-associated poor muscle quality: prevalence and association with age, sex, and body mass index. *BMC Musculoskelet Disord.* 2020;21(1): 1-8.

15. Lester EL, Padwal RS, Birch DW, et al. The real-world cost-effectiveness of bariatric surgery for the treatment of severe obesity: a cost–utility analysis. *CMAJ Open.* 2021;9(2):E673-9. .

16. Montesi L, El Ghoch M, Brodosi L, Calugi S, Marchesini G, Dalle Grave R. Long-term weight loss maintenance for obesity: a multidisciplinary approach.

Diabetes Metab Syndr Obes. 2016;9:37–46.

17. Nguyen NT, Varela JE. Bariatric surgery for obesity and metabolic disorders: state of the art. *Nat Rev Gastroenterol Hepatol*. 2017;14(3):160–9.

18. Campanha-Versiani L, Pereira DA, Ribeiro-Samora GA, et al. The effect of a muscle weight-bearing and aerobic exercise program on the body composition, muscular strength, biochemical markers, and bone mass of obese patients who have undergone gastric bypass surgery. *Obes Surg*. 2017;27:2129-37.

19. Coral RV, Bigolin AV, Machry MC, et al. Improvement in muscle strength and metabolic parameters despite muscle mass loss in the initial six months after bariatric surgery. *Obes Surg*. 2021;31:4485-91.

20. Gil S, Kirwan JP, Murai IH, et al. A randomized clinical trial on the effects of exercise on muscle remodelling following bariatric surgery. *J Cachexia Sarcopenia Muscle*. 2021;12(6):1440-55.

21. Brown JC, Harhay MO, Harhay MN. The muscle quality index and mortality among males and females. *Ann Epidemiol.* 2016; 26(9): 648-53.

22. Reinders I, Murphy RA, Brouwer IA, et al. Muscle quality and myosteatosis: novel associations with mortality risk: the Age, Gene/Environment Susceptibility (AGES)-Reykjavik Study. *Am J Epidemiol*. 2016;183(1):53-60.

23. Mastino D, Robert M, Betry C, et al. Bariatric surgery outcomes in sarcopenic obesity. *Obes Surg*. 2016 Oct;26(10):2355-62.

24. Gaillard M, Tranchart H, Maitre S, Perlemuter G, Lainas P, Dagher I. Preoperative detection of sarcopenic obesity helps to predict the occurrence of gastric leak after sleeve gastrectomy. *Obes Surg*. 2018;28(8):2379-85.

25. Voican CS, Lebrun A, Maitre S, et al. Predictive score of sarcopenia occurrence one year after bariatric surgery in severely obese patients. *PLoS One*. 2018;13(5):e0197248.

26. Buckinx F, Aubertin-Leheudre M. Relevance to assess and preserve muscle strength in aging field. *Prog Neuropsychopharmacol Biol Psychiatry*. 2019;94:109663.

27. Molero J, Olbeyra R, Flores L, et al. Prevalence of low skeletal muscle mass following bariatric surgery. *Clin Nutr ESPEN*. 2022;49:436-41.

28. Page MJ, McKenzie JE, Bossuyt PM, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. *BMJ*. 2021;372:n71.

29. Higgins JPT, Green S. Cochrane Handbook for Systematic Reviews of Interventions. Cochrane; 2011.

30. Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan—a web and mobile app for systematic reviews. *Syst Rev*. 2016;5(1):210.

31. Verhagen A, De Vet H, De Bie RA, et al. The Delphi list: A criteria list for quality assessment of randomized clinical trials for conducting systematic reviews developed by Delphi consensus. *J Clin Epidemiol*. 1998;51(12):1235-41.

32. de Morton NA. The PEDro scale is a valid measure of the methodological quality of clinical trials: A demographic study. *Aust J Physiother.* 2009;55(2):129-33.

33. Maher CG, Sherrington C, Herbert RD, Moseley AM, Elkins M. Reliability of the PEDro scale for rating quality of randomized controlled trials. *Phys Ther.* 2003;83(8):713-21.

34. Study quality assessment tools. National Heart, Lung and Blood Institute website. https://www.nhlbi.nih.gov/health-topics/study-

quality-assessment-tools. Published in 2013, updated in July 2021. Accesed April 4, 2023.

35. Cohen J. A power primer. *Psychol Bull*. 1992;112(1):155-9.
36. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials*. 1986;7(3):177-88.
37. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. *BMJ*. 2011;343(7829):d5928.
38. Irwig L, Macaskill P, Berry G, Glasziou P. Bias in meta-analysis detected by a simple, graphical test. Graphical test is itself biased. *BMJ*. 1998;316(7129):1-11.
39. Sterne JAC, Gavaghan D, Egger M. Publication and related bias in meta-analysis: Power of statistical tests and prevalence in the literature. *J Clin Epidemiol*. 2000;53(11):1119-29.
40. Berkey CS, Hoaglin DC, Mosteller F, Colditz GA. A random effects regression model for meta-analysis. *Stat Med*. 1995;14(4): 395-411.
41. Handrigan G, Hue O, Simoneau M, et al. Weight loss and muscular strength affect static balance control. *Int J Obes (Lond)*. 2010;34(5):936-42.
42. Alba DL, Wu L, Cawthon PM, et al. Changes in lean mass, absolute and relative muscle strength, and physical performance after gastric bypass surgery. *J Clin Endocrinol Metab.* 2019;104(3):711-20.
43. In G, Taskin HE, Al M, et al. Comparison of 12-week fitness protocols following bariatric surgery: aerobic exercise versus aerobic exercise and progressive resistance. *Obes Surg*. 2021;31:1475-84.
44. Oppert JM, Bellicha A, Roda C, et al. Resistance training and protein supplementation increase strength after bariatric surgery: a randomized controlled trial. *Obesity.* 2018;26(11):1709-20.

45. Noack-Segovia JP, Sánchez-López AM, García-García I, Rodríguez-Blanque R, León-Ríos XA, Aguilar-Cordero MJ. Physical exercise and grip strength in patients intervened through bariatric surgery. Aquichan. 2019;19(3).

46. Wiklund M, Olsén MF, Olbers T, Cider Å. Physical fitness and physical activity in Swedish women before and one year after roux-en-Y gastric bypass surgery. *Open Obes J*. 2014;6(1).

47. Diniz-Sousa F, Veras L, Boppre G, et al. How does bariatric surgery affect fall risk factors?. *Obes Surg*. 2021;31:3506-13.

48. Greco AV, Mingrone G, Giancaterini A, et al. Insulin resistance in morbid obesity: reversal with intramyocellular fat depletion. *Diabetes*. 2002;51(1):144-51.

49. Miller GD, Carr JJ, Fernandez AZ. Regional fat changes following weight reduction from laparoscopic Roux-en-Y gastric bypass surgery. *Diabetes Obes Metab*. 2011;13(2):189-92.

50. Lyytinen T, Liikavainio T, Pääkkönen M, Gylling H, Arokoski JP. Physical function and properties of quadriceps femoris muscle after bariatric surgery and subsequent weight loss. *J Musculoskelet Neuronal Interact*. 2013;13(3):329-8.

51. Auclair A, Piché ME, Biertho L, Marceau S, Poirier P. Changes in fat-free mass and muscle mass at 6 and 12 months after biliopancreatic diversion with duodenal switch surgery. *Surg Obes Relat Dis*. 2020;16(7):878-85.

52. Nachit M, Kwanten WJ, Thissen JP, et al. Muscle fat content is strongly associated with NASH: a longitudinal study in patients with morbid obesity. *J Hepatol*. 2021;75(2):292-301.

53. Hue O, Berrigan F, Simoneau M, et al. Muscle force and force control after weight loss in obese and morbidly obese men. *Obes Surg*. 2008;18:1112-8.

54. Miller GD, Nicklas BJ, You T, Fernandez A. Physical function improvements

after laparoscopic Roux-en-Y gastric bypass surgery. *Surg Obes Relat Dis*. 2009;5(5):530-7.

