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Universidad del País Vasco
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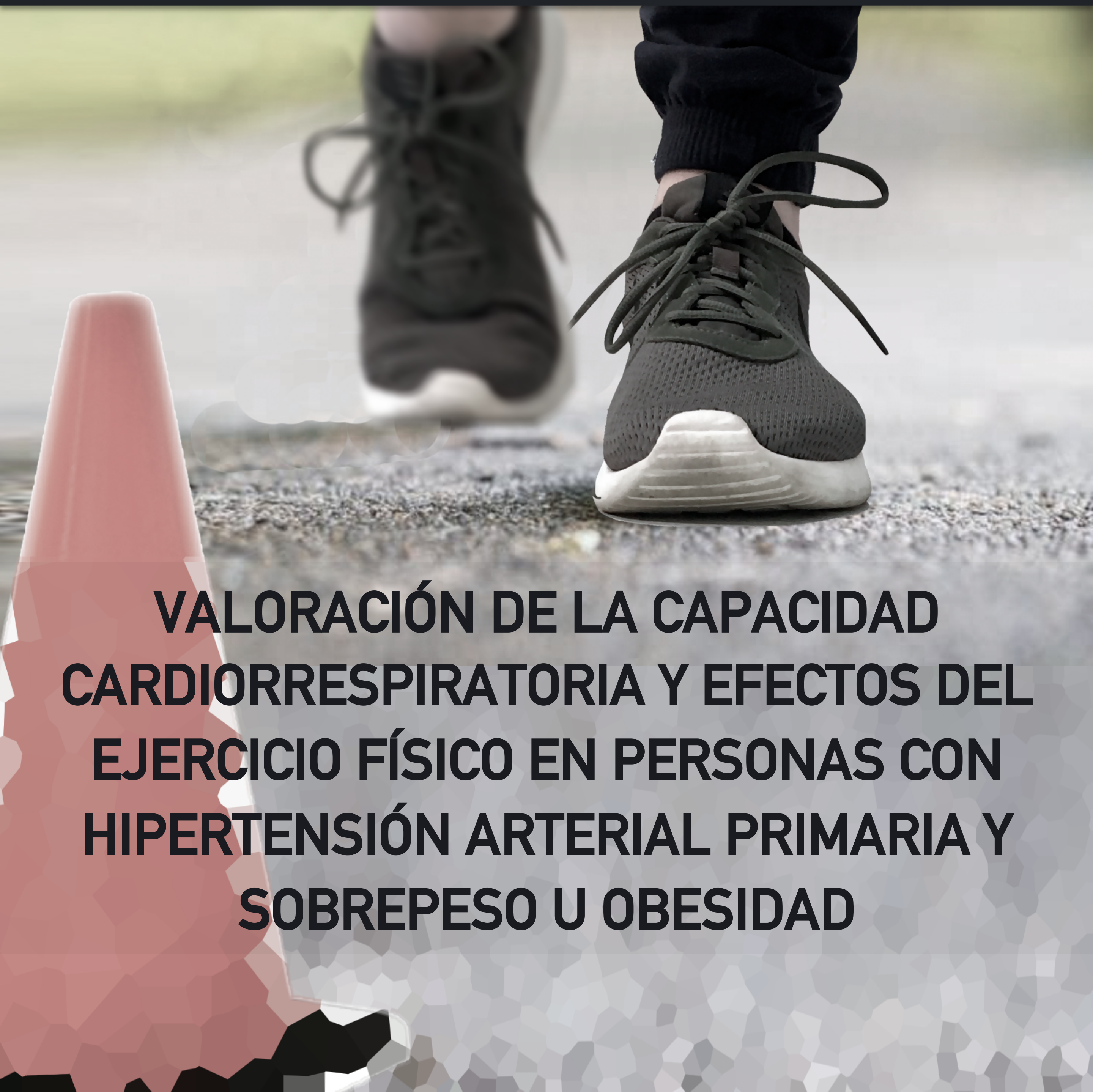
Tesis doctoral – 2018

Dirigida por la Dra. Sara Maldonado Martín



VALORACIÓN DE LA CAPACIDAD CARDIORRESPIRATORIA Y EFECTOS DEL EJERCICIO FÍSICO EN PERSONAS CON HIPERTENSIÓN ARTERIAL PRIMARIA Y SOBREPESO U OBESIDAD

A mi familia;
es la que habría elegido.

A mis amigas y amigos;
los volvería a elegir.

PROGRAMA DE DOCTORADO

Ciencias de la Actividad Física y del Deporte

TESIS DOCTORAL

Valoración de la capacidad cardiorrespiratoria y efectos del ejercicio físico en personas con hipertensión arterial primaria y sobrepeso u obesidad.

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“La felicidad del cuerpo se funda en la salud; la del entendimiento, en el saber”

Tales de Mileto

“Es de importancia para quien desee alcanzar una certeza en su investigación, el saber dudar a tiempo”

Aristóteles

AGRADECIMIENTOS

La presente tesis doctoral ha sido un esfuerzo en el que me han acompañado muchas personas sin cuyo apoyo y colaboración su consecución no habría sido posible. Me gustaría que estas líneas sirvieran para agradecer a todas las personas que han aportado su grano de arena en este proyecto, pese a que no pueda nombrar a todas ellas.

A Sara Maldonado Martín, directora y líder de este proyecto de investigación, por la propuesta y orientación del mismo, pero ante todo por tu entrega, por contagiar tu pasión y por la confianza que me has dado. A la universidad, a la facultad y al departamento por permitir que cuando haya curiosidad se pueda observar. A Ilargi Gorostegi, Pablo Corres, Aitor Mtz. de Aguirre y demás compañeras y compañeros de grado y posgrado que han venido e ido a lo largo de los años. A quienes han apoyado y aportado desde otras especialidades, especialmente a Ignacio Camacho Azkargorta, Peter H. Brubaker, Javier Pérez Asenjo y Rodrigo Aispuru. A las cientos de personas que de forma voluntaria habéis participado en las intervenciones de esta investigación. A la familia, kuadrilla, amigos e Iker, por el cariño y la paciencia. Esker mila aunitz.

DECLARACIÓN

El autor de esta tesis doctoral ha participado en todo el proceso de investigación, desde el diseño hasta el producto final en forma de publicaciones. Para ello, ha revisado la bibliografía existente, participado en el diseño de las intervenciones y en su puesta en práctica, así como en las distintas valoraciones y en la obtención y análisis de datos, y ha tratado de hacer una buena discusión tras haber interpretado los resultados en profundidad. Por otro lado, ha sido responsable, junto con la directora de la tesis, del proceso de divulgación en forma de publicación de artículos en revistas científicas.

Este trabajo no podría haberse llevado a cabo sin la supervisión de la tutora y directora del mismo, quien ha sido parte activa durante todo el proceso, y ha contado con la participación de alumnado de grado en prácticas obligatorias y de alumnado de posgrado, así como de colaboradores externos que han participado en la valoración de las personas participantes para su inclusión en el estudio.

La investigación se ha llevado a cabo en instalaciones y con recursos de la Universidad del País Vasco/Euskal Herriko Unibertsitatea (UPV/EHU), Facultad de Educación y Deporte (Sección Ciencias de la Actividad Física y del Deporte) y del Departamento de Educación Física y Deportiva de la UPV/EHU. Además, las becas de la UPV/EHU (GIU14/21 y EHU14/08) así como la beca SAIOTEK del Gobierno Vasco (SAI12/217) han ayudado en la financiación de la investigación. El Igualatorio Médico Quirúrgico (IMQ) de Vitoria-Gasteiz ha participado de forma altruista con la colaboración de sus especialistas médicos Javier Pérez Asenjo y Rodrigo Aispuru. Exercycle S.L. (BH Fitness Company) ha donado material deportivo que ha facilitado la intervención de ejercicio físico. Tres integrantes del grupo de investigación que han participado de forma activa en este proyecto disfrutan de una beca predoctoral del Gobierno Vasco (Ilargi Gorostegi, Pablo Corres y Aitor Mtz. de Aguirre).

No ha existido conflicto de interés alguno a la hora de realizar esta investigación, y las becas y ayudas no han repercutido en los resultados obtenidos y presentados.

