UNIVERSIDAD POLITÉCNICA DE MADRID

**FACULTAD DE CIENCIAS DE LA ACTIVIDAD FÍSICA Y DEL
DEPORTE (INEF)**

**Influencia de un programa de nutrición y actividad física sobre
parámetros cardiorrespiratorios, hemodinámicos, metabólicos y
comportamentales**

Impact of a nutrition and physical activity program in cardiorespiratory,
hemodynamic, metabolic and behavior parameters

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DEPORTE (INEF)

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Por vezes sentimos que aquilo que fazemos não é
senão uma gota de água no mar. Mas o mar seria
menor se lhe faltasse uma gota.

(Madre Teresa de Calcutá)

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CERTIFICA:

Que la Tesis Doctoral titulada *“Influencia de un programa de nutrición y actividad física sobre parámetros cardiorrespiratorios, hemodinámicos, metabólicos y comportamentales”* que presenta Dña. **ELIANE APARECIDA DE CASTRO** al superior juicio del Tribunal que designe la Universidad Politécnica de Madrid, ha sido realizada bajo mi dirección durante los años 2013-2017. El trabajo presentado cumple con todos los criterios científicos y técnicos exigidos, y demuestra la capacidad de su autora para ser mecedora del Título de Doctora con Mención Internacional, siempre y cuando así lo considere el citado Tribunal.

Fdo. Ana Belén Peinado Lozano

En Madrid, a 18 de abril de 2017

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Fdo. Rocío Cupeiro Coto

En Madrid, a 18 de abril de 2017

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List of abbreviations

ACSM: American College of Sports Medicine.

ANCOVA: Analysis of covariance.

ANOVA: Analysis of variance.

BMI: Body mass index.

BP: Blood pressure.

BW: Body weight.

CAPES: *Coordenação de Aperfeiçoamento de Pessoal de Nível Superior*.

CHO: Carbohydrate.

CVD: Cardiovascular diseases.

DBP: Diastolic blood pressure.

E: Endurance training group.

FEMEDE: *Federación Española de Medicina del Deporte*.

Fig.: Figure.

FM: Fat mass.

G: Intervention group.

HDL: High density cholesterol.

HR: Heart rate.

HR_{max}: Maximal heart rate.

HULP: *Hospital Universitario La Paz.*

LBM: Lean body mass.

LIPA: Light-intensity physical activity.

LoA: Limits of agreement.

MAP: Mean arterial pressure.

MVPA: Moderate-vigorous physical activity.

O: Obese.

PA: Physical activity recommendations group.

PAL: Physical activity level.

PP: Pulse pressure.

PRO: Protein.

PRONAF: *Programas de nutrición y actividad física para el tratamiento de la obesidad.*

RM: Repetitions maximum.

RMR: Resting metabolic rate.

S: Strength training group.

SBP: Systolic blood pressure.

SD: Standard deviation.

SE: Combined strength and endurance training group.

SMR: Standing metabolic rate.

SPSS: Statistical Package for Social Science.

SUP: Supervised training group.

T: Time.

TC: Total cholesterol.

TEI: Total energy intake.

UPM: *Universidad Politécnica de Madrid*.

VO₂: Oxygen consumption.

VO_{2peak}: Peak oxygen consumption or peak oxygen uptake.

VT₁: First ventilatory threshold.

VT₂: Second ventilatory threshold.

W: Overweight.

WC: Waist circumference.

WHO: World Health Organization.

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RESUMEN

Introducción: La obesidad es una patología metabólica que se ha convertido en un complejo problema de salud pública. En la mayoría de los casos se produce cuando la ingesta calórica supera al gasto energético, aunque son múltiples los factores que están influyendo en el incremento del peso corporal. Sin embargo, los mecanismos que impulsan la ingesta y el gasto en el llamado ambiente obesogénico son extremadamente complicados, y han sido atribuidos al estilo de vida y a cambios en los hábitos alimenticios. La obesidad viene acompañada de una disminución de la condición física y de la tasa metabólica de reposo, además de estar asociada a trastornos cardiovasculares y alimenticios, como puede ser la presión arterial elevada y la ingesta calórica inadecuada. La actividad física desempeña un papel importante en la prevención y el tratamiento de muchos cambios y trastornos causados por la obesidad. Entender cómo el ejercicio contribuye en la reducción de las consecuencias derivadas de estos cambios, podría ayudar a los entrenadores y profesionales de la salud pública en el manejo de esta enfermedad.

Objetivo: En este contexto, el objetivo general de esta tesis doctoral fue verificar la influencia de un programa de actividad física y nutrición en los parámetros cardiorrespiratorios (Estudio I), hemodinámicos (Estudio III), metabólicos (Estudio IV) y de comportamiento alimentario (Estudio V), así como desarrollar ecuaciones de predicción del consumo de oxígeno pico ($VO_{2\text{pico}}$) para individuos con sobrepeso y obesidad (Estudio II).

Métodos: Los datos de esta tesis doctoral derivan del proyecto PRONAF: “PROgramas de Nutrición y Actividad Física para el tratamiento de la obesidad”. Este estudio fue un ensayo clínico aleatorizado, desarrollado en población española con sobrepeso y obesidad, y llevado a cabo a lo largo de tres años. Los sujetos incluidos fueron

asignados aleatoriamente a uno de los cuatro grupos de intervención: entrenamiento de fuerza, entrenamiento de resistencia, entrenamiento combinado fuerza + resistencia y un grupo de entrenamiento basado en las recomendaciones de actividad física, asegurando una distribución homogénea de la edad y el género entre los grupos. El grupo de recomendaciones siguió pautas generales de actividad física. Los sujetos de los demás grupos entrenaron tres veces por semana y todas las sesiones de entrenamiento fueron cuidadosamente supervisadas por entrenadores personales certificados, licenciados en Ciencias de la Actividad Física y del Deporte. Todos los participantes fueron sometidos a una intervención dietética individualizada basada en una dieta hipocalórica prescrita por dietistas expertos. La dieta tenía como objetivo una reducción del 25-30% del gasto energético diario. La intervención duró 22 semanas y todas las evaluaciones de las variables utilizadas en esta tesis tuvieron lugar una semana antes (pre) y después (post) de la intervención.

Resultados: Los principales resultados fueron: se observó una mejora del $\text{VO}_{2\text{pico}}$ en hombres con sobrepeso y obesidad (valores pre y post en L/min, respectivamente, sobrepeso = $3,2 \pm 0,6$ vs $3,7 \pm 0,5$, $p < 0,001$, obesos = $3,6 \pm 0,6$ vs $3,8 \pm 0,6$, $p = 0,013$), así como en mujeres con sobrepeso ($2,0 \pm 0,3$ vs $2,3 \pm 0,4$, $p < 0,001$), sin diferencias entre los grupos de intervención (Estudio I). La siguiente ecuación de predicción presentó el mayor coeficiente de determinación ($R^2 = 0.885$), utilizando los datos de la prueba de esfuerzo para los sujetos considerados activos tras la intervención: $\text{VO}_{2\text{pico}}$ (L/min) = $-5,017 + (0,040 \times \text{peso corporal}) + (0,127 \text{ tiempo de ejercicio}) + (0,046 \times \text{porcentaje de masa corporal magra}) + (-0,010 \times \text{edad})$ (Estudio II). La presión arterial sistólica (PAS) y la presión arterial media (PAM) disminuyeron en hombres con sobrepeso (PAS: -7,9%, $p < 0,001$; PAM: -9,6%, $p < 0,001$) y obesos (PAS: -3,0% 0,033; PAM: -4,9%, $p = 0,001$). Además en los hombres, la presión arterial diastólica

(PAD) también se redujo (-8,3%, $p < 0,001$). En las mujeres PAS, PAM, PAD y presión de pulso disminuyeron significativamente alrededor del 5% ($p < 0,05$), sin diferencias entre los grupos de intervención (Estudio III). El riesgo cardiovascular calculado por la función de Framingham-REGICOR reducía solamente en los hombres (-25,7%, $p < 0,001$) (Estudio III). La tasa metabólica de reposo disminuyó en mujeres sin interacción entre grupos de intervención y tiempo (pre: 1592.8 ± 272.3 , post: 1461.2 ± 266.6 , $p = 0.001$), y los hombres no la cambiaron (Estudio IV). Los sujetos disminuyeron la ingesta de energía y grasa, y aumentaron la ingesta de carbohidratos y proteínas desde la pre hasta la post-intervención ($p < 0,001$), sin interacciones significativas para grupos de intervención, categoría de índice de masa corporal o sexo (Estudio V). Las interacciones entre género y tiempo fueron observadas para la motivación al ejercicio y sólo las mujeres aumentaron su motivación después de la intervención (pre: $17,6 \pm 0,3$, post: $18,2 \pm 0,3$, $p = 0,034$), mientras que los hombres la mantuvieron (Estudio V).

Conclusiones: Las conclusiones principales fueron: nuestros hallazgos sugieren que: (a) no hay efecto sustancial del tipo de ejercicio en la respuesta cardiovascular (con mejoras observadas en hombres y mujeres con sobrepeso y en hombres obesos) (Estudio I); en la respuesta de la presión arterial (reducción de la presión arterial en todos los individuos) (Estudio III); en el riesgo cardiovascular (todas las intervenciones disminuyeron el riesgo cardiovascular en hombres) (Estudio III); en la tasa de metabolismo de reposo (ninguna de las intervenciones pudo evitar la reducción de tasa de metabolismo de reposo en mujeres) (Estudio IV); y tampoco en la ingesta energética o la selección de macronutrientes (Estudio V); (b) nuestros hallazgos también mostraron múltiples diferencias entre sexos en respuesta a las intervenciones, lo que sugiere una posible necesidad de mayor intensidad o duración del ejercicio para los cambios en los riesgos cardiovasculares en mujeres (Estudio III), o el mantenimiento de la tasa

metabólica en reposo (Estudio IV), para la mejora cardiorrespiratoria en mujeres obesas (Estudio I); (c) después de un programa de pérdida de peso de 22 semanas, la motivación relacionada con la dieta o el ejercicio no se redujo, demostrando una buena aceptación del programa, especialmente en el grupo de mujeres, que aumentaron la motivación para la realización de ejercicio (Estudio V); (d) las ecuaciones de predicción desarrolladas en este estudio, incluyendo edad, peso corporal, porcentaje de masa magra y tiempo de ejercicio fueron más adecuadas para predecir el $\text{VO}_{2\text{pico}}$ en sujetos con sobrepeso y obesidad, que las ecuaciones comúnmente utilizadas en la literatura (Estudio II).

Palabras clave: obesidad; sobrepeso; ejercicio; actividad física; consumo de oxígeno; presión arterial sanguínea; tasa metabólica de reposo; comportamiento alimentario; salud.

ABSTRACT

Introduction: Obesity is a metabolic pathology that has become a complex public health problem. In most cases, it occurs when the caloric intake exceeds the energy expenditure, although there are multiple factors that are influencing the increase in body weight. However, the mechanisms that drive intake and expenditure, in the so-called obesogenic environment, are extremely complicated, and have been attributed to lifestyle and changes in eating habits. Obesity is accompanied by a decrease in physical condition and resting metabolic rate, in addition to being associated with cardiovascular and eating disorders, such as high blood pressure and inadequate caloric intake. Physical activity plays an important role in the prevention and treatment of many changes and disorders caused by obesity. Understanding how exercise contributes to reducing the consequences of these changes could help coaches and public health professionals in management of this disease.

Objective: In this context, the general aim of this doctoral thesis was to verify the influence of a physical activity and nutrition program in cardiorespiratory (Study I), hemodynamic (Study III), metabolic (Study IV) and eating behavior (Study V) parameters, as well as to develop prediction equations for estimating peak oxygen consumption (VO_{2peak}) in individuals with weight excess (Study II).

Methods: Data for this doctoral thesis were derived from PRONAF project: “PROgramas de Nutrición y Actividad Física para el tratamiento de la obesidad”, a randomized trial developed in overweight and obese Spanish population during three years. Subjects included were randomly assigned to one of the four intervention groups: strength training, endurance training, combined strength+endurance training and a guideline-based physical activity, assuring a homogeneous distribution of age and gender among groups. The guideline-based physical activity group followed general

physical activity recommendations from the American College of Sports Medicine. Subjects of training groups trained three times per week. All training sessions were carefully supervised by certified personal trainers with Sports Science degrees. All participants underwent an individualized dietary intervention based on a hypocaloric diet prescribed by expert dietitians. The diet aimed at a 25-30% reduction on the total daily energy expenditure. The intervention lasted 22 weeks and all assessments for the variables utilized in this thesis took place one week before (baseline) and after (post) the intervention.

Resultados: The main results were: $\text{VO}_{2\text{peak}}$ improved in overweight and obese males (pre and post values in L/min, respectively; overweight = 3.2 ± 0.6 vs. 3.7 ± 0.5 , $p < 0.001$; obese = 3.6 ± 0.6 vs. 3.8 ± 0.6 , $p = 0.013$) as well as in overweight females (2.0 ± 0.3 vs. 2.3 ± 0.4 , $p < 0.001$), without interaction between intervention groups and time (Study I). The following equation presented the highest determination coefficient ($R^2 = 0.885$), using effort test data for active subjects: $\text{VO}_{2\text{peak}}$ (L/min) = $-5.017 + (0.040 \times \text{body weight}) + (0.127 \times \text{time of exercise}) + (0.046 \times \text{lean body mass percentage}) + (-0.010 \times \text{age})$ (Study II). In men, systolic BP (SBP) and mean arterial pressure (MAP) decreased in overweight (SBP: -7.9%, $p < 0.001$; MAP: -9.6%, $p < 0.001$) and obese (SBP: -3.0%, $p = 0.033$; MAP: -4.9%, $p = 0.001$). Diastolic blood pressure (DBP) also reduced in males (-8.3%, $p < 0.001$). In women no interactions were found for body mass category or groups and SBP, MAP, DBP, pulse pressure decreased significantly about 5% ($p < 0.05$), without interaction between intervention groups and time (Study III). Cardiovascular risk calculated by Framingham-REGICOR function reduced only in males (-25.7%, $p < 0.001$) (Study III). Resting metabolic rate decreased in women without interaction between intervention groups and time (pre: 1592.8 ± 272.3 , post: 1461.2 ± 266.6 , $p = 0.001$) and men did not change it (Study IV). Subjects decreased

energy and fat intakes and increased carbohydrate and protein intakes from pre- to post-intervention ($p < 0.001$) without significant interactions with intervention groups, body mass index category or sex (Study V). Interaction between sex and time was observed for motivation to exercise and only women increased their motivation after the intervention (pre: 17.6 ± 0.3 , post: 18.2 ± 0.3 , $p = 0.034$), while men maintained it (Study V).

Conclusions: The main conclusions were: (a) our findings suggested no substantial effect of type of exercise on cardiovascular fitness response (with improvement observed in overweight subjects and obese males) (Study I); on blood pressure response (blood pressure reduction in all individuals) (Study III); on cardiovascular risk (all interventions decreased cardiovascular risk in men) (Study III); on resting metabolic rate (none of the interventions was able to avoid the reduction in resting metabolic rate in women) (Study IV); on energy intake or macronutrient selection (Study V); (b) our findings also showed sex difference in several responses to interventions, suggesting a possible need for more intensity or duration of the exercise for changes in cardiovascular risks in women (Study III), or maintenance resting metabolic rate (Study IV), as well as cardiorespiratory improvement in obese women (Study I); (c) after 22-weeks weight loss program, motivation related to diet or exercise did not reduce, demonstrating good acceptance and suitability of the program, especially in women, that increase their motivation to exercise (Study V); (d) prediction equations developed in this study including age, body weight, lean body mass percentage, and time of effort test were more adequate to predict VO_{2peak} in overweight and obese subjects than those most commonly used equations in the literature (Study II).

Keywords: obesity; overweight; exercise; physical activity; oxygen consumption; blood pressure; resting metabolic rate; eating behavior; health.

1.INTRODUCTION

INTRODUCTION

Body weight excess: epidemiology, risk factors and treatments

Obesity is a complex metabolic disorder (Laffin et al., 2016), which has been considered as a major public health problem (Vallgarda, 2015). Obesity is associated with number of diseases, especially cardiovascular disease, hypertension, dyslipidemia and diabetes; and evidences indicate that even with treatment for mediate these diseases, obese individuals will continue to have significantly raised risk (Lu et al., 2014). In 2008, over 50% of both men and women in the World Health Organization (WHO) European Region were overweight, and approximately 23% of women and 20% of men were obese, representing double the data observed in 1980 (Bischoff et al., 2016). In Spain, body weight excess also achieves over half of the adult population (54% and 71%, women and men, respectively), with obesity prevalence reaching 24.4% in men and 21.4% in women (Gutierrez-Fisac et al., 2012).

Fat distribution seems to play an important role in the relationship between obesity and cardiovascular disease; and central abdominal obesity becomes a main risk factor contributing to cardiovascular disease risk (Laffin et al., 2016). Besides considerable prevalence of obesity in Spanish population, abdominal obesity is also presented in a very high percentage (51%) in this population (Casanueva et al., 2010).

There is a very small probability of cardiovascular diseases when a population reaches 50 years of age with total cholesterol <180mg/dl, blood pressure <120/<80mmHg and without having ever smoked. In Spanish population, this amount does not exceed 6% (Marrugat et al., 2011). This data indicates that there is still large scope for preventive action.

Although obesity, in the vast majority of cases, occurs when energy intake exceeds energy expenditure (Romieu et al., 2017); the mechanisms that drive intake and

expenditure in the prevailing obesogenic environment are extremely complex (Hopkins and Blundell, 2016).

In the last years, the adipocyte has been considered as a “metabolically active cell” due to its capacity to produce various adipokines and inflammatory substances that, in many occasions, stimulate hormonal changes (Laffin et al., 2016). These changes are responsible for many metabolic modifications that can lead to a vicious cycle of increasing of the adipose tissue (Hopkins and Blundell, 2016). In obese individuals there seems to be a fat oxidation economy at resting, represented by a higher respiratory quotient compared to lean individuals (Shook et al., 2016). Furthermore, fat mass, through of leptin secretion, has a strong inhibitory effect on food intake in lean subjects, but this effect appears to weak dramatically as adipose tissue increases, interfering appetite control (Blundell et al., 2015). Moreover, the accumulation of adipose tissue *per se* may also promote overconsumption, sedentariness and further weight gain (Hopkins and Blundell, 2016).

In addition, subjects with weight excess have lower cardiorespiratory fitness, muscle deconditioning, and lower resting metabolic rate; besides greater endothelial dysfunction and peripheral resistance, that contribute for blood pressure increasing and onset of cardiovascular diseases (McMurray et al., 2014, Miller et al., 2012, Van Gaal et al., 2006, Wang et al., 2010, Salvadori et al., 1999, Filozof and Gonzalez, 2000).

Collectively, alterations mentioned above, could to contribute in the imbalance between energy intake and expenditure, leading to progressive increases in body weight and fat stores. The figure 1 illustrates the changes induced by obesity and indicates where each study that composes this work will focus.

Fig. 1. Obesogenic environment.

There are many techniques to measure the adipose tissue, from more sophisticated instruments (such as dual-energy X-ray absorptiometry or computed tomography) to simpler and cheaper techniques (anthropometry). Body mass index (BMI) is the most often obesity indicator utilized as an easy, quick and inexpensive measure to apply to large populations. Moreover, BMI also has been used as inclusion criteria in many randomized controlled trials. Although some researches affirm that BMI could mask a real increase in the obesity epidemic (Visscher et al., 2015), its direct association with body fat, mainly in sedentary individuals (Bradbury et al., 2017) and its strong relation to cardiovascular disease (Aune et al., 2016), become it in an extremely useful instrument.

Regardless of the method used to measure obesity, obesity treatment requires a multidisciplinary approach, both at the level of prevention and therapy including weight loss and maintenance (Bischoff et al., 2016). Since obesity is a chronic systemic disease associated to others diseases, non-pharmacological approaches through weight loss, diet

modification and behavioral changes should be a part of the global response to this problem.

Physical activity plays an important role in the prevention and treatment of many disorders, including obesity (Martin et al., 2016). Exercise aims improving body composition and correcting various metabolic abnormalities that occur with obesity, which would ultimately be the cause of high co-morbidities presented by obese subjects (Koch et al., 2005). Clinicians should to keep emphasizing that exercise is medicine (Eijssvogels and Thompson, 2015).

The pharmacological effect of myokines became exercise into one of the most important agents in the prevention and treatment of obesity, and object of interest of a growing number of studies. Moreover, results from a limited number of studies conducted in primary care settings demonstrate that the promotion of physical activity may be a cost-effective approach (Katzmarzyk, 2011).

Despite the existence of effective physical activity interventions, studies about exercise types and doses for obesity treatment are still needed.

Types of exercise for obesity treatment

Usually, obesity is accompanied by a decrease in physical condition and resting metabolic rate, in addition to being associated with cardiovascular and eating disorders, such as high blood pressure and inadequate caloric intake. Therefore, treating obesity means promoting changes in the parameters that are associated with this disease. Furthermore, regular exercise has many beneficial effects on several health parameters even if weight loss does not occur.

Below are presented the implications of different types of exercise in some parameters affected by obesity and which are discussed throughout this work.

Improvement of cardiorespiratory fitness

Peak oxygen uptake ($\text{VO}_{2\text{peak}}$) is used for measure cardiorespiratory fitness and has been considered the best predictor for cardiovascular mortality and morbidity (Kurl et al., 2003). Data regarding the effect of different training methods for improving cardiovascular fitness in obese subjects are still inconsistent. In the Table 1 are presented the $\text{VO}_{2\text{peak}}$ response for different types of exercise in studies with overweight and obese individuals.

Table 1. Absolute $\text{VO}_{2\text{peak}}$ response to strength, aerobic and combined trainings in different studies with or without diet.

Authors (year)	Strength	Aerobic	Combined	Control	Diet
Ahmadizad et al (2007)	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	----	NS	No
Aioke et al. (2011)	----	$\text{VO}_{2\text{peak}} \uparrow$	----	----	No
Al Saif & Alsenany (2015)	----	$\text{VO}_{2\text{peak}} \uparrow$	----	----	Yes
Ballor et al. (1996)	NS	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	----	----	Yes
Bateman et al. (2011)	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	----	No
Boyd et al. (2013)	----	$\text{VO}_{2\text{peak}} \uparrow$	----	----	No
Christiansen et al. (2010)	----	$\text{VO}_{2\text{peak}} \uparrow$	----	NS	Yes
Christ-Roberts et al. (2004)	----	$\text{VO}_{2\text{peak}}^{\neq} \uparrow$	----	----	No
Cox et al. (2003)	----	$\text{VO}_{2\text{peak}} \uparrow$	----	----	Yes
Davidson et al. (2009)	NS	$\text{VO}_{2\text{peak}} \uparrow$	$\text{VO}_{2\text{peak}} \uparrow$	NS	Yes
Glowacki et al. (2004)	NS	$\text{VO}_{2\text{peak}} \uparrow$	NS	----	No
Hakkinen et al. (2003a)	----	----	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	----	No
Hakkinen et al. (2003b)	NS	----	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	----	No
Himeno et al. (2001)	----	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	----	----	Yes
Hinton et al. (2006)	----	$\text{VO}_{2\text{peak}} \uparrow$	----	----	Yes
Ho et al. (2012a)	NS	NS	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	----	No
Jakicic et al. (2003)	----	$\text{VO}_{2\text{peak}}^{\S} \uparrow$	----	----	Yes

Table 1. (Continued).

Authors (year)	Strength	Aerobic	Combined	Control	Diet
Janssen et al. (2002)	NS	VO _{2peak} ↑	----	----	Yes
Jorge et al. (2011)	NS	VO _{2peak} [§] ↑	NS	NS	No
Keating et al. (2014)	----	VO _{2peak} [§] ↑	----	----	No
Kelley & Kelley (2006)	----	VO _{2peak} [§] ↑	----	----	No
Colak & Ozcelik (2004)	----	VO _{2peak} ↑	----	NS	Yes
Kraemer et al. (1999)	----	VO _{2peak} ↑	VO _{2peak} ↑	NS	Yes
Leggate et al. (2012)	----	VO _{2peak} ↑	----	----	No
Melanson et al. (2004)	----	NS	----	----	Yes
Park et al. (2003)	----	VO _{2peak} ↑	VO _{2peak} ↑	NS	No
Rice et al. (1999)	NS	VO _{2peak} ↑	----	----	Yes
Ross & Rissanen (1994)	NS	VO _{2peak} ↑	----	----	Yes
Salvadori et al. (2014)	----	NS	----	----	Yes
Sanches et al. (2013)	----	----	VO _{2peak} ↑	----	Yes
Sarsan et al. (2006)	VO _{2peak} ↑	VO _{2peak} ↑	----	NS	No
Sartorio et al. (2003c)	----	VO _{2peak} ↑	----	----	Yes
Sartorio et al.(2003b)	----	VO _{2peak} ↑	----	----	Yes
Sartorio et al. (2003a)	----	VO _{2peak} ↑	VO _{2peak} ↑	----	Yes
Schjerve et al. (2008)	VO _{2peak} [±] ↑	VO _{2peak} [±] ↑	----	----	No
Schwingshackl et al. (2013)*	NS	VO _{2peak} [§] ↑	VO _{2peak} [§] ↑	----	No
Sillanpaa et al. (2009a)	NS	VO _{2peak} [§] ↑	VO _{2peak} [§] ↑	NS	No
Sillanpaa et al. (2009b)	NS	VO _{2peak} [§] ↑	VO _{2peak} [§] ↑	NS	No
Stensvold et al. (2010)	NS	VO _{2peak} [§] ↑	VO _{2peak} [§] ↑	NS	No
Tuomainen et al. (2005)	----	NS	----	----	No
Willis et al. (2012)	VO _{2peak} [§] ↑	VO _{2peak} [§] ↑	VO _{2peak} [§] ↑	----	No
Yavari et al. (2012)	VO _{2peak} [§] ↑	VO _{2peak} [§] ↑	VO _{2peak} [§] ↑	NS	No

VO_{2peak}: peak oxygen consumption; NS: non-significant changes; [±]VO_{2peak} related to lean body mass; [§]VO_{2peak} related to body mass; *meta-analysis study.

As can be seen in Table 1, most of the studies obtained improvements in cardiorespiratory fitness with aerobic training and few included diet in their interventions. The effects of strength and combined trainings remain uncertain.

Oxygen consumption prediction

As previously mentioned, cardiorespiratory fitness represents one of the strongest predictors of mortality, emphasizing the importance of exercise testing in daily clinical practice (Laukkanen et al., 2002). However, effort test performance is not always possible, since a number of factors (economic, psychological, etc.) are involved. For this reason, it is important to provide mechanisms through which be possible to predict the cardiorespiratory capacity of an individual.

The most of equations were developed for subjects within a normal weight range (Coquart et al., 2014). Among the few equations developed for obese subjects, most of them used the cycle ergometer on effort test. Therefore, specific equations should be created for the overweight and obese population utilizing treadmill-specific tests, since walking and running are more familiar and habitual modes of exercise for most individuals. Moreover, the inclusion of body composition and physical activity data could provide more accuracy to the estimates.

Effects of exercise on blood pressure

Excess body weight is responsible for more than 60% of the risk for hypertension in men and women (Calhoun and Sharma, 2010). Regardless of the traditional routes of aldosterone secretion, adipose tissue is able to produce factors that also can stimulate aldosterone secretion from the adrenal gland. Aldosterone stimulates kidney to retain salt and water, which increase blood volume and pressure (Xie and Bollag, 2016).

There is a strong evidence supporting that aerobic exercise should be prescribed as prevention, treatment, and control of hypertension (Pescatello et al., 2015, Pescatello et al., 2004, Cornelissen and Fagard, 2005). However, as can be observed in the Table 2, recent studies also indicate the potential contribution of strength training in the prevention and treatment of this disease (Cornelissen et al., 2011, Strasser et al., 2010, Cornelissen and Smart, 2013, Hayashino et al., 2012). Nevertheless, more investigation establishing frequency, intensity, duration of exercise as well as the most efficient combination of aerobic and resistance exercise that provide greater blood pressure benefits among overweight and obese adults is needed (Vanhees et al., 2012, Pescatello et al., 2015). Thus, the optimal training regime to reduce factors associated to cardiovascular abnormalities remains undefined.

Table 2. Systolic and diastolic blood pressure responses after strength, aerobic and combined trainings in different studies with or without diet.

Authors (year)		Strength	Aerobic	Combined	Control	Diet
Barbato et al. (2006)	SBP	----	NS	----	----	Yes
	DBP	----	↓*	----	----	
Barone et al. (2009)	SBP	----	----	NS	NS	No
	DBP	----	----	↓	NS	
Chaudhary et al. (2010)	SBP	↓	↓	----	NS	No
	DBP	NS	↓	----	NS	
Christiensen et al. (2011)	SBP	----	↓	----	----	Yes
	DBP	----	↓	----	----	
Cornelissen et al. (2009)	SBP	----	↓	----	----	No
	DBP	----	↓	----	----	
Figueroa et al. (2014)	SBP	----	----	↓ [#]	----	No
	DBP	----	----	NS	----	
Ghroubi et al. (2009)	SBP	↓	----	↓	NS	Yes
	DBP	NS	----	↓	NS	
Ghroubi et al. (2016)	SBP	----	↓	↓	----	Yes
	DBP	----	↓	↓	----	
Ha & So (2012)	SBP	----	----	↓	NS	No
	DBP	----	----	↓	NS	

Table 2. (Continued).