55. Hassannejad A, Khalaj A, Mansournia MA, Rajabian Tabesh M, Alizadeh Z. The effect of aerobic or aerobic-strength exercise on body composition and functional capacity in patients with BMI≥ 35 after bariatric surgery: a randomized control trial. *Obes Surg*. 2017;27:2792-801.
56. Mundbjerg LH, Stolberg CR, Bladbjerg EM, Funch-Jensen P, Juhl CB, Gram B. Effects of 6 months supervised physical training on muscle strength and aerobic capacity in patients undergoing Roux-en-Y gastric bypass surgery: a randomized controlled trial. *Clin Obes*. 2018;8(4):227-35.
57. Cole AJ, Kuchnia AJ, Beckman LM, et al. Long-term body composition changes in women following Roux-en-Y gastric bypass surgery. *JPEN J Parenter Enteral Nutr.* 2017;41(4):583-91.
58. Mahawar KK. Defining short-term, medium-term, long-term, and very long-term follow-up after bariatric surgery. *Obes Surg*. 2018; 28(5):1425-6.
59. Reinmann A, Gafner SC, Hilfiker R, Bruyneel AV, Pataky Z, Allet L. Bariatric surgery: consequences on functional capacities in patients with obesity. *Front Endocrinol*. 2021;12:646283.
60. Stegen S, Derave W, Calders P, Van Laethem C, Pattyn P. Physical fitness in morbidly obese patients: Effect of gastric bypass surgery and exercise training. *Obes Surg*. 2011;21(1):61-70.
61. Gallart-Aragón T, Fernández-Lao C, Castro-Martín E, Cantarero-Villanueva I, Cózar-Ibáñez A, Arroyo-Morales M. Health-related fitness improvements in morbid obese patients after laparoscopic sleeve gastrectomy: a cohort study. *Obes Surg*. 2017;27:1182-8.
62. Ibacache P, Cano-Cappellacci M, Miranda-

Fuentes C, Rojas J, Maldonado P, Bottinelli A. Physical fitness and physical activity in women with obesity: short term effects of sleeve gastrectomy. Nutr. Hosp. 2019:840-5.

63. Neunhaeuserer D, Gasperetti A, Savalla F, et al. Functional evaluation in obese patients before and after sleeve gastrectomy. *Obes Surg*. 2017;27:3230-9.
64. Otto M, Kautt S, Kremer M, Kienle P, Post S, Hasenberg T. Handgrip strength as a predictor for post bariatric body composition. *Obes Surg*. 2014;24:2082-8.
65. Schollenberger AE, Karschin J, Meile T, Küper MA, Königsrainer A, Bischoff SC. Impact of protein supplementation after bariatric surgery: a randomized controlled double-blind pilot study. *Nutrition*. 2016;32(2):186-92.
66. Zhou N, Scoubeau C, Forton K, et al. Lean mass loss and altered muscular aerobic capacity after bariatric surgery. *Obes Facts*. 2022;15(2):248-56.
67. Zibellini J, Seimon RV, Lee CM, Gibson AA, Hsu MS, Sainsbury A. Effect of diet-induced weight loss on muscle strength in adults with overweight or obesity–a systematic review and meta-analysis of clinical trials. *Obes Rev*. 2016;17(8):647-63.
68. Herring LY, Stevinson C, Davies MJ, et al. Changes in physical activity behaviour and physical function after bariatric surgery: a systematic review and meta-analysis. *Obes Rev*. 2016;17(3):250-61.
69. Tallis J, James RS, Seebacher F. The effects of obesity on skeletal muscle contractile function. *J Exp Biol*. 2018;221(13):jeb163840.
70. Pellegrinelli V, Rouault C, Rodriguez-Cuenca S, et al. Human adipocytes induce inflammation and atrophy in muscle cells during obesity. *Diabetes*. 2015;64(9):3121-34.
71. Collins KH, Herzog W, MacDonald GZ, et al.

Obesity, metabolic syndrome, and musculoskeletal disease: common inflammatory pathways suggest a central role for loss of muscle integrity. *Front Physiol*. 2018;9:112.

72. Allen DL, Hittel DS, McPherron AC. Expression and function of myostatin in obesity, diabetes, and exercise adaptation. *Med Sci Sports Exerc*. 2011;43(10):1828.
73. Juiz-Valiña P, Pena-Bello L, Cordido M, et al. Altered GH-IGF-1 axis in severe obese subjects is reversed after bariatric surgery-induced weight loss and related with low-grade chronic inflammation. *J Clin Med*. 2020;9(8):2614.
74. Sohouli MH, Baniasadi M, Nabavizadeh R, et al. Trends in insulin-like growth factor-1 levels after bariatric surgery: a systematic review and meta-analysis. *Int J Obes (Lond).* 2022;46(5):891-900.
75. Faramia J, Ostinelli G, Drolet-Labelle V, Picard F, Tchernof A. Metabolic adaptations after bariatric surgery: adipokines, myokines and hepatokines. *Curr Opin Pharmacol*. 2020;52:67-74.
76. Haghighat N, Kazemi A, Asbaghi O, et al. Long-term effect of bariatric surgery on body composition in patients with morbid obesity: A systematic review and meta-analysis. *Clin Nutr*. 2021;40(4):1755-66.
77. Nuijten MA, Eijsvogels TM, Monpellier VM, Janssen IM, Hazebroek EJ, Hopman MT. The magnitude and progress of lean body mass, fat-free mass, and skeletal muscle mass loss following bariatric surgery: a systematic review and meta-analysis. *Obes Rev*. 2022;23(1):e13370.
78. Frühbeck G. Bariatric and metabolic surgery: A shift in eligibility and success criteria. *Nat Rev Endocrinol*. 2015;11(8):465-77.
79. Di Lorenzo N, Antoniou SA, Batterham RL, et al. Clinical practice guidelines of the European Association for Endoscopic Surgery (EAES)

on bariatric surgery: update 2020 endorsed by IFSO-EC, EASO and ESPCOP. *Surg Endosc*. 2020;34:2332-58.

80. Tabesh MR, Maleklou F, Ejtehadi F, Alizadeh Z. Nutrition, physical activity, and prescription of supplements in pre-and post-bariatric surgery patients: a practical guideline. *Obes Surg*. 2019;29:3385-400.
81. Rostron ZP, Green RA, Kingsley M, Zacharias A. Associations between measures of physical activity and muscle size and strength: A systematic review. *Arch Rehabil Res Clin Transl*. 2021;3(2):100124.
82. Nielsen MS, Alsaoodi H, Hjorth MF, Sjödin A. Physical activity, sedentary behavior, and sleep before and after bariatric surgery and associations with weight loss outcome. *Obes Surg*. 2021;31 (1):250-9.
83. Donini LM, Busetto L, Bischoff SC, et al. Definition and diagnostic criteria for sarcopenic obesity: ESPEN and EASO consensus statement. *Obes Facts*. 2022;15(3):321-35.
84. Ravussin E, Lillioja S, Knowler WC, et al. Reduced rate of energy expenditure as a risk factor for body-weight gain. *N Eng J Med*. 1988;318(8):467-72.
85. Lamarca F, Melendez-Araújo MS, Porto de Toledo I, Dutra ES, de Carvalho KM. Relative energy expenditure decreases during the first year after bariatric surgery: a systematic review and meta-analysis. *Obes Surg*. 2019;29 (8):2648-59.
86. An Z, Wang H, Mokadem M. Role of the autonomic nervous system in mechanism of energy and glucose regulation post bariatric surgery. *Front Neurosci*. 2021;15:770690.
87. Rosenbaum M, Hirsch J, Murphy E, Leibel RL. Effects of changes in body weight on carbohydratemetabolism, catecholamine excretion, and thyroid function. *Am J Clin Nutr*. 2000;71(6):1421-32.

88. Ibacache P, Cárcamo P, Miranda C, et al. Improvements in heart rate variability in women with obesity: short-term effects of sleeve gastrectomy. *Obes Surg*. 2020;30(10):4038-45.

89. Li K, Shi W, Zhao F, et al. Changes in energy expenditure of patients with obesity following bariatric surgery: a systematic review of prospective studies and meta-analysis. *Obes Surg*. 2019;29:2318-37.

90. Faria SL, Kelly E, Faria OP. Energy expenditure and weight regain in patients submitted to Roux-en-Y gastric bypass. *Obes Surg*. 2009;19 (7):856-9.

91. Turicchi J, O'Driscoll R, Finlayson G, et al. Associations between the proportion of fat-free mass loss during weight loss, changes in appetite, and subsequent weight change: results from a randomized 2-stage dietary intervention trial. *Am J Clin Nutr*. 2020;111(3):536-44.