RECOMENDACIONES PARA LA LECTURA

La tesis doctoral que tiene entre manos se ha realizado en forma de compendio de artículos. Para seguir el hilo de los contenidos que forman este trabajo, se debe partir de la introducción en el primer capítulo, que sirve como justificación de la necesidad de este estudio, da cohesión a los apartados siguientes, y establece el estado de la cuestión referente a las pruebas de valoración de la capacidad cardiorrespiratoria y a los efectos del ejercicio físico en personas con hipertensión arterial primaria y sobrepeso u obesidad.

En el segundo capítulo se marcan los objetivos y se plantean las hipótesis de investigación que se han resuelto siguiendo la metodología descrita en el tercer capítulo.

Los capítulos 4-6 ahondan en el estado de la cuestión de los distintos objetivos de investigación de forma más específica, concretan la medología que se tiene en cuenta para cada apartado, y presentan los resultados de investigación; se trata de tres artículos científicos publicados en revistas internacionales indexadas en *Journal Citation Reports* y/o en *Scopus*. El capítulo cuarto corresponde al artículo "*Association between modified shuttle walk test and cardiorespiratory fitness in overweight/obese adults with primary hypertension: EXERDIET-HTA study"*, que presenta la adaptación de un test de campo para la valoración de la capacidad cardiorrespiratoria, de forma que se ajuste a las características de la población de estudio. En el siguiente capítulo, el artículo *"Validity of the modified shuttle walk test to assess cardiorespiratory fitness after exercise intervention in overweight/obese adults with primary hypertension"* comprueba si la adaptación del test creada es válida para hacer el seguimiento de la capacidad cardiorrespiratoria a lo largo del tiempo y después de una intervención con ejercicio físico. Por último, en el capítulo sexto, el artículo *"Effects of different exercise training programmes on cardiorespiratory fitness in overweight/obese adults with hypertension: a pilot study"* compara los efectos de distintos tipos, intensidades y duraciones de ejercicio físico aeróbico en la salud cardiovascular de las personas participantes en un estudio piloto previo a un ensayo controlado y aleatorizado.

En la parte final de esta tesis se presentan las conclusiones (cap.7), las limitaciones del trabajo y las propuestas para futuras investigaciones (cap.8).

Esta tesis se ha elaborado en castellano, pero al haber sido los artículos que la componen redactados en inglés, algunos capítulos están escritos en inglés; por lo tanto, a lo largo de este documento se van a encontrar las dos lenguas. En las primeras páginas del documento podrá leer dos listas de abreviaturas, en castellano e inglés, respectivamente. El formato de los artículos ha sido cambiado para crear un trabajo más homogéneo y hacer más fácil su lectura, aunque existe copia de los originales en los anexos al final del documento.

ABREVIACIONES

AC: grupo de atención-control.

AF: actividad física.

ACC: Colegio Americano de Cardiología.

AHA: Sociedad Americana del Corazón.

CCR: capacidad cardiorrespiratoria.

CEISH: Comité de Ética para la Investigación relacionada con Seres Humanos.

CG: grupo control.

CPET: test de esfuerzo cardiopulmonar.

CV: cardiovascular.

ECG: electrocardiograma.

ECV: enfermedad cardiovascular.

EF: ejercicio físico.

ESC: Sociedad Europea de Cardiología.

ESH: Sociedad Europea de Hipertensión.

FC: frecuencia cardiaca.

FITT: principio *FITT*; frecuencia, intensidad, tiempo y tipo.

HIIT: entrenamiento interválico de intensidad vigorosa.

HTA: hipertensión arterial.

HV-HIIT: entrenamiento interválico de intensidad vigorosa y volumen alto.

IMC: índice de masa corporal.

IPAQ: cuestionario internacional de actividad física.

ISWT: test incremental de ida y vuelta caminando.

LV-HIIT: entrenamiento interválico de intensidad vigorosa y volumen bajo.

MAPA: monitor ambulatorio de presión arterial.

MET: costo metabólico del EF.

MICT: entrenamiento continuo de intensidad moderada.

MSWT: test de ida y vuelta caminando modificado.

n: tamaño muestral.

OMS: Organización Mundial de la Salud.

PA: presión arterial.

PAD: presión arterial diastólica.

PAS: presión arterial sistólica.

RCV: riesgo cardiovascular.

RER: intercambio respiratorio.

RPE: escala de percepción del esfuerzo.

UPV/EHU: Universidad del País Vasco/Euskal Herriko Unibertsitatea.

UV_1: umbral ventilatorio 1.

UV_2: umbral ventilatorio 2.

$\dot{V}CO_2$: producción de dióxido de carbono.

$\dot{V}O_2$: consumo de oxígeno.

$\dot{V}O_{2pico}$: consumo de oxígeno pico.

ABBREVIATIONS

AC: attention-control group.

AGA: ambulatory gas analyzer.

ANCOVA: analysis of covariance.

BM: body mass.

BMI: body mass index.

BP: blood pressure.

CEISH: Ethics Committee for the Research with Human Beings.

CG: control group.

CI: confidence interval.

COPD: chronic obstructive pulmonary disease.

CRF: cardiorespiratory fitness.

CPET: cardiopulmonary exercise test.

CVD: cardiovascular disease.

CVR: cardiovascular risk.

DBP: diastolic blood pressure.

ECG: electrocardiogram.

f: effect size, Cohen's *f.*

FITT: *FITT* principle; frecuency, intensity, time, type.

g: effect size, Hedge's *g.*

HTN: arterial hypertension.

HR: heart rate.

HV-HIIT: high-volume and high-intensity interval training.

ICC: intraclass correlation coefficient.

ISWT: incremental shuttle walk test.

LV-HIIT: low-volume and high-intensity interval training.

MET: metabolic equivalent of task.

MICT: moderate-intensity continuous training.

MSWT: modified shuttle walk test.

n: sample size.

P: *P*-value, significant differences.

r: Pearson's coefficient of correlation.

r^2: coefficient of determination.

RER: respiratory exchange.

RPE: rate of perceived exertion.

SBP: systolic blood pressure.

SD: standard deviation.

SEE: standard error of estimate.

UPV/EHU: University of the Basque Country.

$\dot{V}O_2$: oxygen uptake.

$\dot{V}O_{2peak}$: peak oxygen uptake.

WHO: World Health Organization.

WHR: waist-to-hip circumference ratio.

Índice

ÍNDICE

Resumen

Finalidad: esta tesis doctoral la componen distintos estudios que se basan en **(a)** la creación y evaluación de una nueva ecuación aplicable al Modified Shuttle Walk Test (MSWT) para realizar la valoración indirecta y el seguimiento de la capacidad cardiorrespiratoria (CCR) tras una intervención de ejercicio físico (EF), y **(b)** la comparación de los efectos que se producen en la CCR tras intervenciones de EF de intensidad, duración y tipo distintos.

Métodos: entre los años 2011 y 2017, un total de 265 personas adultas y sedentarias diagnosticadas con hipertensión arterial (HTA) primaria y sobrepeso u obesidad participaron en el proyecto de investigación EXERDIET-HTA. Esas personas fueron aleatoriamente asignadas a uno de los grupos de intervención de EF aeróbico supervisado (entrenamiento continuo a intensidad moderada, MICT; o entrenamiento interválico a intensidad vigorosa, HIIT), o a un grupo control (CG). Antes de comenzar y después de haber finalizado las intervenciones que duraron 8, 12 o 16 semanas, cada participante realizó distintas pruebas de valoración, entre las que se incluyeron mediciones antropométricas, un test de esfuerzo cardiopulmonar con protocolo incremental en rampa sobre cicloergómetro, y un test de campo de velocidad incremental conocido como MSWT. Los dos test se desarrollaron hasta el agotamiento, o hasta obtener valores pico en la CCR. En ambos test se registraron valores de reposo, submáximos durante la prueba y valores pico de variables como la frecuencia cardiaca, percepción del esfuerzo, presión arterial, y distancia recorrida, así como variables ventilatorias en el test cardiopulmonar, especialmente el consumo de oxígeno pico ($\dot{V}O_{2pico}$), indicador predilecto de la CCR.