Authors (year)		Strength	Aerobic	Combined	Control	Diet
Ho et al. (2012a)	SBP	NS	NS	↓	↓	No
	DBP	NS	NS	NS	↓	
Hsieh et al. (2016)	SBP	NS	----	----	NS	No
	DBP	NS	----	----	NS	
Jorge et al. (2011)	SBP	↓	↓	↓	↓	No
	DBP	↓	↓	↓	↓	
Lamina et al. (2013)	SBP	----	↓	----	NS	No
	DBP	----	↓	----	NS	
Lee et al. (2013)	SBP	↑	↓	----	----	No
	DBP	↑	↓	----	----	
Mathieu et al. (2008)	SBP	----	----	↓	----	No
	DBP	----	----	NS	----	
Moeini et al. (2015)	SBP	----	↓	↓	----	No
	DBP	----	NS	NS	----	
Molmen-Hansen et al. (2012)	SBP	----	↓	----	NS	No
	DBP	----	↓	----	NS	
Potteiger et al. (2012)	SBP	↓	↓	----	----	Yes
	DBP	↓	↓	----	----	
Schjerve et al. (2008)	SBP	NS	NS	NS	----	No
	DBP	NS	↓	NS	----	
Seo et al. (2011)	SBP	----	----	NS	NS	No
	DBP	----	----	↓	NS	
Sigal et al. (2007)	SBP	NS	NS	↓	NS	Yes
	DBP	NS	NS	↓	NS	
Stenvold et al. (2010)	SBP	NS	NS	NS	NS	No
	DBP	NS	NS	NS	NS	
Yang et al. (2011)	SBP	----	----	↓	----	No
	DBP	----	----	↓	----	
Yavari et al. (2012)	SBP	↓	↓	↓	NS	No
	DBP	↓	↓	↓	NS	
Yoo et al. (2013)	SBP	↓	↓	↓	----	No
	DBP	↓	↓	↓	----	
Zois et al. (2009)	SBP	----	----	↓	NS	Yes
	DBP	----	----	NS	NS	

SBP: systolic blood pressure; DBP: diastolic blood pressure; NS: non-significant changes; *physical activity recommendations;

[#]with a whey or casein supplementation.

Impact of exercise on resting metabolic rate

Resting metabolic rate (RMR) varies greatly among individuals, but significant proportion of this variability is related to differences in fat free mass, fat mass, age and sex (Filozof and Gonzalez, 2000). The acute effects of exercise on resting metabolic rate are well documented, but the long-term influences of exercise training seem to be small and still unclear (Bouchard et al., 1993).

Exercise may prevent reductions on RMR by muscle mass maintenance when weight loss by energy restriction is adopted (Herrmann et al., 2015). However, data are controversies and more studies are warranted about the type of exercise that could promote greater effects in the resting metabolic rate maintenance after weight loss. Furthermore, as can be seen in the Table 3, there are few studies that analyzed the RMR response after an endurance plus resistance training and their results are inconsistent (Dolezal and Potteiger, 1998, Donnelly et al., 1991, Whatley et al., 1994, Byrne and Wilmore, 2001, Gremeaux et al., 2012, Petelin et al., 2014).

Table 3. Resting metabolic rate and lean body mass responses to strength, aerobic and combined trainings in different studies with or without diet.

Authors (year)		Strength	Aerobic	Combined	Control	Diet
Antunes et al. (2005)	RMR	----	↓	----	↓	No
	LBM	----	NS	----	NS	
Ballor et al. (1996)	RMR	NS	NS	----	----	Yes
	LBM	↑	↓	----	----	
Bélanger et al. (2005)	RMR	----	↑	----	----	No
	LBM	----	----	----	----	
Broeder et al. (1992)	RMR	NS	NS	----	NS	No
	LBM	↑	NS	----	NS	
Bryner et al. (1999)	RMR	↑	↓	----	----	Yes
	LBM	NS	↓	----	----	
Byrne & Wilmore (2001)	RMR	↑	----	↓	----	No
	LBM	↑	----	↑	----	

Table 3. (Continued).

Authors (year)		Strength	Aerobic	Combined	Control	Diet
Caudwell et al. (2013)	RMR	----	NS	----	----	No
	LBM	----	↑	----	----	
Dolezal & Pottleiger (1998)	RMR	↑	NS	↑	----	No
	LBM	↑	NS	↑	----	
Donnelly et al. (1991)	RMR	↓	↓	↓	↓	Yes
	LBM	↓	↓	↓	↓	
Geliebter et al. (1997)	RMR	↓	↓	----	↓	Yes
	LBM	↓	↓	----	↓	
Geliebter et al. (2014)	RMR	----	----	----	----	Yes
	LBM	↓	↓	----	↓	
Gremeaux et al. (2012)	RMR	----	----	NS	----	Yes
	LBM	----	----	NS	----	
Hambro et al. (2012)	RMR	↑	----	----	----	No
	LBM	↑	----	----	----	
Herrmann et al. (2015)	RMR	----	NS	----	----	No
	LBM	----	NS	----	----	
Hill et al. (1987)	RMR	↓	----	----	↓	Yes
	LBM	----	----	----	----	
Keim et al. (1990)	RMR	----	NS	----	↓	Yes
	LBM	----	↓	----	↓ [§]	
Kirk et al. (2009)	RMR	↑	----	----	NS	No
	LBM	↑	----	----	NS	
Kraemer et al. (1997)	RMR	NS	NS	NS	NS [#]	Yes
	LBM	NS	NS	NS	NS [#]	
Kraemer et al. (1999)	RMR	----	↓	NS	NS	Yes
	LBM	----	NS	NS	↓	
Lopes et al. (2013)	RMR	----	↑	----	NS	Yes
	LBM	----	NS	----	↓	
Martin et al. (2007)	RMR	----	↓	----	↓	Yes
	LBM	----	----	----	----	
Petelin et al. (2014)	RMR	----	----	↓	----	Yes
	LBM	----	----	----	----	
Sénéchal et al. (2010)	RMR	----	----	----	NS	Yes
	LBM	----	----	----	↓ [*]	
Shinkai et al. (1994)	RMR	----	NS	----	NS	No
	LBM	----	NS	----	NS	

Table 3. (Continued).

Authors (year)		Strength	Aerobic	Combined	Control	Diet
Whatley et al. (1994)	RMR	----	----	NS	NS	Yes
	LBM	----	----	NS	NS	
Willis et al. (2014)	RMR	----	NS	----	NS	No
	LBM	----	----	----	----	
Yavari et al. (2012)	RMR	NS	NS	NS	NS	No
	LBM	↑	↑	↑	NS	

RMR: resting metabolic rate; LBM: lean body mass; NS: non-significant changes; diet alone[§] NS for diet alone or control groups;

[§]diet plus aerobic training.

Eating behaviors changes after physical activity programs

Energy balance is a dynamic process and there are reciprocal effects between food intake and energy expenditure. It has recently been demonstrated that RMR is a potential driver of energy intake (Cameron et al., 2016), and physical activity, through the preservation of lean body mass, an important influence factor on mechanisms of satiety and appetite control (Blundell et al., 2015).

However, the type of exercise that would be able to induce greater physiological and behavioral changes related to eating behavior and food intake remains unclear. Almost all studies involved aerobic exercise (see Table 4). More studies are needed for understanding of the relationship between exercise and long-term diet adherence which should include the macronutrient composition of the diet.

Table 4. Total energy intake and macronutrient on diet after strength, aerobic and combined trainings in different studies with or without diet.

Authors (year)	Strength				Aerobic				Combined				Control				Diet
	TEI	CHO	FAT	PRO	TEI	CHO	FAT	PRO	TEI	CHO	FAT	PRO	TEI	CHO	FAT	PRO	
Washburn et al. (2015)	----	----	----	----	NS	NS	NS	NS	----	----	----	----	NS	NS	NS	NS	No
Van Etten et al. (1997)	NS	NS	NS	NS	----	----	----	----	----	----	----	----	NS	NS	NS	NS	No
Shaw et al. (2010)	----	----	----	----	↓	NS	↓	NS	↓	↓	↓	↓	NS	NS	NS	NS	No
Rosenkilde et al. (2012)	----	----	----	----	NS	NS	NS	NS	----	----	----	----	NS	NS	NS	NS	Yes
Ready et al. (1996)	----	----	----	----	NS	NS	NS	NS	----	----	----	----	NS	NS	NS	NS	Yes
Ready et al. (1995)	----	----	----	----	NS	NS	NS	NS	----	----	----	----	NS	NS	NS	NS	No
Reseland et al. (2001)	----	----	----	----	↓	NS	↓	↓	----	----	----	----	↓	↓	↓	↓	Yes
Nordby et al. (2012)	----	----	----	----	NS	NS	NS	NS	----	----	----	----	NS	NS	NS	NS	Yes
Nieman et al. (1990)	----	----	----	----	NS	↓	NS	NS	----	----	----	----	NS	NS	NS	NS	No
Miyashita et al. (2010)	----	----	----	----	NS	NS	NS	NS	----	----	----	----	NS	NS	NS	NS	No
Kirkwood et al. (2007)	----	----	----	----	NS	NS	NS	NS	----	----	----	----	↓	NS	NS	NS	Yes
Jakicic et al. (2011)	----	----	----	----	NS	NS	NS	NS	----	----	----	----	NS	NS	NS	NS	No
Foster-Schubert et al. (2012)	----	----	----	----	NS	NS	↓	NS	----	----	----	----	NS	NS	↓	NS	Yes
Donnelly et al. (2000)	----	----	----	----	NS	NS	NS	NS	----	----	----	----	NS	NS	NS	NS	No

Table 4. (Continued).

Authors (year)	Strength				Aerobic				Combined				Control				Diet
	TEI	CHO	FAT	PRO	TEI	CHO	FAT	PRO	TEI	CHO	FAT	PRO	TEI	CHO	FAT	PRO	
Donnelly et al. (2003)	----	----	----	----	NS	NS	NS	↑ [#]	----	----	----	----	NS	NS	NS	NS	No
Church et al. (2009)	----	----	----	----	↓	NS	NS	NS	----	----	----	----	↓	NS	NS	NS	Yes
Cox et al. (2003)	----	----	----	----	↓	↑	↓	↑	----	----	----	----	↓	↑	↓	↑	Yes
Bryner et al. (1997)	----	----	----	----	NS	NS	NS	NS	----	----	----	----	NS	NS	NS	NS	No
Broeder et al. (1992)	NS	NS	NS	NS	NS	NS	NS	NS	----	----	----	----	NS	NS	NS	NS	No
Brandon et al. (2006)	----	----	----	----	↑ [§]	↑ [§]	NS	NS	----	----	----	----	NS	NS	NS	NS	No
Bales et al. (2012)	NS	NS	NS	NS	↓	↓	↓	↓	↓	NS	↓	↓	----	----	----	----	No

TEI: total energy intake; CHO: carbohydrate; PRO: protein; NS: non-significant changes; [#]in men; [§]in African American women.

Main expected contribution of this thesis

Methodologies comparing different types of exercise that take into account duration and intensity variables in all trainings are needed. The vast majority of the studies that include combined training in their interventions compared the effects of endurance and resistance trainings alone with a linear combination of both (sum of both protocols). Thus, there was an imbalance in the volume of each session, which *per se* could promote different responses. In addition, there is little literature about circuit training, which has been used in many fitness centers for some years.

Therefore, we hope to contribute to the advancement of knowledge regarding effectiveness and viability of different types of training for improvement in cardiorespiratory, hemodynamic, metabolic and behavior parameters in overweight and obese individuals. In addition, we hope to provide simple and accurate equations to estimate oxygen consumption for this population.

2. HYPOTHESES AND OBJECTIVES

HYPOTHESES AND OBJECTIVES

Cardiorespiratory, hemodynamic, metabolic and behavior parameters can be influenced by diet and exercise interventions for weight loss. The overall aim of this thesis was to contribute for an advance of knowledge about the influence of different types of exercise in combination with diet on these parameters. The work was structured in five sequential studies representing the subsections of this thesis.

Hypothesis and objectives of Study I

Hypothesis: Combined aerobic and resistance training could promote a greater $\text{VO}_{2\text{peak}}$ improvement in overweight and obese subjects.

Objective 1: To analyze the effect of a weight loss program on cardiovascular fitness in overweight and obese subjects.

Objective 2: To compare the effectiveness of isolated and combined aerobic and resistance training on $\text{VO}_{2\text{peak}}$ in overweight and obese subjects.

Hypothesis and objective of Study II

Hypothesis: A prediction equation created from body composition and physical condition data predict better $\text{VO}_{2\text{peak}}$ in overweight and obese subjects than standard equations.

Objective 1: To develop equations for estimating $\text{VO}_{2\text{peak}}$ in sedentary and active, overweight and obese subjects.

Objective 2: To compare the newly created equations with standard equations widely used.

Hypothesis and objective of Study III

Hypothesis: There are differences among the four interventions in the hemodynamic responses in overweight and obese subjects.

Objective 1: To analyze the effect of a weight loss program on blood pressure in overweight and obese subjects, comparing the effectiveness of isolated and combined aerobic and resistance training.

Objective 2: To analyze the effect of a weight loss program on cardiovascular risk in overweight and obese subjects, comparing the effectiveness of isolated and combined aerobic and resistance training.

Hypothesis and objective of Study IV

Hypothesis: Strength training could avoid decreases in resting metabolic rate in obese men and women.

Objective 1: To analyze the effect of a six-month weight loss program focused in different types of exercise on resting metabolic rate in obese subjects.

Objective 2: To analyze gender differences on resting metabolic rate responses of obese individuals.

Hypothesis and objective of Study V

Hypothesis: The type of exercise could influence compliance with the prescribed diet in overweight and obese subjects.

Objective 1: To examine if there is a type of exercise or a marker of physical activity level that favors a better compliance with the prescribed diet in overweight and obese subjects.

Objective 2: To examine if there is a type of exercise or a marker of physical activity level that favors a higher motivation relation to diet or exercise in overweight and obese subjects.

3. METHODS, RESULTS AND DISCUSSION

METHODS, RESULTS AND DISCUSSION

As mentioned before, data for this doctoral thesis were derived from PRONAF proyect (*PROgramas de Nutrición y Actividad Física para el tratamiento de la obesidad*) whose main objective was the comparison of four interventions of diet and exercise in the body weight reduction in overweight (years 2009-2010) and obese individuals (years 2010-2011). The PRONAF study was executed in three phases: the first, comparing different protocols testing for energy expenditure (circuit weight training: free weights, machines and a free weights plus aerobic exercise combination) in 30 young subjects physically active, realized in 2009; the second, comparing the effects of the four interventions (strength training, endurance training, combined training and physical activity recommendations) in 119 overweight subjects (2010); and the last one, with the same design as the previous one, but in 120 subjects with obesity (2011). Furthermore, a three years follow-up was realized for phases II and III (2013 and 2014, respectively).

All variables presented in this thesis were part of the PRONAF study phases II and III.

The complete methodology of PRONAF study can be seen in Zapico et al (2012) (appendix).

Sections “Methods”, “Results” and “Discussion” are presented below for each contribution that constitutes the present Doctoral Thesis.

WHAT IS THE MOST EFFECTIVE EXERCISE PROTOCOL TO IMPROVE CARDIOVASCULAR FITNESS IN OVERWEIGHT AND OBESE SUBJECTS?

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Abstract

Background: Increased peak oxygen consumption ($\text{VO}_{2\text{peak}}$) can reduce cardiovascular risks associated with obesity. Our aim was to analyze the effect of a weight loss program on cardiovascular fitness in overweight (W) and obese (O) subjects. *Methods:* One hundred and sixty-seven subjects (77 males and 90 females), aged 18–50 years, performed a modified Bruce protocol before (pre) and after (post) a weight loss program of 24 weeks. This program combined physical training (strength, S; endurance, E; combined strength + endurance, SE; or physical activity recommendation, PA) 3 times per week, with a 25%-30% caloric restriction diet. *Results:* $\text{VO}_{2\text{peak}}$ improved in overweight and obese males (pre and post values in L/min, respectively; W = 3.2 ± 0.6 vs. 3.7 ± 0.5 , $p < 0.001$; O = 3.6 ± 0.6 vs. 3.8 ± 0.6 , $p = 0.013$) as well as in overweight females (2.0 ± 0.3 vs. 2.3 ± 0.4 , $p < 0.001$). VO_2 in the first ventilatory threshold (VT_1) increased for all 4 interventions in males ($p < 0.05$), except for S in the obese group (1.6 ± 0.2 vs. 1.7 ± 0.3 , $p = 0.141$). In females, it increased in E (0.9 ± 0.2 vs. 1.4 ± 0.3 , $p < 0.001$), SE (0.9 ± 0.2 vs. 1.2 ± 0.4 , $p = 0.003$), and PA (0.9 ± 0.1 vs. 1.2 ± 0.2 , $p = 0.006$) overweight groups. Time-to-exhaustion improved in all subjects except for females in PA group (15.7 ± 0.3 vs. 15.9 ± 0.3 , $p = 0.495$). *Conclusion:* Our results suggest that all methods, including the recommendation of physical activity, can improve cardiovascular fitness in overweight subjects and obese males.

Keywords: combined training; endurance training; obesity; oxygen consumption; physical activity; strength training; ventilatory threshold.

Introduction

From a clinical point of view, obesity is associated with many comorbidities and represents an important health problem (Lu et al., 2014). Studies have suggested that

lower aerobic fitness is also associated with a less favorable coronary or cardiovascular risk factor profile and an increase in peak oxygen consumption ($\text{VO}_{2\text{peak}}$) in the amount of 1 metabolic equivalent, correlated with a 13% reduction of all-cause mortality as well as with a 15% decrease in cardiovascular risk (Carnethon et al., 2005, Kodama et al., 2009). In general, obese individuals have lower cardiovascular fitness than lean counterparts (Wang et al., 2010). Results suggest that increased fitness could reduce the risks associated with obesity (Donnelly et al., 2009).

Data regarding the effect of different training methods for improving cardiovascular fitness in obese subjects are still inconsistent. Some found improvements in $\text{VO}_{2\text{peak}}$ only with aerobic and/or combined (aerobic/resistance) training (Davidson et al., 2009, Glowacki et al., 2004, Hakkinen et al., 2003b, Ho et al., 2012a, Jorge et al., 2011), whereas others also found improvements applying resistance training (Ahmadizad et al., 2007, Al Saif and Alsenany, 2015, Bateman et al., 2011, Sarsan et al., 2006, Schjerve et al., 2008, Willis et al., 2012, Yavari et al., 2012). Aerobic training promotes changes in aerobic capacity, increasing mitochondrial oxidative capacities and capillary density in skeletal muscle (Daussin et al., 2008), whereas resistance training increases muscle mass, which should increase maximal aerobic capacity (Caruso et al., 2014). Therefore, it is reasonable to suggest that both types of training together can contribute to the improvement in cardiorespiratory fitness. In fact, many authors have found combined training to have a greater influence on cardiorespiratory response (Aguiar et al., 2014, Schwingshackl et al., 2013). However, the comparison among studies is difficult owing to the different training methodologies used. It is therefore still unknown which method is the one achieving greatest enhancements (Schwingshackl et al., 2013). Along this line, and to the best of our knowledge, no study has compared the effects of different training methods applying the same volume and intensity, and

therefore assuring that the distinct results were due only to the change in the type of training. In addition, there is little literature about circuit training, which has been used in many fitness centers for some years. There are also few studies reporting data regarding aerobic and anaerobic threshold changes after a weight loss program (Boni et al., 1995, Hakkinen et al., 2003b, Salvadori et al., 2014). These data could uncover interesting information about the cardiovascular fitness response of overweight and obese people following this kind of program. The improvement in these parameters is also related to a longer duration of exercise in the same intensity and consequently a longer period of fatty acid oxidation or increased intensity of exercise, which can ensure excess post-exercise oxygen consumption and contribute to weight loss (Burleson et al., 1998, Kirk et al., 2009). Finally, some authors have suggested that if dietary intervention is associated with the training program, VO_{2peak} will improve even more (Melanson et al., 2004).

Therefore, the main objective of this study was to analyze the effect of a weight loss program on cardiovascular fitness in overweight and obese subjects, comparing the effectiveness of isolated and combined aerobic and resistance training on VO_{2peak} .

Methods

Participants

This study was performed as part of the Nutrition and Physical Activity for Obesity Study (the PRONAF study according to its Spanish initials), the aim of which was to assess the usefulness of different types of physical activity (PA) and nutrition programs for the treatment of obesity. The inclusion criteria specified adult subjects, aged 18 to 50 years, who were overweight or obese (body mass index [BMI]: ≥ 25 to < 35 kg/m²), sedentary (< 30 min PA/day), normoglycemic, and non-smoking. Only

females with regular menstrual cycles were included. A total of 167 participants (77 males and 90 females) completed all the tests. Adherences to diet (80%) and exercise (90%) were included in the analysis. All participants were informed about the risks and benefits of the study and signed a document of informed consent. The PRONAF study was approved by the Human Research Review Committee of the University Hospital La Paz (HULP) (No.NCT01116856).

Study protocol

The complete methodology and the flow diagram can be found in Zapico et al. (2012). Briefly, subjects who fulfilled the inclusion criteria were randomly assigned to 1 of the 4 interventions detailed here, assuring a homogeneous distribution of age and gender among groups. The intervention programs lasted 22 weeks, and the assessment tests took place 1 week before (baseline) and after (post) the intervention.

Exercise protocols

Four different interventions were performed: strength training (S), endurance training (E), combined strength + endurance training (SE) groups followed the corresponding supervised exercise program plus the dietary intervention, and the PA group followed dietary intervention and was instructed about the general recommendations about PA from the American College of Sports Medicine (ACSM) (Donnelly et al., 2009). The exercise of the PA group was not supervised, only registered with an accelerometer. Subjects in the S, E, and SE groups trained 3 times per week for 22 weeks. All training sessions were carefully supervised by certified personal trainers. The exercise programs were designed according to the subject's muscle strength and heart rate reserve. Muscle strength was measured using the 15-repetition maximum testing method in the S and SE groups. Resting heart rate was calculated as

the average heart rate during 10 min in a lying position, and maximal heart rate (HR_{max}) was obtained by means of the cardiovascular maximal effort test.

In the S group the session routine consisted of the execution of 8 scheduled exercises (i.e., shoulder press, squat, barbell row, lateral split, bench press, front split, biceps curl, and French press for triceps). For group E, running, cycling, or elliptical (self-selected) exercises were the main components of the session routine, whereas the routine for the SE group consisted of a combination program using cycle ergometry, treadmill, or elliptical machine intercalated with squatting, rowing machine, bench press, and front split.

Both volume and intensity of the 3 training programs increased progressively (Fig. 2). The S and SE participants performed 15 repetitions of each strength exercise or 45 seconds of aerobic exercise (only SE participants) with a rest period of 15 seconds between them. Feedbacks of training loads were evaluated with the Rate of Perceived Exertion scale once a month, following a similar methodology used elsewhere (Shaibi et al., 2006).

Fig. 2. Timeline of the study. S = strength training group; E = endurance training group; SE = combined strength and endurance training group; PA = physical activity recommendations group; RM = repetitions maximum.

Hypocaloric diet

All groups underwent an individualized and hypocaloric diet (between 1200 and 3000 kcal) prescribed by expert dieticians in the Nutrition Department of HULP. The diet aimed for a 25% reduction of the total daily energy expenditure measured using the SenseWear Pro Armband accelerometer (BodyMedia, Inc., Pittsburgh, PE, USA).

Measurements

Cardiovascular fitness

The test evaluating cardiovascular fitness was maximal ergospirometry following the modified Bruce protocol with a computerized treadmill (H/P/COSMOS 3PW 4.0; H/P/Cosmos Sports & Medical, Nussdorf-Traunstein, Germany). $\text{VO}_{2\text{peak}}$ was measured with the gas analyzer Jaeger Oxycon Pro (Erich Jaeger; Viasys Healthcare; Hoechberg, Germany). Heart response was continuously monitored with a 12-lead electrocardiogram. The effort test was maintained until exhaustion. The mean of the 3 highest measurements was used as $\text{VO}_{2\text{peak}}$ and HR_{max} .

The first and the second ventilatory thresholds (VT_1 and VT_2 , respectively) were set at the point of maximum agreement of the most common methods of assessment published previously (Rabadan et al., 2011). All tests were evaluated by 2 researchers in a double-blind process. $\text{VO}_{2\text{peak}}$ was expressed in several values: absolute (L/min), relative to body mass (mL/kg/min), and relative to lean body mass (mL/kg_{LBM}/min). Ventilatory thresholds were expressed in absolute (L/min) and percentage terms of $\text{VO}_{2\text{peak}}$.

Subjects were classified in fitness categories according to their absolute $\text{VO}_{2\text{peak}}$ (L/min) and age. Subjects who scored “very poor”, “poor”, “fair”, or “average” were deemed unfit; and subjects who scored “good”, “very good”, or “excellent” were deemed fit in relation to age-specific norms (O'Donovan et al., 2012).

Body composition

Body composition was assessed by dual-energy X-ray absorptiometry scan (Version 6.10.029GE Encore 2002, GE Lunar Prodigy; GE Healthcare, Madison, WI, USA). Height was measured using a seca stadiometer (Quirumed, Valencia, Spain), which has a range of 80–200 cm. Body mass was measured using a TANITA BC-420MA balance (Bio Lógica Tecnología Médica S.L, Barcelona, Spain). BMI was calculated as body mass/height (kg/m^2).

Statistical analysis

Data are presented as mean $\pm$ SD. Repeated 3-way analysis of covariance (ANCOVA) measures were used to determine any differences among the 4 interventions (S, E, SE, and PA) and the BMI category (overweight and obese) at baseline and post-intervention. Analyses were performed in men and women separately, and age was used as covariate. The Bonferroni *post hoc* test was employed to locate specific differences. Differences between the PA group and the exercise groups in fitness category frequencies were calculated using a χ^2 test. SPSS Statistic for Windows Version 20.0 (IBM Corp., Armonk, NY, USA) was used. The significance level was set at $\alpha = 0.05$.

Results

Characteristics of all participants are summarized in Table 5. In both men and women, baseline characteristics were significantly different between overweight and obese subjects, except for age, height, and $\text{VO}_{2\text{peak}}$ values relative to body mass. No differences were observed among the groups within the same gender.

Table 5. Characteristics at baseline (mean $\pm$ SD).

Variables	Male		Female	
	Overweight	Obese	Overweight	Obese
Age (years)	36.3 $\pm$ 8.0	38.6 $\pm$ 7.5	33.3 $\pm$ 8.5	38.4 $\pm$ 7.7
Body weight (kg)	87.5 $\pm$ 6.9	101.2 $\pm$ 7.9**	73.5 $\pm$ 5.8	86.3 $\pm$ 8.5**
Height (cm)	175.3 $\pm$ 6.4	176.7 $\pm$ 5.9	162.0 $\pm$ 6.1	163.0 $\pm$ 7.0
Body mass index (kg/m ²)	28.4 $\pm$ 1.1	32.4 $\pm$ 1.9**	28.0 $\pm$ 1.3	32.4 $\pm$ 1.9**
Percentage fat (%)	33.7 $\pm$ 4.6	38.2 $\pm$ 4.0**	43.3 $\pm$ 3.7	47.1 $\pm$ 3.6**
Lean body mass (kg)	55.7 $\pm$ 5.5	59.8 $\pm$ 5.0*	40.3 $\pm$ 4.2	44.1 $\pm$ 4.7**
Fat mass (kg)	28.5 $\pm$ 5.2	37.2 $\pm$ 5.8**	30.7 $\pm$ 3.7	39.5 $\pm$ 6.5**
VO _{2peak} (L/min)	3.2 $\pm$ 0.6	3.6 $\pm$ 0.6**	2.0 $\pm$ 0.3	2.5 $\pm$ 0.4**
VO _{2peak} (ml/kg/min)	36.5 $\pm$ 1.1	36.1 $\pm$ 0.8	27.7 $\pm$ 0.5	28.2 $\pm$ 0.5

* $p < 0.05$; ** $p < 0.001$, compared to overweight. Abbreviation: VO_{2peak} = peak oxygen consumption.

VO_{2peak}

Interactions between time of measurement and BMI category were found for absolute VO_{2peak} values ($F = 10.316$, $p = 0.002$), VO_{2peak} values relative to body mass ($F = 7.714$, $p = 0.007$), and VO_{2peak} values relative to lean body mass ($F = 9.911$, $p = 0.002$) in men (Table 6). Absolute and relative (to body and to lean mass) VO_{2peak} improved in overweight and obese men. Overweight men had greater improvement, about 12% more than obese men, in absolute VO_{2peak} compared to baseline values. On the other hand, interactions between time and BMI category for absolute VO_{2peak} values ($F = 12.863$, $p = 0.001$), relative to body mass ($F = 12.309$, $p = 0.001$), and VO_{2peak} values relative to lean body mass ($F = 12.951$, $p = 0.001$) in women showed that being overweight increased all VO_{2peak} values. In obese females, VO_{2peak} values improved only relative to body mass, in general 12% less than in overweight women (Table 6).

Table 6. Peak oxygen consumption before and after weight loss intervention.