92. Morales-Marroquin E, Kohl HW, Knell G, de la Cruz-Muñoz N, Messiah SE. Resistance training in post-metabolic and bariatric surgery patients: a systematic review. *Obes Surg*. 2020;30 (10):4071-80.

93. Bellicha A, van Baak MA, Battista F, et al. Effect of exercise training before and after bariatric surgery: A systematic review and meta-analysis. *Obes Rev*. 2021;22:e13296.

94. Vieira FT, de Oliveira GS, Gonçalves VS, Neri SG, de Carvalho KM, Dutra ES. Effect of physical exercise on muscle strength in adults following bariatric surgery: A systematic review and meta-analysis of different muscle strength assessment tests. *Plos One*. 2022;17(6):e0269699.

95. Yoshiko A, Watanabe K, Akima H. Relative contribution of neuromuscular activation, muscle size, and muscle quality to maximum strength output of the thigh muscles in young

individuals. *Physiol Rep*. 2023;11(1):e15563.

96. Goodpaster BH, Park SW, Harris TB, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. *J Gerontol A Biol Sci Med Sci*. 2006;61(10):1059-64.

97. Chen L, Nelson DR, Zhao Y, Cui Z, Johnston JA. Relationship between muscle mass and muscle strength, and the impact of comorbidities: a population-based, cross-sectional study of older adults in the United States. *BMC Geriatr*. 2013;13(1):1-8.

98. Bollinger LM. Potential contributions of skeletal muscle contractile dysfunction to altered biomechanics in obesity. *Gait Posture.* 2017;56:100-7.

99. Verdijk LB, Van Loon L, Meijer K, Savelberg HH. One-repetition maximum strength test represents a valid means to assess leg strength in vivo in humans. *J Sports Sci*. 2009;27(1):59-68.

100. Dvir Z, Müller S. Multiple-joint isokinetic dynamometry: a critical review. *J Strength Cond Res*. 2020;34(2):587-601.

101. Sizoo D, de Heide LJ, Emous M, van Zutphen T, Navis G, van Beek AP. Measuring muscle mass and strength in obesity: a review of various methods. *Obes Surg*. 2021;31 (1):384-93.

102. McGuigan MR, Newton MJ, Winchester JB, Nelson AG. Relationship between isometric and dynamic strength in recreationally trained men. *J Strength Cond Res*. 2010;24(9):2570-3.

Impacto de la cirugía bariátrica en la variabilidad del ritmo cardiaco

Estudio 4

Sección 2

Sección 2

Estudio 4

Improvements in heart rate variability in women with obesity: short-term effects of sleeve gastrectomy

Obesity Surgery (2020)

https://doi.org/10.1007/s11695-020-04721-y

Paulina Ibacache, Paulina Cárcamo, Claudia Miranda, Andrés Bottinelli, Jaime Guzmán, Elena Martínez-Rosales, Enrique G. Artero, Marcelo Cano-Cappellacci

Abstract

Purpose. Obesity has been associated with reduced vagal function and increased sympathetic activity. Cardiac autonomic dysfunction has emerged as a major risk factor in the development of cardiovascular disease. Cardiac autonomic function (CAF) can be assessed by heart rate variability (HRV), an independent predictor of mortality based on the changes in time intervals between adjacent heartbeats (RR). Bariatric surgery is considered the most effective treatment for obesity and its comorbidities, being sleeve gastrectomy (SG) the most frequent bariatric procedure. There are few studies on HRV changes in women with obesity after SG. The aim of this study was to evaluate the short-term impact of SG on CAF and its relationship with weight loss.

Materials and Methods. An observational cohort study was conducted. Twenty-three female patients were assessed before SG and at one and three months after surgery. CAF was evaluated by analyzing HRV from 5-minute records of RR intervals while the subject was supine. HRV was analyzed in time and frequency domains, and with a nonlinear method.

Results. Patients (36.0±11.1 years old, BMI 35.1±3.4 kg/m^2) presented higher HRV values, on average, in all domains both at one and three months after SG ($p<0.05$). In addition, all anthropometric parameters improved ($p<0.001$) although there was no relationship between HRV improvements and anthropometric changes.

Conclusion. SG seems to be effective at reducing excess weight and improving HRV at short-term, and these changes are detectable as early as the first month after surgery. HRV assessment appears as a promising low-cost tool that deserves further research.

Keywords: Obesity, bariatric surgery, autonomic nervous system, weight loss.

Introduction

Obesity is a disease which affects over 650 million adults worldwide [1] with a higher prevalence in women [2]. It has been reported that obesity implies a greater cardiovascular disease (CVD) risk for women than men [3]. Obesity is associated with numerous comorbidities such as dyslipidemia, diabetes, osteoarthritis, some cancers [4], hypertension, atrial fibrillation, heart failure, stroke, and coronary heart disease [5-8]. CVD may occur due to structural and functional changes of the myocardium induced by the excess adipose tissue and other mechanisms related to obesity [5,9].

Obesity is also characterized by autonomic dysfunction with elevated sympathetic and decreased parasympathetic system activity, leading to an autonomic imbalance across the cardiovascular system [10]. Hormonal changes observed in subjects with obesity, such as an increase in insulin and leptin plasmatic levels, have been established as factors that contribute to autonomic dysfunction and the development of obesity-related cardiac diseases [11,12]. It has been described that a 10% increase in body weight is enough to decrease parasympathetic activity and to increase the activity of the sympathetic system, the latter would be an adaptive mechanism to increase the energy expenditure at rest and to promote the restoration of the previous weight [12].

Altered cardiovascular autonomic regulation resulting from obesity can be detected by assessing heart rate variability (HRV), the change in time intervals between adjacent heartbeats [13]. HRV has been widely described [14-19], proving to be an independent predictor of mortality [14, 20-24] associated with cardiac health [25].

HRV reductions in obese women have been previously reported

[13], with a higher rate of sudden cardiac death among obese people, compared to adults with normal body weight [26-28].

Conventional obesity treatment has shown limited success in reducing body weight over time [29]. The number of bariatric procedures has increased over recent years [30] and more than 70% of these have been performed on women [31]. Although evidence exists regarding the efficacy of bariatric surgery on weight reduction and comorbidities [32-35], there is insufficient information on the changes that sleeve gastrectomy (SG), the most common bariatric procedure in the world [30], can induce on HRV. The aim of this study was to describe the short-term HRV changes following SG, and their relationship to weight loss.

Materials and Methods

Study design, participants and procedures

In this analytical observational cohort study, participants were recruited over a 2-year period (2015 and 2016). The sample size was calculated with an alpha error of 5% and a statistical power of 90%, considering previously reported high frequency (HF) power data [36], which gave a required cohort size of 17 patients. The present study included 23 adult women with obesity (BMI ≥30 kg/m²) who were undergoing SG. Participants with arrhythmias, severe CVD, chronic renal insufficiency, chronic obstructive pulmonary disease, a smoking habit, used beta blockers, a postmenopausal status or who had undergone previous bariatric surgery were excluded.

All subjects followed the usual bariatric post-surgical diet indications [37] and were given recommendations for increasing physical activity levels.

Subjects were asked to fast for at least three hours before each evaluation; they were also asked to wear comfortable clothes and to refrain from drinking caffeinated and alcoholic beverages and performing intense physical exercise over the preceding 24 hours. All assessments were performed in the morning to avoid variations in the circadian rhythm.

A complete assessment of anthropometric parameters and HRV were conducted 7-14 days prior to surgery, as well as one month and three months following the SG.

All procedures were performed in accordance with the standards set out in the 1964 Helsinki Declaration and its later amendments, and all patients signed an informed consent.

Anthropometrics

The body mass index (BMI) and the waist circumference (at the level of the iliac crests) were determined using a DETECTO 439 balance scale and a Rosscraft anthropometric tape, respectively [38]. Weight loss was expressed as the percentage of total weight loss (%TWL) and the percentage of excess weight loss (%EWL) [39].

Heart rate variability

The duration of RR intervals was recorded using a Polar RS800CX telemetry heart rate monitor (Polar Electro Oy, Kempele, Finland) [40-42]. After resting in the supine position for five minutes, the heart rate RR intervals were continuously recorded for ten minutes in the same position in a quiet, temperature-controlled room (22–24°C) while breathing at a controlled rate (14 breaths per minute) using a metronome [43]. The time domain, frequency domain and nonlinear analysis of HRV were determined from the five-minute resting RR record with the lowest average heart rate.