Resultados: **(a)** el $\dot{V}O_{2pico}$ medido mostró una correlación fuerte ($r = 0.72$, $P < 0.001$; error de estimación de 4.35 $mL·kg^{-1}·min^{-1}$, 19 %) con una combinación de variables registradas en el MSWT (distancia total, frecuencia cardiaca de reposo, masa corporal y sexo) antes de comenzar la intervención, con lo que se creó una ecuación para estimar la CCR aplicada al MSWT. Se evaluó la validez de la ecuación creada con registros obtenidos tras las intervenciones de EF: la correlación entre el $\dot{V}O_{2pico}$ medido y el estimado resultó fuerte ($r = 0.76$, $P < 0.001$; error de estimación de 4.9 $mL·kg^{-1}·min^{-1}$, 17 %), con un nivel de fiabilidad moderado ($ICC = 0.69$; *95 % CI* 0.34-0.82; $P < 0.001$) que mostró mayor precisión cuando se tenía en cuenta solo a las personas obesas ($ICC = 0.76$; *95 % CI* 0.52-0.87; $n = 128$). El cambio medido en la CCR tras la intervención de EF correlacionó de forma débil con el calculado a través de la ecuación de estimación ($r = 0.42$, $P < 0.001$; con 31 % de error de estimación) y obtuvo un nivel de fiabilidad bajo ($ICC = 0.31$; *95 % CI* 0.06-0.49; $P < 0.001$). **(b)** En lo que respecta a los efectos en la CCR tras las diferentes intervenciones de EF, se observaron incrementos del $\dot{V}O_{2pico}$ en los grupos de EF supervisado (MICT, 3.8 ± 3.3 $mL·kg^{-1}·min^{-1}$, $g = 0.6$; HIIT, 4.2 ± 4.7 $mL·kg^{-1}·min^{-1}$, $g = 0.7$; $P < 0.001$). Las diferencias respecto a los CG en los que no se observaron cambios ($g < 0.1$) fueron sustanciales ($P < 0.02$; $g > 0.8$), principalmente debido al efecto del HIIT. Las mejoras en la CCR ocurrieron en las intervenciones de EF supervisado de 12 y 16 semanas, y no en las de 8 semanas o CG que mostraron efectos pequeños.

Conclusión: (a) los resultados indican que la estimación de la CCR a través de la ecuación creada para ser aplicada al MSWT en personas con HTA primaria y sobrepeso u obesidad reporta un error de estimación sustancial, sobre todo a la hora de hacer un seguimiento de la CCR tras una intervención, por lo que su validez es cuestionable; este método de valoración podría tener utilidad en personas con HTA y obesidad (no sobrepeso), cuando la valoración directa con test cardiopulmonar no esté disponible. **(b)** este estudio muestra que las intervenciones con MICT y HIIT producen efecto cardioprotector en personas con HTA primaria y sobrepeso u obesidad. Las intervenciones de corta duración (< 12 semanas) no parecen ser efectivas para la mejora de la CCR, y el HIIT podría resultar en mayores ganancias de CCR, que parecen aumentar al alargar la duración de la intervención.

Palabras clave: consumo de oxígeno pico, test de campo, ecuación de estimación, actividad física, diseño de ejercicio físico, enfermedad cardiovascular.

Capítulo 1.

Introducción

1. Introducción

Las enfermedades cardiovasculares (ECV) son la causa principal de morbilidad y mortalidad en el mundo provocando un enorme impacto en la calidad de vida y en costes relacionados con el cuidado de la salud.[1] En el año 2016, 17.8 millones de muertes se debieron a ECV, que supusieron el 31.4 % de las defunciones a nivel mundial.[2] También en el conjunto de la población española, las ECV constituyen la primera causa de morbilidad y mortalidad: en 2016 causaron 119 778 muertes (328 muertes cada día), lo que supone el 29.2 % de todas las defunciones,[3] y supusieron el 14.8 % de todas las estancias hospitalarias y el 12.5 % de todas las altas hospitalarias.[4] Además, cinco de las diez principales amenazas mundiales para la salud están relacionadas con las ECV, como la hipertensión arterial (HTA), el tabaquismo, el consumo de alcohol, la hipercolesterolemia y la obesidad o el sobrepeso.[5] El 9 % del gasto sanitario total de la Unión Europea en 2009 (106 000 millones de euros) fue destinado a la prevención de ECV, lo que supone una carga económica que requiere medidas.[6]

Es fundamental conocer los factores de riesgo que predisponen a padecer ECV, especialmente los factores de riesgo modificables. La implementación de un tratamiento que disminuya los valores excesivos de presión arterial (PA), de masa grasa, y de otros factores de riesgo modificables, como la hipercolesterolemia, diabetes mellitus tipo 2, sedentarismo/inactividad física, estrés, tabaquismo y alcoholismo es esencial para contribuir a reducir la incidencia de ECV y para paliar la elevada tasa de mortalidad por causas cardiovasculares (CV).[7,8]

España presenta un patrón de muerte coronaria semejante al de otros países mediterráneos, claramente inferior al de los países del centro y norte de Europa y Norteamérica. Esa tasa inferior de mortalidad coronaria se atribuye a la dieta mediterránea y a otros hábitos de vida como la actividad física (AF).[5] Se ha observado una tendencia a la baja en las tasas de mortalidad por ECV desde 1975, con un descenso anual medio del 3.1 % hasta 2004,[5] mientras que a partir del 2005 el descenso anual medio ha sido del 0.5 %;[9] sin embargo, la tendencia a nivel mundial es al alza (desde el año 2000 las muertes por ECV han aumentado un 3.5 % más que la población, y la tasa de muerte por causa CV ha aumentado un 4.1 %, hasta el 31.4 % actual)[2]. En lo que respecta a la tendencia de las tasas de morbilidad hospitalaria de las ECV, ha ido en aumento en los últimos años.[4]

La tasa de mortalidad CV aumenta exponencialmente a medida que incrementa la edad, siendo la causa líder a partir de los 79 años (33.6 % de los fallecidos de este grupo de edad), y la segunda causa de muerte a partir de los 40 años. Sin embargo, dado que los ancianos son los que tienen las tasas de mortalidad más elevadas, para el conjunto de todas las edades las ECV ocupan el primer lugar como causa de muerte, y la segunda causa en cuanto a años potenciales de vida perdidos de personas menores de 79 años (19 %), después de los tumores (44 %). Por sexo, son más mujeres (54 %) que hombres las que mueren por estas causas, siendo los tumores la principal causa de muerte entre varones, seguido de las ECV.[3]

Según la Guía de Manejo de la Hipertensión arterial del 2013,[10] distintos estudios han considerado la HTA como factor de riesgo principal que predispone a padecer ECV y lesiones derivadas. El sobrepeso u obesidad y la HTA coexisten frecuentemente en la misma persona siendo aditivos en términos de riesgo cardiovascular (RCV).

1.1. Hipertensión arterial

La PA es la presión o fuerza que ejerce la sangre a su paso por las paredes de las arterias, y se cuantifica con dos valores: PA sistólica (PAS) y PA diastólica (PAD), medidas en milímetros de mercurio (mm Hg). La PAS representa el pico de presión que corresponde con la contracción ventricular, durante la sístole, mientras que la PAD representa la presión durante la relajación ventricular, la diástole.[11]

Los valores de PA tienen una distribución normal en la población, y no hay un punto de corte natural sobre el cual se pueda considerar la existencia de HTA, ni bajo el que la PA se considere normal o baja. Sin embargo, queda demostrado en diversos estudios epidemiológicos que el incremento de los valores de PA mantenida en el tiempo puede causar lesiones y enfermedad asociada a la PA en distintos órganos. Así, el RCV aumenta de forma progresiva y lineal por encima de mediciones de 115/75 mm Hg (donde 115 representa la PAS, y 75 la PAD), y el riesgo de padecer eventos CV se dobla por cada 20/10 mm Hg que se eleva la PA. Teniendo en cuenta estas estimaciones del riesgo para la salud que supone la PA alta, se establece un umbral de PA como criterio que determina la presencia de HTA. La HTA se refiere a la mayoría de la población con valores de PA elevados de forma crónica, y el umbral de HTA lo concretan los valores de PA sobre el que el tratamiento puede reducir la evolución de la enfermedad, dando así unos límites con valores ≥ 140 mm Hg para la PAS y/o ≥ 90 mm Hg para la PAD según la Sociedad Europea de la Hipertensión (ESH) y la Sociedad Europea de Cardiología (ESC) (Tabla 1)[10,11].