	Male				
	Overweight	Obese	<i>P</i>	Observed Power	η^2
VO_{2peak} (L/min)					
Baseline	3.2 ± 0.6	3.6 ± 0.6 [†]	T <0.001	>0.99	0.38
Post-intervention	3.7 ± 0.5**	3.8 ± 0.6*	TxG 0.171	0.43	0.07
Delta	0.5 ± 0.4	0.2 ± 0.5	TxBMI 0.002	0.89	0.13
			TxGxBMI 0.127	0.48	0.08
VO_{2peak} (mL/kg/min)					
Baseline	37.4 ± 6.2	36.0 ± 5.9	T <0.001	>0.99	0.65
Post-intervention	46.6 ± 5.6**	41.4 ± 6.9 ^{‡**}	TxG 0.058	0.62	0.10
Delta	9.2 ± 5.7	5.4 ± 5.6	TxBMI 0.007	0.78	0.10
			TxGxBMI 0.482	0.22	0.03
VO_{2peak} (mL/kg_{LBM}/min)					
Baseline	57.9 ± 8.3	60.5 ± 8.1 [†]	T <0.001	>0.99	0.41
Post-intervention	67.3 ± 6.7**	63.9 ± 7.7**	TxG 0.229	0.37	0.06
Delta	9.4 ± 8.1	3.4 ± 8.3	TxBMI 0.002	0.87	0.13
			TxGxBMI 0.220	0.38	0.06
	Female				
	Overweight	Obese	<i>P</i>	Observed Power	η^2
VO_{2peak} (L/min)					
Baseline	2.0 ± 0.3	2.5 ± 0.4 [†]	T <0.001	0.96	0.15
Post-intervention	2.3 ± 0.4**	2.5 ± 0.4 [‡]	TxG 0.308	0.31	0.04
Delta	0.3 ± 0.3	-0.1 ± 0.3	TxBMI 0.001	0.94	0.14
			TxGxBMI 0.332	0.30	0.04
VO_{2peak} (mL/kg/min)					
Baseline	27.7 ± 3.8	28.2 ± 3.3	T <0.001	>0.99	0.55
Post-intervention	33.8 ± 5.6**	31.0 ± 4.6 ^{‡**}	TxG 0.135	0.48	0.07
Delta	6.1 ± 4.4	2.8 ± 4.2	TxBMI 0.001	0.93	0.13
			TxGxBMI 0.477	0.22	0.03
VO_{2peak} (mL/kg_{LBM}/min)					
Baseline	50.7 ± 6.2	55.8 ± 6.1 [†]	T <0.001	>0.99	0.22
Post-intervention	57.0 ± 8.4**	56.5 ± 7.7	TxG 0.124	0.49	0.07
Delta	6.3 ± 6.5	0.7 ± 7.3	TxBMI 0.001	0.94	0.14
			TxGxBMI 0.252	0.36	0.05

Note: Data in bold for the *p* value indicate significant difference.

* *p* < 0.05, ***p* < 0.001, compared with baseline.

[‡] *p* < 0.05, compared with overweight.

Abbreviations: T = time; G = intervention group; BMI = body mass index classification; VO_{2peak} = peak oxygen consumption.

For men who improved from unfit to fit after the intervention, 43% were in the supervised training programs (S, E, and SE) and 38% were in PA, whereas in females, 29.6% were in the supervised training groups and 15.8% were in PA. However, χ^2 analysis showed no significant association between type of intervention and percentage

changes (Table 7).

Table 7. VO_{2peak} classified as fit at baseline and post-intervention (%).

	Male		Female	
	PA	SUP	PA	SUP
Baseline	6.0	13.0	5.3	1.4
Post-intervention	44.0	56.0	21.1	31.0
Δ	38.0	43.0	15.8	29.6

Abbreviations: PA = physical activity group; SUP = supervised training group.

VO_2 in VT_1 and VT_2

In males, a significant triple interaction (time–BMI category–intervention) was found for absolute VO_2 in VT_1 ($F = 3.864$, $p = 0.013$). All 4 interventions in overweight men increased these values (S: 43.0%, $p < 0.001$; E: 35.7%, $p = 0.005$; SE: 15.1%, $p = 0.028$; PA: 47.6%, $p < 0.001$). This occurred in obese men as well, except for the S group (E: 18.6%, $p = 0.012$; SE: 34.2%, $p < 0.001$; PA: 17.8%, $p = 0.007$). In females, interactions between time and BMI category ($F = 16.328$, $p < 0.001$) and between time and intervention ($F = 7.117$, $p < 0.001$) were found for absolute VO_2 in VT_1 . Considering the pairwise comparison, differences between the pre- and post-measurements were found in E (+20%, $p < 0.001$), SE (+37.5%, $p < 0.001$), and PA (+19.2%, $p = 0.010$) groups, but only for overweight women. Concerning percentage of VO_2 in VT_1 with respect to VO_{2peak} , interactions between time and BMI category ($F = 5.991$, $p = 0.017$) and time and intervention ($F = 5.063$, $p = 0.003$) were found only in females. This percentage improved in overweight women in E ($p < 0.001$) and SE ($p = 0.015$) groups. In males, only time ($F = 22.377$, $p < 0.001$) was significant. Regarding VT_2 , the main effect was observed in oxygen consumption for men ($F = 33.629$, $p < 0.001$) and for women ($F = 8.849$, $p = 0.004$). Percentage of VO_2 in VT_2 with respect to the peak did not change in any group (Table 8).

Time-to-exhaustion

An interaction between time and intervention was observed ($F = 3.027$, $p = 0.034$) in females, demonstrating a significant improvement in all supervised training programs, i.e., S (+8.9%, $p < 0.001$), E (+8.5%, $p < 0.001$), SE (+4.4%, $p = 0.018$), and PA (+1.3%, $p = 0.495$). In males, only time was significant ($F = 63.512$, $p < 0.001$) for this variable, i.e., S (+7.4%), E (+8.2%), SE (+10.3%), and PA (+7.1%) (Fig. 3).

Fig. 3. Time-to-exhaustion delta in minutes. Error bars represent one standard error of the mean. * $p < 0.05$, ** $p < 0.001$, baseline-post differences; S = strength training group; E = endurance training group; SE = combined strength + endurance training group; PA = physical activity recommendation group.

Table 8. Oxygen consumption in VT1 and VT2 before and after weight loss intervention (mean $\pm$ SD).

	Overweight				Obese				<i>P</i>	Observed Power	η^2
	S	E	SE	PA	S	E	SE	PA			
Male											
VO₂ in VT₁ (L/min)									T <0.001	>0.99	0.54
Baseline	1.2 $\pm$ 0.2	1.2 $\pm$ 0.1	1.5 $\pm$ 0.4	1.3 $\pm$ 0.2	1.6 $\pm$ 0.2	1.5 $\pm$ 0.2	1.6 $\pm$ 0.3	1.6 $\pm$ 0.2	TxG 0.863	0.10	0.01
Post-intervention	1.7 $\pm$ 0.2**	1.6 $\pm$ 0.4*	1.7 $\pm$ 0.3*	1.9 $\pm$ 0.4**	1.7 $\pm$ 0.3	1.8 $\pm$ 0.3*	2.1 $\pm$ 0.2** [†]	1.8 $\pm$ 0.4*	TxBMI 0.177	0.27	0.03
Delta	0.5 $\pm$ 0.2	0.4 $\pm$ 0.4	0.2 $\pm$ 0.3	0.6 $\pm$ 0.3	0.1 $\pm$ 0.4	0.3 $\pm$ 0.3	0.5 $\pm$ 0.3	0.3 $\pm$ 0.4	TxGxBMI 0.013	0.80	0.15
VO₂ in VT₁ (%)									T <0.001	>0.99	0.25
Baseline	38.9 $\pm$ 3.1	37.9 $\pm$ 2.9	44.9 $\pm$ 2.2	42.6 $\pm$ 3.2	42.8 $\pm$ 2.1	46.1 $\pm$ 2.4	42.6 $\pm$ 2.3	43.7 $\pm$ 2.2	TxG 0.619	0.17	0.03
Post-intervention	46.1 $\pm$ 2.9	45.3 $\pm$ 2.7	44.1 $\pm$ 2.0	52.3 $\pm$ 2.9	45.9 $\pm$ 2.0	51.0 $\pm$ 2.2	50.9 $\pm$ 2.1	50.4 $\pm$ 2.1	TxBMI 0.976	0.05	0.00
Delta	7.2 $\pm$ 4.2	7.4 $\pm$ 3.9	-0.8 $\pm$ 3.0	9.7 $\pm$ 4.3	3.1 $\pm$ 2.9	4.9 $\pm$ 3.3	8.3 $\pm$ 3.1	6.7 $\pm$ 3.0	TxGxBMI 0.152	0.45	0.07
VO₂ in VT₂ (L/min)									T <0.001	>0.99	0.33
Baseline	2.6 $\pm$ 0.7	2.7 $\pm$ 0.3	2.6 $\pm$ 0.5	2.6 $\pm$ 0.6	3.2 $\pm$ 0.7	2.6 $\pm$ 0.4	2.9 $\pm$ 0.5	2.9 $\pm$ 0.5	TxG 0.311	0.31	0.05
Post-intervention	3.3 $\pm$ 0.6	3.0 $\pm$ 0.5	3.2 $\pm$ 0.9	2.9 $\pm$ 0.7	3.1 $\pm$ 0.6	3.0 $\pm$ 0.4	3.5 $\pm$ 0.6	3.2 $\pm$ 0.5	TxBMI 0.234	0.22	0.02
Delta	0.8 $\pm$ 0.3	0.3 $\pm$ 0.5	0.6 $\pm$ 1.0	2.9 $\pm$ 0.5	-0.2 $\pm$ 0.3	0.4 $\pm$ 0.3	0.6 $\pm$ 0.6	0.2 $\pm$ 0.4	TxGxBMI 0.093	0.54	0.09
VO₂ in VT₂ (%)									T 0.149	0.30	0.03
Baseline	80.4 $\pm$ 4.0	84.6 $\pm$ 3.7	80.5 $\pm$ 2.8	83.5 $\pm$ 4.1	82.5 $\pm$ 2.7	79.0 $\pm$ 3.1	79.4 $\pm$ 3.0	81.8 $\pm$ 2.8	TxG 0.928	0.08	0.01
Post-intervention	86.2 $\pm$ 5.7	84.0 $\pm$ 5.3	85.0 $\pm$ 4.0	79.7 $\pm$ 5.8	83.1 $\pm$ 3.9	85.9 $\pm$ 4.4	84.6 $\pm$ 4.2	87.6 $\pm$ 4.0	TxBMI 0.470	0.11	0.01
Delta	5.8 $\pm$ 7.2	-0.6 $\pm$ 6.7	4.5 $\pm$ 5.1	-3.7 $\pm$ 7.3	0.6 $\pm$ 4.9	6.9 $\pm$ 5.6	5.2 $\pm$ 5.3	5.8 $\pm$ 5.1	TxGxBMI 0.627	0.16	0.02

Table 8. (Continued)

	Overweight				Obese				<i>P</i>	Observed Power	η^2
	S	E	SE	PA	S	E	SE	PA			
Female											
VO₂ in VT₁ (L/min)									T <0.001	>0.99	0.30
Baseline	1.0 ± 0.2	0.9 ± 0.2 [#]	0.9 ± 0.2	0.9 ± 0.1	1.4 ± 0.2	1.2 ± 0.2	1.3 ± 0.2	1.2 ± 0.3	TxG <0.001	0.98	0.21
Post-intervention	1.1 ± 0.3	1.4 ± 0.2**	1.2 ± 0.4*	1.2 ± 0.2*	1.3 ± 0.3	1.3 ± 0.3	1.4 ± 0.2	1.2 ± 0.2	TxBMI <0.001	0.98	0.17
Delta	0.8 ± 0.3	0.5 ± 0.3	0.3 ± 0.3	0.2 ± 0.1	0.1 ± 0.1	0.1 ± 0.3	0.2 ± 0.3	0.1 ± 0.2	TxGxBMI 0.146	0.46	0.06
VO₂ in VT₁ (%)									T <0.001	0.98	0.17
Baseline	48.0 ± 2.2	43.5 ± 2.0	43.8 ± 2.5	46.7 ± 2.3	54.8 ± 2.2	49.9 ± 2.0	48.8 ± 2.2	53.7 ± 2.5	TxG 0.003	0.91	0.16
Post-intervention	49.2 ± 2.6	60.0 ± 2.4	50.0 ± 2.9	52.7 ± 2.8	51.0 ± 2.6	53.9 ± 2.3	54.5 ± 2.6	55.3 ± 2.9	TxBMI 0.017	0.68	0.07
Delta	1.2 ± 3.2	16.5 ± 2.8	6.2 ± 3.5	6.0 ± 3.3	3.8 ± 3.2	4.0 ± 2.8	5.7 ± 3.2	1.6 ± 3.5	TxGxBMI 0.247	0.36	0.05
VO₂ in VT₂ (L/min)									T 0.004	0.84	0.10
Baseline	1.7 ± 0.3	1.6 ± 0.2	1.5 ± 0.2	1.7 ± 0.3	2.1 ± 0.3	2.1 ± 0.4	2.1 ± 0.3	1.8 ± 0.2	TxG 0.376	0.27	0.04
Post-intervention	1.7 ± 0.4	2.0 ± 0.3	1.8 ± 0.6	1.7 ± 0.3	2.1 ± 0.4	2.1 ± 0.4	2.2 ± 0.3	2.0 ± 0.3	TxBMI 0.105	0.37	0.03
Delta	0.0 ± 0.3	0.3 ± 0.3	0.2 ± 0.4	0.1 ± 0.4	-0.0 ± 0.3	-0.0 ± 0.5	0.1 ± 0.3	0.1 ± 0.1	TxGxBMI 0.167	0.44	0.06
VO₂ in VT₂ (%)											
Baseline	82.5 ± 2.2	82.3 ± 2.0	77.2 ± 2.5	82.5 ± 2.3	83.7 ± 2.2	85.9 ± 2.0	80.7 ± 2.2	83.3 ± 2.5	T 0.836	0.05	<0.01
Post-intervention	80.6 ± 2.9	84.6 ± 2.6	76.2 ± 3.2	78.1 ± 3.1	85.2 ± 2.9	84.8 ± 2.6	84.4 ± 2.9	86.7 ± 3.2	TxG 0.966	0.06	<0.01
Delta	-1.9 ± 3.8	2.3 ± 3.4	-1.0 ± 4.2	-4.4 ± 4.0	1.5 ± 3.8	-1.1 ± 3.4	3.7 ± 3.8	3.4 ± 4.2	TxBMI 0.251	0.21	0.02
									TxGxBMI 0.464	0.23	0.03

Data are presented as mean ± SD. Baseline-post differences: **p* < 0.05; ***p* < 0.001. [†] Significant difference between S and SE groups. [#] Significant difference between E and S groups. T: time; G: intervention group; BMI: body mass index classification; VO₂: oxygen consumption; VT₁: aerobic ventilatory threshold; VT₂: anaerobic ventilatory threshold or respiratory compensation point; S: strength training group; E: endurance training group; SE: combined strength + endurance training group; PA: physical activity recommendations group.

Discussion

The main finding of this study was that all four protocols were effective in improving cardiovascular fitness in overweight and obese males and overweight females.

Because age and gender have been proved to modify oxygen consumption (Loe et al., 2013, Rojo-Tirado et al., 2013), we performed the analysis separately by gender and corrected for age. Another factor that influences oxygen consumption is body mass (Wang et al., 2010). Obese subjects had significantly lower estimated $\text{VO}_{2\text{peak}}$ relative to body mass than non-obese adults but similar $\text{VO}_{2\text{peak}}$ to overweight subjects (Wang et al., 2010). Our data also showed similar $\text{VO}_{2\text{peak}}$ relative to body mass or to lean body mass and greater absolute oxygen consumption in obese subjects compared with overweight subjects. $\text{VO}_{2\text{peak}}$ values were low in both categories of BMI and both genders. Compared with a Norwegian study that included 3816 subjects with heterogeneous BMI (Loe et al., 2013), our data were 20% lower in men and 25% lower in women.

Our data showed that in overweight and obese males, $\text{VO}_{2\text{peak}}$ relative to body mass increased by 26.8% and 16%, respectively, while females improved by 22.5% and 10.7%, respectively. Previous studies showed lesser improvements in relative to body mass $\text{VO}_{2\text{peak}}$: between 8% (Himeno et al., 2001) and 17% (Al Saif and Alsenany, 2015) for overweight and obese individuals combining aerobic exercise with a mild hypocaloric diet, or 5% for overweight males performing aerobic or resistance training (Ahmadizad et al., 2007). These differences could be due to the weight loss generated by our program, which was greater than in those studies. As reported elsewhere, the average weight loss in our sample was 9.6 kg (Benito et al., 2015), which could contribute to a considerable improvement in oxygen consumption relative to body mass.

For instance, our data indicated that absolute $\text{VO}_{2\text{peak}}$ did not increase in obese females, whereas its relative value improved, most likely as a result of weight loss and not cardiorespiratory adaptations. Therefore, in a weight loss program, it seems to be more interesting to evaluate cardiovascular fitness by means of absolute $\text{VO}_{2\text{peak}}$. Wheatley et al. (2014) observed that females presented limitations in cardiac performance and demonstrated that females need greater cardiac output than males to meet the same external work demand.

Another study in obese adolescents showed that gender differences exist in VO_2 uptake on-kinetics during moderate exercise, indicating an enhanced potential for male subjects to deliver and/or use oxygen (Franco et al., 2014). Greater volume and intensity could be necessary to promote cardiovascular changes in obese women.

Our data also showed that all interventions were effective for improving $\text{VO}_{2\text{peak}}$ in overweight males and females and in obese males, which is in accordance with other studies (Ahmadizad et al., 2007, Bateman et al., 2011, Willis et al., 2012, Yavari et al., 2012). Several studies found significant increases in $\text{VO}_{2\text{peak}}$ only for aerobic and/or combined training. However, in these studies, strength training involved shorter sessions (Bateman et al., 2011, Davidson et al., 2009, Hakkinen et al., 2003b, Willis et al., 2012) or fewer sessions than did aerobic or combined training (Glowacki et al., 2004, Sarsan et al., 2006). In our study, intensity and volume were monitored to ensure the comparison among the different types of training, and the control of these parameters may have been responsible for the lack of differences. Finally, caloric restriction in our study appeared to be appropriate to allow an oxygen consumption increase, because significant increase in $\text{VO}_{2\text{max}}$ can be achieved only by moderate energy intake preservation (Sarsan et al., 2006).

Although oxygen consumption is the most-used cardiovascular variable to measure the response to training, other variables may also provide important or interesting information. Few studies have assessed responses of thresholds, ventilation, and other cardiorespiratory parameters (Salvadori et al., 2014). PA performed at moderate intensity causes changes in VT_1 (Tuomainen et al., 2005), which agrees with the training loads applied. In the same way as for VO_{2peak} , obese women did not show an improvement in the absolute and relative values to lean mass oxygen consumption in VT_1 . Unlike the study by Salvadori et al. (2014), which did not show changes in VT_1 , our data indicated that in overweight males, VO_2 in VT_1 improved in all interventions, as well as in overweight females and obese males, except for the S group. Strength training may lead to peripheral changes that could be considered antagonistic to aerobic power development (Hakkinen et al., 2003b). As also suggested by our data absolute and relative to lean body mass VO_2 in VT_1 in obese people, other studies with appropriate comparison methodologies indicated increased VO_{2peak} only for aerobic or combined training and not for strength training (Ho et al., 2012a, Jorge et al., 2011). When obese men and women were analyzed together, only the combined group showed an improvement in absolute VO_{2peak} (Benito et al., 2015). If we consider time commitments and health benefits, combined training may be more appropriate and less monotonous in inducing certain cardiorespiratory adaptations and adherence in obese people (Coquart et al., 2008).

On the other hand, no interactions were observed for VO_{2peak} in the VT_2 . Therefore, the intensity adopted does not seem enough to cause interactions in this threshold (Elliott et al., 2015). Finally, the last parameter analyzed to predict improvement in cardiovascular fitness was the Time-to-exhaustion on a treadmill test, which was the only parameter that improved in obese women. Even without changes in

oxygen consumption, quality of oxygen utilization and neuromuscular adaptations caused by training may have led to a greater ability to tolerate high workloads (at or above the VT_2) over longer periods of time before fatigue occurred (Lucia et al., 2002). Our data showed improvements in time-to-exhaustion in overweight and obese females in S, SE, and E groups. However, in obese females, PA did not alter oxygen consumption or time-to-exhaustion. Interventions with exercise seemed more effective in obese women: dropout rates in PA were 68.4% for women and 31.6% for men. Moreover, within our supervised training programs, the percentage of men who improved from the unfit class to the fit class was 12.7% greater than the percentage in women. This difference between men and women increased to 23.0% in the PA group. Nevertheless, it is also important to consider the learning effect of the ergospirometry effort test, which may have influenced the findings in regard to this variable because most women in this study had never climbed on a treadmill.

Important strengths of this study include (1) the randomized design; (2) the inclusion of 4 different training programs in the same study combined with caloric restriction in all interventions; (3) the direct supervision of exercise for all training sessions; and (4) inclusion of appropriate programs of strength and combined training to provide an adequate stimulus and comparison among groups. The study is limited by the fact that it did not include a “no treatment” control group, but rather compared the intervention with previously described exercise recommendations that are broadly accepted from an ethical point of view and in clinical practice. Gains in VO_{2peak} observed in all interventions might have been the result of the fact that the participants initially consented to participate in a study that would prescribe and counsel about exercise with the goal of increasing PA and improving fitness. Given that our

supervised programs or recommendations required only minimal training and equipment, they could be implemented in a wide range of PA practices.

Conclusion

Interventions of exercise or recommendations of PA plus diet were effective in improving cardiovascular fitness in overweight males and females and obese males. Time-in-effort test was the only variable that increased in obese females, except for those in the PA recommendation group. Obese women seem to need greater intensity and volume of training to achieve cardiovascular changes. As practice applications, aerobic training between 50% and 60% of heart rate reserve and strength training for large muscle groups between 50% and 60% of 15 maximum repetitions, or a combination of both, 3 times per week and conducted in a circuit, may be more appropriate to induce adequate cardiorespiratory adaptations in obese people.

PEAK OXYGEN UPTAKE PREDICTION IN OVERWEIGHT AND OBESE ADULTS

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Abstract

Peak oxygen uptake ($\text{VO}_{2\text{peak}}$) is an important risk predictor for cardiovascular mortality and morbidity. The main aim of this study was to develop equations for estimating $\text{VO}_{2\text{peak}}$ in sedentary and active overweight and obese subjects. The second objective was to compare the newly created equations with the standard equations that are widely used. One hundred and twenty-nine overweight and obese subjects (57 males), aged 18-50 years, were randomized into two groups: development group ($n = 94$) and validation group ($n = 35$). Individuals performed a modified Bruce protocol before (sedentary) and after (active) a 24-week weight loss program. Body composition was measured by bioelectrical impedance analysis. Stepwise multiple regression models were performed; the following factors: age, body weight (BW), lean body mass percentage (%LBM), and time of effort test (TIME) were included in the model. Four equations were developed: with and without effort test data for sedentary and active subjects. In the validation group, equations with and without TIME underestimated $\text{VO}_{2\text{peak}}$ values in sedentary ($p = 0.002$ and $p = 0.008$, respectively), but not in active subjects. Furthermore, the equations derived from this study presented the greatest determination coefficients and the lowest values for the standard errors of estimate, for both development and validation groups. The following equation presented the highest determination coefficient, using effort test data for active subjects: $\text{VO}_{2\text{peak}} \text{ (L/min)} = -5.017 + (0.040 \times \text{BW}) + (0.127 \times \text{TIME}) + (0.046 \times \% \text{LBM}) + (-0.010 \times \text{AGE})$. The predicted $\text{VO}_{2\text{peak}}$ values using the Bruce equation were significantly lower than the measured values in active participants ($p = 0.046$); whereas those predicted by ACSM's equation were significantly higher in comparison to the measured $\text{VO}_{2\text{peak}}$ levels in sedentary and active subjects ($p < 0.001$), for both groups. In conclusion, equations developed in this study were adequate to predict $\text{VO}_{2\text{peak}}$ in overweight and obese subjects, whilst the

most commonly used equations in the literature, ACSM and Bruce, reported an inaccurate estimation of $\text{VO}_{2\text{peak}}$.

Keywords: oxygen consumption; sedentary; active; prediction equations.

Introduction

Peak or maximum oxygen consumption ($\text{VO}_{2\text{peak}}$) represents cardiovascular fitness and is recognized as an important predictor for cardiovascular mortality and morbidity (DeFina et al., 2015). Moreover, $\text{VO}_{2\text{peak}}$ is an important factor for exercise prescription and control (da Cunha et al., 2011). $\text{VO}_{2\text{peak}}$ measured by indirect calorimetry has been used to assess cardiorespiratory fitness, using a variety of ergometers until the highest level of physiologic exertion is reached. Although $\text{VO}_{2\text{peak}}$ testing is considered the “gold standard” for assessing aerobic capacity, it is often unfeasible and challenging to achieve a true value as its practice may be influenced by variables such as fatigue, motivation, injuries and physical limitations (Evans et al., 2014, Gellish et al., 2007). Therefore, a wide variety of equations to predict $\text{VO}_{2\text{peak}}$ have been developed and published over the last 10 years (Evans et al., 2014). Notwithstanding this, most of equations were developed for subjects within a normal weight range (Coquart et al., 2014). As a result, errors may occur when applying these equations to an overweight/obese population because obese individuals have lower cardiovascular fitness than lean subjects (Wang et al., 2010). Therefore, specific equations for the overweight and obese population should be created. Cycle ergometer testing is a popular mode for assessing $\text{VO}_{2\text{peak}}$ in overweight and obese individuals (Coquart et al., 2011, Coquart et al., 2009). Cycle ergometer testing is influenced by peripheral fatigue and often do not reflect the actual consumption of oxygen (Faulkner and Eston, 2007, Sarzynski et al., 2013, Wright et al., 2013). Body composition,

particularly lean body mass (LBM) may influence $\text{VO}_{2\text{peak}}$. Since LBM is a reflection of metabolically active tissues, it should be considered when predicting $\text{VO}_{2\text{peak}}$ (O'Donovan et al., 2012). In addition, walking and running are more familiar and habitual modes of exercise for the average individual, thus it would be beneficial to develop equations for treadmill-specific tests (Eston et al., 2012). Moreover, another factor that influences oxygen consumption is the level of physical activity; hence equations estimating $\text{VO}_{2\text{peak}}$ should continue to include this variable (Eston et al., 2008, Evans et al., 2013). Therefore, the aim of this study was two-fold. Firstly, to develop equations for estimating $\text{VO}_{2\text{peak}}$ in sedentary and active overweight and obese subjects. Secondly, to compare the equations developed with other widely used equations. A cross-validation study with an independent sample was conducted to determine the accuracy of the new equations.

Material and method

Participants

The present study was part of a randomized clinical trial by *Nutrition and Physical Activity Programs for Obesity Treatments* (PRONAF according to its Spanish initials); the aim of which was to assess the usefulness of different types of physical activity and nutrition programs for the treatment of adult obesity. The inclusion criteria included subjects living in the region of Madrid, aged 18 to 50 years, overweight or obese (body mass index [BMI]: ≥ 25 to $< 35 \text{ kg/m}^2$), sedentary (< 30 min physical activity/day), normoglycaemic and non-smoker. In agreement with the guidelines of the Declaration of Helsinki (Rickham, 1964), regarding research on human subjects, all participants were carefully informed about the possible risks and benefits of the present study and signed an institutionally approved document of informed consent. The

PRONAF study was approved by the Human Research Review Committee of the University Hospital La Paz (HULP) (PI-643).

Study design

The intervention consisted of a 6-month diet and exercise-based program, with a particular focus on creating a behavior change. Participants entered the study in two sample waves (overweight and obese phase) they were then split into four randomly assigned groups, stratified by age and sex. The following groups were: strength, endurance, combined strength and endurance, and the control group, adhering to physical activity recommendations. All participants were measured pre- and post-intervention, in week 1 and week 24, respectively. Physical activity was assessed by a SenseWear Pro3 Armband™ accelerometer (Body Media, Pittsburgh, PA). Participants wore the monitor continuously for 5 days following general recommendations (Murphy, 2009). Daily energy expenditure was calculated using the Body Media propriety algorithm (Interview Research Software Version 6.0). Additionally, participants were asked to report physical activity habits and chronicle their food consumption during the intervention through a personal diary. From a total of 180 participants, who concluded the PRONAF study, 129 participants (57 males and 72 females) completed all the tests and were included in this study. Individuals of the control group were excluded from the analyzes because their physical activities were not supervised. Individuals were randomized into two groups: development group ($n=94$) and validation group ($n=35$), both groups included the same ratio of men to women and a proportional representation of training groups (strength, endurance and combined). With the development and validation groups representing 73% and 27% of the total sample, respectively. The data of development group were used to create the equations, while the data of validation group were used to validate these equations. According to classifications of physical

activity level used elsewhere (Eston et al., 2012), individuals on baseline and post-intervention were considered sedentary and active, respectively. For both classifications, sedentary and active, two equations with the same variables were created; however, one considered the effort test, whilst the other did not. Moreover, measured $\text{VO}_{2\text{peak}}$ was compared to predicted values by American College of Sport Medicine (ACSM, 2006) and Bruce (Bruce et al., 1973) equations (Table 9).

Table 9. ACSM and Bruce equations utilized.

ACSM Equation
$\text{VO}_{2\text{peak}} (\text{L/min}) = (((\text{SPEED} \times 0.1) + (\text{SPEED} \times \text{GRADE} \times 1.8) + 3.5) / 1000) \times \text{BW}$
Bruce Equation
$\text{VO}_{2\text{peak}} (\text{L/min}) = ((85.42 - (13.73 \times \text{SEX}) - (0.409 \times \text{AGE}) - (3.24 \times \text{PAS}) - (0.114 \times \text{BW})) / 1000) \times \text{BW}$
<small>$\text{VO}_{2\text{peak}}$ – peak oxygen uptake; speed in miles; grade in decimal percentage (10% = 0.1); BW – body weight (in kilograms); sex (1 = male, 2 = female); age in years; PAS – physical activity status (active = 1; sedentary = 2).</small>

Diet intervention

Before initiating the intervention, negative energy balance was calculated for all participants; taking into account their own daily energy expenditure based on accelerometry data and the 3-day food log. As a result, they followed an individualized hypo-caloric diet with a 25-30% caloric restriction. Macronutrient distribution was set according to the Spanish Society of Community Nutrition recommendations (Serra-Majem and Aranceta, 2001).

Exercise intervention

All exercise training groups followed an individualized training program; which consisted of three exercise sessions per week, for 22-weeks. All exercise sessions were carefully supervised by certified personal trainers. Details of the different protocols developed by the groups are described elsewhere (Zapico et al., 2012).