RR data were analyzed with Kubios HRV Premium software (3.0.2 version) and preprocessed to remove abnormal intervals and artifacts [43,44]. The time domain HRV variables analyzed were standard deviation of all RR intervals (SDNN), root mean square of successive differences in RR intervals (RMSSD), and percentage of consecutive RR intervals that differ by more than 50 ms (pNN50) [16,23]. The frequency domain analysis was computed using the fast Fourier transform and the measures included the low frequency (LF) power, HF power and LF to HF power ratio (LF/HF) [14]. HF and LF were expressed in absolute and logarithm values (Ln). Nonlinear parameters included from Poincaré Plot were standard deviation 1 (SD1), that represents short-term variability, the major axis represents standard deviation 2 (SD2), meaning long-term variability (compared with SD1) and the sample entropy, which measures the regularity and complexity of a time series [18,25]. The ratio of change of the HRV variables was expressed as a percentage and was calculated by subtracting the pre-surgical value from the post-surgical data and dividing it by the pre-surgical values.

Surgical technique

The surgical procedures were performed by three certified bariatric surgeons. All the patients underwent laparoscopic SG, as described previously [45], leaving an estimated stomach capacity of 120-150 ml.

Statistical Analysis

For data distribution, the Shapiro-Wilk normality test was used. All HRV values were expressed as medians [minimum - maximum] whereas the anthropometric values were expressed as means ± standard deviation (SD). Differences in HRV over the three time points were analyzed using the Friedman test, with the Wilcoxon test being employed for pairwise comparison. To compare the anthropometric measurements over the three assessments, we used ANOVA with Bonferroni post-hoc analysis. The Spearman test was applied for correlation analysis. Statistical analysis was performed using SPSS 21.0 software (SPSS Inc, Chicago, IL, U.S.). A p-value of <0.05 was considered statistically significant.

Results

Thirty-five women with an indication for SG were recruited; however, five of them were excluded and two patients did not consent to participate in the study. Of the 28 patients initially included, five were loss during the study (Fig. 1).

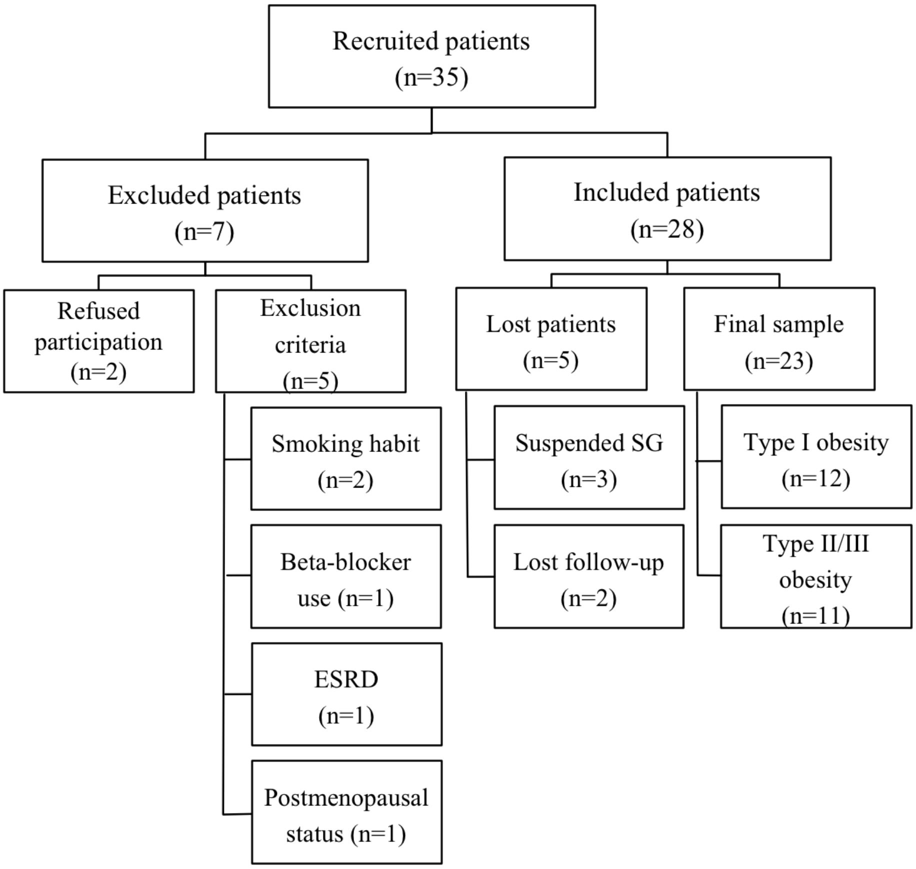


Fig. 1. Flow diagram of patient recruitment. *ESRD* End-stage renal disease.

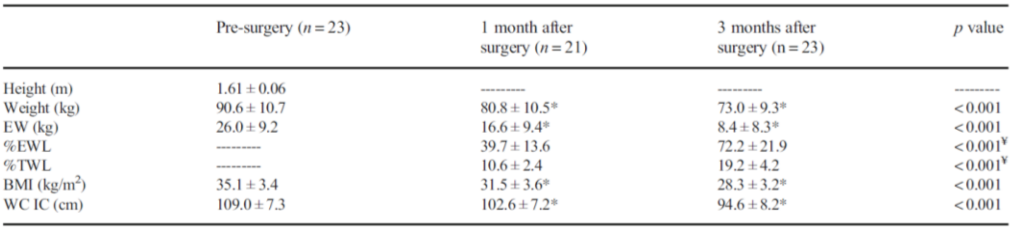
The study finally included 23 women (36.0 ± 11.1 years old; excess weight 26.0 ± 9.2 kg; BMI 35.1 ± 3.4 kg/m^2), two of which did not participate in the 1-month postoperative evaluation.

Regarding comorbidities, 2 of them had controlled arterial hypertension, 7 had controlled hypothyroidism, and 14 had non-alcoholic fatty liver disease.

There was a significant improvement in all the anthropometric measurements both at the first and the third month after surgery (Table 1). Regarding the HRV analysis, an improvement in all time domain variables was observed among the three assessments, SDNN (p=0.003; Cohen's d=0.68), RMSSD (p=0.006; Cohen's d=0.87), and pNN50 (Fig. 2) (Cohen's d=0.80), with all the improvements being statistically significant from the first month post-surgery (Table 2). In the frequency domain analysis, there was an improvement in HF power from the preoperative to postoperative assessments (both in absolute and Ln values, p=0.015; a Cohen's d for absolute HF power=0.75), with a higher spectral power from the first month following SG (Table 2). On the other hand, the LF power showed a tendency to improve among the three assessment points (p=0.076), with a significant change only between the preoperative assessment and the third month in absolute values (p=0.030; Cohen's d=0.22) and Ln values (p=0.007; Cohen's d=0.58) (Table 2). There were no significant changes in the LF/HF ratio (p=0.201).

The nonlinear analysis showed an improvement in SD1 and SD2 (Fig. 3), and no changes in sample entropy (p=0.217), with higher variability in the Poincaré plot from the first month in SD1 and SD2 (Table 2) (Cohen's d for SD1=0.87). There was no relationship between the weight changes and HRV improvements observed in our patients.

Table 1. Anthropometric characteristics at baseline and during follow-up after SG



	Pre-surgery ($n = 23$)	1 month after surgery ($n = 21$)	3 months after surgery (n = 23)	p value
Height (m)	1.61 ± 0.06	---------	---------	---------
Weight (kg)	90.6 ± 10.7	80.8 ± 10.5*	73.0 ± 9.3*	< 0.001
EW (kg)	26.0 ± 9.2	16.6 ± 9.4*	8.4 ± 8.3*	< 0.001
%EWL	---------	39.7 ± 13.6	72.2 ± 21.9	< 0.001¥
%TWL	---------	10.6 ± 2.4	19.2 ± 4.2	< 0.001¥
BMI (kg/m^2)	35.1 ± 3.4	31.5 ± 3.6*	28.3 ± 3.2*	< 0.001
WC IC (cm)	109.0 ± 7.3	102.6 ± 7.2*	94.6 ± 8.2*	< 0.001

Data are presented as means ± SD.
SG Sleeve gastrectomy, *EW* Excess weight, *%EWL* Percentage excess weight loss, *%TWL* Percentage total weight loss, *BMI* Body mass index, *WC IC* Waist circumference at the level of the iliac crests.
ANOVA *p* value. * *p*<0.001 compared with preoperative values. ¥ T Test *p* value.