Tabla 1. Definiciones y clasificación de los valores de presión arterial (mm Hg).[10]

Categoría	PAS		PAD
Óptima	< 120	y	< 80
Normal	120-129	y/o	80-84
Normal alta	130-139	y/o	85-89
Hipertensión grado 1	140-159	y/o	90-99
Hipertensión grado 2	160-179	y/o	100-109
Hipertensión grado 3	≥ 180	y/o	≥ 110

PAD = presión arterial diastólica; PAS = presión arterial sistólica.

Se pueden distinguir dos tipos de HTA, dependiendo de la o las causas que la hayan originado: primaria y secundaria. La HTA primaria o idiopática se refiere a que no existe una causa obvia o identificable que haya promovido su desarrollo. El 90 % de las personas con HTA padece de este tipo desconocido, mientras que el 10 % restante, responde a la denominada HTA secundaria, que puede ocurrir por distintas causas específicas: adenoma de Conn, enfermedad reno- vascular, feocromocitoma, hipotiroidismo o hipertiroidismo, apnea obstructiva del sueño, acromegalia, o consumo de drogas. Los casos de HTA secundaria, donde hay una causa identificable, suelen ser más abundantes en personas menores de 40 años.[11]

Un gran número de estudios observacionales ha puesto de manifiesto que la morbilidad y mortalidad CV mantienen una relación continua con la PA, incluso cuando las elevaciones son ligeras,[5,10] por lo que la HTA representa un factor de riesgo independiente, común y elevado de sufrir ECV y sus consiguientes eventos en el corazón y/o vasos sanguíneos (accidente cerebro vascular, infarto de miocardio, insuficiencia cardiaca, ECV periférica), así como enfermedad crónica de riñón, deterioro cognitivo, y muerte prematura.[11,12] Tanto la PAS como la PAD muestran una relación independiente y gradual con todas estas ECV y otras relacionadas.[10]

La HTA es sorprendentemente común en el contexto internacional, especialmente en la población europea, y su prevalencia se ve influenciada por factores como la edad y el estilo de vida. La elevación de la PAS es la característica dominante de HTA en personas de mayor edad, mientras que quienes suelen tener la PAD más elevada son más jóvenes (menores de 50 años). Al menos un cuarto de la población adulta a nivel mundial tiene HTA. Del total de afectados por HTA, 1/3 corresponde a países económicamente desarrollados, y los restantes 2/3, a países en vías de desarrollo en los que la tasa de HTA es cada vez mayor.[12-14] En el caso de los Estados Unidos de América (EEUU), se calcula que 98 millones de adultos (casi el 30 % de la población adulta) tienen HTA,[15] aunque la nueva Guía para la HTA en personas adultas de la Sociedad Americana del Corazón (AHA) y del Colegio Americano de Cardiología (ACC)[16] define las categorías de PA de un modo más estricto, no considerando que haya valores óptimos sino normales, definiendo como PA elevada lo que para la ESH y la ESC son valores normales, y disminuyendo el umbral considerado como HTA a lo que eran valores normales altos, de modo que la prevalencia de HTA ha crecido, y la cantidad de personas potenciales receptoras de tratamiento para la reducción de la PA ha aumentado un 14 % en el país, llegando a afectar al 46 % de la población adulta.[17] La prevalencia de HTA en la población adulta de España es elevada: aproximadamente el 35 % de personas mayores de 18 años tienen HTA (PA ≥ 140/90 mm Hg o en tratamiento farmacológico anti-hipertensivo). Estas cifras se elevan exponencialmente cuanto mayor es la edad de la población, subiendo al 40-50 % en edades medias, y al 68 % en mayores de 60 años.[5] Se prevé que la prevalencia de HTA y la necesidad de tratamientos sigan creciendo, ya que la población es cada vez de mayor edad, más sedentaria y más obesa,[5,11,12] tres de los factores que afectan de manera directa a la PA. De hecho, según un análisis sobre la tendencia de la carga que supone la HTA a nivel mundial, se estima que las personas afectadas por HTA en el año 2025 serán 1.5 billones, pasando del 26.4 % en 2000, al 29.2 % de la población adulta.[13,18]

Los riesgos para la salud que supone la PA alta, junto con la gran prevalencia de HTA en la población, explica que en un informe de la Organización Mundial de la Salud (OMS) se haya citado la HTA como primera causa de muerte en todo el mundo,[10] que en 2010 provocó la pérdida del 7 % del total de años de vida y 9.4 millones de muertes, 2.1 millones de muertes más que en 1990;[6] al considerarse el factor principal de afecciones CV, también es la causa de ECV modificable más potente, relacionada con estilos de vida cada vez más sedentarios, con una mala alimentación, y tendentes a tasas de sobrepeso y obesidad cada vez mayores.[14]

1.2. Sobrepeso y obesidad

La obesidad o tener sobrepeso se consideran condiciones médicas en las que se presenta un exceso de acumulación de grasa corporal que puede tener efectos perjudiciales para la salud. Los puntos de corte de porcentaje de masa grasa más habituales para definir el sobrepeso son 20.1 % y 30.1 %, y para definir la obesidad 25 % y 35 %, para hombres y mujeres, respectivamente.[19] El índice de masa corporal (IMC) es un indicador simple de la relación entre la masa corporal y la talla que se utiliza junto con otras medidas antropométricas para identificar el sobrepeso y la obesidad en personas adultas; se calcula dividiendo la masa corporal de una persona en kilogramos por el cuadrado de su talla en metros ($kg \cdot m^{-2}$).[20] La OMS clasifica como sobrepeso los valores de IMC ≥ 25 $kg \cdot m^{-2}$ y como obesidad el IMC ≥ 30 $kg \cdot m^{-2}$ (Tabla 2).[21] El IMC proporciona la medida más útil del sobrepeso y la obesidad en la población, puesto que es la misma para personas adultas de cualquier edad y sexo. Sin embargo, debe ser considerada a título indicativo porque es posible que no se corresponda con el mismo nivel de adiposidad en diferentes personas, ya que no distingue la masa muscular de la grasa.[22] Se recomienda medir el perímetro de cintura como indicador de grasa visceral, para obtener información adicional sobre la composición corporal y poder detectar cambios en la misma;[23] de hecho, se estima que usando solo el IMC no se detecta la mitad de la población con exceso de grasa.[19,22] El IMC junto con el perímetro de cintura sirven para estimar el RCV relacionado con la adiposidad. Los valores de perímetro de cintura ≥ 94 cm en hombres y ≥ 80 cm en mujeres en Europa se asocian con obesidad central y RCV y metabólico más elevado[24] (los umbrales de perímetro de cintura para valorar la obesidad varían según grupos étnicos)[21]. A las mediciones antropométricas mencionadas para la valoración de la composición corporal se les puede añadir métodos más sofisticados como la absorciometría dual de rayos X (DEXA), o la impedancia bioeléctrica, que determina la proporción de masa corporal correspondiente a masa grasa midiendo el agua corporal correspondiente a masa muscular.[25]

Tabla 2. Clasificación de la OMS sobre el estado nutricional de acuerdo con el IMC.[20]

Categoría	IMC (kg·m^{-2})
Masa corporal insuficiente	< 18.50
Normopeso	18.50 – 24.99
Sobrepeso	≥ 25.00
Grado I	25.00 – 27.49
Grado II	27.50 – 29.99
Obesidad	≥ 30.00
Grado I	30.00 – 34.99
Grado II	35.00 – 39.99
Grado III/Mórbida	≥ 40.00

IMC = índice de masa corporal.