Measurements

Cardiovascular fitness

Evaluation of cardiovascular fitness was conducted through a maximal effort test with the modified Bruce protocol, broadly used in overweight and obese populations (Ghroubi et al., 2009, Hunter et al., 2008), with a computerized treadmill (H/P/COSMOS 3PW 4.0, H/P/Cosmos Sports & Medical, Nussdorf-Traunstein, Germany). During testing, minute ventilation (VE), oxygen uptake (VO_2), and carbon dioxide expiration (VCO_2) were constantly measured through indirect calorimetry using the gas analyzer Jaeger Oxycon Pro (Erich Jaeger, Viasys Healthcare, Germany). $\text{VO}_{2\text{peak}}$ was assessed using calculations that evaluated the volume and composition of expired gas using the Haldane transformation. All subjects were asked to refrain from intense exercise/physical activity 24 hours preceding the test. The measurements took place in similar environmental conditions. The analyzer was calibrated using certified gas mixtures before each run. Heart rate, in response to increasing exercise, was continuously monitored with a 12-lead electrocardiographic monitor. The following criteria were used to determine $\text{VO}_{2\text{peak}}$: performance must attain $\geq 85\%$ of the theoretical maximum heart rate, achieve a superior respiratory exchange ratio (RER) to 1.10 and perform until exhaustion (Balady et al., 2010). The mean of the three highest measurements determined $\text{VO}_{2\text{peak}}$ (Cortes et al., 2014). All tests were evaluated by two researchers in a double blind process. The coefficient of variation between the assessments of these two studies and those of a highly-experienced expert was 1.3%. The time of effort test (TIME) was used as the independent variable in the equations, with regards to the effort test.

Body composition

A Tanita BC 418 body composition analyzer (Tanita Corp., Tokyo, Japan) was used for the bioelectrical impedance analysis (BIA). Subjects stood with the ball of their feet and heels in contact with the metallic electrodes. Once weight was recorded, subjects were instructed to grasp the hand grips and hold them down by their sides so that the metallic electrodes were in contact with the palm and thumb. The precision error for BIA measures in our laboratory was 0.52% of body fat percentage. All measurements were done in agreement with the normal protocol at least 3 hours after a meal (including drinks), and subjects were instructed to refrain from strenuous exercise 12 hours prior to the measurements. Subjects were asked to empty their bladder before the measurements. Females were not measured during their menstrual period (Deurenberg et al., 2001). Body weight (BW), fat mass percentage (%FM) and lean body mass percentage (%LBM) measures were obtained. Height was measured using a SECA stadiometer (range 80-200 cm, Valencia, Spain). BMI was calculated as: body mass (kg)/height (m)².

Statistical Analysis

The arithmetic mean and standard deviation were used as descriptive statistics. Stepwise multiple regression models were performed to verify the influence of certain variables in the VO_{2peak} . In each case, the dependent variable was VO_{2peak} and the independent variables were age, gender, BW, BMI, %FM and %LBM, and TIME. If the slope for an independent variable was not found to be statistically significantly different than zero at $\alpha = 0.05$, that independent variable was excluded from the model. Independent variables selected for the final regressions were age, BW and %LBM and TIME. The validity of the model was assessed through the analysis of colinearity statistics and Q-Q plots of unstandardized residuals. Pearson correlation coefficients (r)

and determination coefficients (R^2) were calculated. Differences between the coefficients of determination from the validation and elaboration groups would be within 0.075. Standard error of estimate (SEE) was calculated. Bland-Altman plots 95% limits of agreement analysis (LoA) were constructed to determine the level of agreement between the measured and predicted VO_{2peak} for each equation. In addition, Lin's concordance correlation coefficients were obtained and classified according McBride (2007) where values >0.99 is considered almost perfect, $>0.95-0.99$ substantial, $>0.90-0.95$ moderate and ≤ 0.90 poor. Independent samples t test was used to compare characteristics at baseline between development and validation groups. Paired samples t tests were performed to compare measured and predicted VO_{2peak} values. The analyzes were conducted using SPSS statistical software (Version 17; SPSS, Inc, Chicago, IL) and MedCalc (Medical Calculator) software (version 12.1.4.0). The statistical significance level was set at 5% ($p < 0.05$).

Results

The characteristics of participants at baseline were similar in the development and validation groups (Table 10). Percentages of men were 43.6 and 45.7 in the development and validation group, respectively. All tests were considered maximum, in accordance to the criteria described in methods. Multiple regression models with exercise included BW, TIME, %LBM and age. Models without exercise included the same variables, except TIME. Equations before (sedentary, 1a and 1b) and after (active, 2a and 2b) the intervention were developed (Table 11).

Table 10. Characteristics at baseline.

	Development Group (n=94)	Validation Group (n=35)
Age	37.3 ± 7.3	39.0 ± 8.9
Body weight (kg)	88.8 ± 13.8	88.0 ± 11.9
Height (cm)	169.1 ± 9.3	168.2 ± 9.5
Body mass index (kg/m ²)	30.9 ± 3.2	31.0 ± 2.6
Percentage fat (%)	35.6 ± 7.0	36.1 ± 7.5
Fat mass (kg)	31.7 ± 8.3	31.8 ± 8.0
Lean body mass (kg)	54.2 ± 10.0	53.4 ± 9.6

Data are presented as mean ± SD. No significant differences were found between development and validation groups for any of the variables.

Table 11. Equations obtained in this study.**Equation 1a (sedentary with effort test)**

$$\text{VO}_{2\text{peak}} (\text{L/min}) = -4.119 + (0.038 \times \text{BW}) + (0.147 \times \text{TIME}) + (0.027 \times \% \text{LBM}) + (-0.014 \times \text{AGE})$$

Equation 1b (sedentary without effort test)

$$\text{VO}_{2\text{peak}} (\text{L/min}) = -3.519 + (0.045 \times \text{BW}) + (0.050 \times \% \text{LBM}) + (-0.020 \times \text{AGE})$$

Equation 2a (active with effort test)

$$\text{VO}_{2\text{peak}} (\text{L/min}) = -5.017 + (0.040 \times \text{BW}) + (0.127 \times \text{TIME}) + (0.046 \times \% \text{LBM}) + (-0.010 \times \text{AGE})$$

Equation 2b (active without effort test)

$$\text{VO}_{2\text{peak}} (\text{L/min}) = -4.849 + (0.046 \times \text{BW}) + (0.069 \times \% \text{LBM}) + (-0.010 \times \text{AGE})$$

$\text{VO}_{2\text{peak}}$ – peak oxygen uptake; BW – body weight (in kilograms); TIME – time of effort test (in minutes); %LBM – lean body mass percentage.

The equations derived from this study reported the greatest determination's coefficients and lowest values of SEE, for both development and validation groups. In the development group, $\text{VO}_{2\text{peak}}$ predicted values, using the Bruce equation, were significantly lower than the measured values after the intervention ($p = 0.046$); whereas those predicted by ACSM's equation were significantly higher compared to the measured $\text{VO}_{2\text{peak}}$ levels before and after the intervention ($p < 0.001$) (Table 12).

Table 12. Measured and predicted peak oxygen uptake in development group (n=94).

Sedentary					
	Measured VO_{2peak}	Equation 1a	Equation 1b	ACSM (2006)	Bruce et al. (1973)
Mean ± SD (L/min)	2.830 ± 0.805	2.729 ± 0.707	2.786 ± 0.691	3.630 ± 0.888 [#]	2.876 ± 0.866
95% LoA (L/min)	---	-0.074 ± 0.374	-0.017 ± 0.411	0.826 ± 0.677	0.073 ± 0.483
r	---	0.885*	0.859*	0.684*	0.835*
R ²	---	0.757	0.738	0.468	0.697
SEE (L/min)	---	0.383	0.414	1.077	0.491
CCC	---	0.874	0.849	0.460	0.830
Active					
	Measured VO_{2peak}	Equation 2a	Equation 2b	ACSM (2006)	Bruce et al. (1973)
Mean ± SD (L/min)	3.038 ± 0.852	3.065 ± 0.782	3.052 ± 0.755	3.625 ± 0.889 [#]	2.941 ± 0.832 [#]
95% LoA (L/min)	---	0.026 ± 0.339	0.013 ± 0.401	0.586 ± 0.520	-0.097 ± 0.464
r	---	0.917*	0.882*	0.825*	0.849*
R ²	---	0.841	0.778	0.681	0.721
SEE (L/min)	---	0.342	0.403	0.790	0.477
CCC	---	0.914	0.876	0.672	0.842

* $p < 0.001$; [#] $p < 0.05$ - mean differences between predicted and measured values; analysis of the 95% limits of agreement (LoA) expressed as bias (± 1.96 SD diff); SEE - standard error of estimate; CCC – concordance correlation coefficient; VO_{2peak} – peak oxygen consumption; ACSM – American College of Sport Medicine.

In the validation group, equations 1a and 1b underestimated VO_{2peak} values at baseline ($p = 0.002$ and $p = 0.008$, respectively); similarly, Bruce's equation also underestimated these values at post intervention ($p = 0.019$). Equally for the elaboration group, ACSM's equation overestimated VO_{2peak} measured values, before and after the intervention ($p < 0.001$) (Table 13).

Table 13. Measured and predicted peak oxygen uptake in validation group (n=35).

Sedentary					
	Measured VO_{2peak}	Equation 1a	Equation 1b	ACSM (2006)	Bruce et al. (1973)
Mean ± SD (L/min)	2.888 ± 0.778	2.678 ± 0.653 [#]	2.698 ± 0.665 [#]	3.596 ± 0.740 [#]	2.813 ± 0.776
95% LoA (L/min)	---	-0.211 ± 0.373	-0.191 ± 0.396	0.707 ± 0.475	-0.075 ± 0.469
r	---	0.879*	0.860*	0.805*	0.817*
R ²	---	0.772	0.740	0.648	0.667
SEE (L/min)	---	0.436	0.448	0.873	0.483
CCC	---	0.828	0.821	0.556	0.814
Active					
	Measured VO_{2peak}	Equation 2a	Equation 2b	ACSM (2006)	Bruce et al. (1973)
Mean ± SD (L/min)	3.019 ± 0.859	3.025 ± 0.759	2.991 ± 0.746	3.516 ± 0.756 [#]	2.846 ± 0.753 [#]
95% LoA (L/min)	---	0.004 ± 0.294	-0.030 ± 0.337	0.494 ± 0.397	-0.176 ± 0.417
r	---	0.941*	0.921*	0.886*	0.874*
R ²	---	0.885	0.848	0.785	0.764
SEE (L/min)	---	0.298	0.343	0.649	0.461
CCC	---	0.934	0.912	0.738	0.846

* $p < 0.001$; [#] $p < 0.05$ - mean differences between predicted and measured values; analysis of the 95% limits of agreement (LoA) expressed as bias (± 1.96 SD diff); SEE - standard error of estimate; CCC - concordance correlation coefficient; VO_{2peak} – peak oxygen consumption; ACSM – American College of Sport Medicine.

Before the intervention, concordance correlation coefficients were considered “poor” for all the equations. However, the highest values were reported by the equations from the present study. After the intervention, concordance correlation coefficients were classified as “moderate” for the equations 2a and 2b in the validation group. ACSM’s equation presented the lowest values of concordance correlation coefficients in all the cases. Bland and Altman plots indicated that, on average, the equations of this study in the validation group underestimated VO_{2peak} by 0.200L/min (standard errors of mean) in sedentary subjects ($p < 0.05$) (Fig. 4). However, the standard errors of mean for the same subjects for ACSM and Bruce equations were -0.707 L/min and 0.076 L/min, respectively.

Fig. 4. Bland and Altman's limits-of-agreement plot between measured and estimated $\text{VO}_{2\text{peak}}$; calculated through equations 1a (sedentary with effort test) (above) and 1b (sedentary without effort test) (below) in subjects of the validation group. — Observed average agreement; ---- 95% Limits of agreement: $y = 0$ signifies the line of perfect agreement.

On the other hand, when the subjects were active, the equations predicted $\text{VO}_{2\text{peak}}$ well, with the mean differences close to zero (Fig. 5). ACSM and Bruce equations presented standard errors of mean of -0.496 and 0.174, respectively.

Fig. 5. Bland and Altman's limits-of-agreement plot between measured and estimated $\text{VO}_{2\text{peak}}$; calculated through equations 2a (active with effort test) (left) and 2b (active without effort test) (right) in subjects of the validation group. — Observed average agreement; ---- 95% Limits of agreement: $y = 0$ signifies the line of perfect agreement.

Discussion

The purpose of the present study was to develop equations for predicting $\text{VO}_{2\text{peak}}$, with and without effort test data in overweight and obese subjects, before and after a weight loss intervention. Our results revealed that BW, %LBM, age and TIME, used in combination, is an adequate method to predict $\text{VO}_{2\text{peak}}$ in this population, explaining almost 80% of the variation in $\text{VO}_{2\text{peak}}$. Moreover, our data showed that equations commonly used in the literature inaccurately estimate $\text{VO}_{2\text{peak}}$.

Several studies found differences between men and women in the oxygen consumption (Dagan et al., 2013, Loe et al., 2013). In our data, other variables, such as BW and %LBM, were better predictors than gender. Body composition, particularly muscle mass, seems to have a stronger correlation with the development of some physical capacities than genetic sexual characteristics (Perez-Gomez et al., 2008, Schantz et al., 1983). Furthermore, hormone responses also seem to relate to body size, and greater values of BMI could blunt a sexual dimorphism (Zugel et al., 2016). It is important to note that many variables influence the muscle mass percentage values obtained by bioimpedance. For this reason, it is recommended that the conditions should be the same, as previously indicated in this study's methodology, to ensure better precision in the equations.

Besides BW and %LBM, age was also included as a predictor of $\text{VO}_{2\text{peak}}$ in the equations of this study. This is in agreement with the results of Loe et al. (2013), which indicated that the oxygen consumption decreases approximately 6% every decade between the second and fifth decade of life in both genders.

Furthermore, TIME was included in the equations instead of velocity, since the Bruce protocol is not graded and time is a simple and easy variable to measure (Bires et al., 2013).

Although our equations at baseline in the validation group presented significantly different values compared to measured values, equations developed in the present study obtained the best concordance correlation coefficients and greatest determination coefficients compared to ACSM and Bruce equations. Moreover, these equations reported lower values than measured ones. Nonetheless, when working with obese individuals, who commonly have some pathology associated with excess weight, it is better to underestimate than overestimate $\text{VO}_{2\text{peak}}$ predictions. A greater health risk could be incurred if $\text{VO}_{2\text{peak}}$ values were overestimated, and subsequently utilized for the purpose of an intervention program (Noble, 1982). ACSM's equation overestimated all $\text{VO}_{2\text{peak}}$ values in this study as well as in other studies (Dalleck et al., 2005, Foster et al., 1996, Peterson et al., 2003). Also, determination coefficients of this study were higher than coefficients showed in other studies in different populations (Almeida et al., 2014, Coquart et al., 2010, Coquart et al., 2009, Dagan et al., 2013, Eston et al., 2008). It is important in the selection of an equation to consider certain factors, such as population, medical conditions or medication, the mode of ergometer in terms of safety, familiarity and availability (Gellish et al., 2007). Therefore, our equations could be used in other populations with similar characteristics to our sample.

The prediction of $\text{VO}_{2\text{peak}}$ through models without exercise can be a viable alternative for the evaluation of cardiorespiratory fitness in epidemiological studies. It is beneficial for prescribing exercise programs when is not possible to perform an effort test and to estimate $\text{VO}_{2\text{peak}}$, and relate it to life expectancy (Maranhao Neto Gde et al., 2004). Bruce and colleagues (Bruce et al., 1973) established prediction equations without exercise, demonstrating that oxygen consumption could be predicted by variables such as gender, age, weight and physical activity habits. These authors were the first to use adults and to consider lifestyle factors such as daily physical activity, in

addition to anthropometric characteristics. However, in our study Bruce equation showed significant differences in the estimated oxygen consumption after the intervention. This fact may be due to the sample used by the authors that included elderly individuals which probably altered the regression results, particularly with improving VO_{2peak} levels after a training period (Bruce et al., 1973). Furthermore, Bruce equation did not use the effort test; similar to our equations, specifically those without effort test data presented a satisfactory estimation of VO_{2peak} .

According to Eston et al. (Eston et al., 2008) sedentary individuals are understandably unfamiliar to the associated signals of exertion emanating from acute cardiorespiratory, thermal, and metabolic changes associated with an increase in exercise intensity. Our results reported improvement in the accuracy of VO_{2peak} prediction after the intervention, as suggested by others (Eston et al., 2006, Evans et al., 2013).

Duration of the intervention allowed verifying changes in predictive variables due to training, detected by models with and without exercise. Our data contributed to the rectification of the lack of studies in clinical populations, since there are few studies specifically focused on the development of models applied to special groups. And when they are presented, they have a low potential for widespread use due to reduced samples used in their development. In addition, BIA, an easy and low cost instrument, prevents measurement errors of the evaluators and expands its use to different populations. Skinfolds, for example, require well-trained operators to adequately collect data and often use other equations to predict the percentage of fat, which increase errors (Dogra et al., 2015). In this line, dual X-ray absorptiometry is still an expensive and impractical procedure for general population.

Limitations of this study include the relatively small sample size and joint treatment for females and males. However, the difference between genders for oxygen consumption was reflected in the equations when considering the lean body mass. Additionally, we have to take into account that the predicted $\text{VO}_{2\text{peak}}$ values would be the theoretical value obtained by the subject in a Bruce protocol test on the treadmill with indirect calorimetry.

In conclusion, equations developed in this study including the variables age, BW, %LBM and TIME, were adequate to predict $\text{VO}_{2\text{peak}}$ in overweight and obese subjects. ACSM and Bruce equations, commonly used in the literature, showed inaccurately estimation of $\text{VO}_{2\text{peak}}$.

BLOOD PRESSURE RESPONSE AND CARDIOVASCULAR RISK AFTER DIFFERENT TYPES OF TRAINING IN OVERWEIGHT AND OBESE ADULTS

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Abstract

Background: Studies indicate that weight excess has a direct relationship with blood pressure (BP) and cardiovascular risk, but mechanisms that could mediate the hypertension linked to obesity are still unclear. Our aim was to analyze the effect of a weight loss program on BP and cardiovascular risk in overweight and obese subjects.

Methods: One hundred and eight overweight and obese individuals (84 males), aged 18–50 years, were randomized in 4 intervention groups: strength (S); endurance (E); combined strength + endurance (SE) or physical activity recommendation (PA) during 22 weeks with a 25%-30% caloric restriction diet. Blood pressure, coronary heart disease risk (Framingham-REGICOR function) and associated diseases risk by World Health Organization (WHO' diseases risk) were measured before and after the program.

Results: In men, systolic BP (SBP) and mean arterial pressure (MAP) decreased in overweight (SBP: -7.9%, $p < 0.001$; MAP: -9.6%, $p < 0.001$) and obese (SBP: -3.0%, $p = 0.033$; MAP: -4.9%, $p = 0.001$). Diastolic BP (DBP) also reduced in males (-8.3%, $p < 0.001$). In women no interactions were found for body mass category or groups and SBP, MAP, DBP, pulse pressure decreased significantly about 5% ($p < 0.05$). Resting heart rate decreased in SE (-7.1%, $p = 0.015$) and PA (-9.7%, $p = 0.001$) groups in males and in S (-11.7%, $p < 0.001$), E (-5.8%, $p = 0.017$) and PA (-7.2%, $p = 0.033$) in females. Framingham-REGICOR function reduced only in males (-25.7%, $p < 0.001$). Percentage of subjects included in each category of WHO' diseases risk before and after the intervention was significantly different ($p < 0.001$). WHO' diseases risk was positively associated to body weight, fat and lean body mass percentages, waist circumference, body mass index, android fat percentage and negatively associated to peak oxygen consumption in both genders ($p < 0.05$). *Conclusion:* All the interventions were effective for decrease BP in subjects with weight excess. Associated diseases risk

as diabetes, hypertension and cardiovascular diseases also decreased in both genders, but coronary heart disease risk reduced only in men.

Keywords: systolic blood pressure; diastolic blood pressure; coronary heart disease, body mass index, obesity.

Introduction

High blood pressure (BP) and a crescent increase of obesity and diabetes are the main features of the cardiometabolic epidemic of the 21st century (Ezzati and Riboli, 2013). High BP was considered the leading risk factor for deaths due to cardiovascular diseases (CVD), chronic kidney disease and diabetes, contributing with approximately 40% of worldwide deaths from these diseases in 2010 (Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration, 2014). The prevalence of hypertension in Spain is high; approximately 25% of men and 15% of women adults were considered hypertensive according to the data from the World Obesity Federation (www.worldobesity.org). Furthermore, hypertension is also a main cardiovascular risk factor in Spain, achieving 40% from 35 years in both genders (Banegas, 2005). In turn, CVD is the leading cause of death in Spain (Bertomeu and Castillo-Castillo, 2008). The absolute individual risk to develop CVD depends not only of BP levels, but also other cardiovascular risk factors and associated clinical disorders, such as obesity (Casanueva et al., 2010, Global Burden of Metabolic Risk Factors for Chronic Diseases Collaboration, 2014) and sedentary lifestyle (Fagard, 2012, Vanhees et al., 2012). In addition, from the total deaths and cardiovascular deaths occurred in Spanish population in the 90s related to blood pressure ($\geq 120/80$ mmHg), 20% approximately relapsed into normal or normal-high BP levels (Banegas, 2005). Therefore, decline in blood pressure

in normotensive individuals, as well as weight reduction and lifestyle changes have several advantages for cardiovascular risk improvement.

In general population, higher values of body mass index (BMI) are related to higher values of adipose tissue (Amato et al., 2013) and studies indicate that BMI has a direct relationship with BP (Li et al., 2006, Ortiz-Galeano et al., 2012, Whitlock et al., 2009). There are multiple mechanisms that could mediate the hypertension linked to obesity (Xie and Bollag, 2016), although this interrelation is still not entirely understood (Neter et al., 2003). Adipose tissue is now appreciated as a metabolically active organ that releases a large number of cytokines and bioactive mediators (Van Gaal et al., 2006), which could stimulate hormonal changes (Laffin et al., 2016) and adaptations in cardiac structure and hemodynamic function in obese individuals (Poirier et al., 2006). In fact, the reduction of one kilogram of body weight implies of about 1mmHg in systolic BP (SBP) (Neter et al., 2003). Moreover, there is a clear relationship between magnitude of central obesity and cardiovascular risk in adults (Laffin et al., 2016, Casanueva et al., 2010). Therefore, weight loss programs aimed to decreasing the amount of total and central adipose tissue could have a very positive implication on cardiovascular risk and could contribute to the prevention of hypertension in normotensive subjects (Fagard, 2011).

Physical activity is associated with a marked reduction in cardiovascular and all-cause mortalities, even after adjustment for other relevant risk factors (Fagard, 2012, Rossi et al., 2012). The role of habitual physical activity in the primary prevention of coronary heart disease is consistent (Pescatello et al., 2004, Rossi et al., 2012, Ezzati and Riboli, 2013, Fagard, 2011, Fagard, 2012) and there is a strong evidence that aerobic exercise should be prescribed as the primary type of exercise for the prevention, treatment, and control of hypertension (Pescatello et al., 2015, Pescatello et al., 2004,

Cornelissen and Fagard, 2005). However, in the last years, many authors found significant improvements in BP with resistance or strength training alone or in combination with aerobic training (Jorge et al., 2011, Potteiger et al., 2012, Yoo et al., 2013, Ghroubi et al., 2016, Zois et al., 2009, Ha and So, 2012, Ho et al., 2012b, Hsieh et al., 2016). Although recent studies are encouraging about the potential contribution of strength training in the prevention and treatment of hypertension (Cornelissen et al., 2011, Strasser et al., 2010, Cornelissen and Smart, 2013, Hayashino et al., 2012), data are not conclusive. More investigation establishing frequency, intensity, duration of exercise as well as the most efficient combination of aerobic and resistance exercise that elicit the greatest BP benefit among adults is necessary (Vanhees et al., 2012, Pescatello et al., 2015). Thus, the optimal training regime to prevention and treatment of factors associated to cardiovascular abnormalities remains undefined. Therefore, the purpose of the present study was to analyze the effect of a weight loss program on BP and cardiovascular risk in overweight and obese subjects, comparing the effectiveness of isolated and combined aerobic and resistance training.

Methods

Participants

The present study was performed as part of *Nutrition and Physical Activity Programs for Obesity Treatment* (PRONAF Study according to its Spanish initials); the aim of which was to assess the usefulness of different types of physical activity and nutrition programs for the treatment of adult obesity. The inclusion criteria specified adult subjects, aged 18 to 50 years, overweight or obese (BMI: ≥ 25 to < 35 kg/m²), sedentary (< 30 min physical activity/day), normoglycaemic and non-smoker. Only females with regular menstrual cycles were included. Adherences to diet (80%) and

exercise (90%) were required. In total, data of 176 participants (83 men) were included in the analysis of this study. In agreement with the guidelines of the Declaration of Helsinki, regarding research on human subjects, all participants were carefully informed about the possible risks and benefits of the study and signed a document of informed consent. The PRONAF study was approved by the Human Research Review Committee of the University Hospital La Paz (HULP) (PI-643).

Study design

The complete methodology and the flow diagram can be found in Zapico et al. (2012). Briefly, subjects who fulfilled the inclusion criteria were included into four randomly assigned groups, stratified by age and sex. The intervention programs lasted 22 weeks, and the assessment tests took place one week before (baseline) and after (post) the intervention.

Exercise protocols

Four different interventions were performed: strength training (S), endurance training (E), combined strength + endurance training (SE) groups followed the corresponding supervised exercise program plus the dietary intervention, and the physical activity recommendation (PA) group followed dietary intervention and was instructed about the general recommendations about physical activity from the American College of Sports Medicine (ACSM) (Donnelly et al., 2009).

Subjects in the S, E, and SE groups trained three times per week. All training sessions were carefully supervised by certified personal trainers with Sports Science degrees. The exercise programs were designed according to the subject's muscle strength and heart rate (HR) reserve. All exercise programs were performed in circuit. Sessions routine consisted of: eight strength exercises in S group; aerobic exercise (running, cycling, or elliptical) in E group; and a combination of four bouts of aerobic

exercise intercalated with four strength exercises in SE group. Participants performed 15 repetitions of each strength exercise or 45 seconds of aerobic exercise in each aerobic exercise bout. The recovery period between exercises lasted 15 seconds. Both volume and intensity of the three training programs increased progressively from one lap to the circuit at an intensity of 50% of the heart rate reserve and/or the 15RM, to three laps at an intensity of 60%.

Hypocaloric diet

All groups underwent an individualized and hypocaloric diet (between 1200 and 3000 kcal) prescribed by expert dietitians. The diet aimed for a 25-30% reduction of the total daily energy expenditure calculated using the Body Media propriety algorithm (Interview Research Software Version 6.0) based on accelerometry data. Macronutrient distribution was set according to the Spanish Society of Community Nutrition recommendations (Serra-Majem and Aranceta, 2001).

Measurements

Blood Pressure

Blood pressure measurements were made manually on the right arm in supine position by a trained physician using a standard stethoscope and sphygmomanometer after the subject had been lying quietly for 5 minutes. Pulse pressure (PP) was calculated as the difference between SBP and diastolic BP (DBP). Mean arterial pressure (MAP) was obtained by the following formula: $DBP + 1/3 * (PP)$.

Body composition and anthropometry

Body composition was assessed by dual-energy X-ray absorptiometry scan (Version 6.10.029GE Encore 2002, GE Lunar Prodigy; GE Healthcare, Madison, WI, USA); obtaining values for body weight, fat mass, lean body mass and android fat mass. Height was measured using a SECA stadiometer and waist circumference (WC) was

obtained employing a SECA 201 steel tape (Quirumed, Valencia, Spain) and measured at the level of the iliac crest at the end of a normal expiration. BMI was calculated as body mass/height (kg/m^2).

Cardiovascular Fitness

The test evaluating cardiovascular fitness was a maximal ergospirometry following the modified Bruce protocol with a computerized treadmill (H/P/COSMOS 3PW 4.0; H/P/Cosmos Sports & Medical, Nussdorf-Traunstein, Germany). Peak oxygen consumption ($\text{VO}_{2\text{peak}}$) was measured with the gas analyzer Jaeger Oxycon Pro (Erich Jaeger; Viasys Healthcare; Hoechberg, Germany). Heart response was continuously monitored with a 12-lead electrocardiogram. The subjects maintained the effort test until exhaustion. The mean of the three highest measurements was used as $\text{VO}_{2\text{peak}}$ and maximal heart rate. Resting HR was calculated as the average heart rate during 10 min in a lying position before the effort test.

Blood Samples

All blood samples were taken after 12 hours fast between 7:00 and 9:00 a.m. at baseline and post-intervention, always 72 hours after the last training day to avoid acute effects of training on blood lipids. Total cholesterol (TC) and high-density lipoprotein cholesterol (HDL) were determined using enzymatic methods with Olympus reagents by automated spectrophotometry performed on Olympus AU5400 (Olympus Diagnostica, Hamburg, Germany).

Assessment Coronary and Disease Risk

We used two models for predicting coronary (Framingham-REGICOR function) and associated diseases risk (WHO' diseases risk). Firstly, the calibrated Framingham-REGICOR function (Marrugat et al., 2003a, Marrugat et al., 2003b), validated in Spanish population (Marrugat et al., 2007, Marrugat et al., 2014, Marrugat et al., 2011)

was calculated for estimation 10-year stroke and coronary heart disease risk. Framingham-REGICOR function is a score that includes a combination of the following risk factors: smoking, diabetes, SBP, DBP and lipid profile (TC and HDL). As this function was developed for people from 35 years of age, analyzes were performed only for those subjects who fulfilled this requirement ($n = 121$, men = 57). Secondly, the classification suggested by Spanish Guidelines of Hypertension (Guía Española de Hipertensión Arterial, 2005) adapted of the World Health Organization (WHO) for associated diseases risk (type 2 diabetes, hypertension and cardiovascular diseases) (WHO' diseases risk) also was obtained. This classification ranks the individuals according to their BMI and WC in increased, high, very high and extremely high risks.