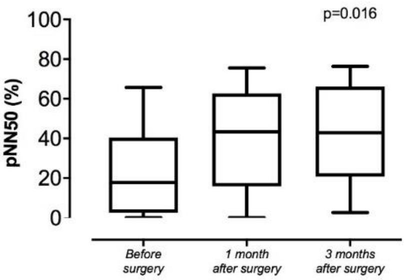


Fig. 2. Improvement in pNN50 after sleeve gastrectomy. pNN50 Percentage of RR intervals with differences above 50 ms. Friedman *p* value.

Discussion

This study showed that SG is effective at inducing significant weight loss and improving HRV indices, beginning as soon as the first month after surgery.

Only three previous studies have reported the effect of SG on HRV [36,46,47]. The study by Casellini et al. (on 56 patients with SG) showed an improvement in the HRV time domain 6 months after bariatric surgery. Unfortunately, the authors did not include either a frequency domain analysis or a nonlinear HRV analysis [46].

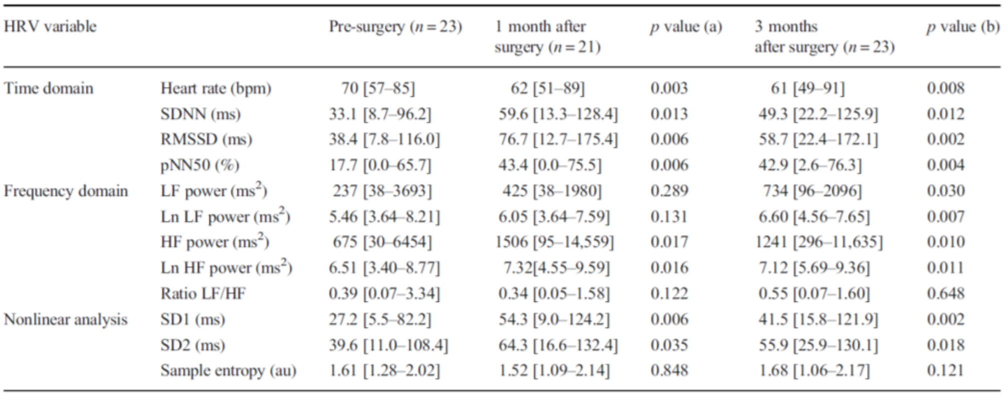
The work of Kokkinos et al. (on 23 patients with SG) showed similar results to our study related to improved HF and LF power both 3 and 6 months after SG, with no changes in the LF/HF ratio. The authors did not include time domain or nonlinear analysis results. There was also no information regarding the gender distribution of the sample [36].

Finally, in the work by Wu et al. on a sample of 18 patients with SG (50% women), the authors found statistically significant HRV improvements six months after SG, both in terms of the time and frequency domain analyses, although these changes were not apparent three months after surgery. Moreover, they found no changes in the nonlinear analysis. The findings of Wu et al. clearly differ from our results and theirs is the only work that showed changes in the LF/HF ratio after SG [47].

The increase in the RMSSD and pNN50 following SG that we observed in our study, which is directly related to vagus nerve activity [19], indicates enhanced parasympathetic activity [48]. The spectral power in HF, which increased in our patients from the first month following SG, is a well-known marker of parasympathetic tone [19]. In contrast, the LF, which only increased three months after SG in our study, reflects both sympathetic and vagal influences [19]. Likewise, the improvement we observed in the Poincaré plot indexes, SD1 and SD2, has been described as a reliable indicator of better parasympathetic system functioning [17].

Moreover, the SDNN, which also increased from the first month post SG in our study, is negatively influenced by the sympathetic

Table 2. HRV at baseline and during follow-up after SG



HRV variable		Pre-surgery ($n = 23$)	1 month after surgery ($n = 21$)	p value (a)	3 months after surgery ($n = 23$)	p value (b)
Time domain	Heart rate (bpm)	70 [57–85]	62 [51–89]	0.003	61 [49–91]	0.008
	SDNN (ms)	33.1 [8.7–96.2]	59.6 [13.3–128.4]	0.013	49.3 [22.2–125.9]	0.012
	RMSSD (ms)	38.4 [7.8–116.0]	76.7 [12.7–175.4]	0.006	58.7 [22.4–172.1]	0.002
	pNN50 (%)	17.7 [0.0–65.7]	43.4 [0.0–75.5]	0.006	42.9 [2.6–76.3]	0.004
Frequency domain	LF power (ms^2)	237 [38–3693]	425 [38–1980]	0.289	734 [96–2096]	0.030
	Ln LF power (ms^2)	5.46 [3.64–8.21]	6.05 [3.64–7.59]	0.131	6.60 [4.56–7.65]	0.007
	HF power (ms^2)	675 [30–6454]	1506 [95–14,559]	0.017	1241 [296–11,635]	0.010
	Ln HF power (ms^2)	6.51 [3.40–8.77]	7.32[4.55–9.59]	0.016	7.12 [5.69–9.36]	0.011
	Ratio LF/HF	0.39 [0.07–3.34]	0.34 [0.05–1.58]	0.122	0.55 [0.07–1.60]	0.648
Nonlinear analysis	SD1 (ms)	27.2 [5.5–82.2]	54.3 [9.0–124.2]	0.006	41.5 [15.8–121.9]	0.002
	SD2 (ms)	39.6 [11.0–108.4]	64.3 [16.6–132.4]	0.035	55.9 [25.9–130.1]	0.018
	Sample entropy (au)	1.61 [1.28–2.02]	1.52 [1.09–2.14]	0.848	1.68 [1.06–2.17]	0.121

Data are presented as medians [minimum-maximum]. *SG* Sleeve gastrectomy, *SDNN* Standard deviation of RR intervals duration, *RMSSD* Root mean square of successive differences in RR intervals, *pNN50* Percentage of RR intervals with differences above 50 ms, *LF* Low frequency, *Ln* Natural logarithm, *HF* High frequency, *SD* Standard deviation (from Poincaré plot), *au* Arbitrary units.
p value(a): Comparison of HRV variation from pre-surgery to one month after surgery; *p* value(b): Comparison of HRV variation from pre-surgery to three months after surgery.

component of the autonomic nervous system [15,19]. This might be due to the fact that, after bariatric surgery, there is a severe caloric restriction, mainly in the first months. It has been reported that these dietary changes produce a global reduction in sympathetic activity [49,50] with implications regarding resting energy expenditure as an adaptive response to a caloric restriction [50,51].

The improvement in parasympathetic tone following SG that we observed in our patients may be beneficial to their cardiovascular system, as previously reported [52-54], although it has not yet been established how much the vagal activity markers need to increase to provide protection for the heart.

Few studies have reported beneficial effects on cardiac function after SG. One study showed an improvement in systolic function and global longitudinal strain on the left ventricle that correlated with weight loss [55]. Also, after SG, a reduction in the interventricular septum, the thickness of the posterior wall and the mass of the left ventricle has been demonstrated [56].

A recent meta-analysis showed that SG has a greater effect on the parasympathetic tone than the gastric bypass procedure [57]. The SG surgical technique preserves the vagal trunk of the stomach's lesser curvature [57], and it has been suggested that the effects of bariatric surgery on the brain-gut axis could be influenced by the surgically induced anatomical alterations [12].

In our patients, we observed improved HRV in the time and frequency domains, as well as in the nonlinear analysis, with no additional intervention. In contrast, it has been previously reported that patients who have undergone a gastric bypass may only show improved HRV if there is a physical training program, with no change in those patients who only received the surgery [58]. This differs from the studies carried out by Bobbioni-Harsch et al., who found improvements in the time domain [59], and by Kokkinos et al., who reported improvements in the frequency domain - in both cases, there was no physical exercise training following surgery [36].