La obesidad es una enfermedad crónica, multifactorial, de prevalencia creciente, que junto con el sobrepeso, afecta a más de la mitad de la población en los países desarrollados, por lo que fue considerada por el Grupo de Trabajo Internacional por la Obesidad y la OMS, como la epidemia del siglo XXI.[26] El incremento en la masa adiposa corporal y del IMC que se ha producido en las últimas décadas va acompañada de profundos cambios sociales, demográficos y culturales, y se debe fundamentalmente a dos factores: por un lado, el consumo excesivo de alimentos de gran contenido calórico y, por otro, la disminución de la AF, imponiéndose un estilo de vida cada vez más sedentario.[27-29] Las enfermedades asociadas al sobrepeso y la obesidad suponen un amplio espectro de complicaciones, desde la HTA, hiperinsulinemia, dislipidemia, diabetes mellitus tipo 2, inflamación sistémica, eventos CV y hasta el agravamiento de enfermedades relacionadas con el asma bronquial.[6,30,31] Así, la obesidad, tiene para la sociedad importantes costes directos e indirectos que exigen múltiples recursos sanitarios y económicos; es responsable del 10-13 % de las defunciones y del 2-8 % de los costes económicos en los países de la Unión Europea.[32] El sobrepeso y la obesidad están asociados con el aumento del RCV y con el riesgo de muerte por cualquier causa,[6] y al igual que la HTA, también constituyen factores de riesgo de ECV modificables.[29,33]

1.3. Riesgo cardiovascular

Se denomina RCV a la probabilidad de desarrollar un episodio CV, y suele expresarse en forma de riesgo de que ocurra en un plazo de 10 años. El RCV lo determinan los valores de PA, la presencia de lesiones en los órganos diana, ECV establecida (isquemia, insuficiencia cardiaca, enfermedad cerebro vascular…), y otros factores de riesgo para la ECV, como estilos de vida no saludables en cuyo cambio habrá que insistir (dieta, tabaquismo, obesidad, inactividad, sedentarismo), diabetes y dislipidemia.[10,11]

Diversos estudios[11] han examinado y evaluado el RCV que supone la presencia en mayor o menor medida de HTA: se ha comprobado que la reducción de 20/10 mm Hg en la PA habitual de hombres y mujeres con edades comprendidas entre los 40 y 89 años, está asociada con una disminución a la mitad de muertes debidas a eventos relacionados con accidentes cerebro vasculares o enfermedad isquémica de corazón, o que la reducción de 5, 7.5 y 10 mm Hg en la PAS correlaciona con reducciones de accidente cerebro vascular del 34 %, 46 % y 56 %, respectivamente, y reducciones de enfermedad coronaria del 21 %, 29 % y 37 %, respectivamente.

Tal y como se observa en la Figura 1, para estratificar el RCV, además de tener en cuenta la clasificación de la PA (Tabla 1), se califican otros factores o enfermedades que aumentan el riesgo. Cuanto mayor sea el grado de HTA y más factores añadidos se observen, mayor tenderá a ser el RCV.[10]

Otros factores de riesgo, LO asintomática o enfermedad de órganos	**Presión arterial**			
	Normal alta	**HTA grado 1**	**HTA grado 2**	**HTA grado 3**
Sin otros factores de riesgo		RCV bajo	RCV moderado	RCV alto
1-2 factores de riesgo	RCV bajo	RCV moderado	RCV moderado-alto	RCV alto
3 o más factores de riesgo	RCV bajo-moderado	RCV moderado-alto	RCV alto	RCV alto
LO, ERC en fase 3, o diabetes	RCV moderado-alto	RCV alto	RCV alto	RCV alto-muy alto
ECV sintomática, ERC fase ≥ 4, o diabetes con LO/otros factores de riesgo.	RCV muy alto	RCV muy alto	RCV muy alto	RCV muy alto

Figura 1. Estratificación del RCV en categorías, en relación a la PA y otros factores de riesgo.[10]

ECV = enfermedad cardiovascular; ERC = enfermedad renal crónica; HTA = hipertensión arterial; LO = lesión de órganos; RCV = riesgo cardiovascular.

Se ha comprobado que las personas con HTA también suelen tener sobrepeso u obesidad, y que son físicamente inactivas,[34] siendo todos ellos factores aditivos en cuanto al RCV.[35] Los estudios indican que la HTA y la obesidad son dos de las causas de morbilidad y mortalidad prematura más prevenibles a nivel mundial, que pueden ser tratadas de forma efectiva, disminuyendo de esta forma la ocurrencia de las ECV, y que si la HTA no es tratada, está asociada a una elevación progresiva en la PA, a menudo culminando en estado resistente al tratamiento, debido a daño vascular y renal asociado.[5,11]

Como medida para la reducción del RCV, se proponen distintos tratamientos; dependiendo de la estratificación del RCV se recomiendan cambios en el estilo de vida, y adicionalmente tratamiento farmacológico.[10] Se calcula que el 80 % de ECV puede prevenirse mediante cambios en los estilos de vida.[14] Los aspectos principales dentro de los estilos y hábitos de vida que pueden tener relación con los cambios en el RCV, especialmente en la PA, son la dieta, una baja ingesta de calcio, consumo de alcohol y tabaco, cafeína, suplementos de potasio y magnesio, sal (sodio), el sobrepeso, terapias de relajación, y AF entre otros.[11] Se hace hincapié en la baja eficacia del habitual consejo "*come menos y haz más ejercicio*", ya que la dieta y el ejercicio físico (EF) son dos de los principales objetivos de intervención, y recalca que para que estos tratamientos funcionen, además de disminuir la ingesta calórica y aumentar el gasto energético, resulta fundamental completarlos con técnicas para cambios de conducta,[6] que aumentan la eficacia de la adherencia a los nuevos estilos de vida.[29]

1.4. Coste-efectividad de los cambios en el estilo de vida en el riesgo cardiovascular

Varios estudios han puesto de manifiesto que, en pacientes de RCV alto o muy alto, el tratamiento de la obesidad y principalmente el de la HTA tienen una relación coste-efectividad muy favorable, es decir, que la reducción de la incidencia de ECV y muerte, compensan ampliamente los gastos de hospitalización y el coste del tratamiento, aunque este deba mantenerse durante toda la vida. De hecho, es probable que los efectos beneficiosos observados sean aun mayores que los calculados mediante el número de eventos CV evitados por año de tratamiento y expresados mediante el número de pacientes que es necesario tratar.[15,36]

Los cambios en el estilo de vida que se pueden llevar a cabo para disminuir el RCV son principalmente el cambio conductual, evitar comportamientos sedentarios y aumentar los niveles de AF, una alimentación saludable, y posibles restricciones en el consumo de algunos nutrientes, así como evitar el consumo de alcohol y tabaco. Considerando estas medidas en el estilo de vida como carentes de coste, y teniendo en cuenta la efectividad en que resultan, la relación coste-efectividad es más que considerable.[6]

1.5. Capacidad cardiorrespiratoria

La capacidad cardiorrespiratoria (también condición o fitness cardiorrespiratorio, CCR) se conoce como la capacidad que tienen los sistemas respiratorio y circulatorio de aportar oxígeno a la musculatura esquelética durante una AF continuada.[37,38] La valoración de la CCR representa una conclusión clínica importante en la evaluación del RCV, de gran interés como indicador para barajar comorbilidades. Recientemente, se ha considerado signo vital, ya que es un predictor fuerte e independiente de mortalidad por toda causa.[37] Resulta esencial como punto de partida para la evaluación y seguimiento del RCV, y para la programación de intervenciones no farmacológicas como el EF o la dieta.[6,10,37]

Este proyecto de investigación consta de dos áreas de interés principales en relación a la salud de las personas con HTA primaria y sobrepeso u obesidad, que están estrechamente ligadas al concepto de RCV: (1) valoración de la CCR, y (2) efectos del EF en la CCR.