Statistical Analysis

Data are presented as mean $\pm$ SD. Three-way repeated measures analysis of covariance (ANCOVA) were used to determine any differences among the four intervention groups (S, E, SE and PA) and BMI category (overweight and obese subjects) by time (pre and post-intervention). Analyses were performed in men and women separately, and weight loss percentage was used as covariate. The Bonferroni *post hoc* tests were employed to locate specific differences. Effect size was calculated by partial eta-squared (η_p^2) and small, moderate and large effect corresponded to values equal or greater than 0.001, 0.059, and 0.138, respectively (Richardson, 2011). Differences between disease risk categories were calculated using a χ^2 test and residuals' analysis were performed. Pearson correlations were calculated to verify the association between Framingham-REGICOR function, disease risks and body composition and VO_{2peak} changes. Proportional changes were calculated through the standard formula: change (%) = [(pre-test score – post-test score)/pre-test score]*100.

All analyses were conducted in SPSS-PC v20 (IBM SPSS Statistics, Armonk, NY USA), and level of significance was set at $p < 0.05$.

Results

The characteristics of participants at baseline were similar among intervention groups in the same gender ($p > 0.05$ for all variables) (Table 14).

Table 14. Characteristics at baseline.

Variables	MEN (n = 83)				WOMEN (n = 93)			
	S	E	SE	PA	S	E	SE	PA
Age	38.3 ± 9.0	37.3 ± 7.6	38.0 ± 7.3	37.9 ± 8.0	37.1 ± 8.8	38.2 ± 7.5	37.3 ± 7.0	38.5 ± 9.1
Body weight (kg)	96.8 ± 10.1	95.1 ± 10.2	94.6 ± 12.1	96.2 ± 8.8	81.0 ± 9.8	79.7 ± 9.5	80.3 ± 12.6	77.4 ± 5.4
Height (cm)	177.1 ± 6.9	175.2 ± 7.2	176.8 ± 6.1	175.5 ± 5.8	162.8 ± 6.2	163.1 ± 6.6	162.5 ± 8.1	161.1 ± 5.2
Body mass index (kg/m ²)	30.8 ± 2.3	31.0 ± 2.7	30.2 ± 2.7	31.2 ± 2.4	30.5 ± 2.4	29.9 ± 2.5	30.3 ± 3.4	29.9 ± 2.8
Fat mass (%)	35.8 ± 4.5	36.4 ± 4.7	35.7 ± 5.4	37.4 ± 4.5	45.8 ± 2.6	44.4 ± 4.3	45.7 ± 5.4	44.8 ± 3.4
Android fat mass (%)	45.6 ± 6.3	45.3 ± 6.8	46.0 ± 6.8	47.5 ± 6.3	50.6 ± 4.1	48.8 ± 7.1	49.2 ± 8.1	49.6 ± 5.1
Lean body mass (kg)	59.8 ± 5.3	56.3 ± 5.4	58.4 ± 5.5	58.1 ± 5.9	42.3 ± 5.0	42.5 ± 5.3	42.3 ± 5.6	41.1 ± 3.0
Waist circumference (cm)	106.0 ± 5.4	104.5 ± 6.8	104.6 ± 7.1	104.3 ± 7.2	96.0 ± 6.3	95.5 ± 7.0	94.9 ± 6.9	94.7 ± 8.6
VO _{2peak} (L/min)	3.6 ± 0.7	3.2 ± 0.5	3.5 ± 0.5	3.4 ± 0.6	2.3 ± 0.4	2.2 ± 0.4	2.3 ± 0.5	2.1 ± 0.3
VO _{2peak} (ml/kg/min)	36.8 ± 7.1	35.6 ± 6.4	37.1 ± 4.8	35.2 ± 5.9	28.0 ± 3.4	27.9 ± 3.5	28.6 ± 4.3	27.4 ± 3.1
SBP (mmHg)	127.4 ± 9.9	126.3 ± 9.2	126.1 ± 11.3	126.9 ± 12.0	118.6 ± 11.9	114.8 ± 8.9	118.5 ± 14.0	122.9 ± 13.3
DBP (mmHg)	85.3 ± 7.8	81.8 ± 8.2	79.6 ± 9.2	82.1 ± 7.5	76.8 ± 9.0	76.5 ± 6.9	73.3 ± 8.0	78.0 ± 11.9
MAP (mmHg)	99.2 ± 7.6	96.5 ± 7.9	95.0 ± 8.7	96.9 ± 8.2	90.6 ± 9.5	89.1 ± 6.6	88.2 ± 8.9	92.9 ± 12.0

Data are presented as mean ± SD. S: strength training group; E: endurance training group; SE: combined strength + endurance training group; PA: physical activity recommendations group; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure.

Interaction between BMI category and time was found for SBP ($F_{(1,74)} = 6.885, p = 0.011, \eta_p^2 = 0.085$), and MAP ($F_{(1,74)} = 5.194, p = 0.026, \eta_p^2 = 0.066$) in men. SBP and MAP decreased in both BMI categories, and overweight men (SBP: $p < 0.001, \eta_p^2 = 0.277$; MAP: $p < 0.001, \eta_p^2 = 0.324$) achieved greater reduction than obese men (SBP: $p = 0.033, \eta_p^2 = 0.060$; MAP: $p = 0.001, \eta_p^2 = 0.137$), as observed by effect size. Only a significant main effect for time ($F_{(1,74)} = 34.763, p < 0.001, \eta_p^2 = 0.320$) was found for DBP in men. Main effect of time was also found for SBP ($F_{(1,74)} = 29.820, p < 0.001, \eta_p^2 = 0.287$) and MAP ($F_{(1,74)} = 45.619, p < 0.001, \eta_p^2 = 0.381$) in men. The remaining interactions were not significant (Figure 6a). In women no interactions between intervention groups or BMI category and time were found in SBP, MAP or DBP, with only a significant main effect of time in all these variables ($F_{(1,84)} = 26.856, p < 0.001, \eta_p^2 = 0.242$; $F_{(1,84)} = 21.551, p < 0.001, \eta_p^2 = 0.204$; $F_{(1,84)} = 12.101, p = 0.001, \eta_p^2 = 0.126$; respectively) (Figure 6b). The remaining interactions were not significant.

Fig. 6. A - SBP, MAP and DBP at baseline and post-intervention in men (a) and women (b). SBP: systolic blood pressure; MAP: mean arterial pressure; DBP: diastolic blood pressure.

There was interaction between time and intervention groups for resting HR in men, showing a decrease for SE ($p = 0.015$, $\eta_p^2 = 0.078$) and PA ($p = 0.001$, $\eta_p^2 = 0.150$) groups. Main effect of time was also found for resting HR in men. Pulse pressure did not change in men. A triple interaction was observed in women for resting HR. Overweight women of S ($p < 0.001$, $\eta_p^2 = 0.183$), E ($p = 0.017$, $\eta_p^2 = 0.071$) and PA ($p = 0.033$, $\eta_p^2 = 0.057$) groups reduced resting HR, while obese women showed no change. An interaction between time and BMI category also showed that only overweight women decreased resting HR and main effect of time was also found for this variable. Pulse pressure improved about 5% only in women, without interactions between intervention groups or BMI category. The remaining interactions were not significant (Table 15).

Table 15. Resting heart rate and pulse pressure before and after weight loss program.

MEN												
	S	E	SE	PA	TOTAL	F	P	η_p^2				
Resting HR (bpm)						T: 12.425	0.001	0.145				
Baseline	57.7 ± 8.2	58.3 ± 9.8	57.9 ± 7.6	63.7 ± 7.0	59.4 ± 8.4	TxG: 2.851	0.043	0.105				
Post-intervention	56.3 ± 5.7	59.0 ± 7.4	53.7 ± 6.7*	57.5 ± 9.9*	56.5 ± 7.7*	TxBMI 0.069	0.794	0.001				
						TxGxBMI 0.865	0.464	0.034				
PP (mmHg)						T : 0.098	0.755	0.001				
Baseline	----	----	----	----	44.6 ± 8.8	TxG: 0.462	0.710	0.018				
						TxBMI: 0.904	0.345	0.012				
Post-intervention	----	----	----	----	45.0 ± 9.6	TxGxBMI: 0.196	0.899	0.008				
WOMEN												
	OVERWEIGHT				OBESE				TOTAL	F	P	η_p^2
	S	E	SE	PA	S	E	SE	PA				
Resting HR (bpm)										T: 14.021	0.001	0.152
Baseline	68.3 ± 7.7	65.0 ± 8.2	62.8 ± 5.3	63.9 ± 5.4	62.5 ± 5.2	59.9 ± 6.7	69.3 ± 6.9	67.1 ± 6.5	64.7 ± 7.1	TxG: 0.560	0.643	0.021
Post-intervention	60.3 ± 5.1**	61.2 ± 6.0*	62.3 ± 8.4	59.3 ± 6.9*	64.8 ± 5.6	57.6 ± 8.6	67.0 ± 7.3	64.7 ± 7.1	62.0 ± 7.3**	TxBMI: 5.079	0.027	0.061
										TxGxBMI: 3.372	0.023	0.115
PP (mmHg)										T: 4.260	0.042	0.048
Baseline	----	----	----	----	----	----	----	----	42.1 ± 8.7	TxG: 1.103	0.353	0.038
										TxBMI: 0.010	0.922	0.000
Post-intervention	----	----	----	----	----	----	----	----	40.0 ± 7.8*	TxGxBMI: 0.101	0.959	0.004

Data are presented as mean ± SD. Baseline-post differences: *p < 0.05; **p < 0.001. T: time; G: intervention groups; BMI: body mass index category; S: strength training group; E: endurance training group; SE: combined strength + endurance training group; PA: physical activity recommendations group; HR: heart rate; PP: pulse pressure.

Coronary heart disease risk by Framingham-REGICOR function decreased only in men

($F_{(1,48)} = 46.197, p < 0.001, \eta_p^2 = 0.490$) for about 26%, without interactions (Figure 7).

Fig. 7. Framingham-REGICOR function at baseline and post-intervention in men and women.

According to χ^2 analysis, percentage of subjects included in each category of WHO' diseases risk before and after the intervention was significantly different $\chi^2(6) = 37.03, p < 0.001$. Residuals' analysis showed that percentage in the "very high risk" category before the intervention was significantly four times higher than after the intervention in men (Figure 8a). Regarding to women, χ^2 test also showed differences in percentages of WHO' diseases risk in the different categories before and after the intervention $\chi^2(6) = 55.39, p < 0.001$. Similarly, the "very high risk" category for women decreased about a 30% at when comparing baseline and post-intervention (Figure 8b). Furthermore, after the intervention a new category "without risk" was included for both genders.

Fig. 8. WHO' diseases risk categories distribution at baseline and post-intervention in men (a) and women (b).

No correlations ($p > 0.05$) were found between Framingham-REGICOR function change and body composition or VO_{2peak} changes. However, WHO' diseases risk low was moderately associated with body weight, fat and lean body mass percentages, waist circumference, body mass index, android fat percentage and VO_{2peak} in both genders (Table 16).

Table 16. Correlations between cardiovascular risk and body composition or fitness variables changes.

MEN								
	Body weight	Fat mass (%)	Lean body mass (%)	BMI	WC	Android fat mass (%)	Visceral Android Tissue (kg)	VO _{2peak}
Framingham-REGICOR function	0.217	0.190	-0.142	0.225	0.149	0.180	0.132	0.149
WHO' diseases risk	0.544**	0.525**	-0.502**	0.604**	0.514**	0.514**	0.476**	-0.359*
WOMEN								
	Body weight	Fat mass (%)	Lean body mass (%)	BMI	WC	Android fat mass (%)	Visceral Android Tissue (kg)	VO _{2peak}
Framingham-REGICOR function	0.036	0.096	-0.069	0.150	0.194	0.053	-0.038	0.018
WHO' diseases risk	0.414**	0.546**	-0.488*	0.411**	0.498**	0.356**	0.449**	-0.269*

*p<0.05; **p<0.001. BMI: body mass index; WC: waist circumference; VO_{2peak}: peak oxygen consumption.

Discussion

The main findings of the current study were: (1) that all four interventions, included strength training, were effective in reducing BP and disease risk in no hypertensive overweight and obese subjects; (2) that overweight males improved SBP more than obese males.

Several studies evaluated the association between BP and CV risk. Every 7 to 10 mmHg reduction in SBP decreased significantly about 13% relative coronary heart and all-cause mortality risks (Ettehad et al., 2016, Xie and Bollag, 2016). In our study, reductions in SBP and DBP were around 6 mmHg and 4-7mmHg, respectively, for both genders, without differences among interventions groups. Others investigations showed lower reductions in SPB compared to our results when utilized strength training (Ho et al., 2012b, Chaudhary et al., 2010, Schjerve et al., 2008, Stensvold et al., 2010, Sigal et al., 2007), endurance training (Chaudhary et al., 2010, Ho et al., 2012b, Schjerve et al., 2008, Stensvold et al., 2010, Sigal et al., 2007, Cornelissen et al., 2009, Moeini et al., 2015) or combined training (Ho et al., 2012b, Seo et al., 2011, Stensvold et al., 2010, Barone et al., 2009, Sigal et al., 2007, Figueroa et al., 2014, Mathieu et al., 2008). However, other authors found greater reductions than our study in the different training protocols: strength (Yoo et al., 2013, Hsieh et al., 2016, Jorge et al., 2011), endurance (Jorge et al., 2011, Lamina et al., 2013, Ghroubi et al., 2016, Molmen-Hansen et al., 2012, Potteiger et al., 2012, Yoo et al., 2013, Ghroubi et al., 2009) and combined (Ha and So, 2012, Yoo et al., 2013, Ghroubi et al., 2016, Moeini et al., 2015, Yang et al., 2011, Ghroubi et al., 2009, Zois et al., 2009). All studies that achieved greater improvements than ours involved participants with higher baseline values (hypertensive, diabetic or individuals with metabolic syndrome). Nevertheless, methodological aspects or others differences in sample characteristics difficult deeper

comparisons. Our study was the only one in which subjects from all training groups performed the exercises in circuit (i.e. with small recovery periods among exercises).

Cornelissen & Fagard (Cornelissen and Fagard, 2005) in their meta-analysis concluded that aerobic endurance training favorably affects BP and that physical activity was important in the prevention and management of hypertension. Significant reductions in resting SBP and DBP were more pronounced in the 30 hypertensive study groups (-6.9/-4.9) than normotensive (-2.4/-1.6 mm Hg) or pre-hypertensive groups (-1.7/-1.7 mm Hg) (Cornelissen and Fagard, 2005). In our results, 80% of the subjects would be considered pre-hypertensive. Despite of this, our results were more similar to those found for the hypertensive subjects of the meta-analysis mentioned above, which could be related to the different training methodologies of the studies and, and especially, to the fact that in the hypertensive group the subjects had a greater BMI, similar to our subjects. On the other hand, exercise intensity seems to be an important factor in the BP response of hypertensive subjects (Cornelissen and Smart, 2013). A recent study showed that aerobic interval training, but not moderate continuous training, improved variables related to BP, through decreased in total peripheral resistance and increase of flow mediated dilatation (Molmen-Hansen et al., 2012); although both improved blood pressure (reduction of 12 mmHg and 4.5 mmHg, respectively). The volume and intensity of exercise in our interventions was more similar to the intensity of continuous training performed in the study previously cited (our subjects trained, on average, 10% less intensity and about 10-20% more in volume than continuous training cited). However our results were more similar to those of aerobic interval training. This fact could be related to a longer term of our program (three months more), a performance of the exercises in circuit, an exhaustive daily control of the intensity through rate of perceived exertion scale, a progressive increment of the intensity, besides

other mechanisms involved in the BP response to training (Cornelissen and Fagard, 2005).

In contrast to the large amount of evidence of endurance training for BP improvement and maintenance, research was insufficient to support the role of strength training in the hypertension prevention and treatment (Hurley et al., 2011, Strasser et al., 2010). Another meta-analysis of Cornelissen and colleagues (Cornelissen et al., 2011) did not find significant differences in BP reduction in hypertensive participants, while resistance training induced a significant BP reduction in normotensive or pre-hypertensive study groups (-3.9 mmHg for both, SBP and DBP). However, only 4 of the 30 dynamic resistance study groups involved hypertensive patients and the poor methodological quality of many trials should be acknowledged when interpreting the results (Cornelissen et al., 2011). Regarding combined training, further researches are still required (Pattyn et al., 2013). Results of a meta-analysis (Cornelissen and Smart, 2013) demonstrated that combined, as well as endurance, dynamic resistance, and isometric resistance trainings significantly reduced DBP and all except combined training decreased SBP. As the authors did not discuss the reasons that could influence BP non-responsiveness for combined training and did not clarify the studies included in their analysis, it is difficult to compare our results with this finding. On the other hand, most articles evaluating combined training effects did not ensure the same intensity and volume for the different types of training used, and thus failing when comparing them. In PRONAF, exercise intensity and volume for all training interventions were systematically controlled, and no differences were found in other parameters, such weight loss (Benito et al., 2015) and $\dot{V}O_{2peak}$ (Castro et al., 2016). BP reductions found in our study have a clinical importance, since even a reduction of 2 mmHg in SBP would involve a decrease of about 10% in stroke mortality and of about 7% in mortality

from ischemic heart disease or other vascular causes in middle age (Lewington et al., 2002).

Our intervention also had an impact on other variables related to BP and CV risk, such as MAP, PP and resting HR. Although important, few studies have evaluated MAP, presenting similar results to ours (Potteiger et al., 2012). Pulse pressure seems to have an additional prognostic role to predict CV risk, although more significant in older people. In our study, PP only changed in females, but with a small effect size. Higher resting HR also seems to be independently associated with an increased risk of mortality (Zhao et al., 2017), although there may be a relationship with age, affecting old but not younger people (Li et al., 2016). However, our findings do not differ much from others found in the literature, respecting differences in baseline values (Ghroubi et al., 2016, Ho et al., 2012b, Zois et al., 2009, Molmen-Hansen et al., 2012, Cornelissen et al., 2009, Figueroa et al., 2014, Mathieu et al., 2008, Ghroubi et al., 2009). In general, in our data men presented worse results for BP variables than women from the point of view of health. This could be due to the fact that participants' age allowed women to still be on the protective effect of sex hormones (Orshal and Khalil, 2004).

In relation to BP changes comparing BMI categories, our results showed that overweight men improved more than obese counterparts in some variables. Although we cannot explain this difference with our results, elevated levels of aldosterone are present in obese patients with resistant hypertension (Laffin et al., 2016). Adipocyte-derived leptin appears also modulate aldosterone secretion, and this could explain, at least in part, the effect of obesity on BP (Xie and Bollag, 2016). This fact could be a hypothesis for explaining the difference between BMI categories. In addition, metabolic adaptation discussed in recent studies about weight loss, where obese subjects obtained

lower than expected weight loss (Lam and Ravussin, 2017), could also influence other variables.

In our study, men decreased the risk by Framingham-REGICOR function, while women did not change it, probably because they presented very low risk already at baseline. In turn, WHO' diseases risk showed a large benefit effect of the intervention in both genders. A new category "without risk" that was not present at baseline, included more of 13.3% of the subjects in the post-intervention. A study showed that overall 51% of almost 18000 Spanish subjects presented abdominal obesity measured by waist circumference, which is strongly associated with dyslipidemia and hypertension (Casanueva et al., 2010). Abdominal obesity seems to be a better marker of cardiovascular risk than BMI, because it is a main predictive factor of the metabolic syndrome (Amato et al., 2013). Our results were in accordance with previous study (Casanueva et al., 2010) which showed a direct relationship of the abdominal obesity with CVD at all levels of BMI. In our study, significant associations were also found between WHO' diseases risk and abdominal obesity (by waist circumference and android fat mass percentage).

Although the utilities of CV risk predictions are indisputable, they have also some limitations. The main ones are that young adults (especially women) will have small possibilities to be considered at high risk even if they have one or more important risk factors. On the other hand, older adults are often included in very high risk category. The latter fact could orient public investments only in older subjects and give little importance to young people. However the long-term exposures to an increased risk in the younger may lead to a situation of partially irreversible high risk later in life (Guía Española de Hipertensión Arterial, 2005).

Some limitation can be pointed in this research. The lack of additional measures throughout the program impedes to evaluate the dynamics BP reduction in the different types of intervention. Another limitation was no follow-up, without which the duration of the adaptations caused in BP by the program cannot be assessed.

In conclusion, endurance, strength, combined trainings and physical activity recommendations were effective for decrease BP in subjects with weight excess. Overweight males improve more than obese males. WHO' diseases risk also decreased in both genders, but coronary heart diseases risk by the Framingham-REGICOR function was reduced only in men.

RESTING METABOLIC RATE REPOSE AFTER WEIGHT LOSS PROGRAM

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Abstract

Background: Resting metabolic rate (RMR) is the major component of daily energy expenditure and exercise could mitigate the decline caused by weight loss programs.

Objective: to analyze the effect of a six-month weight loss program focused in different types of exercise on RMR in obese subjects, comparing the responses between men and women.

Methods: 95 obese individuals (48 men), aged 18–50 years, were randomized in 4 intervention groups: strength (S); endurance (E); combined strength + endurance (SE) or physical activity recommendation (PA) during 22 weeks with a 25%-30% caloric restriction diet. Standing metabolic rate (SMR) and RMR was measured by indirect calorimetry, and body composition was assessed by dual-energy X-ray absorptiometry. *Results:* RMR and SMR decreased in women without interactions between intervention groups and time (pre: 1592.8 ± 272.3 , post: 1461.2 ± 266.6 , $p = 0.001$; pre: 1708.4 ± 355.1 , post: 1518.8 ± 304.8 ; $p < 0.001$, respectively). There was interaction between intervention groups and time for SMR in men and SE (pre: 2235.3 ± 229.2 , post: 1964.5 ± 347.9 , $p = 0.003$) and PA (pre: 2492.2 ± 235.6 , post: 2046.6 ± 254.6 , $p < 0.001$) decrease SMR. RMR did not change in men. Absolute LBM decreased (pre: 44.1 ± 4.7 , post: 43.6 ± 4.8 , $p = 0.013$) and percentage LBM increased (pre: 51.3 ± 3.3 , post: 55.7 ± 4.3 , $p = 0.001$) in women after the intervention, without interactions between intervention groups and time. There was an interaction between intervention groups and time in men for absolute LBM, and only PA decreased it (pre: 60.9 ± 3.7 , post: 59.3 ± 2.5 , $p < 0.001$). Percentage LBM increased in men without interaction between intervention groups and time (pre: 59.7 ± 3.8 , post: 64.8 ± 4.6 , $p < 0.001$). Significant associations were found between RMR and LBM and between RMR and $\text{VO}_{2\text{peak}}$, in the pre and post-intervention for both sexes ($p < 0.005$). *Conclusion:* All

the interventions caused a reduction in RMR in women, but not in men. Future studies about sexual dimorphism related to RMR are required.

Keywords: standing metabolic rate; body mass index; obesity; lean body mass, training.

Introduction

Obesity occurs when energy intake exceeds energy expenditure (Romieu et al., 2017). In habitual conditions, resting metabolic rate (RMR) is the major component of daily energy expenditure (Ravussin et al., 1986). In general, low RMR is associated with weight gain (Lam and Ravussin, 2017) and RMR reduction caused by weight loss programs is a frequent concern as it could facilitate weight regains (Johannsen et al., 2012). Thus, RMR maintenance after weight loss interventions could be an important factor in weight management.

Lean body mass (LBM) is the largest contributor to RMR (Blundell et al., 2012), explaining about 60% of the variance in this variable (Caudwell et al., 2013). The muscle mass maintenance and, consequently, of a higher RMR, could prevent weight gain (Yaskolka Meir et al., 2016). Although endurance training promote a number of benefits for weight loss (such improve of the cardiorespiratory capacity and reduction of fat mass) (Dolezal and Potteiger, 1998, Geliebter et al., 1997), also have been shown that resistance training induced skeletal muscle hypertrophy and could be more effective to stimulate higher metabolic activity (Byrne and Wilmore, 2001, Cheema et al., 2014). In this line, some studies have been demonstrated that interventions with endurance exercise decrease RMR (Willis et al., 2014, Antunes et al., 2005, Dolezal and Potteiger, 1998, Donnelly et al., 1991, Bryner et al., 1999, Geliebter et al., 1997), while interventions with strength exercise maintain or increase it (Dolezal and Potteiger, 1998, Byrne and Wilmore, 2001, Hambre et al., 2012, Kirk et al., 2009, Bryner et al., 1999).

However, data are controversies and several studies also indicated a RMR reduction after resistance training (Donnelly et al., 1991, Geliebter et al., 1997).

There are few studies that analyzed the RMR response in combination endurance and resistance training, and results are inconsistent (Dolezal and Potteiger, 1998, Donnelly et al., 1991, Whatley et al., 1994, Byrne and Wilmore, 2001, Gremeaux et al., 2012, Petelin et al., 2014). Combined training could be a very interesting type of exercise (Koch et al., 2005) focused on metabolic activity improvement by a dual pathway, i.e. through increasing lean mass and improving cardiorespiratory fitness, since recent studies have supported the relation between oxygen consumption and RMR (Miller et al., 2012, Shook et al., 2014, McMurray et al., 2014).

Another factor that influence in the RMR response after a weight loss program is the caloric restriction (Martin et al., 2007). Most of the studies include a diet in their intervention programs (Donnelly et al., 1991, Whatley et al., 1994, Kraemer et al., 1997, Lopes et al., 2013, Martin et al., 2007, Petelin et al., 2014, Bryner et al., 1999, Geliebter et al., 1997, Shinkai et al., 1994, Kraemer et al., 1999). Although current recommendations for obesity suggest that increasing energy expenditure may be more effective for reducing body fat than caloric restriction (Hume et al., 2016), in many times diet prescription is determinant for promote weight loss, especially for sedentary individuals, who have more difficulty following a longer and a more intense program of physical activity.

Lastly, there is also a great influence of sex on RMR (McMurray et al., 2014). In general, men exhibit higher values compared to women (Hirsch et al., 2016), but often, studies analyzing the influence of exercise on RMR do not present any sex distinction (Geliebter et al., 1997, Gremeaux et al., 2012, Kirk et al., 2009, Lopes et al., 2013, Martin et al., 2007). Furthermore, acute effects of exercise as a more robust increase on

RMR in men than women after an exercise bout are well documented (Bouchard et al., 1993, Henderson, 2014). However, studies about the long-term influences of exercise training alone, or exercise in combination with energy restriction, on RMR considering interactions of sex, age, and body composition are warranted (McMurray et al., 2014, Herrmann et al., 2015). Therefore, the purpose of the present study was to analyze the effect of a six-month weight loss program focused in different types of exercise on RMR in men and women obese individuals.

Methods

Participants

The present research was performed as part of *Nutrition and Physical Activity Programs for Obesity Treatment* (PRONAF Study according to its Spanish initials); the aim of which was to assess the usefulness of different types of physical activity and nutrition programs for the treatment of adult obesity. The inclusion criteria specified adult subjects, aged 18 to 50 years, obese (body mass index [BMI]: ≥ 30 to < 35 kg/m²), sedentary (< 30 min physical activity/day), normoglycaemic and non-smoker. Only females with regular menstrual cycles were included. Adherences to diet (80%) and exercise (90%) were required. In total, data of 95 participants (48 men) were included in the analysis of this study. All participants were carefully informed about the possible risks and benefits of the study and signed a document of informed consent. The PRONAF study was approved by the Human Research Review Committee of the University Hospital La Paz (HULP) (PI-643).

Study design

The complete methodology and the flow diagram can be found in Zapico et al. (2012). Briefly, subjects who fulfilled the inclusion criteria were included into four

randomly assigned groups, stratified by age and sex. The intervention programs lasted 22 weeks, and the assessment tests took place one week before (baseline) and after (post) the intervention.

Exercise protocols

Four different interventions were performed: strength training (S), endurance training (E), combined strength + endurance training (SE) groups followed the corresponding supervised exercise program plus the dietary intervention, and the physical activity recommendation (PA) group followed dietary intervention and was instructed about the general recommendations about physical activity from the American College of Sports Medicine (ACSM) (Donnelly et al., 2009). All Participants wore the monitor continuously for 5 days following general recommendations (Murphy, 2009).

Subjects in the S, E, and SE groups trained three times per week. All training sessions were carefully supervised by certified personal trainers with Sports Science degrees. The exercise programs were designed according to the subject's muscle strength and heart rate (HR) reserve. All exercise programs were performed in circuit. Sessions routine consisted of: eight strength exercises in S group; 8 bouts of aerobic exercise (running, cycling, or elliptical) in E group; and a combination of four bouts of aerobic exercise intercalated with four strength exercises in SE group. Participants performed 15 repetitions of each strength exercise or 45 seconds of aerobic exercise in each aerobic exercise bout. The recovery period between exercises lasted 15 seconds. Both volume and intensity of the three training programs increased progressively every four weeks from one lap to the circuit at an intensity of 50% of the heart rate reserve and/or the 15RM, to three laps at an intensity of 60%.

Hypocaloric diet

All groups underwent an individualized and hypocaloric diet (between 1200 and 3000 kcal) prescribed by expert dietitians. The diet aimed for a 25-30% reduction of the total daily energy expenditure calculated using the Body Media propriety algorithm (Interview Research Software Version 6.0) based on accelerometry data. Macronutrient distribution was set according to the Spanish Society of Community Nutrition recommendations (Serra-Majem and Aranceta, 2001).

Measurements

Resting Metabolic Rate

Subjects were asked to refrain from any exercise for at least 24 h before the test. To assess RMR, participants were cited between 7 am to 10 am, after a nine hours overnight fasted period. RMR was then measured by indirect calorimetry standing up (during 10 min) and in a lying position (additional 20 min). Oxygen uptake and carbon dioxide production were recorded by a gas analyzer Jaeger Oxycon Pro (Erich Jaeger, Viasys Healthcare, Germany), and resting heart rate was measured using a heart rate monitor (Polar Electro Oy, Kempele, Finland). All these parameters were averaged during the last 5 min of the standing up position (standing metabolic rate; SMR) and the last 10 min of the lying position (RMR). Oxygen uptake and carbon dioxide production data were used to calculate RMR according to the formula of Weir (Weir, 1949).