Our results suggest a recovery in cardiac autonomic function and a reversal of vagal impairment following weight loss [19]; this was demonstrated by the increase in SDNN, RMSSD, pNN50, HF, LF, SD1 and SD2, with a predominantly large or medium effect size. However, a difference in HRV between men and women has been described [60] so our results cannot be applied to the male bariatric population. It is also important to consider that age and initial BMI of our participants are lower than mean values previously reported worldwide [31] and might have influenced these positive results.

As HRV is a predictor of cardiovascular disease and early mortality [24] and considering the physiological changes that SG induces on autonomic function, repeatedly measurements of HRV may provide the data necessary for evaluating cardiac risk and other post-surgical complications [61]. However, we suggest additional research involving larger cohorts (ideally with higher BMI and including older patients and male population), with at least 12-month follow up, to confirm our findings and assess the utility of including HRV assessment in routine practice of bariatric patients.

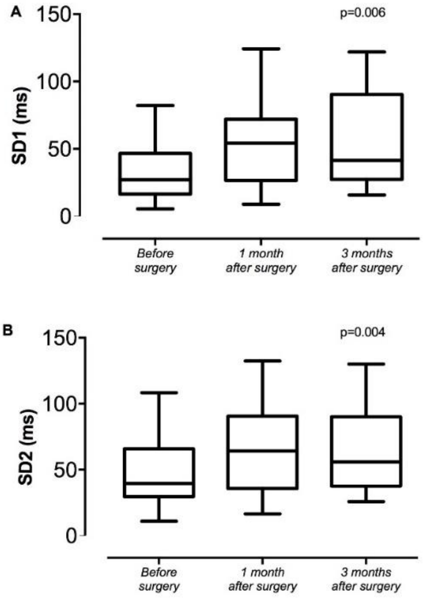


Fig. 3. Improvement in SD1 and SD2 after sleeve gastrectomy. *SD1* Standard Deviation from 45° axis on Poincaré plot. *SD2* Standard Deviation from 135° axis on Poincaré plot. Friedman *p* value.

We should acknowledge that the main limitation of this study is its inability to determine whether weight loss and HRV improvements will be permanent due to the short-term nature of the follow up. In addition, had we included a control group made up of obese patients who had not undergone surgery, or diet-induced weight loss patients, it would have enabled us to compare the results. Regarding the study’s main strength, we would like to point out that, so far, this is the most comprehensive HRV analysis conducted on a sample of women who have undergone exclusively SG.

Compliance with Ethical Standards

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee (registered number 149-2014) and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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

Informed/Written Consent Informed consent was approved by the institutional research ethics committee and was obtained from all individual participants included in the study.

References

1. World Health Organization. Obesity and overweight. [Internet]. [cited 2020 Feb 12]. Available from: www.who.int/mediacentre/factsheets/fs311/en/
2. Inoue Y, Qin B, Poti J, Sokol R, Gordon-Larsen P. Epidemiology of obesity in adults: Latest trends. Curr Obes Rep. 2018;7(4):276–288. doi:10.1007/s13679-018-0317-8
3. Garcia M, Mulvagh SL, Merz CN, Buring JE, Manson JE. Cardiovascular disease in women: Clinical Perspectives. Circ Res. 2016;118(8):1273-1293. doi:10.1161/CIRCRESAHA.116.307547
4. Williams EP, Mesidor M, Winters K, Dubbert PM, Wyatt SB. Overweight and obesity: prevalence, consequences, and causes of a growing public health problem. Curr Obes Rep. 2015;4(3):363-370. doi:10.1007/s13679-015-0169-4
5. Mandviwala T, Khalid U, Deswal A. Obesity and cardiovascular disease: a risk factor or a risk marker? Curr Atheroscler Rep. 2016;18(5):21. doi:10.1007/s11883-016-0575-4

6. Pareek M, Bhatt DL, Schiavon CA, Schauer PR. Metabolic surgery for hypertension in patients with obesity. Circ Res. 2019;124(7):1009-1024. doi:10.1161/CIRCRESAHA.118.313320
7. GBD 2015 Obesity Collaborators, Afshin A, Forouzanfar MH, Reitsma MB, Sur P, Estep K, et al. Health effects of overweight and obesity in 195 countries over 25 years. N Engl J Med. 2017;377:13-27. doi:10.1056/NEJMoa1614362
8. Lavie CJ, De Schutter A, Parto P, Jahangir E, Kokkinos P, Ortega FB, et al. Obesity and prevalence of cardiovascular diseases and prognosis—the obesity paradox updated. Prog Cardiovasc Dis. 2016;58(5):537-547. doi:10.1016/j.pcad.2016.01.008
9. Alpert M, Omran J, Mehra A, Ardhanari S. Impact of obesity and weight loss on cardiac performance and morphology in adults. Prog Cardiovasc Dis. 2014;56(4):391-400. doi:10.1016/j.pcad.2013.09.003
10. Wijngaarden MA, Pijl H, van Dijk KW, Klaassen ES, Burggraaf J. Obesity is associated with an altered autonomic nervous system response to nutrient restriction. Clin Endocrinol. 2013;79(5):648-651. doi:10.1111/cen.12100
11. Straznicky NE, Lambert GW, Lambert EA. Neuroadrenergic dysfunction in obesity: an overview of the effects of weight loss. Curr Opin Lipidol. 2010;21(1):21-30. doi:10.1097/MOL.0b013e3283329c62

12. Guarino D, Nannipieri M, Iervasi G, Taddei S, Bruno RM. The role of the autonomic nervous system in the pathophysiology of obesity. Front Psychol. 2017;8:665. doi:10.3389/fphys.2017.00665
13. Triggiani AI, Valenzano A, Ciliberti MA, Moscatelli F, Villani S, Monda M, et al. Heart rate variability is reduced in underweight and overweight healthy adult women. Clin Physiol Funct Imaging. 2017;37(2):162-167. doi:10.1111/cpf.12281
14. Shaffer F, McCraty R, Zerr CL. A healthy heart is not a metronome: an integrative review of the heart's anatomy and heart rate variability. Front Psychol. 2014;5:1040. doi:10.3389/fpsyg.2014.01040
15. Xhyheri B, Manfrini O, Mazzolini M, Pizzi C, Bugiardini R. Heart rate variability today. Prog Cardiovasc Dis. 2012;55(3):321-331. doi:10.1016/j.pcad.2012.09.001
16. Vigo DE, Siri LN, Cardinali DP. Heart rate variability: a tool to explore autonomic nervous system activity in health and disease. In: Gargiulo P, Mesones Arroyo H, editors. Psychiatry and Neuroscience Update. Cham: Springer; 2019. p. 113-126.
17. Rahman S, Habel M, Contrada RJ. Poincaré plot indices as measures of sympathetic cardiac regulation: Responses to psychological stress and associations with pre-ejection period. Int J Psychophysiol. 2018;133:79-90.

doi:10.1016/j.ijpsycho.2018.08.005

18. Kubičková A, Kozumplík J, Nováková Z, Plachý M, Jurák P, Lipoldová J. Heart rate variability analysed by Poincaré plot in patients with metabolic syndrome. J Electrocardiol. 2016;49(1):23-28. doi:10.1016/j.jelectrocard.2015.11.004
19. Task Force of the European Society of Cardiology and the North American Society of Electrophysiology. Heart rate variability, standards of measurement, physiological interpretation and clinical use. Eur Heart J. 1996;17(3):354-381.
20. Ziegler D, Zentai CP, Perz S, Rathmann W, Haastert B, Döring A, et al. Prediction of mortality using measures of cardiac autonomic dysfunction in the diabetic and nondiabetic population: the MONICA/KORA Augsburg Cohort Study. Diabetes Care. 2008;31(3):556-561. doi:10.2337/dc07-1615
21. Koko KR, McCauley BD, Gaughan JP, Fromer MW, Nolan RS, Hagaman AL, et al. Spectral analysis of heart rate variability predicts mortality and instability from vascular injury. J Surg Res. 2018;224:64-71. doi:10.1016/j.jss.2017.11.029
22. Sessa F, Anna V, Messina G, Cibelli G, Monda V, Marsala G, et al. Heart rate variability as predictive factor for sudden cardiac death. Aging. 2018;10(2):166-177. doi:10.18632/aging.101386
23. Shaffer F, Ginsberg JP. An overview of heart rate

variability metrics and norms. Front Public Health. 2017;5:258. doi:10.3389/fpubh.2017.00258