1.5.1. Valoración de la capacidad cardiorrespiratoria

El consumo de oxígeno ($\dot{V}O_2$) pico ($\dot{V}O_{2pico}$) es la medida de referencia (*gold standard*) de la CCR.[34] Algunos estudios concluyen que el $\dot{V}O_{2pico}$ es el parámetro a utilizar para valorar el nivel de salud; así, las personas con mayor $\dot{V}O_{2pico}$ tienden a vivir más tiempo, incluso aunque muestren factores de riesgo ya establecidos asociados a ECV u obesidad.[39,40] La unidad de medida del $\dot{V}O_2$ puede expresarse de forma absoluta o de forma relativa a la masa corporal, indicando el consumo en volumen de oxígeno por minuto: $L \cdot min^{-1}$ y $mL \cdot kg^{-1} \cdot min^{-1}$, respectivamente. Otra medida para expresar la capacidad cardiorrespiratoria es el *MET* (*metabolic equivalent of task)*, que indica el costo energético de la AF y equivale a un $\dot{V}O_2$ de 3.5 $mL \cdot kg^{-1} \cdot min^{-1}$. El *MET* se usa como referencia de la intensidad del EF, que se calculará a partir del gasto metabólico de reposo, o lo que es lo mismo, el costo energético en *MET*s cuando no se está practicando AF.[41] El incremento de cada 1 *MET* en el $\dot{V}O_{2pico}$ aumenta la esperanza de vida de las personas en un 10-25 %.[37]

El $\dot{V}O_{2pico}$ se conoce a través de medición directa en un test de esfuerzo cardiopulmonar (CPET, del inglés *cardiopulmonary exercise test*); este procedimiento no está siempre disponible y su precio es elevado, por lo que existen gran variedad métodos para estimar la CCR o valores de $\dot{V}O_2$ submáximos sin medición directa, como pruebas de esfuerzo, diversos test de campo que simulan el CPET, y ecuaciones de regresión para estimar el $\dot{V}O_{2pico}$. Los métodos alternativos al CPET son cada vez más utilizados y en poblaciones clínicas más específicas, pero la estimación indirecta de la CCR[38] conlleva un error de estimación entre 4.2 y 7.0 mL de $O_2 \cdot kg^{-1} \cdot min^{-1}$, por lo que se recomienda la obtención de esta información a través de un modo objetivo y directo cuando esté disponible, especialmente para la valoración de personas con RCV.[37]

Los test de campo y demás métodos de estimación del $\dot{V}O_{2pico}$ resultan en una valoración eficaz que permite hacer seguimiento de la CCR a lo largo del tiempo, y en el caso de tratamientos con EF, facilitan el diseño de la intensidad de ejercicio.[38] Ejemplo de ello es el test incremental de ida y vuelta caminando (incremental shuttle walk test, ISWT),[42] o su variante (modified shuttle walk test, MSWT),[43] test de campo de aplicación sencilla que han sido probados y validados para estimar el $\dot{V}O_{2pico}$ en distintas poblaciones a partir de la distancia recorrida y otras variables registradas en la misma prueba.[44] El ISWT y el MSWT no han sido validados para personas con HTA y sobrepeso u obesidad; si estos test pudiesen ofrecer la información que se obtiene a través de CPET de forma válida, fiable y precisa, supondría un avance en la medición y valoración de la CCR, en la estimación del RCV y en la programación de EF de estas personas, ya que simplificaría y abarataría el proceso.

1.5.2. Efectos del ejercicio físico en factores de riesgo cardiovascular y recomendaciones actuales

Según se ha podido comprobar, los hábitos de vida sedentarios o la práctica reducida de EF aeróbico son fuertes predictores de futura ECV y de toda causa de mortalidad,[18] independientemente de la AF.[45] Al mismo tiempo, la ESC, la ESH, la AHA, el ACC y el Colegio Americano de Medicina del Deporte recomiendan la práctica habitual de EF aeróbico, con el fin contrario, la prevención CV, induciendo mejoras sustanciales en la salud física y mental.[6,46-48]

Todas las guías internacionales[6,10,16,24,48-50] promueven la AF como estilo de vida efectivo y una prioridad para prevenir y tratar la HTA primaria y la obesidad, así como terapia no farmacológica para reducir el RCV y minimizar la necesidad de medicación. Son muchos los estudios realizados en torno al efecto que tiene el EF en la PA, tanto en personas con HTA como con normo-tensión, así como en la composición corporal de personas con distintos niveles de IMC. El EF afecta de forma favorable a los factores de RCV: además de la reducción de la PA, trae consigo otros beneficios para la salud CV, como reducción de la masa corporal, de la adiposidad visceral y total, y del perímetro de cintura, e incremento en el uso de la glucosa, aumento de sensibilidad a la insulina y de concentraciones de lipoproteínas de alta densidad, y reducción de concentraciones de lipoproteínas de baja densidad.[6,10,51,52] El RCV se ve también disminuido por la mejora de la CCR, por pequeña que esta sea;[53] el riesgo resulta menor cuanto mayor es la capacidad aeróbica, llegando a considerar que las personas en baja forma física tienen el doble de riesgo de muerte, independientemente del IMC.[54]

Se ha analizado la respuesta de la PA, composición corporal y CCR frente a estímulos de EF, de frecuencia, intensidad, tiempo o duración, y tipo variados (variables de la carga de entrenamiento que con sus iniciales determinan el principio *FITT*). El entrenamiento aeróbico es la modalidad de EF más estudiada y recomendada. Se diferencian dos tipos de EF aeróbico principales: entrenamiento aeróbico continuo, cuando se lleva a cabo una sesión en un periodo de tiempo de forma continua a una intensidad moderada-vigorosa; y entrenamiento aeróbico interválico, que consiste en alternar periodos de corta duración e intensidad vigorosa, con periodos de recuperación desarrollados a menor intensidad o incluso sin carga.[55]

Los resultados obtenidos con distintas combinaciones de los componentes *FITT* son muy diversos. Así, se ha observado que el efecto anti-hipertensivo del EF aeróbico reduce la PAS entre 3 y 10.5 mm Hg, y la PAD entre 2 y 7.6 mm Hg.[46,47,52] Aunque se haya demostrado que existe relación lineal entre la dosis de EF y la reducción en la PA, no siempre ha sido una relación estadísticamente significativa.[56] Las distintas instituciones internacionales recomiendan la práctica de EF aeróbico como principal método de entrenamiento para la reducción de la PA. Los estudios diseñados para comparar los efectos de EF de distintas intensidades concluyen que el EF aeróbico de intensidad baja y moderada (60 % - 85 % frecuencia cardiaca (FC) pico) son más eficaces que los de mayor intensidad para reducir la PA, lo que sugiere que el efecto anti-hipertensivo del EF ocurre en AF moderada, sin cambios sustanciales a partir de esa intensidad;[46,47,57,58] sin embargo, las últimas guías de práctica clínica de Europa también recomiendan realizar ejercicio aeróbico de intensidad vigorosa (hasta el 93 % FC máxima) y menor duración,[6] complementándolo con entrenamiento de fuerza muscular y ejercicios físicos neuromotores, a lo que otras guías añaden ejercicio de fuerza isométrica en extremidades superiores.[16]

La dosis de EF recomendada para el tratamiento de la obesidad no varía en exceso de unas guías a otras.[24,49] Se recomienda EF aeróbico de intensidad moderada por más de 150 minutos a la semana, repartidos en la mayoría de días posible para una modesta pérdida de masa corporal y para no aumentarla. Estas recomendaciones contrastan con otras que se hacían anteriormente, y que recomendaban 200-300 minutos a la semana para disminuir la masa corporal a largo plazo.[59] Aconsejan combinar el entrenamiento aeróbico con 3 sesiones no consecutivas de entrenamiento de fuerza a la semana. El entrenamiento de fuerza no disminuye la masa corporal, pero resulta en cambios de la composición corporal, aumentando la masa muscular y disminuyendo la masa grasa.[24]

Las guías de práctica clínica citadas[6,16] se centran primordialmente en los indicadores de RCV más conocidos, como la PA y composición corporal, y consideran otros indicadores como la CCR para barajar comorbilidades, y para evaluar y hacer seguimiento de la condición física. En lo que respecta a las recomendaciones de EF para mejorar la CCR, diversos estudios han demostrado que el EF aeróbico interválico de intensidad vigorosa mejora la forma física y reduce varios factores de riesgo relacionados con las ECV en mayor medida que el EF aeróbico continuo de intensidad moderada, también en personas con HTA.[60-65] Así, cabe mencionar estudios como el de Molmen-Hansen *et al.*, en el que se observó un incremento significativo del $\dot{V}O_2$ máximo tras entrenamientos continuos a intensidad baja, que resultó más pronunciado cuando se entrenó a intervalos de intensidad vigorosa (> 5 % *vs.* > 15 %), y en el que el EF aeróbico interválico de intensidad vigorosa se consideró superior al continuo de intensidad moderada en cuanto a mejora de la función cardiaca y de la capacidad aeróbica.[56]

Las más recientes recomendaciones en EF aeróbico para la prevención CV[6] concretan de la siguiente forma los componentes del principio *FITT*:

- *F*recuencia: mínimo 3 sesiones por semana, preferiblemente a diario.
- *I*ntensidad: moderada (64-76 % de la FC máxima) o vigorosa (77-93 % de la FC máxima).
- *T*iempo: al menos 150 minutos de AF moderada o 75 minutos de AF vigorosa por semana, que se pueden acumular en sesiones de más de 10 minutos. También se pueden combinar distintas intensidades.
    - Para un control más exhaustivo de la masa corporal se recomienda mayor volumen, en sesiones de mayor duración (60-90 minutos al día).
- *T*ipo: EF continuo (caminar, jogging, nadar…); el método interválico no se recomienda por el momento, y hasta que haya mayor evidencia sobre su seguridad y eficacia.