Body composition

Body composition was assessed by dual-energy X-ray absorptiometry scan (Version 6.10.029GE Encore 2002, GE Lunar Prodigy; GE Healthcare, Madison, WI, USA); obtaining values for body weight, fat mass, lean body mass (LBM) and android fat mass. Height was measured using a SECA stadiometer and waist circumference (WC) was obtained employing a SECA 201 steel tape (Quirumed, Valencia, Spain) and

measured at the level of the iliac crest at the end of a normal expiration. BMI was calculated as body mass/height (kg/m^2).

Cardiovascular Fitness

The test evaluating cardiovascular fitness was a maximal ergospirometry following the modified Bruce protocol with a computerized treadmill (H/P/COSMOS 3PW 4.0; H/P/Cosmos Sports & Medical, Nussdorf-Traunstein, Germany). Peak oxygen consumption ($\dot{V}\text{O}_{2\text{peak}}$) was measured with the gas analyzer Jaeger Oxycon Pro (Erich Jaeger; Viasys Healthcare; Hoechberg, Germany). Heart response was continuously monitored with a 12-lead electrocardiogram. The subjects maintained the effort test until exhaustion. The mean of the three highest measurements was used as $\dot{V}\text{O}_{2\text{peak}}$ and maximal heart rate. Resting HR was calculated as the average heart rate during 10 min in a lying position before the effort test.

Statistical Analysis

Data are presented as mean $\pm$ SD. Normality was proven by Kolmogorov Smirnov test. Two-way repeated measures analysis of variance (ANOVA) were used to determine any differences among the four intervention groups (S, E, SE and PA) by time (pre and post-intervention) in RMR, SMR and LBM. Two-way repeated measures ANOVA also were used to determine differences between quartiles (first and fourth) of absolute LBM change by time. Analyses were performed in men and women separately. Bonferroni *post hoc* tests were employed to locate specific differences. Effect size was calculated by partial eta-squared (η_p^2) and small, moderate and large effect corresponded to values equal or greater than 0.001, 0.059, and 0.138, respectively (Richardson, 2011). One-way ANOVA was used to analyze differences among the four interventions at baseline. Pearson' correlations were calculated to verify the association between RMR, LMB and $\dot{V}\text{O}_{2\text{peak}}$ at baseline, post-intervention and changes.

Proportional changes were calculated through the standard formula: $\text{change (\%)} = [(\text{pre-test score} - \text{post-test score}) / \text{pre-test score}] * 100$. All analyses were conducted in SPSS-PC v20 (IBM SPSS Statistics, Armonk, NY USA), and level of significance was set at $p < 0.05$.

Results

The characteristics of participants at baseline were similar among intervention groups in the same sex ($p > 0.05$ for most variables), except for SMR in men, with differences between S or E and PA groups; and for absolute fat mass in women, with differences between SE and PA groups (Table 17).

Table 17. Characteristics at baseline.

Variables	MEN (n = 48)				WOMEN (n = 47)			
	S	E	SE	PA	S	E	SE	PA
Age	38.3 ± 9.4	37.2 ± 8.7	37.3 ± 7.3	38.9 ± 7.1	37.6 ± 9.3	37.7 ± 7.0	38.6 ± 7.5	38.5 ± 7.5
Body weight (kg)	100.7 ± 8.8	99.4 ± 8.2	103.3 ± 9.1	101.5 ± 5.7	88.1 ± 7.9	87.9 ± 7.7	89.9 ± 10.2	81.2 ± 6.1
Height (cm)	177.5 ± 6.6	174.8 ± 6.7	178.4 ± 5.0	176.0 ± 5.0	164.7 ± 6.5	165.1 ± 7.8	164.9 ± 7.6	159.0 ± 4.7
BMI (kg/m ²)	31.9 ± 1.9	32.6 ± 2.5	32.4 ± 1.6	32.8 ± 1.6	32.4 ± 1.7	32.2 ± 1.4	33.0 ± 2.4	32.1 ± 1.9
Fat mass (kg)	36.4 ± 5.1	34.7 ± 5.5	40.1 ± 7.2	37.3 ± 5.2	40.0 ± 5.0	39.2 ± 4.4	43.8 ± 8.4	35.7 ± 5.6 [#]
Fat mass (%)	37.7 ± 3.8	37.8 ± 5.1	39.3 ± 4.0	37.9 ± 3.4	46.8 ± 2.1	46.5 ± 3.5	49.1 ± 3.6	46.0 ± 4.2
LBM (kg)	60.0 ± 5.2	57.2 ± 5.8	61.2 ± 4.6	60.9 ± 3.7	45.3 ± 4.3	45.2 ± 5.3	44.9 ± 5.0	41.6 ± 3.3
LBM (%)	60.2 ± 3.5	60.2 ± 4.8	58.8 ± 3.8	60.0 ± 3.3	51.6 ± 2.0	51.9 ± 3.2	49.5 ± 3.4	52.3 ± 3.9
RMR	1905.8 ± 208.6	1884.7 ± 302.0	1948.0 ± 409.6	2113.3 ± 223.0	1589.4 ± 170.3	1575.7 ± 271.7	1717.9 ± 302.2	1470.4 ± 300.6
SMR	2163.4 ± 247.2	2151.4 ± 358.3	2235.3 ± 229.2	2492.2 ± 235.6 [§]	1639.5 ± 338.6	1783.1 ± 366.6	1855.1 ± 334.3	1503.5 ± 310.9

Data are presented as mean ± SD. [‡] Difference between S and PA groups; [§] difference between E and PA groups; [#] difference between SE and PA groups. S: strength training group; E: endurance training group; SE: combined strength plus endurance training group; PA: physical activity recommendations group; LBM: lean body mass; RMR: resting metabolic rate; SMR: standing metabolic rate.

A significant main effect of time ($F_{(1,43)} = 12.296, p = 0.001, \eta_p^2 = 0.222$) was found for RMR in women, without interaction for intervention groups. Men did not change this variable, although there was a tendency of interaction between intervention groups and time ($F_{(3,44)} = 2.454, p = 0.076, \eta_p^2 = 0.143$) and only PA group decreased RMR (change: -203.9 kcal, $p = 0.018, \eta_p^2 = 0.121$) (Figure 9a). Similar results were found for RMR related to LBM, with women decreasing this variable without interaction between intervention groups and time ($F_{(1,40)} = 10.047, p = 0.003, \eta_p^2 = 0.201$) and men without changes or interaction (Figure 9b).

Fig. 9. (a): resting metabolic rate at baseline and post-intervention in men and women; (b): resting metabolic rate related to lean body mass at baseline and post-intervention in men and women.

SMR decreased in women ($F_{(1,43)} = 23.733, p < 0.001, \eta_p^2 = 0.356$) without interaction for intervention groups (Figure 10a). In men, interaction between intervention groups and time was found for SMR ($F_{(3,44)} = 6.020, p = 0.002, \eta_p^2 = 0.296$), and SE (change: -270.7 kcal, $p = 0.003, \eta_p^2 = 0.186$) and PA groups (change: -445.7 kcal, $p < 0.001, \eta_p^2 = 0.403$) decrease it (Figure 10b). A significant main effect of time was also found for SMR in men ($F_{(1,44)} = 25.376, p < 0.001, \eta_p^2 = 0.371$).

Fig. 10. Standing metabolic rate in the pre- and post-intervention in men (a) and women (b).

There was an interaction between intervention groups and time in men for absolute LBM, and only PA decreased it (change: -1.6 kg, $p < 0.001$, $\eta_p^2 = 0.327$). A significant main effect of time was also found for absolute LBM in men. Percentage LBM increased in men, without interaction between intervention groups and time. Absolute LBM decreased and percentage LBM increased in women after the intervention, without interaction between intervention groups and time (Table 18).

Table 18. Absolute and percentage lean body mass before and after weight loss program.

MEN								
	S	E	SE	PA	TOTAL	<i>F</i>	<i>P</i>	η_p^2
LBM (kg)								
Baseline	60.0 ± 5.2	57.1 ± 6.2	61.2 ± 4.6	60.9 ± 3.7	59.9 ± 5.0	T 7.487	0.009	0.148
Post-intervention	60.2 ± 5.4	57.0 ± 6.3	60.7 ± 4.7	59.3 ± 2.5**	59.3 ± 4.9*	TxG 4.957	0.005	0.257
LBM (%)								
Baseline	60.2 ± 3.5	59.8 ± 4.9	58.8 ± 3.8	60.0 ± 3.3	59.7 ± 3.8	T 173.594	<0.001	0.801
Post-intervention	65.4 ± 4.1	65.3 ± 5.5	63.9 ± 4.4	64.7 ± 4.9	64.8 ± 4.6**	TxG 0.224	0.879	0.015
WOMEN								
	S	E	SE	PA	TOTAL	<i>F</i>	<i>P</i>	η_p^2
LBM (kg)								
Baseline	45.3 ± 4.3	44.7 ± 5.4	44.3 ± 4.6	41.6 ± 3.5	44.1 ± 4.7	T 6.743	0.013	0.141
Post-intervention	45.4 ± 4.6	44.3 ± 5.6	43.3 ± 4.5	40.9 ± 3.1	43.6 ± 4.8*	TxG 1.549	0.216	0.102
LBM (%)								
Baseline	51.6 ± 2.0	52.2 ± 3.1	49.3 ± 3.5	52.3 ± 4.1	51.3 ± 3.3	T 148.725	0.001	0.784
Post-intervention	56.2 ± 4.1	56.8 ± 3.4	53.1 ± 4.5	56.7 ± 5.1	55.7 ± 4.3**	TxG 0.261	0.853	0.019

Data are presented as mean ± SD. Baseline-post differences: * $p < .05$; ** $p < .001$. T: time; G: intervention groups; S: strength training group; E: endurance training group; SE: combined strength + endurance training group; PA: physical activity recommendations group; LBM: lean body mass.

When absolute LBM change was divided in first and fourth quartiles, no significant differences were found for men between two quartiles, and women decreased RMR in both ($F_{(1,22)} = 16.389, p = 0.001, \eta_p^2 = 0.427$) (Figure 11).

MEN

1° QUARTILE LBM CHANGE

4° QUARTILE LBM CHANGE

WOMEN

1° QUARTILE LBM CHANGE

4° QUARTILE LBM CHANGE

Fig. 11. Resting metabolic rate response in the first and fourth quartiles in men and women. * $p < 0.05$. LBM: lean body mass. Highlighted lines indicate total value for each quartile in men and women.

Significant associations were found between RMR and LBM, before and after intervention for both sexes. In the same way, positive correlations also were observed between RMR and VO_{2peak} in the pre and post-intervention for men and women. However, association between proportional changes was found only in men between RMR and VO_{2peak} . When RMR and VO_{2peak} were expressed related to LBM, no associations were observed, except in men, where a significant positive correlation was found for proportional changes (Table 19).

Table 19. Pearson's correlations between RMR and LBM and VO_{2peak} in the pre, post-intervention and proportional changes.

Men			
RMR			
	Pre-intervention	Post-intervention	%
LBM (kg)	0.375*	0.424*	-0.132
VO_{2peak}	0.509**	0.608**	0.290*
RMR related to LBM			
	Pre-intervention	Post-intervention	%
VO_{2peak} related to LBM	0.055	-0.071	0.343*
Women			
RMR			
	Pre-intervention	Post-intervention	%
LBM (kg)	0.586**	0.631**	-0.163
VO_{2peak}	0.693**	0.499*	0.077
RMR related to LBM			
	Pre-intervention	Post-intervention	%
VO_{2peak} related to LBM	0.065	0.227	0.043

RMR: resting metabolic rate; LBM: lean body mass; VO_{2peak} : peak oxygen consumption. * $p < .05$; ** $p < .001$.

Discussion

The main findings of the current study were: (1) that women decreased RMR after a six-month weight loss program while men did not present changes in this variable; (2) that percentage LBM increased in both genders, and absolute LBM

decreased in women similarly in all intervention groups while in men only PA group decreased it.

It is extremely important to understand physiological differences between men and women in response to exercise (Henderson, 2014). The large majority of studies about RMR response after an exercise program that included men and women in the same design analyzed the results of both genders together (Ballor et al., 1996, Belanger and Boulay, 2005, Bryner et al., 1999, Geliebter et al., 1997, Gremeaux et al., 2012, Kirk et al., 2009, Lopes et al., 2013, Martin et al., 2007). The few and more recent studies that considered sex in analyzes did not find differences between men and women in the RMR response. In some of these studies RMR decreased significantly after aerobic (Willis et al., 2014) and combined training (Petelin et al., 2014) or remained unchanged after aerobic training (Caudwell et al., 2013, Herrmann et al., 2015). With the exception of the study by Petelin et al. (2014), the other studies did not include diet in their intervention programs, and weight loss in which RMR did not change was considerably lower compared to our study (Caudwell et al. (2013) = 0.77% for women and 2.45% for men, Herrmann et al. (2015) = 8.40% for responders to weight loss and 0.04% kg for non-responders, versus 10.10% in our subjects (Benito et al., 2015). Diet performed by participants of Petelin et al. (2014) was similar to that performed in the present study, although the little information regarding the training provided by the authors did not allow comparison. In addition, the inclusion of more than 60% of women in their sample may have been another factor of similarity between their and ours results (Petelin et al., 2014).

Although RMR varies greatly among individuals, significant proportion of this variability is related to differences in fat free mass (Filozof and Gonzalez, 2000). When RMR related to LBM was analyzed, similar results to mentioned above were obtained,

with women decreasing RMR and men without changes. It is known that men experience a more robust increase in RMR than women after a single endurance exercise bout (Henderson and Alderman, 2014), but the reasons why women exhibit a lower response are still unclear (Henderson, 2014). In general, women appear to be more precisely homeostatic than men, with ovarian hormone playing a role in the precision of homeostatic control of metabolic processes (Henderson, 2014). Although we have not measured, baseline concentrations of testosterone in men also appear to be correlated with RMR (Geliebter et al., 2014). Furthermore, endocrine differences, which can affect sympathoadrenal activity, as higher norepinephrine level after exercise in men (Henderson, 2014) and lower level of this hormone in obese women (Astrup et al., 1992) also may be involved in the RMR response. Lastly, greater growth hormone response in men could favor the increment in the cell metabolic activity (Henderson, 2014).

As mentioned anteriorly, RMR is highly correlated with LBM (Caudwell et al., 2013, Cunningham, 1982). The classic physical functions of muscle tissue are well recognized, but it is gaining a greater prominence in recent years (Argiles et al., 2016). In our study women with some gain in LBM (included in the fourth quartile) also decreased RMR; although LBM loss was similar to men (about 0.5 kg or 1%). Change in fat-free mass is not always related to change in RMR (Kraemer et al., 1997, Speakman and Selman, 2003, Senechal et al., 2010, Geliebter et al., 2014). However, women presented a LBM reduction about 16 kg or 10% compared to men in initial and final values. In addition, other study including only men showed that the increase in RMR was higher than expected from the increase in lean body mass (Hambrey et al., 2012). Women may need more attention in relation to maintaining muscle mass due to a less favorable physiological environment of muscle growth. The majority of work on

exercise has been conducted on males, so additional work on women is needed to further extend our understanding of sexual dimorphism (Henderson, 2014). In the future, it may be of benefit to discover ways to alter the response of resting metabolism to exercise, which currently appear to be sex-dependent, in order to help in the management of obesity.

When SMR was analyzed, women presented again a reduction in this metabolic variable regardless intervention group. However, ANOVA showed an interaction between intervention groups and time in men. Although combined training group also decreased SMR in men, reduction observed in the physical activity recommendation group was almost twice more. Standing metabolic rates include the metabolic cost of muscular activation for balance and maintaining an upright posture (Weyand et al., 2009) and the reduction in absolute LBM observed in the physical activity recommendation group could be responsible for decrease in SMR, due to lower muscular activation. A tendency also was observed for RMR in men, where only PA group seemed to decrease it. Hambre and colleagues (2012) verified that almost half of the men who reported that followed recommendations of resistance training after 1 year also showed RMR and muscle mass at similar levels as at baseline and lower than those achieved in the final of their intervention. The authors affirmed that to accomplish a more permanent increase in RMR it is required that the exercise activities become routine in every-day life and have the appropriate intensity for these changes (Hambre et al., 2012). The lack of differences in the other intervention groups in our study could be related to the performance of the exercises in circuit, exhaustive daily control of the intensity and duration of exercises and progressive increment of the intensity in all intervention groups.

Recent studies support the hypothesis that lower RMR is associated with lower maximal aerobic capacity (Shook et al., 2014, Miller et al., 2012, McMurray et al., 2014). In our study, the participants were sedentary, but these that had higher VO_{2peak} at the beginning and final of the intervention had higher RMR too. Obesity may be a vicious cycle of elevated BMI, reduced cardiorespiratory fitness, muscle deconditioning, and lower RMR (Miller et al., 2012).

Some limitations of this research include: lack of additional measures throughout the program that impedes to evaluate the dynamics RMR in the different types of intervention and between sex; no weight balance before RMR measure; and no follow-up, without which the duration of the adaptations observed cannot be assessed. However, the exhaustive control and equality in trainings, as well as the novel circuit methodology used, convert the results of this work in relevant findings to current literature.

In conclusion, faced with a weight loss program of the same duration and frequency, women decreased RMR, while men maintained it. In addition, supervised training interventions were able to maintain lean mass in men, but appeared not to be adequate enough to prevent loss in women.

IMPACT OF PHYSICAL ACTIVITY ON EATING BEHAVIOR IN OVERWEIGHT AND OBESE ADULTS

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Abstract

Background: The way by which different types of exercise induce physiological and behavioral changes related to food remains unclear. *Objective:* to examine if there is a type of exercise or a marker of physical activity level that favors a better compliance with the prescribed diet, a higher eating-related motivation, and a healthier diet composition in overweight and obese subjects. *Methods:* One hundred and sixty-two (males $n=79$) overweight and obese subjects, aged 18-50 years, were randomized in four interventions groups during 24 weeks: strength training (S), endurance training (E), combined strength + endurance training (SE) and guideline-based physical activity (PA). All in combination with a 25-30 % caloric restriction diet. All food and beverages consumed by the participants were recorded using a food frequency questionnaire and a “3-day food and drink record” before (pre) and after (post-intervention) the program. Kilocalories consumed in the diet and macronutrient percentages were calculated using the DIAL software. Motivation was evaluated with a questionnaire specifically developed for this study. This questionnaire consisted of 10 questions, rated on a 10-point Likert-type scale. Eight questions were related to diet motivation and two to exercise motivation. *Results:* No interaction was observed between intervention groups and time and all of them decreased energy intake ($p < .001$). Carbohydrate and protein intakes increased, and fat intake decreased from pre- to post-intervention without significant interactions with intervention groups, BMI category or gender ($p < .001$). Diet-related motivation showed a tendency to increase from pre to post-intervention (70.0 ± 0.5 vs 71.0 ± 0.6 , $p = .053$), without significant interactions with intervention groups, BMI category or gender. Regarding motivation to exercise, interaction between gender and time were observed ($F_{(1,146)} = 7.452$, $p = .007$), and only women increased their motivation after the intervention (pre: 17.6 ± 0.3 , post: 18.2 ± 0.3 , $p = .034$), while

men maintained it. *Conclusion:* The findings suggest no substantial effect of type of exercise on energy intake or macronutrient selection. After six-month weight loss program, individuals did not reduce their motivation related to diet or exercise, demonstrating good acceptance and suitability of the program, especially in women. More research is required to determine the mechanisms through which exercise training may affect and improve appetite regulation.

Keywords: macronutrients; energy intake; motivation to diet; motivation to exercise; weight loss program.

Introduction

Despite the considerable increase in studies about obesity, the number of overweight people increases every year worldwide (Lobstein and Brinsden, 2014). In addition, obesity is a public health problem, since it is related to numerous risk factors for cardiovascular disease and comorbidities (Lu et al., 2014); fact that points out the need for further studies. It is known that healthy habits of physical activity and nutrition work together to maintain body weight at desirable levels (Dombrowski et al., 2014). Although diet contributes to a greater extent for short-term weight loss (Fisher et al., 2011, Christiansen et al., 2010, Janssen et al., 2002), exercise seems to have an important role in maintaining this loss (Swift et al., 2014, Fogelholm et al., 2000). Thus, exercise might also facilitate long-term adherence to healthy eating habits and behaviors.

Several studies have analyzed if exercise was able to modulate food intake (Schubert et al., 2014, Martins et al., 2008, Elder and Roberts, 2007), indicating that participation in physical activity as well as its duration and intensity, could contribute to appetite regulation (Martins et al., 2010, Broom et al., 2007), total calorie intake

(Whybrow et al., 2008) and macronutrient composition of the diet (Jokisch et al., 2012, Alkahtani et al., 2014), resulting in an appropriate energy balance. Other studies have also shown an association between regular physical activity and psychosocial and motivational factors related to a healthier eating behavior (Lowe et al., 2014, Andrade et al., 2010).

However, the type of exercise that would be able to induce greater physiological and behavioral changes related to eating behavior and food intake remains unclear. Regarding the intensity of effort, some authors found that more intense exercise reduced feelings of hunger during and after its practice as well as a few hours later (Jokisch et al., 2012, Westerterp-Plantenga et al., 1997, King and Blundell, 1995). Other authors have shown that absolute caloric intake was superior in high-intensity exercise, in spite of small energy compensations (lower energy consumed vis-à-vis the energy expended) (Whybrow et al., 2008, Pomerleau et al., 2004). As to the mode of exercise, most of the studies involved aerobic exercises and regular weight individuals (Broom et al., 2007, Jokisch et al., 2012, Whybrow et al., 2008), and the results are not very consistent. In addition, the literature lacks studies on the relationship between exercise and long-term diet adherence, and that consider the composition of the diet. Therefore, the present study aimed at examining if there is a type of exercise or a marker of physical activity level that favors a better compliance with the prescribed diet, a higher eating-related motivation, and a healthier diet composition in overweight and obese subjects.

Methods

Participants

Data for this study were derived from the Nutrition and Physical Activity for Obesity Treatment (PRONAF), a randomized trial which aimed to assess the usefulness of different types of physical activity and nutrition programs for the treatment of obesity. The inclusion criteria specified adult subjects, aged 18 to 50 years, who were overweight or obese (body mass index [BMI]: ≥ 25 to < 35 kg/m²), sedentary (< 30 min physical activity/day), normoglycemic, non-smoking and, if females, with regular menstrual cycles. A total of 180 participants (84 males) complying with at least 90% of the training sessions and an 80% adherence to the diet were included in the analysis. Of these total, 162 subjects were included in the analyses regarding the type of exercise and 91 participants in the analyses concerning the markers of physical activity level. All participants were informed about the risks and benefits of the study and signed a written informed consent. The PRONAF study was approved by the Human Research Review Committee of the University Hospital La Paz (HULP) (No.NCT01116856).

Study Design and Intervention

The intervention lasted 22 weeks and the assessments took place one week before (baseline) and after (post) the intervention. Subjects included were randomly assigned to one of the four intervention groups – strength training (S), endurance training (E), combined strength+endurance training (SE) and a guideline-based physical activity (PA), assuring a homogeneous distribution of age and gender among groups. The complete methodology and the diagram flow can be found in Zapico et al. (2012).

Exercise protocols

The PA group followed general physical activity recommendations from the American College of Sports Medicine (ACSM) (Donnelly et al., 2009). Exercise from this group was not supervised, like a classical intervention. Subjects in the S, E, and SE groups trained three times per week. All training sessions were carefully supervised by certified personal trainers with Sports Science degrees. The exercise programs were designed according to the subject's muscle strength and heart rate reserve. All exercise programs were performed in circuit. Sessions routine consisted of: eight strength exercises in S group; aerobic exercise (running, cycling, or elliptical) in E group; and a combination of four bouts of aerobic exercise intercalated with four strength exercises in SE group. Participants performed 15 repetitions of each strength exercise or 45 seconds of aerobic exercise in each aerobic exercise bout. The recovery period between exercises lasted 15 seconds. Both volume and intensity of the three training programs increased progressively every from two laps to the circuit at an intensity of 50% of the heart rate reserve and/or the 15RM, to three laps at an intensity of 60% (Fig. 12).

Fig. 12. Timeline of the study. S = strength training group; E = endurance training group; SE = combined strength and endurance training group; PA = physical activity recommendations group; RM = repetitions maximum.

Hypocaloric diet

All participants underwent an individualized dietary intervention based on a hypocaloric diet prescribed by expert dietitians. The diet aimed at a 25-30% reduction on the total daily energy expenditure. Macronutrient distribution was set according to the Spanish Society of Community Nutrition recommendations (Serra-Majem and Aranceta, 2001).

Assessments

Physical Activity

Habitual physical activity was measured using the SenseWear Pro3 ArmbandTM (Body Media, Pittsburgh, PA). Subjects were instructed to wear the monitor continuously for six consecutive days, 24 hours per day on the non-dominant arm. Following general recommendations, only data from subjects who had a minimum of three days of recording, including at least one weekend day, and worn the monitors >95% of the day (22 hours and 48 minutes) were included in the analyses (Almeida et al., 2011, Camiletti-Moiron et al., 2015, Scheers et al., 2012). Data were recorded by 1-minute intervals. Minutes per day spent on sedentary activities, light-intensity physical activity (LIPA), moderate-vigorous physical activity (MVPA), daily steps and physical activity level (PAL) were provided by the accelerometer. Three daily steps' categories considering initial data (before intervention) were established (< 7500, 7500 - 10000, > 10000 steps) (Tudor-Locke et al., 2011). Daily energy expenditure was calculated using the Body Media propriety algorithm (Innerview Research Software Version 6.0).

Eating behavior

All food and beverages consumed by the participants were recorded using a food frequency questionnaire and a "three-day food and drink record", validated for the Spanish population (Ortega et al., 2003), at baseline and at the end of the intervention.

Participants were instructed to write down everything they ate and drank for two weekdays and one weekend day. Also, participants were asked to measure the amount of food consumed with household measurements (e.g., cups, teaspoons, tablespoons) or to write down the quantity written on commercial packaging. Total energy intake (TEI) or kilocalories consumed in the diet and macronutrient percentages (carbohydrate [CHO], fat and protein [PRO]) were calculated using the DIAL software (Alce Ingeniería, 2004). Diet compliance was calculated as the estimated Kcal of the diet divided by the real Kcal intake ($[\text{estimated kcal of diet} / \text{real Kcal intake}] \cdot 100$), representing perfect adherence values equal to 100. Values superior or inferior to 100 indicated a greater caloric deficit or a caloric excess, respectively.

Motivation

Motivation was evaluated with a questionnaire specifically developed for this study. This questionnaire consisted of 10 questions, rated on a 10-point Likert-type scale. Eight questions were related to diet motivation and two remaining to exercise motivation. Participants punctuated their diet-related motivation on a scale of de 0 to 10 by answering the following questions: “What is your motivation...” 1) to make changes in diet; 2) to go to dietary control appointments; 3) to reduce fat consumption (sausages, sauces, breaded, snacks, etc.); 4) to reduce the consumption of sugars (candies, chocolates, cakes, etc.); 5) to reduce the consumption of alcohol (if the participant did not consume alcohol, he should punctuate 10); 6) to increase fruit consumption; 7) to increase consumption of vegetables; 8) to increase fish consumption. Also, subjects scored their exercise-related motivation by answering the following questions: “What is your motivation...” 1) to exercise regularly; 2) to perform the physical exercise tasks recommended in the program. Total scores for diet and exercise-related motivation were calculated by summing the scores of the respective questions. Subscales of motivations

to diet and exercise showed acceptable internal consistency, with Cronbach's alphas of 0.73 and 0.84, respectively.

Body composition

Body composition was assessed by dual-energy X-ray absorptiometry scan (GE Lunar Prodigy; GE Healthcare, Madison, WI, USA; version 6.10.029GE Encore 2002). Height was measured using a Seca Stadiometer (Quirumed, Valencia, Spain), which has a range of 80–200 cm. Body mass was measured using a TANITA BC-420MA balance (Bio Lógica Tecnología Médica S.L, Barcelona, Spain). Body mass index was calculated as body mass/height² (kg/m²).

Statistical Procedures

Data are presented as mean $\pm$ SD. One-way analysis of variance (ANOVA) was utilized to analyze differences at baseline into the four intervention groups (S, E, SE, and PA). Normality was proven by Kolmogorov Smirnov test. Four-way repeated measures ANOVA were used to determine differences among the four intervention groups or among the three daily steps' categories (<7500, 7500-10000, >10000), BMI categories (overweight and obesity) and gender (men and women) by time (pre and post-intervention). Bonferroni *post-hoc* tests were employed to locate specific differences. Effect size was calculated by partial eta-squared (η_p^2) and small, moderate and large effect corresponded to values equal or greater than 0.001, 0.059, and 0.138, respectively (Richardson, 2011). Pearson's partial correlations controlling for the intervention groups were used to test associations between eating behavior, physical activity and motivations changes. Proportional changes were calculated through the standard formula: change (%) = [(post-test score – pre-test score)/pre-test score]*100. All analyses were conducted in SPSS-PC v20 (IBM SPSS Statistics, Armonk, NY USA), and level of significance was set at $p < .05$.

Results

Participants' baseline characteristics are described in Table 20. No differences were observed among intervention groups for any variable.

Table 20. Baseline characteristics.