24. Wulsin LR, Horn PS, Perry JL, Massaro JM, D'Agostino RB. Autonomic imbalance as a predictor of metabolic risks, cardiovascular disease, diabetes, and mortality. J Clin Endocrinol Metab. 2015;100(6):2443-2448. doi:10.1210/jc.2015-1748
25. Rajendra Acharya U, Paul Joseph K, Kannathal N, Lim CM, Suri JS. Heart rate variability: a review. Med Biol Eng Comput. 2006;44(12):1031-1051. doi:10.1007/s11517-006-0119-0
26. Sabbag A, Sidi Y, Kivity S, Beinart R, Glikson M, Segev S, et al. Obesity and exercise-induced ectopic ventricular arrhythmias in apparently healthy middle aged adults. Eur J Prev Cardiol. 2016;23(5):511-517. doi:10.1177/2047487315591442
27. Adabag S, Huxley RR, Lopez FL, Chen LY, Sotoodehnia N, Siscovick D, et al. Obesity related risk of sudden cardiac death in the atherosclerosis risk in communities study. Heart. 2015;101(3):215-221. doi:10.1136/heartjnl-2014-306238
28. Chiuve SE, Sun Q, Sandhu RK, Tedrow U, Cook NR, Manson JE, et al. Adiposity throughout adulthood and risk of sudden cardiac death in women. JACC Clin Electrophysiol. 2015;1(6):520-528. doi:10.1016/j.jacep.2015.07.011
29. Montesi L, El Ghoch M, Brodosi L, Calugi S, Marchesini G, Dalle Grave R. Long-term weight loss

maintenance for obesity: a multidisciplinary approach. Diabetes Metab Syndr Obes. 2016;9:37-46. doi:10.2147/DMSO.S89836

30. Angrisani L, Santonicola A, Iovino P, Vitiello A, Higa K, Himpens J, et al. IFSO Worldwide Survey 2016: primary, endoluminal, and revisional procedures. Obes Surg. 2018;28(12):3783-3794. doi:10.1007/s11695-018-3450-2
31. Welbourn R, Pournaras DJ, Dixon J, Higa K, Kinsman R, Ottosson J, et al. Bariatric surgery worldwide: baseline demographic description and one-year outcomes from the second IFSO Global Registry Report 2013–2015. Obes Surg. 2018;28(2):313-322. doi:10.1007/s11695-017-2845-9
32. Jakobsen GS, Småstuen MC, Sandbu R, Nordstrand N, Hofsø D, Lindberg M, et al. Association of bariatric surgery vs medical obesity treatment with long-term medical complications and obesity-related comorbidities. JAMA. 2018;319(3):291-301. doi:10.1001/jama.2017.21055
33. Nguyen NT, Varela JE. Bariatric surgery for obesity and metabolic disorders: state of the art. Nat Rev Gastroenterol Hepatol. 2017;14(3):160-169. doi:10.1038/nrgastro.2016.170
34. Yu J, Zhou X, Li L, Li S, Tan J, Li Y, et al. The long-term effects of bariatric surgery for type 2 diabetes: systematic review and meta-analysis of randomized and non-randomized evidence.

Obes Surg. 2015;25(1):143-158. doi:10.1007/s11695-014-1460-2

35. Bower G, Toma T, Harling L, Jiao LR, Efthimiou E, Darzi A, et al. Bariatric surgery and non-alcoholic fatty liver disease: a systematic review of liver biochemistry and histology. Obes Surg. 2015;25(12):2280-2289. doi:10.1007/s11695-015-1691-x
36. Kokkinos A, Alexiadou K, Liaskos C, Argyrakopoulou G, Balla I, Tentolouris N et al. Improvement in cardiovascular indices after roux-en-y gastric bypass or sleeve gastrectomy for morbid obesity. Obes Surg. 2013;23(1):31-38. doi:10.1007/s11695-012-0743-8
37. Snyder-Marlow G, Taylor D, Lenhard MJ. Nutrition care for patients undergoing laparoscopic sleeve gastrectomy for weight loss. J Am Diet Assoc. 2010;110(4):600-607. doi:10.1016/j.jada.2009.12.022
38. Redberg RF, Benjamin EJ, Bittner V, Braun LT, Goff DC Jr, Havas S, et al. AHA/ACCF 2009 Performance measures for primary prevention of cardiovascular disease in adults. Circulation.2009;120(13):1296-1336. doi:10.1161/CIRCULATIONAHA.109.192617
39. Brethauer SA, Kim J, El Chaar M, Papasavas P, Eisenberg D, Rogers A, et al. Standardized outcomes reporting in metabolic and bariatric surgery. Obes Surg. 2015;25(4):587-606. doi:10.1016/j.soard.2015.02.003

40. Barbosa MP, da Silva NT, de Azevedo FM, Pastre CM, Vanderlei LC. Comparison of Polar® RS800G3™ heart rate monitor with Polar® S810i™ and electrocardiogram to obtain the series of RR intervals and analysis of heart rate variability at rest. Clin Physiol Funct Imaging. 2016;36(2):112-117. doi:10.1111/cpf.12203
41. Hernando D, Garatachea N, Almeida R, Casajús JA, Bailón R. Validation of heart rate monitor Polar RS800 for heart rate variability analysis during exercise. J Strength Cond Res. 2018;32(3):716-725. doi:10.1519/jsc.0000000000001662
42. Williams DP, Jarczok MN, Ellis RJ, Hillecke TK, Thayer JF, Koenig J. Two-week test-retest reliability of the Polar® RS800CX™ to record heart rate variability. Clin Physiol Funct Imaging. 2017;37(6):776-781. doi:10.1111/cpf.12321
43. Gisselman AS, D'Amico M, Smoliga JM. Optimizing inter-session reliability of heart rate variability – the effects of artefact correction and breathing type. J Strength Cond Res. 2017. doi:10.1519/JSC.0000000000002258
44. Tarvainen MP, Niskanen JP, Lipponen JA, Ranta-Aho PO, Karjalainen PA. Kubios HRV—heart rate variability analysis software. Comput Methods Programs Biomed. 2014;113(1):210-220. doi:10.1016/j.cmpb.2013.07.024
45. Kissler HJ, Settmacher U. Bariatric surgery to treat obesity. Semin Nephrol.

2013;33(1):75-89. doi:10.1016/j.semnephrol.2012.12.004

46. Casellini CM, Parson HK, Hodges K, Edwards JF, Lieb DC, Wohlgemuth SD, et al. Bariatric surgery restores cardiac and sudomotor autonomic C-fiber dysfunction towards normal in obese subjects with type 2 diabetes. PLoS One. 2016;11(5):e0154211. doi:10.1371/journal.pone.0154211
47. Wu JM, Yu HJ, Lai HS, Yang PJ, Lin MT, Lai F. Improvement of heart rate variability after decreased insulin resistance after sleeve gastrectomy for morbidly obesity patients. Surg Obes Relat Dis. 2015;11(3):557-563. doi:10.1016/j.soard.2014.09.011
48. Poirier P, Hernandez TL, Weil KM, Shepard TJ, Eckel RH. Impact of diet-induced weight loss on the cardiac autonomic nervous system in severe obesity. Obes Res. 2003;11(9):1040-1047. doi:10.1038/oby.2003.143
49. Straznicky NE, Lambert EA, Lambert GW, Masuo K, Esler MD, Nestel PJ. Effects of dietary weight loss on sympathetic activity and cardiac risk factors associated with the metabolic syndrome. J Clin Endocrinol Metab. 2005;90(11):5998-6005. doi:10.1210/jc.2005-0961
50. Rosenbaum M, Hirsch J, Murphy E, Liebel RL. Effects of changes in body weight on carbohydrate metabolism, catecholamine excretion, and thyroid function. Am J Clin Nutr. 2000;71(6):1421-1432. doi:10.1093/ajcn/71.6.1421