Además del entrenamiento aeróbico, se recomiendan al menos dos sesiones semanales de trabajo de fuerza muscular dinámica (bandas elásticas, calistenia, trabajo físico intenso), realizando en cada sesión 2-3 series de 8-12 repeticiones al 60-80 % de la repetición máxima individual, y ejercicios de equilibrio, agilidad, coordinación y marcha para los que no especifica la dosis recomendada.

Estudios de metodología similar que comparan distintas intervenciones de EF, concluyen en algunos casos que una dosis de EF es más efectiva a la hora de disminuir la PA, en otros casos es otra la que da mejores resultados, y en otros no se encuentran diferencias significativas entre ellas, por lo que lo publicado hasta el momento resulta contradictorio o confuso en muchos casos.[56,66] Las guías de prevención de ECV y tratamiento de la HTA y obesidad recomiendan dosis diferentes en las distintas modalidades de EF que contemplan. Así, los tipos de ejercicio, y límites máximos y mínimos de intensidad y duración que aconsejan varían de unas a otras, y existen contradicciones en cuanto a prácticas recomendadas o no recomendadas.[6,10,16] Debido a la ausencia de evidencia científica suficiente en aspectos relacionados con el diseño del EF y el RCV, las características adecuadas para un programa de EF siguen abiertas a debate,[51] ya que es complicado sacar conclusiones respecto a cuál es la mejor combinación de los componentes del principio *FITT*, es decir, la cuantificación de la dosis de EF necesaria, para que el beneficio trasladado a la salud sea óptimo y/o que conlleve el menor riesgo.[56] El mayor reto en el ámbito de la HTA + sobrepeso/obesidad y EF es concretar la mejor intervención para cada caso individual. Por ello, se deben comparar entrenamientos con diversas combinaciones de los componentes *FITT* que pueden afectar de diferente manera en la PA, composición corporal y CCR dependiendo de variables como el sexo, la edad, la raza, el grado de PA o IMC del que se parte, y otros factores de riesgo o enfermedades.[47]

Capítulo 2.

Objetivos e hipótesis

2. OBJETIVOS E HIPÓTESIS DE LA INVESTIGACIÓN

2.1. Objetivos

- Evaluar la relación entre el MSWT y la CCR en población con HTA y sobrepeso u obesidad, y desarrollar una ecuación para estimar la CCR en esa población.
- Evaluar la validez de la ecuación creada para la estimación de la CCR después de un programa de intervención de EF.
- Evaluar y comparar el efecto de dos programas de EF aeróbico de diferentes intensidades (continuo-moderado e interválico-vigoroso) en intervenciones de diferente duración (8, 12 y 16 semanas) en variables cardiorrespiratorias de personas con HTA y sobrepeso u obesidad, en un estudio piloto.

2.2. Hipótesis

- La ecuación existente para la estimación de la CCR en población con insuficiencia respiratoria tendrá un error de estimación grande en la población de estudio, aunque la relación entre el MSWT y la CCR sea grande. La nueva ecuación permitirá una estimación más precisa.
- Después del programa de intervención con EF, el MSWT permitirá una valoración precisa y válida de la CCR, aunque el error de estimación aumente.
- El programa de EF de mayor intensidad (interválico) provocará mejoras superiores en variables de la condición física en comparación con el EF de intensidad moderada en modo continuo.

Capítulo 3.

Metodología

3. METODOLOGÍA

El diseño, criterios de selección y procedimientos del estudio EXERDIET-HTA han sido previamente descritos.[67] El protocolo del estudio ha sido aprobado por el Comité de Ética para las Investigaciones relacionadas con Seres Humanos (CEISH) del Vicerrectorado de Investigación de la Universidad del País Vasco/Euskal Herriko Unibertsitatea (UPV/EHU, CEISH/56/2010 y CEISH/279/2014) y el Comité de Ética de Investigación Clínica del Hospital Universitario de Araba (2015-030). (Identificador Clinical Trials.gov, NCT02283047). Todas las pruebas y mediciones fueron realizadas en el mismo laboratorio de Análisis del Rendimiento Deportivo del Departamento de Educación Física y Deportiva de la UPV/EHU y por el mismo grupo de investigación.

3.1. Diseño

El presente estudio es un ensayo controlado aleatorizado abierto llevado a cabo entre los años 2011 y 2017, creándose dentro del mismo cuatro sub-estudios (Figura 2):

- ESTUDIO 1 (año 2011): intervención de EF de ocho (8) semanas de duración.
- ESTUDIO 2 (año 2012): intervención de EF de doce (12) semanas de duración.
- ESTUDIO 3 (año 2013): intervención de EF de dieciséis (16) semanas de duración.
- ESTUDIO 4 (años 2014-17): intervención de EF de dieciséis (16) semanas de duración e intervención nutricional (dieta hipocalórica).

En cada uno de los estudios, las personas participantes fueron asignadas a diferentes grupos experimentales paralelos:

- Grupo control (CG): recomendaciones generales de estilo de vida saludable, incluyendo AF no supervisada. En el ESTUDIO 4 fue grupo de atención-control (AC), que además recibió intervención nutricional.
- Grupo de EF continuo a intensidad moderada (MICT).
- Grupo de EF interválico a intensidad vigorosa y volumen alto (HV-HIIT*).*
- Grupo de EF interválico a intensidad vigorosa y volumen bajo (LV-HIIT*).* Este grupo experimental se añadió a partir del ESTUDIO 3.