Variables	S (n = 39)	E (n = 48)	SE (n = 42)	PA (n = 33)
Age	38.1 ± 8.9	37.4 ± 7.9	38.7 ± 6.6	38.4 ± 7.9
Body weight (kg)	88.5 ± 12.5	84.3 ± 11.2	88.8 ± 15.6	88.5 ± 12.6
Height (cm)	169.5 ± 9.8	167.9 ± 9.1	170.2 ± 10.3	169.5 ± 9.4
Body mass index (kg/m ²)	30.7 ± 2.2	30.4 ± 2.6	30.2 ± 3.1	30.8 ± 2.6
Fat (%)	41.4 ± 6.0	41.2 ± 6.2	40.8 ± 7.0	40.6 ± 5.7
Lean body mass (%)	56.7 ± 5.7	56.9 ± 5.8	57.3 ± 6.6	57.5 ± 5.4
Total Energy Intake (kcal)	2578.4 ± 964.0	2598.74 ± 1122.8	2412.2 ± 727.0	2512.3 ± 709.2
Physical Activity Level	1.4 ± 0.2	1.3 ± 0.2	1.4 ± 0.2	1.3 ± 0.1
Daily steps (n°)	11231.5 ± 3648.7	10130.1 ± 3760.1	10064.5 ± 3134.2	9409.6 ± 2189.3

Data are presented as mean ± SD. S: strength training group; E: endurance training group; SE: combined strength plus endurance training group; PA: physical activity recommendations group.

In the tables 21, 22, 23 and 24 all significant correlations between eating behavior, physical activity and motivation are represented in bold. Large negative correlations between diet compliance and TEI and between CHO and FAT intakes were observed in all intervention groups ($p < .001$). In addition, as expected, MVPA, steps and PAL were moderate to strongly correlated in all intervention groups ($p < .05$). Moderate to large correlations between PRO intake and diet compliance and between motivations to diet and to exercise were also observed in all groups ($p < .05$), except in the strength group.

Table 21. Pearson's partial correlations between changes in dietary variables, motivation and physical activity in strength group.

		CHO	PRO	FAT	Diet	Exercise				Motivation	
	TEI	(%)	(%)	(%)	compliance	adherence	MVPA	Steps	PAL	to diet	to exercise
TEI	1										
CHO (%)	-0.10	1									
PRO (%)	-0.18	-0.16	1								
FAT (%)	0.18	-0.80**	-0.16	1							
Diet compliance	-0.92**	0.10	0.27	-0.28	1						
Exercise adherence	0.35*	-0.14	-0.03	0.09	-0.28	1					
MVPA	0.51 *	-0.23	0.07	0.17	-0.34	0.46*	1				
Steps	0.27	-0.07	-0.09	0.06	-0.20	0.51*	0.57*	1			
PAL	0.44*	-0.10	-0.10	0.05	-0.32	0.47*	0.82**	0.78**	1		
Motivation to diet	0.10	0.01	0.07	0.18	-0.18	-0.01	-0.22	-0.14	-0.22	1	
Motivation to exercise	0.28	-0.14	-0.01	0.15	-0.33*	0.39*	-0.15	0.04	0.05	0.18	1

TEI: total energy intake; CHO: carbohydrate; PRO: protein; MVPA: moderate-to-vigorous physical activity; PAL: physical activity level. * $p < .05$; ** $p < .001$.

Table 22. Pearson's partial correlations between changes in dietary variables, motivation and physical activity in aerobic group.

		CHO	PRO	FAT	Diet	Exercise				Motivation	
	TEI	(%)	(%)	(%)	compliance	adherence	MVPA	Steps	PAL	to diet	to exercise
TEI	1										
CHO (%)	0.08	1									
PRO (%)	-0.43*	-0.06	1								
FAT (%)	0.02	-0.66*	-0.33*	1							
Diet compliance	-0.88**	-0.01	0.42*	-0.13	1						
Exercise adherence	0.23	0.21	-0.22	-0.12	-0.10	1					
MVPA	-0.15	-0.25	-0.02	0.13	0.14	-0.01	1				
Steps	-0.02	-0.33	-0.39	0.48*	0.08	-0.01	0.55*	1			
PAL	-0.06	-0.26	-0.32	0.17	0.13	0.08	0.71**	0.68**	1		
Motivation to diet	-0.03	-0.26	-0.13	0.28	-0.09	-0.15	0.33	0.21	0.41*	1	
Motivation to exercise	0.08	-0.13	0.03	0.09	-0.10	0.01	0.07	-0.07	0.02	0.49**	1

TEI: total energy intake; CHO: carbohydrate; PRO: protein; MVPA: moderate-to-vigorous physical activity; PAL: physical activity level. * $p < .05$; ** $p < .001$.

Table 23. Pearson's partial correlations between changes in dietary variables, motivation and physical activity in combined group.

		CHO	PRO	FAT	Diet	Exercise				Motivation	
	TEI	(%)	(%)	(%)	compliance	adherence	MVPA	Steps	PAL	to diet	to exercise
TEI	1										
CHO (%)	-0.29	1									
PRO (%)	-0.27	-0.22	1								
FAT (%)	0.45*	-0.83**	-0.09	1							
Diet compliance	-0.88**	0.20	0.44*	-0.37*	1						
Exercise adherence	0.09	-0.06	0.16	0.16	-0.04	1					
MVPA	0.28	0.31	-0.13	-0.07	-0.14	0.06	1				
Steps	0.18	0.40	-0.24	-0.30	-0.08	0.02	0.54*	1			
PAL	0.23	0.18	-0.01	0.03	-0.07	0.36	0.69**	0.59*	1		
Motivation to diet	-0.13	-0.01	-0.04	0.03	0.10	0.26	-0.01	-0.10	0.21	1	
Motivation to exercise	0.04	0.02	-0.08	0.12	-0.07	0.20	0.01	-0.38	-0.13	0.42*	1-

TEI: total energy intake; CHO: carbohydrate; PRO: protein; MVPA: moderate-to-vigorous physical activity; PAL: physical activity level. * $p < .05$; ** $p < .001$.

Table 24. Pearson's partial correlations between changes in dietary variables, motivation and physical activity in physical activity recommendation group.

		CHO	PRO	FAT	Diet				Motivation	
	TEI	(%)	(%)	(%)	compliance	MVPA	Steps	PAL	to diet	to exercise
TEI	1									
CHO (%)	0.31	1								
PRO (%)	-0.59*	-0.46*	1							
FAT (%)	-0.33	-0.77**	0.19	1						
Diet compliance	-0.93**	-0.27	0.62**	0.29	1					
Exercise adherence										
MVPA	-0.26	0.18	-0.07	-0.04	0.34	1				
Steps	-0.28	0.29	-0.01	-0.16	0.22	0.47*	1			
PAL	-0.12	0.34	-0.11	-0.23	0.12	0.62*	0.58*	1		
Motivation to diet	0.29	-0.03	0.20	-0.11	-0.28	-0.10	-0.12	0.01	1	
Motivation to exercise	0.15	-0.35	0.13	0.25	-0.08	0.03	-0.01	-0.05	0.43*	1

TEI: total energy intake; CHO: carbohydrate; PRO: protein; MVPA: moderate-to-vigorous physical activity; PAL: physical activity level. * $p < .05$; ** $p < .001$.

Analysis of variance showed gender-time interaction ($F_{(1,137)} = 4.783, p = .030, \eta_p^2 = .034$) and BMI category-time interaction ($F_{(1,137)} = 13.233, p < .001, \eta_p^2 = 0.088$) for TEI. Men consumed more calories in the pre and post-intervention than women (differences: 535.7 kcal, $p < .001, \eta_p^2 = .102$; 250.0 kcal, $p = .002, \eta_p^2 = .066$; respectively). Obese subjects showed greater TEI than overweight participants in the pre and post-intervention (differences: 651.8 kcal, $p < .001, \eta_p^2 = .144$; 176.6 kcal, $p = .029, \eta_p^2 = .034$; respectively). However, no interaction was observed between intervention groups and time and all of them decreased energy intake ($F_{(1,137)} = 133.742, p < .001, \eta_p^2 = .494$). The remaining interactions and factors were not significant. CHO and PRO intakes increased and fat intake decreased from pre- to post-intervention (CHO: $F_{(1,137)} = 65.652, p < .001, \eta_p^2 = .324$; PRO: $F_{(1,137)} = 90.606, p < .001, \eta_p^2 = .398$; fat: $F_{(1,137)} = 116.561, p < .001, \eta_p^2 = .460$) without significant interactions with intervention groups, BMI category or gender (Figure 13). The remaining interactions and factors were not significant.

Fig. 13. Total energy intake and macronutrient percentages before and after the intervention. TEI: total energy intake; CHO: carbohydrate; PRO: protein; S: strength training group; E: endurance training group; SE: combined strength plus endurance training group; PA: physical activity recommendations group.

Diet-related motivation showed a tendency to increase from pre to post-intervention ($F_{(1,146)} = 3.799, p = .053, \eta_p^2 = .025$), without significant interactions with intervention groups, BMI category or gender. Regarding motivation to exercise, interaction between gender and time was observed ($F_{(1,146)} = 7.452, p = .007, \eta_p^2 = .049$), and only women increased their motivation after the intervention (pre: 17.6 ± 2.5 , post: $18.3 \pm 2.0, p = .034, \eta_p^2 = 0.031$). There was a tendency of interaction between intervention group and time ($F_{(3,146)} = 2.440, p = .067, \eta_p^2 = .048$) and pairwise comparisons showed that only the PA group decreased motivation to exercise ($p = .045, \eta_p^2 = .027$). No interaction with BMI category was observed. The remaining interactions and factors were not significant (Figure 14).

Fig. 14. Motivation to diet and exercise before and after the intervention. S: strength training group; E: endurance training group; SE: strength and endurance training group; PA: physical activity recommendations group. $**p < .001$.

When the sample was analyzed by daily steps categories ($n = 91$) similar results for TEI, CHO and fat, as well as motivation to exercise, were observed. BMI category-time interaction was also observed for TEI, and obese individuals obtained greater values than overweight in the pre-intervention (difference: 636 kcal, $p = .004$, $\eta_p^2 = .116$). In addition, as observed earlier, CHO and PRO increased and fat decreased. However, individuals who started the intervention program with more daily steps increased PRO compared to individuals who performed less than 7500 daily steps, independently of BMI category or gender ($\geq 7500 < 10000$: $p = .011$, $\eta_p^2 = .090$; ≥ 10000 : $p < .001$, $\eta_p^2 = .435$). Tendency observed above for increase in diet-related motivation by intervention groups, in this case, was significant without interactions for daily steps categories, BMI category or gender. Gender-time interaction was also found for motivation to exercise and only women increased their motivation after the intervention (pre: 17.8 ± 2.4 , post: 18.8 ± 1.8 , $p = .011$, $\eta_p^2 = .080$). The remaining interactions and factors were not significant (Table 25).

Table 25. Dietary and motivation-related variables by categories of daily steps at baseline.

	<7500	≥7500<10000	≥10000	Total	<i>F</i>	<i>P</i>	η_p^2
TEI					T = 41.841	< 0.001	0.377
Baseline	2447.9 ± 1026.8	2434.3 ± 805.2	2766.2 ± 1186.0	2592.9 ± 1044.5	TxS = 3.670	0.060	0.051
Post-intervention	1781.5 ± 448.5	1811.0 ± 563.9	1850.5 ± 651.7	1823.3 ± 580.4**	TxBMI = 6.725	0.012	0.089
					TxC = 1.554	0.219	0.043
					TxSxBMIxC = 2.115	0.128	0.058
CHO (%)					T = 30.129	< 0.001	0.304
Baseline	38.5 ± 7.8	36.3 ± 7.0	37.8 ± 6.2	37.5 ± 6.8	TxS = 1.698	0.197	0.024
Post-intervention	44.0 ± 6.1	43.2 ± 6.1	43.2 ± 6.3	43.4 ± 6.1**	TxBMI = 0.531	0.469	0.008
					TxC = 0.559	0.575	0.016
					TxSxBMIxC = 0.985	0.379	0.028
PRO (%)					T = 36.812	< 0.001	0.348
Baseline	17.3 ± 3.5	17.6 ± 2.1	16.3 ± 2.5	16.9 ± 2.6	TxS < 0.001	0.994	< 0.001
Post-intervention	19.1 ± 2.5	19.2 ± 2.5*	20.3 ± 2.7**	19.7 ± 2.6**	TxBMI = 1.440	0.234	0.020
					TxC = 4.587	0.013	0.117
					TxSxBMIxC = 0.962	0.387	0.027
FAT (%)					T = 48.246	< 0.001	0.411
Baseline	40.7 ± 7.9	41.5 ± 6.9	41.1 ± 6.1	41.2 ± 6.7	TxS = 0.296	0.588	0.004
Post-intervention	33.4 ± 5.5	33.9 ± 6.0	33.4 ± 6.0	33.5 ± 5.8**	TxBMI = 0.716	0.400	0.010
					TxC = 0.316	0.730	0.009
					TxSxBMIxC = 1.674	0.195	0.046
MOTIVATION TO DIET					T = 11.851	0.001	0.130
Baseline	70.0 ± 7.2	71.0 ± 6.9	70.9 ± 6.3	70.7 ± 6.6	TxS = 1.838	0.179	0.023
Post-intervention	73.1 ± 5.6	73.5 ± 6.4	72.2 ± 6.8	72.8 ± 6.4*	TxBMI = 0.496	0.483	0.006
					TxC = 0.704	0.498	0.018
					TxSxBMIxC = 1.170	0.316	0.029

Table 25. (Continued)

	<7500	≥7500<10000	≥10000	Total	<i>F</i>	<i>P</i>	η_p^2
MOTIVATION TO EXERCISE					T = 1.422	0.237	0.018
Baseline	17.5 ± 3.6	18.4 ± 1.7	17.8 ± 2.4	18.0 ± 2.5	TxS = 6.305	0.014	0.074
Post-intervention	18.1 ± 4.5	18.2 ± 3.7	18.4 ± 2.2	18.3 ± 3.3	TxBMI = 2.325	0.131	0.029
					TxC = 0.494	0.612	0.012
					TxSxBMIxC = 0.609	0.546	0.015

TEI: total energy intake; CHO: carbohydrate intake; PRO: protein intake; T: time (pre-post); S: gender; BMI: body mass index category; C: daily steps' categories; * $p < 0.05$; ** $p < 0.001$.

Discussion

The main findings of the current study were: (1) that macronutrients distribution and total caloric intake were not different among strength, endurance, combined or guideline-based physical activity groups, with diet advices maintained during the study; (2) individuals that start the program performing >7500 daily steps have more probability increase protein intake; (3) motivation to exercise increased only in women.

To our knowledge, this is the first study to investigate macronutrients distribution among three different types of exercise intervention in circuit. Our results are in accordance with previous findings that suggested no substantial effect of a specific exercise on macronutrient selection (Elder and Roberts, 2007, Washburn et al., 2015, Halliday et al., 2014). The literature is limited and there are very few trials of sufficient duration (Donnelly et al., 2014). A recent meta-analysis investigating if an increase of exercise or physical activity could alter ad-libitum daily energy intake or macronutrient composition in healthy adults, evaluated 24 randomized trials. Of these randomized trials studies, only two evaluated different types of exercise (Donnelly et al., 2014): Shaw et al. (2010) compared the effects of endurance and combined training in normal weight subjects, while Bales et al. (2012) compared the effects of endurance, resistance and the both linear combination in obese individuals. As in our study, their results also pointed a reduction of energy intake; however these authors did not observe any change in the percentage contribution of each macronutrient.

Our data showed similar decreases in fat intake in all intervention groups. Many studies found consistent negatives associations between fat intake and BMI or waist circumference, besides appointed a contribution of the diet composition, especially saturated fat and refined carbohydrates, in oxidative stress and inflammation (Ahluwalia et al., 2009, Dandona et al., 2010). Thus, decreases observed in this study for fat intake

could contribute to a healthier life, considering that Spanish population are related with excessive consumption of fats (Gonzalez-Solanellas et al., 2011). Our results also showed an increase of CHO and PRO intakes for all intervention groups. This homogeneous change among the four groups in our study could be due to the fact that all individuals received the same diet restriction and advices, which probably influenced these responses. Others factors, as exercise intensity (Alkahtani et al., 2014), genetic (Goni et al., 2015) or social conditions (Riesco et al., 2010) also could induce differences in macronutrient selection. Furthermore, conscious food choices could mask the exercise effects to consume a particular combination of macronutrients (Elder and Roberts, 2007).

A significant decrease was observed in our study in the total energy intake in response to all interventions, demonstrating that various types of exercise and physical activity recommendations allied to diet can be effective to maintain lower energy intake even after the end of the program. The energy deficits achieved in this study (about 780 kcal) can be considered clinically meaningful and relevant for the weight management, since a deficit of 100 kcal and 189 kcal per day has been calculated to prevent weight regain (Sim et al., 2015). Our results confirmed the claim that sedentary individuals who initiate a long-term exercise program do not increase their energy intakes in a compensatory fashion (Bales et al., 2012), if diet advice is included.

In our study, despite of the sample to be sedentary at beginning of the intervention (<30 min physical activity/day), subjects who started the program with more daily steps presented an increase of protein intake, although diet recommendations were equal for all the participants. Others studies observed that active individuals consumed more protein than inactive counterparts (Jokisch et al., 2012, Varlet-Marie et al., 2013). This

fact could be related to the belief that active individuals need to consume more proteins than sedentary individuals (Jokisch et al., 2012).

Regarding to motivation to diet and exercise, our findings indicated a good acceptance of the intervention program by the individuals. Although motivation to exercise increased only in women, men did not decrease it. Our results could be expectable, since previous studies indicated differences in motivation to exercise between men and women (San Mauro Martin et al., 2014), with men more motivated by competitiveness and exceeding limits than women, who in turn were more motivated by aspects related to aesthetics (Balbinotti and Capozzoli, 2008). In the Balbinotti and Capozzoli' study (2008) when controlled by sex and age, the health dimension was the most cited as motivation to practice exercise. On the other hand, body dissatisfaction and BMI seemed to be strongly associated with the different constructs of eating behavior in both sexes (Fortes et al., 2013).

Nutritional education alone may not be sufficient for changing eating behavior (Annesi et al., 2010). In this sense, exercise seems to play an important role, inducing better energy deficit in relation to dietary restriction, through the prevention of nutritional compensatory responses (Thivel et al., 2016, Chang and Lin, 2015). Furthermore, has been observed a strong relationship between exercise and eating behavior, and individuals who reported being internally motivated to eat were significantly more likely to engage in physical activity and presented lower BMI (Gast et al., 2015, Cadena-Schlam and Lopez-Guimera, 2014, Jakicic et al., 2011). In fact, studies indicated that disorders eating, as emotional eating, were related less engagement in physical activity (Whitaker et al., 2014) and higher BMI (van Strien et al., 2012, Stein et al., 2013, Danielsen et al., 2013).

In order to promote action rather than mere motivation, and allow a substantial effect on food choice and exercise level, multifactorial approach should be incorporated in environmental and behavior change strategies (Brug et al., 2005, Gohner et al., 2012, Stacey et al., 2015, Makoundou et al., 2010, Johnson et al., 2012).

Although ANOVA has not showed differences among intervention groups for energy intake, macronutrient distribution or motivations to diet and to exercise, some results appointed by correlations worth to be commented. Some correlations, as motivations to diet and to exercise were found for all groups, except for strength group. In general, the correlations observed in the strength group showed that individuals who ate more also moved more, and those who ate less moved less. Strength group was the only one that, although not significantly, increased absolute lean mass, while endurance group decreased it also not significantly. In other two groups, there was a significant decrease in absolute lean mass (data not shown). Blundell et al. (2012) observed that fat-free mass was positively associated with daily energy intake and hunger levels, which could explain, at least in part, the correlations found in this group. Guelfi and colleagues (2013) found that aerobic exercise was associated with an increase in satiety, while an equivalent period of 12 weeks of resistance training not. It is possible that resistance exercise needs more time to improve the responses related to appetite control and further research should investigate these responses in relation to chronic exercise in a long-time (one year or more).

Nutritional behavior plays an important role in predicting cardiovascular risk for any category of BMI and exercise behavior is also an important predictor for the presence of normal weight or overweight (Huang et al., 2014). Further research is required to determine the mechanisms through which exercise training may affect and improve appetite regulation (Sim et al., 2015), besides to help in the understanding that obesity is

not a simple matter of will power or that eating less and exercising more is the solution (Brown and Kuk, 2016). Success in long-term weight loss and maintenance increases as more behavioral dimensions are involved in the behavioral change process (Westenhoefer, 2001).

Important strengths of this study include: 1) the randomized design; 2) the inclusion of four different training programs in the same study combined with caloric restriction in all interventions; 3) the direct supervision and control of exercise for all training sessions. An important limitation of this study was the fact that it did not include a “no treatment” control group, but rather compared the intervention with a previously described exercise recommendation which is broadly accepted from an ethical point of view and of the clinical practice. Another point would be the limitation of measure instrument itself, which data could be affected by the oft-cited problem of total and/or selective under-reporting (Abbot et al 2008). Moreover, the measure realized at the end of the program, could promote continuity adherence to diet merely because is a recent behavior. Lastly, the lack of blood markers and appetite regulation scales weaken a greater understanding of the responses on behavior eating, seen in our study.

In conclusion, our findings suggest no substantial effect of type of exercise on macronutrient selection or energy intake, but they point out a general change on these parameters when an exercise program is followed. Significant increases in carbohydrate and protein intakes and decreases in fat and total energy intakes were reported, regardless type of exercise, IMC category or gender, as a result of following a weight loss program. Furthermore, in a subsample of this present study, individuals who started the intervention performing higher daily steps number increased more their protein intake than those who performed <7500 daily steps. Lastly, there were increases in diet

and exercise motivations, although motivation to exercise was incremented only in women.

4. CONCLUSIONS

CONCLUSIONS

The overall aim of this thesis was to verify the influence of different types of exercise in combination with diet in cardiorespiratory, hemodynamic, metabolic and behavior parameters. Therefore, conclusions presented below allude to the five contributions of this thesis represented by each of the five studies that compose the subsections of this work.

Conclusions of Study I

Conclusion 1: Our weight loss program was effective for improve cardiovascular fitness in overweight subjects and obese men, but not in obese women.

Conclusion 2: All interventions promoted similar improvement on $\text{VO}_{2\text{peak}}$.

Conclusions of Study II

Conclusion 1: Four equations were developed, with and without effort test data, for sedentary and active subjects, including age, body weight, lean body mass percentage, and time of effort test in the models.

Conclusion 2: Equations developed in this study were adequate to predict $\text{VO}_{2\text{peak}}$ in overweight and obese subjects, whilst the most commonly used equations in the literature, ACSM and Bruce, reported an inaccurate estimation of this parameter.

Conclusions of Study III

Conclusion 1: All interventions were effective for decrease blood pressure in subjects with weight excess.

Conclusion 2: Coronary heart disease risk reduced only in men, without interactions among intervention group.

Conclusions of Study IV

Conclusion 1: There was not difference on resting metabolic rate response among intervention groups.

Conclusion 2: All our interventions caused a reduction on resting metabolic rate in women, but not in men.

Conclusions of Study V

Conclusion 1: There was no substantial effect of type of exercise on energy intake or macronutrient selection, demonstrating that all our interventions were effective in a compliance diet.

Conclusion 2: After six-month weight loss program, individuals did not reduce their motivation related to diet or exercise, demonstrating good acceptance and suitability of the program, especially in women.

5. STRENGTHS AND LIMITATIONS

STRENGTHS

Several strengths of the PRONAF study and of this thesis should be highlighted:

- It was a randomized controlled study.
- Participants who completed the intervention and were included in present thesis, all had an adherence of 90% for exercise and 80% for diet.
- Interventions were conducted by a collaboration of different centers, constituting a multidisciplinary group.
- In the supervised groups, through the 22 weeks, during all the training sessions participants were monitored by certified trainers with Sports Science degrees, ensuring the correct execution of the exercises and the completion of each session.
- Physical activity of each subject was assessed by accelerometry.
- The adequate design and control in the supervised groups, with the same duration and intensity, ensured a correct comparison among the different types of exercise.
- The inclusion of a combined intervention group, with aerobic and strength exercises performed in circuit was a novelty that adds value to the study and contributes to the scientific knowledge.

LIMITATIONS

After carrying out the project, analyzing the data and discussing and comparing our results with other studies, we present a critical view of our work, listing the main limitations below:

- PRONAF study did not included psychological support for the participants.
- Sample size and power was calculated for the main objective of the project i.e. weight loss, therefore for others studies could be underpowered.
- Non-inclusion of individuals with obesity-related pathologies.
- Non-inclusion of a “no treatment” control group, but data comparison with exercise recommendations are broadly accepted from an ethical point of view and in clinical practice.

6. FUTURE RESEARCH LINES

FUTURE RESEARCH LINES

This project has given the possibility to study the influence of a controlled weight loss program in cardiorespiratory, hemodynamic, metabolic and behavior parameters. Learning from it and having a wider view of similar projects, future studies should take into consideration the following points:

- Include subjects with pathologies.
- Include individuals from other age groups, such as children and older adults.
- Organize multi-center collaborations in order to obtain a large sample size to ensure power.
- Add hormones variables and others blood markers in order to expand explanations in the physiological processes involved in obesity.
- Add new technologies for body composition measurement, which allow better evaluation of muscle mass and visceral fat, such computed tomography.
- Include appetite regulation scales for a better understanding on behavior eating responses.
- Include intermediate measures during the intervention, and to evaluate as many variables as possible at follow-up.
- Verify the effectiveness and feasibility of multi-modal trainings in obese individuals (such functional exercise, crossfit training, etc).
- Include follow-up with more variables in order to evaluate adherence and follow changes and improvements achieved during the intervention.

7. PRACTICAL APPLICATIONS

PRACTICAL APPLICATIONS

Experts in sport science and practicing trainers have suggested before that well designed, controlled and supervised exercise with certified trainers is the best way to do physical activity in order to lose weight. In our study physical activity recommendations have also promoted some health benefits, but our results support the suggestion of the experts and demonstrate superiority of supervised interventions for some aspects. Below, we highlight some practical applications considered important obtained from this work:

- All interventions were effective in improving the various parameters studied in overweight and obese individuals; however obese healthy women seem to require a greater training load to achieve increase in cardiovascular capacity, decrease in the cardiovascular risk and to contain the reduction on resting metabolic rate.
- Physical activity recommendations seem not to be able to avoid a lean body mass reduction when a diet is adopted in obese men.
- Physical activity recommendations did not improve exercise time on effort test in obese women.
- Body composition seems to be more relevant in predicting peak oxygen consumption than sex alone. Practicing trainers and coaches should use prediction equations that include body composition data in their calculations;
- Young adult men, despite having a higher cardiovascular risk, may also benefit more than women from a weight loss program to reduce this risk.
- Women have more external motivation to follow training after a weight loss program.

- The proposed dietary was well accepted by the participants and could be a good option for other individuals, with macronutrient proportions that could contribute for a cardiometabolically healthier diet.

8. REFERENCES

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9. SUMMARIZED CV

FORMAL EDUCATION

- 2013 – current** PhD Student in Physical Activity and Sport Science. Universidad Politécnica de Madrid, Spain.
- 2015 - 2016** Postgraduate degree in Personal Trainer. Universidad Politécnica de Madrid, Spain.
- 2010 – 2012** Master's degree in Physical Education. Universidade Federal de Viçosa, Brazil.
- 2004 - 2008** Bachelor's degree in Physical Education. Universidade Federal de Viçosa, Brazil.

PROFESSIONAL EXPERIENCE

- 2013 – 2013** Position: Professor. Faculty: Faculdade de Viçosa, Brazil. Schemes of job: Partial-time. Subject: Volleyball.
- 2012 - 2013** Position: Professor. Faculty: Faculdade Ubaense Ozanan Coelho (FAGOC), Brazil. Schemes of job: Partial-time. Subject: Gym activities I and II.
- 2009 – 2011** Position: Professor. School: Escola Municipal Nossa Senhora de Fátima, Brazil. Schemes of job: Partial-time. Subject: Physical Education in Basic Education.

PUBLICATIONS

- Validity of adiposity index in predicting body fat in a sample of Brazilian women. Cerqueira M, Amorim P, Magalhães F, **Castro E**, Franco F, Franceschini S, Cerqueira L, Marins J, Doimo L. Obesity (IF: 3.614), 21 (12), E696 - E699, 2013.
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- Blood pressure in hypertensive women after aerobics and hydrogymnastics sessions. Loiola A, Lima LM, **Castro EA**, Veras RP, Segheto W, Zanatta TC, Doimo LA. Nutrición Hospitalaria (IF: 1.497), 32: 823-828, 2015.

- What is the most effective exercise protocol to improve cardiovascular fitness in overweight and obese subjects? **Castro EA**, Peinado AB, Benito PJ, Galindo M, González-Gross M, Cupeiro R on behalf of the PRONAF Study Group. Journal of Sport and Health Science (IF: 1.685). In Press. <http://dx.doi.org/10.1016/j.jshs.2016.04.007>
- Peak oxygen uptake prediction in overweight and obese adults. **Castro EA**, Cupeiro R, Benito PJ, Calderón J, Fernández IR, Peinado AB on behalf of the PRONAF Study Group. Archivos de Medicina del Deporte, 34(2):72-79, 2017.
- Impacto da sarcopenia e da qualidade muscular na força e mobilidade funcional de membros inferiores em mulheres pós-menopáusicas. **Castro EA**, Amaral JF, Doimo LA. Revista Portuguesa de Ciências do Desporto. Accepted 10/10/2016.
- Sedentary behavior and compensatory mechanisms in response to different doses of exercise - a randomized controlled trial in overweight and obese adults. **Castro, EA**, Júdice PB, Silva AM, Teixeira PJ, Benito PJ on behalf of the PRONAF Study Group. European Journal of Clinical Nutrition (IF: 2.935). Accepted 04/18/2017.

CONGRESSES CONTRIBUTIONS

- VI International Symposium in Strength Training, Madrid, Spain, December 2013.
- World Conference on Kinanthropometry, Murcia, Spain, October 2014.
- 19th European College Sport Science Congress, Amsterdam, Netherlands, July 2014.
- *Simposio EXERNET - Investigación en Ejercicio y Salud: Presente y Futuro en España*, Granada, Spain, November 2014.