51. Bettini S, Bordigato E, Fabris R, Serra R, Dal Pra' C, Belligoli A, et al. Modifications of resting energy expenditure after sleeve gastrectomy. Obes Surg. 2018;28(8):2481-2486. doi:10.1007/s11695-018-3190-3
52. Olshansky B, Sabbah HN, Hauptman PJ, Colucci WS. Parasympathetic nervous system and heart failure: pathophysiology and potential implications for therapy. Circulation. 2008;118(8):863-871. doi:10.1161/CIRCULATIONAHA.107.760405
53. Guiraud T, Labrunee M, Gaucher-Cazalis K, Despas F, Meyer P, Bosquet L, et al. High-intensity interval exercise improves vagal tone and decreases arrhythmias in chronic heart failure. Med Sci Sports Exerc. 2013;45(10):1861-1867. doi:10.1249/MSS.0b013e3182967559
54. Dimova R, Tankova T, Chakarova N, Groseva G, Dakovska L. Cardiovascular autonomic tone relation to metabolic parameters and hsCRP in normoglycemia and prediabetes. Diabetes Res Clin Pract. 2015;109(2):262-270. doi:10.1016/j.diabres.2015.05.024
55. Leung M, Xie M, Durmush E, Leung DY, Wong VW. Weight loss with sleeve gastrectomy in obese type 2 diabetes mellitus: impact on cardiac function. Obes Surg. 2016;26(2):321-326. doi:10.1007/s11695-015-1748-x
56. Cavarretta E, Casella G, Calì B, Dammaro C, Biondi-Zoccai G, Iossa A, et al. Cardiac remodeling in obese patients after laparoscopic sleeve

gastrectomy. World J Surg. 2013;37(3):565-572. doi:10.1007/s00268-012-1874-8

57. Geronikolou SA, Albanopoulos K, Chrousos G, Cokkinos D. Evaluating the homeostasis assessment model insulin resistance and the cardiac autonomic system in bariatric surgery patients: A meta-analysis. Adv Exp Med Biol. 2017;988:249-259. doi:10.1007/978-3-319-56246-9_20
58. Castello V, Simões RP, Bassi D, Catai AM, Arena R, Borghi-Silva A. Impact of aerobic exercise training on heart rate variability and functional capacity in obese women after gastric bypass surgery. Obes Surg. 2011;21(11):1739-1749. doi:10.1007/s11695-010-0319-4
59. Bobbioni-Harsch E, Sztajzel J, Barthassat V, Makoundou V, Gastaldi G, Sievert K, et al. Independent evolution of heart autonomic function and insulin sensitivity during weight loss. Obesity. 2009;17(2):247-253. doi:10.1038/oby.2008.532
60. Koenig J, Thayer JF. Sex differences in healthy human heart rate variability: a meta-analysis. Neurosci Biobehav Rev. 2016;64:288-310. doi:10.1016/j.neubiorev.2016.03.007
61. Lodder AF, Kamath MV, Armstrong D, Upton ARM. Bariatric Surgery and Its Effects on Heart Rate Variability. In Kamath MV, Watanabe MA, Upton ARM, editors. Heart Rate Variability (HRV) Signal Analysis. Clinical Applications. Boca Raton: CRC Press; 2013. p. 279-302.

Conclusiones generales

CONCLUSIONES GENERALES

Si bien la cirugía bariátrica ha demostrado variados beneficios para la salud, entre ellos la reducción del peso corporal, la mejora de la variabilidad del ritmo cardiaco y la remisión/mejora de las comorbilidades, a corto plazo parece afectar negativamente la capacidad cardiorrespiratoria, la fuerza muscular de las extremidades inferiores y la composición muscular.

Aunque la reducción del peso corporal es el *outcome* más buscado en el manejo de la obesidad (o al menos uno de ellos), que se considera el criterio de éxito por excelencia de la intervención bariátrica, esta se ha asociado con un deterioro de la condición física asociada a la salud. Las meta-regresiones presentadas en esta tesis doctoral mostraron que las personas que experimentaron una mayor disminución de su peso corporal después de la cirugía bariátrica, también sufrieron una mayor reducción de su capacidad cardiorrespiratoria y fuerza muscular. Esto podría explicarse, en parte, porque posiblemente las personas que experimentaron una mayor reducción de su peso corporal también sufrieron una mayor pérdida de masa magra.

Se ha evidenciado que tanto la capacidad cardiorrespiratoria como la fuerza muscular son uno de los indicadores de salud y de expectativa de vida más importantes, tanto en personas sanas, como en aquellas con morbilidades, demostrándose que niveles bajos de estos componentes de la condición física se asocian con un alto riesgo de morbimortalidad, independiente del nivel de IMC. Considerando estos antecedentes y que incluso pequeños incrementos en la capacidad cardiorrespiratoria o en la fuerza muscular pueden afectar el riesgo de morbimortalidad de manera clínicamente significativa, es que la reducción observada en la capacidad cardiorrespiratoria y en la fuerza posteriores a una cirugía bariátrica podría mitigarse prescribiendo un programa de ejercicio físico individualizado y supervisado como parte esencial del manejo de estos usuarios, tanto antes como después de la intervención quirúrgica.

Son necesarios estudios con un seguimiento a largo plazo para confirmar el efecto adverso de la cirugía bariátrica sobre la capacidad cardiorrespiratoria, la fuerza y la composición muscular, así como estudiar las consecuencias de estos cambios en la salud de esta población. La combinación de evaluaciones de la composición corporal, la fuerza muscular y otros *outcomes* de salud, incluido un mayor tamaño muestral y múltiples evaluaciones de seguimiento postquirúrgicas, podría proporcionar una mejor comprensión del vínculo entre la pérdida de peso, los cambios en la masa muscular, la capacidad cardiorrespiratoria y la fuerza/calidad muscular y la salud en esta población.

Finalmente, y en base a la evidencia expuesta, sería conveniente plantearse si la pérdida de peso debiese seguir siendo el enfoque principal del tratamiento de la obesidad. Según lo estudiado en la presente tesis doctoral, se sugiere incorporar *outcomes* de salud tan o más importantes que el peso corporal, tales como la capacidad cardiorrespiratoria y la fuerza muscular en la valoración y manejo de estos usuarios.

OTRAS APORTACIONES CIENTÍFICAS DERIVADAS DE LA TESIS DOCTORAL

Presentaciones en eventos científicos

Fecha	Trabajo presentado	Formato presentación	Evento
Octubre-2019	Aumento temprano de la variabilidad del ritmo cardiaco en mujeres con obesidad sometidas a una cirugía bariátrica - Coautor	Oral	42º Simpósio Internacional de Ciências do Esporte. CELAFISCS. São Paulo, Brasil.
Mayo- 2019	*Association between preoperatory moderate vigorous physical activity and cardiorespiratory fitness one year after bariatric surgery* - Autor principal	Póster	World Confederation for Physical Therapy Congress 2019. Ginebra, Suiza.
Septiembre-2022	*Relationship of physical activity and sedentary behavior with cardiometabolic risk factors in patients awaiting bariatric surgery: EFIBAR Study*- Autor principal	Póster	37th World Congress of Sports Medicine. Federación Internacional de Medicina del Deporte (FIMS). Guadalajara, México.
Junio- 2023	*Effects of bariatric surgery on strength and muscle quality: a systematic review*- Autor principal	Oral	World Physiotherapy Congress 2023. Dubai, Emiratos Árabes.
Junio- 2023	*Association between muscle quality, body composition and physical activity in adults with obesity awaiting bariatric surgery*- Autor principal	Póster	World Physiotherapy Congress 2023. Dubai, Emiratos Árabes.

AGRADECIMIENTOS

Sin duda en primer lugar necesito comenzar agradeciendo a quien permite que abra mis ojos cada día. A mi padre, creador y sustentador.

A mi familia. A mi pequeñita hermosa, que con sus miradas, abrazos y besos mientras escribía esta tesis, sin comprenderlo, me daba las fuerzas que necesitaba para continuar cuando me quedaban pocas. Comencé esta aventura contigo en mi panza y ahora tendré la bendición de concluirla de tu mano.

A mi Marce, que me instó a comenzar este desafío y me apoyo en todo lo que pudo para que pudiera concluirlo exitosamente también.

A mis padres. A mi mamita hermosa que me apoyo con el cuidado de mi Josefinita. A mi papá que me enseño a amar la lectura y la escritura desde pequeña.

A Enrique, quien me animó a comenzar el doctorado y estuvo en todo momento para lo que necesité.

A la Ele, por su siempre desinteresada ayuda.

Finalmente, a mis amigos, mi familia escogida, quienes con su preocupación y comprensión también fueron parte importante de todo este proceso.