- VII International Symposium in Strength Training, Madrid, Spain, December 2014.
- VIII International Symposium in Strength Training, Madrid, Spain, December 2015.
- *21ª Reunión de la Sociedad Española de Hipertensión*, Valencia, Spain, March 2016.
- 21st Annual Congress of the European College of Sport Science, Vienna, Austria, July 2016.
- *Simposio EXERNET - Investigación en Ejercicio, Salud y Bienestar: "Exercise is Medicine"*. Cádiz, Spain, October 2016.
- International Congress Exercise and Health, Sports and Human Development, Évora, Portugal, November 2016.
- IX International Symposium in Strength Training, Madrid, Spain, December 2016.
- *22ª Reunión de la Sociedad Española de Hipertensión*, Madrid, Spain, March 2017.

AWARDS

- Best scientific poster in *Simposio EXERNET*, November 2014.
- 3rd Nutrisport Award in VIII International Symposium in Strength Training, December 2015.
- *Premio FEMEDE a la investigación, convocatoria 2015*.
- Best scientific communication in the poster session "Non-pharmacological treatment" in *21ª Reunión de la Sociedad Española de Hipertensión*, March 2016.

- Best poster presentation and 3rd Oral Communication Award in IX International Symposium in Strength Training, December 2016.
- Best scientific communication in the poster session “Non-pharmacological treatment” in *22^a Reunión de la Sociedad Española de Hipertensión*, March 2017.

10. APPENDIX

STUDY PROTOCOL

Open Access

Nutrition and physical activity programs for obesity treatment (PRONAF study): methodological approach of the project

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Abstract

Background: At present, scientific consensus exists on the multifactorial etiopatogenia of obesity. Both professionals and researchers agree that treatment must also have a multifactorial approach, including diet, physical activity, pharmacology and/or surgical treatment. These two last ones should be reserved for those cases of morbid obesities or in case of failure of the previous ones. The aim of the PRONAF study is to determine what type of exercise combined with caloric restriction is the most appropriate to be included in overweight and obesity intervention programs, and the aim of this paper is to describe the design and the evaluation methods used to carry out the PRONAF study.

Methods/design: One-hundred nineteen overweight (46 males) and 120 obese (61 males) subjects aged 18–50 years were randomly assigned to a strength training group, an endurance training group, a combined strength + endurance training group or a diet and physical activity recommendations group. The intervention period was 22 weeks (in all cases 3 times/wk of training for 22 weeks and 2 weeks for pre and post evaluation). All subjects followed a hypocaloric diet (25–30% less energy intake than the daily energy expenditure estimated by accelerometry). 29–34% of the total energy intake came from fat, 14–20% from protein, and 50–55% from carbohydrates. The mayor outcome variables assesed were, biochemical and inflammatory markers, body composition, energy balance, physical fitness, nutritional habits, genetic profile and quality of life. 180 (75.3%) subjects finished the study, with a dropout rate of 24.7%. Dropout reasons included: personal reasons 17 (28.8%), low adherence to exercise 3 (5.1%), low adherence to diet 6 (10.2%), job change 6 (10.2%), and lost interest 27 (45.8%).

Discussion: Feasibility of the study has been proven, with a low dropout rate which corresponds to the estimated sample size. Transfer of knowledge is foreseen as a spin-off, in order that overweight and obese subjects can benefit from the results. The aim is to transfer it to sports centres. Effectiveness on individual health-related parameter in order to determine the most effective training programme will be analysed in forthcoming publications.

Trial registration: ClinicalTrials.gov NCT01116856

Keywords: Overweight, Obesity, Caloric restriction, Exercise, Weight loss

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Background

The increase in overweight and obesity rates is a major public health concern. In most countries it has affected all population groups regardless of sex, age, race, income or education level, but to varying extents [1]. Based on comparative studies with other European countries, Spain is at the forefront [1], one in four people is overweight or obese, ie 12.5 million people [2]. In fact, two out of three men are overweight and one of every six is obese, with a clear trend to increase in the forthcoming years [3].

Today it is accepted that obesity has a multifactorial origin [4,5] and is a known risk factor for numerous health problems, including high cholesterol, diabetes, hypertension, respiratory problems, musculoskeletal diseases, cardiovascular diseases, and some forms of cancer. Mortality also increases sharply once the overweight threshold is crossed [6,7].

Research has been very active in the last years trying to identify the most effective treatment for adult overweight and obesity [8-40]. A combination of caloric restriction with an increase in energy output by means of exercise has been proven in the hospital setting [41]. Results have been quite conclusive regarding aerobic exercise [9] and very restrictive caloric intake (less than 50% of kcal intake) [35]. But data are still scarce regarding the effect of a combination of strength and aerobic training and a much lesser restrictive hypocaloric diet on weight loss [35]. The PRONAF study wants to get deeper into the latter, also considering the Consensus Paper 2011 from the Spanish Society of Obesity Research (SEEDO), that has stated that the primary goal of treatment should not focus on achieving the ideal body weight, but to have smaller weight losses maintained in the long term [42].

Therefore, the main aim of the PRONAF study was to discover which is the most effective training protocol in combination with caloric restriction for overweight and obese subjects included in a specific intervention program. The aim of this paper is to describe the design and the evaluation methods used for the PRONAF study.

Methods/design

Study design

PRONAF is a 22 week-intervention study performed among Spanish overweight and obese adults, who were randomly assigned to one of the following intervention groups: strength training group (S), endurance training group (E), combined strength plus endurance training group (SE), and physical activity recommendations group (C), which are described in detail below. The study was performed twice, one year apart, first in the overweight group (year 2009/2010) and then in the obese group (year 2010/2011). In total, we had 8 interventions groups.

Population and sample size estimation

The estimation of the sample size was calculated to detect a main effect of the treatment on the percentage of body fat with a 80% statistical power at 5% significance, assuming a 0.80 correlation between repeated measures [43]. The initial calculated sample size per intervention group ($n = 22$) permits the detection of a large effect size (Cohen's $d = -0.8$), as observed in a previous investigation [43].

The initial adjustment of sample size for dropouts carried out used a maximum of 25% of dropouts in each group [37]. Adjusted dropouts sample = $n (1/(1-R))$, where n = number of subjects not lost, and R = expected proportion for dropouts. With our data, the initial necessary sample size was: $88 (1 / 1 - 0.25) = 118$ subjects or 29/30 in each intervention group, this being applicable for both the overweight and the obese interventions groups. A total of two hundred thirty nine people initiated the study, completing it 180 (75.3%), which supposed 59 dropouts for different reasons. For personal reasons 17 (28.8%), low exercise adherence 3 (5.1%), low diet adherence 6 (10.2%), job change 6 (10.2%), and lost interest 27 (45.8%).

Recruitment of the subjects

Subjects were recruited by means of diverse advertisements published in the media and the applicants filtered using different criteria. The voluntary subjects who fulfilled the inclusion criteria and passed the baseline physical examination were stratified by age ranges and body mass index (BMI), and randomized into the different intervention groups (Figure 1).

Inclusion and exclusion criteria

Inclusion criteria included being male or female living in the Region of Madrid, being overweight (BMI 25–29.9 kg/m²) or obese (BMI: 30–34.9 kg/m²), middle-aged (from 18 to 50 years), having a sedentary lifestyles (< 30 min Physical Activity/day), being normoglycaemic, and non-smoker [37,41]. In the case of females, having regular menstrual cycles was required.

The exclusion criteria were suffering from a physical (orthopaedic limitations, stroke, etc.) and/or psychological (anorexia, bulimia, etc.) disease that may have precluded the performance of the requested strength or endurance training, intake of any medication (beta blockers, alcohol, etc.) known to influence physical performance or the interpretation of the results, having a history of systematic strength or endurance training (moderate to high intensity training more than once a week) in the year before the beginning of the study [37,40].

After the intervention period, participants who failed to comply with 90% assistance to the training sessions

and less than 80% adherence to the diet were excluded from further analysis. The characteristics of the final sample (completers) are shown in Table 1.

Ethical issues

The protocols and procedures of the PRONAF study were in agreement with the ethical guidelines on biomedical research on human subjects of the World Medical Association's Declaration of Helsinki (1964) and further

amendments. Before participating in this research, all subjects were carefully informed about the possible risks and benefits of the project, being required to read and sign an institutionally approved informed consent document. PRONAF study was approved by the Human Research Review Committee of the University Hospital La Paz (PI-643).

Access to the database was restricted to the researchers that participated in the PRONAF study. Therefore, the

Table 1 Baseline data (n = 180)

	Overweight n = 84		Obesity n = 96	
	Women	Men	Women	Men
	n = 48	n = 36	n = 48	n = 48
Age (years)	37.29 ± 8.25	37.42 ± 8.02	39.02 ± 7.74	38.79 ± 7.99
Body Weight (kg)	73.5 ± 5.87	88.21 ± 8.13	88.33 ± 10.1	102.04 ± 8.94
Height (m)	1.62 ± 0.06	1.75 ± 0.07	1.64 ± 0.07	1.77 ± 0.06
BMI (kg/m ²)	28.01 ± 1.32	28.57 ± 1.12	32.41 ± 1.85	32.4 ± 1.9
Body fat (%)	43.28 ± 3.62	33.8 ± 4.63	47.11 ± 3.49	38.17 ± 4.02
Body fat free mass (kg)	40.25 ± 4.3	55.99 ± 5.47	44.3 ± 4.71	58.63 ± 8.96
Bone mineral density (g/cm ²)	1.18 ± 0.1	1.26 ± 0.09	1.21 ± 0.11	1.3 ± 0.1

Results are shown as Mean ± SD.

Note. BMI = Body Mass Index. Body fat, Body fat free mass and Bone mineral density calculated by Dual-energy x-ray absorptiometry (DXA).

data and information obtained in the project was considered as confidential following current Spanish legislation regulating personal data protection (Organic Law 15/1999 and Royal Decree 1720/2007).

This trial was registered at clinicaltrials.gov as NCT01116856. <http://clinicaltrials.gov/>.

Intervention

Time line intervention

The assessments took place for all subjects one week before and after 22 weeks of intervention. Additionally, body weight was measured every 15 days, training intensity and physical activity were controlled monthly, and dietary intake was evaluated every three months.

Exercise protocols

Four different intervention groups were involved in the study as stated above. The S, E and SE groups followed the corresponding training program plus the dietary intervention, and the C group followed the dietary intervention and was instructed about the general recommendations regarding physical activity for weight loss from the American College of Sports Medicine (ACSM) [44].

Subjects in the S, E and SE groups performed training 3 times/wk for 22 weeks at a Sports Centre in Madrid (Spain). All training sessions were carefully supervised by certified personal trainers. The exercise programs were designed taking into account each subject's muscle strength (MS) and the heart rate reserve (HRR). MS was measured using the 15-repetition maximum (15 RM) testing method [45] in the S and SE groups (both of which involved strength training). Both volume and intensity of exercise was increased over the study period (Figure 2) according to standard procedures [35,41].

Prior to each training session each subject started with a 5-minute aerobic warm-up routine, followed by the session routine, and concluded with a 5-minute cool down and stretching exercises routine. Moreover, an MP3 audio track was played for each participant to set the execution rhythm of the exercises during all the sessions. In this case, the heart rate (HR) was monitored by a pulse-meter (Polar RS800CX, Polar Electro, Kempele, Finland). The cadence for the resistance exercises was fixed at 1:2 (concentric-eccentric phase). A session routine consisted in the execution on eight scheduled exercises in the case of group S (i.e., shoulder press, squat, barbell row, lateral split, bench press, front split, biceps curl and French press for triceps). Regarding types of exercises, running, cycling or elliptical (self-selected) exercises were the main components of the session routine for group E, while the routine for the SE group consisted in a combination of cycle ergometry, treadmill or elliptical intercalated with squat, row machine, bench press and front split.

The volume and intensity of the three training programs increased progressively. During the adaptation period (cf. weeks 1–4) subjects were taught on the exercise technique. Between the fifth and eighth week, exercises were carried out at an intensity of 50% of 15RM and HRR, performing 2 laps to the circuit (cf. 51 minutes and 15 seconds), then between the 9th and 14th week the intensity was increased up to 60% of 15RM and HRR, and finally during the period between the 15th and 24th week the volume increased from 2 to 3 laps to the circuit (64 minutes). Then, a five-minute recovery period was set between the circuits. The S and SE participants performed 15 repetitions (45") for each exercise with a rest period of 15 seconds between them.

Diet intervention

Hypocaloric diets (between 5028 and 12570 KJ) were prescribed individually for all participants by expert dieticians at the Department of Nutrition, La Paz University Hospital, Madrid. The diet was designed to provide 25–30% less energy than the daily energy expenditure (DEE), as measured using SenseWear Pro3 Armband™ (Body Media, Pittsburgh, PA). Approximately, 29–34% of the energy came from fat, 14–18% from protein, and 50–55% from carbohydrates [46]. In the obesity group, energy provided from protein was increased up to 14–20%.

Before-after measurements

Physical fitness and health

Maximal aerobic power test The test was conducted on a computerized treadmill (H/P/COSMOS 3P® 4.0, H/P/Cosmos Sports & Medical, Nussdorf-Traunstein, Germany). Peak oxygen uptake (VO_2 peak) was measured with the modified Bruce protocol used elsewhere with overweight and obese population [35,47]. Volume and composition of expired gas was analysed with a gas analyzer Jaeger Oxycon Pro (Erich Jaeger, Viasys Healthcare, Germany) which validity and reliability has been demonstrated previously [48,49], and continuous 12-lead electrocardiographic monitoring. The exercise test was maintained until exhaustion. The mean of the three highest measurements was used as VO_2 peak. Identical procedure was carried out to calculate the maximal HR.

Resting metabolic rate

Subjects were asked to refrain from any exercise for at least 24 h before the test. To assess the resting metabolic rate (RMR), participants were cited between 7 am to 10 am, after a 9 h overnight fasted period. RMR was then measured by indirect calorimetry standing up (during 11 min) and in a lying position (additional 20 min). Oxygen uptake (VO_2) and carbon dioxide production (VCO_2) were recorded by a gas analyzer Jaeger Oxycon Pro (Erich Jaeger, Viasys Healthcare, Germany), and resting heart rate (RHR) was measured using a heart rate monitor (Polar Electro Oy, Kempele, Finland). All these parameters were averaged during the last 5 min of the standing up position and the last 10 min of the lying position. Oxygen uptake and VCO_2 data were used to calculate RMR according to the formula of Weir [50].

Maximal dynamic strength

Muscle strength was measured with the 15RM testing method described elsewhere [51] for both strength training groups S and SE. The 15 RM for each exercise was tested twice on different days during the evaluation

periods. The intraclass correlation coefficient of reliability for all the exercises was ICCr = 0,995 and ICCr = 0,994 for men and women, respectively. All the assessments, the data collection sessions and the previous trainings were carried out with the same machines and free weights (Johnson Health Tech. Iberica, Matrix, Spain).

Static strength (dinamometry)

The general strength index (SI) was calculated using previous criteria [52]. This method measures leg and arm strength with respect to body weight via two exercises: the bench press and squat. The dynamometric strength index (DSI) was calculated by measuring muscular strength using a Tecsymp Tkk5002 hand dynamometer and a Tecsymp Tkk5401 leg and back dynamometer (Tecsymp, Barcelona, Spain). The DSI value was calculated as the sum of the values obtained with both apparatuses divided by subject's body weight.

Physical activity and daily energy expenditure

Habitual physical activity (PA) was assessed with a SenseWear Pro3 Armband™ (Body Media, Pittsburgh, PA). Subjects were instructed to wear the monitor continuously for 5 days including weekend days and weekdays following general recommendations [53]. Data was recorded by 15 min intervals. DEE was calculated using the Body Media propriety algorithm (Innerview Research Software Version 6.0).

Energy balance, adherence to diet and exercise

All subjects were instructed to continue their habitual daily activities as before the intervention period. They were required to report the kind, duration, and intensity of any physical activity and the amount of any food undertaken during the intervention period.

At the beginning of the intervention, negative energy balance was calculated taking into account the DEE, and a 3-day food record, in order to decrease the energy intake of the diet by a 25–30% during the intervention.

In one hand, adherence to diet was calculated as the estimated Kcal of the diet divided by the real Kcal intake in percentage ($[\text{estimated kcal of diet} / \text{real Kcal intake}] \cdot 100$), representing the highest adherence the value 100%. Higher values mean a higher restriction and viceversa. On the other hand, adherence to exercise was calculated by the number of sessions completed in regard to the theoretical sessions ($[\text{sessions performed} / \text{total sessions}] \cdot 100$).

Psychological and eating behavior assessment

Quality of life The impact of overweight and non-morbid obesity on Health-Related Quality of Life (HRQL) was assessed using two different questionnaires:

EUROQOL 5D (EQ-5D)

The EQ-5D, is a self-administered questionnaire capable of generating a score reflecting a value associated with a given health status. The EQ-5D™ descriptive system consists of five dimensions: 1. Mobility; 2. Self-care; 3. Usual activities; 4. Pain/discomfort; 5. Anxiety/depression. Each dimension has three levels: “level 1: no health problems”, “level 2: moderate health problems” and “level 3: extreme health problems”. Each unique health state described by the instrument has an associated 5-digit descriptor ranging from 11111 for perfect health to 33333 for the worst possible state. The resulting descriptive system defines 243 health states. The instrument also includes a 20-centimeter visual analogue scale for the self-assessment of current general health [54].

Short Form-36 Health Survey (SF-36) version 1.4, valid for the Spanish population was used [55]. This questionnaire evaluates the individual health status in two dimensions: functional and emotional. Functional status is divided in 6 subscales: Physical Functioning (PF), Role-Physical (RP), Bodily Pain (BP), Vitality (VT), Social Functioning (SF) and Role-Emotional (RE). Emotional status includes Mental Health (MH) and General Health (GH) subscales. Scores on all subscales range from 0 to 100 (higher scores indicate better health status) [56].

Eating behaviour At baseline and at the end of the intervention all food and beverages consumed by the participants were recorded using a food frequency questionnaire and a “3-day food and drink record”, validated for the Spanish population [57]. This recorded all food and drinks consumed at home and away for three days, including 2 weekdays and 1 weekend day. Subjects were instructed to record the weights of food consumed if possible and to use household measurements (spoonfuls, cups, etc.) if not. The energy and nutritional content of the food consumed was then calculated using the DIAL software (Alce Ingeniería, 2004). Then, the values obtained were compared to the recommended dietary intakes for the Spanish population to determine dietary adequacy [58].

Body composition

Anthropometric measurements Body height was measured using a SECA stadiometer (range 80-200 cm, Valencia, Spain). Body weight (BW) was measured using a TANITA BC-420MA balance (Bio Lógica Tecnología Médica S.L, Barcelona, Spain). BMI was calculated as [body weight (kg)/(height (m))²]. Waist circumference (WC) was measured using a SECA 201 steel tape (Quirumed, Valencia, Spain). Body fat percentage was measured using bioelectrical impedance analysis (BIA)

with an OMRON BF 306® analyzer (OMRON HEALTH-CARE Co., Ltd, Ukyo-ku, Kyoto, Japan).

Dual-energy x-ray absorptiometry Dual-energy x-ray absorptiometry (DXA) was used to measure percentage of total fat mass (TFM%), percentage of android fat (AF%), the android gynoid ratio (A/GF) and lean mass (kg), using a GE Lunar Prodigy apparatus (GE Healthcare, Madison, Wisconsin, USA). All DXA scan analyses were performed at the Faculty of Physical Activity and Sport Sciences using GE Encore 2002 software v 6.10.029.

Nuclear magnetic resonance Nuclear Magnetic Resonance (MRI) was used to study the proportion and location of the adipose tissue. The MRI study measured changes at different abdominal adipose tissue compartments: SAT (superficial and deep depots) and VAT (intraperitoneal and retroperitoneal compartments). Images were obtained with a GE Medical Systems 1.5 Tesla whole body scanner using a T1-weighted fast-spin echo pulse sequence at the University Hospital *La Paz* Research Institute. The subjects were examined in supine position with arms positioned parallel along the lateral sides of the body. The subjects were imaged in two half-body volumes. A breath-hold sequence during expiration (approximately 20 seconds per acquisition) was used to minimize the effects of respiratory motion on the images. The total research time was about 5-10 min. All images were acquired on a 256x192 matrix, 16 bits/pixel, with a field of view = 480 mm. Slice thickness was 6 mm and contiguous slices were obtained every 1.5 mm from the first sacral vertebra upwards, until to achieve 30 images per person. For each subject six reference levels were studied, corresponding to intervertebral disc levels L5-S1 to L2-L3, at umbilical and at caudal left kidney positions. The acquired axial MR images were retrieved from the scanner using the DICOM® protocol and after were transferred to an external personal computer running Windows XP. We used specially designed image analysis software Stereonauta for quantitative analysis of the images.

Biochemical, metabolic, inflammatory and genetic profile

Biomarkers Blood samples were taken early in the morning at the La Paz University Hospital Extraction Unit after a 12 h overnight fast by venipuncture from the antecubital vein. Samples were kept at 4- 6°C until analysis, which was always performed within 48 h following standard hospital procedures. The following parameters were measured:

- Hematology was performed in a Pentra 120 DX cell counter (ABX-Horiba, Montpellier, France).

- Serum calcium, phosphorus, total proteins, albumin, creatinine, uric acid, bilirubin, lipase, alkaline phosphatase, creatinase, LDH, GOT and GPT were analyzed by enzymatic-spectrophotometric assay (Olympus AU 5400, Izasa, Porto, Portugal).
- Blood lipid profile (total cholesterol, HDL and LDL cholesterol, triglycerides) and glucose were analyzed by means of a enzymatic-spectrophotometric assay (Olympus AU 5400, Izasa, Porto, Portugal). Apo A and Apo B were determined using a BNII nephelometer (Siemens Healthcare Diagnostics GmbH, Eschborn, Germany). Atherogenic risk ratios were calculated: total cholesterol/HDL, LDL/HDL and Apo B/Apo A1.
- Plasma fasting immunoreactive insulin was measured by enzymatic method in a fluoro-immunochemistry Analyzer (AIA-360, Tosoh Bioscience, Tessenderlo, Belgium). Insulin sensitivity was estimated using the HOMA-IR index [$\text{HOMA-IR} = \text{fasting glucose (mmol/l)} / \text{fasting immunoreactive insulin (mU/ml)} / 22.5$].
- Inflammatory biomarkers: Plasma C-reactive protein concentrations (CRP) were determined using a BNII nephelometer (Siemens Healthcare Diagnostics GmbH, Eschborn, Germany). Plasma fibrinogen was measured by coagulometric methods (ACL TOP 700, Izaasa, Porto, Portugal). Plasma leptin, IL-6 and TNF- α plasma concentrations were determined using a Luminex[®]-LX200 Analyzer (Millipore Corp, Billerica, Massachusetts, USA) and a MILLIPLEX MAP human circulating cancer biomarker magnetic bead panel (HCCBP1MAG-58 K) (Millipore, St. Charles, Missouri, USA). All samples were analyzed in duplicate. Data were analyzed using 3.1 xPONENT Software (Millipore, St. Charles, Missouri, USA). The intra and inter-assay coefficients of variation for the cytokine assays all fell in the 5-10% range.
- 25-hydroxyvitamin D was measured by chemiluminescent immunoassay using the LIAISON[®] Analyzer family (Palex Medical, Barcelona, Spain).
- Serum TSH was measured by an electrochemiluminescence immunoassay (ECLIA) by using an E170 analyser (Roche Diagnostics, Mannheim, Germany).

Genetic profile We investigated the potential influence of different genetic single nucleotide polymorphisms (SNPs), highly prevalent in the general population, on the response to different training protocols in overweight and obesity treatment. These SNPs are located in genes involved in metabolic pathways related to adiposity

(Beta-Adrenergic and Leptin receptors, and Peroxisome Proliferator-Activated Receptor), and in genes involved in energy metabolism and the production of energy during physical activity (metabolism of lactate and fatty acids). In addition, we have studied the Angiotensin-Converting Enzyme (ACE) Insertion/Deletion (I/D) polymorphism, which has been associated with athletic performance and training adaptation. The potential role for most of the selected polymorphisms is well documented, both as overweight/obesity risk factors and as modulators for the response to different interventions.

With regard to the method used, we firstly reviewed published literature about the techniques for analyzing the polymorphisms [59-68]. Then, we adapted these protocols to the conditions in our laboratory. Whole blood (5 ml) from each patient was collected in EDTA and sent to the Metabolism, Genetics and Nutrition Research Group of the School of Medicine-IFIMAV, in Santander. DNA was extracted from each sample using the "QIAamp[®] DNA Blood Mini Kit" from QIAGEN (Hilden, Germany) and the genotyping was performed for each SNP afterwards. The DNA samples were preserved at -40°C. All subjects signed a specific informed consent which allows storage and genetic characterization in relation to the objectives of the PRONAF study by the Metabolism, Genetics and Nutrition Research Group of the IFIMAV following the protocols of confidentiality and clinical safety, ensuring the anonymity of the samples and their use for research only.

After selecting the most interesting SNPs for the project objectives, the analyses were performed using genotyping assays based on techniques of double PCR, PCR and RFLP or sequencing for Phase II, and real-time PCR (TaqMan[®] SNP Genotyping Assays, Applied Biosystem) for Phase III, which allows the semi-automation of these determinations. All these techniques proved to be reproducible and stable under the conditions of the study. The reliability of the techniques used for genotyping in the different phases of the study has been proved using internal quality controls through different methods: repeated measurements of randomized samples, double-blinded reading of random samples, introduction of positive and negative controls, and random doubled testing of samples by both techniques. We obtained consistent results for any of the techniques used.

Assessment during the follow-up

Training control

Feedbacks for training loads were done once a month with the Rate of Perceived Exertion (RPE) to subjectively evaluate each session and determine where the participant considered the intensity to be at, following a similar methodology previously used [69].

Physical activity control

PA was assessed as described above once a month. All subjects were instructed to continue their habitual daily activities as before the intervention period and were provided with a PA diary to log the type, duration, and intensity of any PA or exercise undertaken during the intervention.

Body weight control

BW was measured as described earlier every fifteen days at the Sports Center. Subjects included in group C used their own scales to monitor BW at home during the intervention.

Dietary intake control

A dietician interviewed each participant at baseline, and at 3 and 6 months after the start of the intervention. All subjects were instructed about how to record their dietary intake using a daily log, and given recommended portion sizes and information on possible food swaps. In addition, voluntary group nutrition education sessions were given by the dieticians. The goal was to equip the participants with the necessary knowledge and skills to achieve gradual, permanent behavioural changes.

Statistical analysis

The main independent variables of the study were: intervention group, age, gender, measurement (baseline – post) and BMI classification (overweight or obese). The delta percentage was calculated through the standard formula: $\text{change (\%)} = [(\text{post-test score} - \text{pre-test score}) / \text{pre-test score}] * 100$. The power calculated previously to find significant differences between groups was 0.8 to fat mass (%).

Standard statistical methods will be used for the calculation of the means and standard deviation for all dependent variables. The statistical analysis will be as follows: 1) Univariate descriptive analysis, study of data distribution, basic statistics such as central and dispersion values. Pair comparison tests with previous analysis of the homogeneity of variance will be used. Pearson correlation coefficients, chi-squared tests and exact probability calculations will be also performed to study the relationship between quantitative and qualitative variables, respectively; 2) General lineal models, such a multivariate analysis (MANOVA) or two way analysis of variance (ANOVA) for repeated measures, will be used to determine differences among the four interventions groups and between baseline and post-training values. Compound symmetry, or sphericity, will be verified by the Mauchly test. When the assumption of sphericity would not be met, the significance of F ratios will be adjusted according to the Greenhouse-Geisser procedure.

Multiple comparisons of ANOVAs will be made with the Bonferroni post-hoc test.

The analysis of the data will be done using statistical package SPSS (SPSS Inc., Chicago, Illinois, USA). The significant level will be set at $\alpha = 0.05$.

Assessment for quality control

Previous to the start of the intervention we developed a protocol book with all the tests carried out in the pre and post intervention, plus the intervention procedures. An external observer followed the pilot study and his observations were included in the protocols. Weekly meetings during the pilot study were made with all the people involved in the project to train them and perform the protocol book.

At the end of the overweight intervention, the subjects filled in a satisfaction questionnaire. The results were included in the design of the obese intervention.

Finally, in order to clean the final data base of possible errors, a double data entry procedure was performed. Also an assessment of missing data and the identification of potential outliers were carried out.

Discussion

The PRONAF study is the first randomized controlled intervention study performed in Spanish overweight and obese adults without any other associated disease with the aim of losing weight and improving several health-related parameters by means of combining caloric restriction and controlled training programs. One of the strengths of the PRONAF study is the multidisciplinary approach. A group of professionals and researchers with expertise in a specific field: physical activity and fitness, nutrition, body composition, genetics and biochemical markers have designed together the study protocols after an in-depth review of the state of the art in the literature [8-40]. Exercise protocols were tested in healthy subjects and study protocols harmonized in a pilot study [70,71].

The PRONAF study has both strengths and limitations. The main limitation is that the study did not include psychological control of the subjects. During the study and in the final questionnaire evaluation the subjects pointed out the need of some psychological support especially when the body weight changes were not so evident.

On the other hand, the PRONAF study has also several strengths: 1) the final sample size of our study was maintained according to the sample size estimation, keeping a low dropout rate similar to other studies [37,40,41]. It is important to note that there were no differences between groups in the number of dropouts. 2) During the training sessions the participants in the study were continuously monitored by certified trainers to ensure the correct execution of the exercises and the

completion of each training session. 3) Inclusion of additional variables as visceral fat, blood lipid profile, and genotyping broadens the dimension of the PRONAF study.

In summary, feasibility of the PRONAF protocol has been proven. Transfer of knowledge is foreseen as a spin-off, in order that overweight and obese subjects can benefit from the results. The aim is to transfer it to sports centers. Effectiveness on individual health-related parameter will be analyzed in forthcoming publications.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

All authors participated in the writing of the paper and provided comments on the drafts and approved the final version.

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