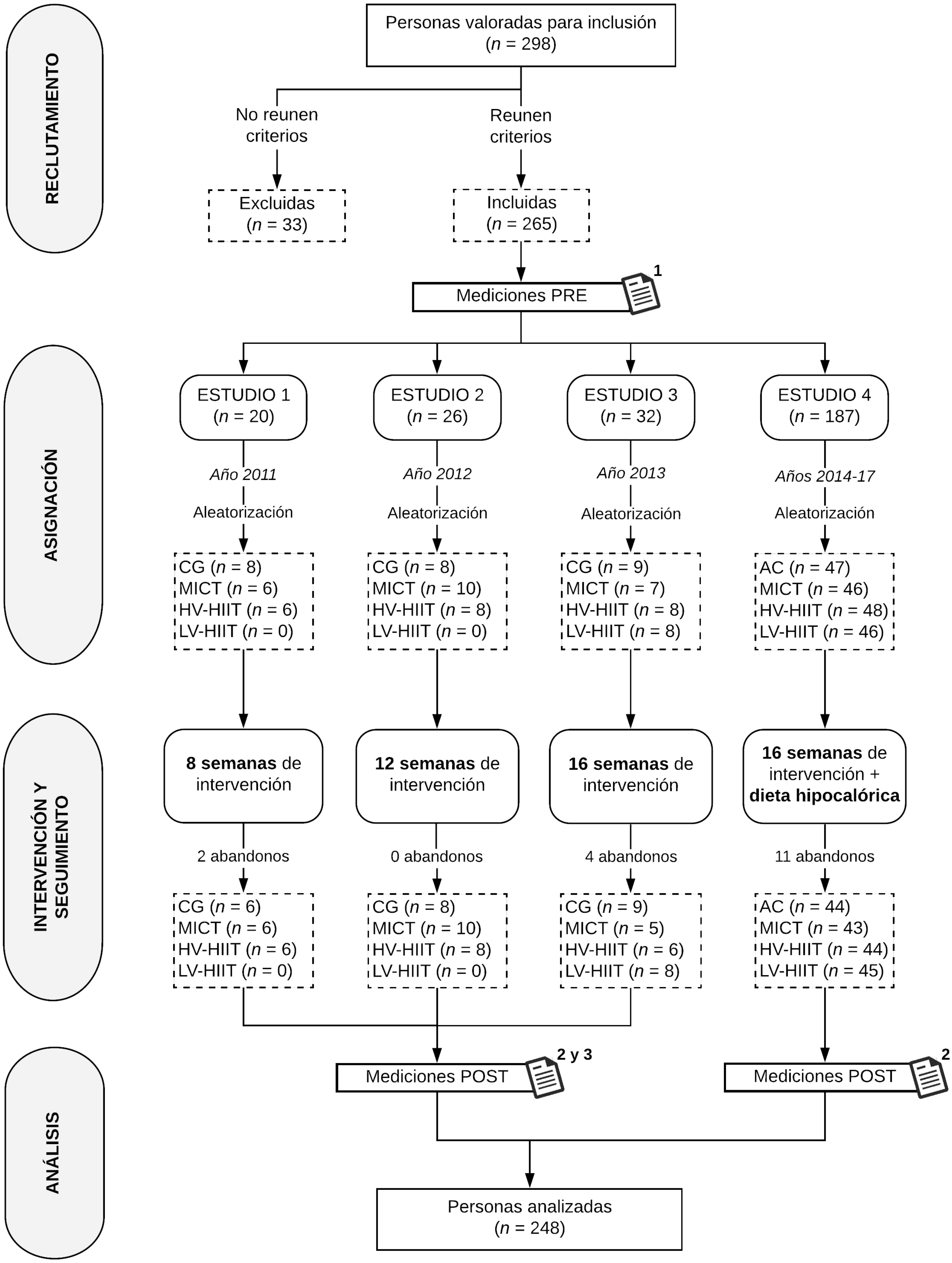

Figura 2. Diagrama de flujo del proyecto de investigación y relación con los artículos publicados y presentados en los capítulos 4-6.

DIVULGACIÓN

1

Jurio-Iriarte et al. (2017) *Association between Modified Shuttle Walk Test and cardiorespiratory fitness in overweight/obese adults with primary hypertension: EXERDIET-HTA study.*

Capítulo 4

2

Jurio-Iriarte et al. (2018) *Validity of the Modified Shuttle Walk Test to assess cardiorespiratory fitness after exercise intervention in overweight/obese adults with primary hypertension.*

Capítulo 5

3

Jurio-Iriarte et al. (2018) *Effects of different exercise training programmes on cardiorespiratory fitness in overweight/obese adults with hypertension: a pilot study.*

Capítulo 6

3.2. Participantes

En este estudio han participado personas con HTA primaria, sobrepeso u obesidad, y hábitos de vida sedentarios. Además de los requisitos citados, las personas participantes debían reunir otras condiciones, como ser mayores de edad y tener disponibilidad horaria para llevar a cabo la intervención. Solo fueron seleccionadas las personas pronosticadas con riesgo bajo-moderado de padecer evento CV en los próximos diez años según la clasificación de la Guía de práctica clínica para el tratamiento de la HTA 2011,[11] y siempre que no estuviesen bajo tratamiento farmacológico que no posibilitase realizar un CPET pico al inicio del estudio. Se tuvieron en cuenta las contraindicaciones para la realización de EF de la ESC,[8] así como para las pruebas de esfuerzo según la Guía de práctica clínica de la Sociedad Española de Cardiología en pruebas de esfuerzo.[68,69] La Tabla 3 recoge todos los criterios de inclusión y exclusión del estudio.

Todas las personas que participaron mantuvieron el tratamiento farmacológico que tuviesen antes de entrar a formar parte del estudio, que no fue modificado a menos que se lo indicase su especialista en atención primaria, medicina interna, nefrología o cardiología.

Tabla 3. Criterios de inclusión y exclusión al estudio.[67]

Criterios de inclusión	– Edad: 18-70 años. – HTA primaria en estadio 1-2: PAS de 140-179 mm Hg, y/o PAD de 90-109 mm Hg, con pronóstico de RCV bajo-moderado.[11,36] – Sobrepeso u obesidad: IMC ≥ 25 $kg \cdot m^{-2}$. – Hábitos de vida sedentarios según escala IPAQ.[70] – Disponibilidad horaria: 90 minutos, dos días a la semana, durante el periodo que dure la intervención.
Criterios de exclusión	– HTA secundaria. – Hipertrofia ventricular izquierda: masa ventricular izquierda estimada hasta 103 g/m^{-2} en hombres y hasta 89 $g \cdot m^{-2}$ en mujeres.[71] – Presencia de un factor de RCV severo o no-controlado, o diabetes mellitus diagnosticada hace más de 10 años, o con organopatía asociada. – Otros estados de salud significativos, incluidos pero no limitados a: desorden pulmonar, gastrointestinal, neuromuscular, neurológico, psiquiátrico o cognitivo crónico o recurrente; discapacidad física que impida llevar a cabo el programa de EF; enfermedades vasculares autoinmunes o del colágeno; enfermedad autoinmune o VIH positivo; anemia, problemas de sangrado, trombosis crónica, estados de hipercoagulabilidad; tumores en los últimos 5 años (excepto cáncer de piel controlado); desorden metabólico o endocrino; incluye diabetes mellitus tipo 1; cualquier estado de salud o enfermedad que amenace la vida o que pueda interferir o ser agravado con el EF. – Estar embarazada o ser lactante. – Tres o más factores de riesgo de ECV.[8] – Haber participado en algún programa para la pérdida de peso durante el último año. – Tener planificado estar más de dos semanas fuera de la ciudad.

ECV = enfermedad cardiovascular; EF = ejercicio físico; HTA = hipertensión arterial; IMC = índice de masa corporal; IPAQ = International Physical Activity Questionnaire; RCV = riesgo cardiovascular; PAD = presión arterial diastólica; PAS = presión arterial sistólica; VIH = virus de inmunodeficiencia humana.

3.3. Material y métodos

Valoración antropométrica

La valoración antropométrica realizada consiste en medición de estatura (SECA 213, Hamburgo, Alemania), masa corporal total (SECA 869, Hamburgo, Alemania), perímetro mínimo de cintura y perímetro máximo de cadera (SECA 200, Hamburgo, Alemania) siguiendo el protocolo de los estándares internacionales para la valoración antropométrica (*International Society for the Advancement of Kinanthropometry*, ISAK).[72] A partir de las mediciones realizadas se calcularon IMC (masa·estatura^{-2}, kg·m^{-2}) e índice de cintura-cadera (cintura·cadera^{-1}, cm·cm^{-1}). Se utilizó la impedancia bioeléctrica (Tanita BF 350, Illinois, EEUU) para la estimación de masa libre de grasa, masa grasa y agua corporal total.

Presión arterial

La PA ambulatoria se valoró con un monitor ambulatorio de PA (MAPA; Welch Allyn 6100, Nueva York, EEUU),[73] siguiendo las recomendaciones de las guías ESH/ESC.[36] El dispositivo registró la PA en intervalos de 30 minutos durante el día, y de 60 minutos durante la noche, para lo que el monitor tuvo que ser configurado teniendo en cuenta los horarios de cada participante. Una vez descargados los datos al ordenador, las horas reales de sueño fueron corregidas con las que cada participante manifestara. El registro se tomó por válido si al menos el 75 % de las mediciones resultaron exentas de error, repitiéndose la valoración en caso contrario.

Actividad física y sedentarismo

La versión corta del International Physical Activity Questionnaire (IPAQ) sirvió para valorar la actividad física y el sedentarismo. Esta versión del IPAQ está compuesta por 8 preguntas, que estiman el tiempo total por semana empleado en AF de diferentes intensidades: vigorosa, moderada, baja o caminar, y sedente.[70]

Test de esfuerzo cardiopulmonar (CPET)

La prueba de rendimiento cardiopulmonar pico limitada por síntomas se realizó en el cicloergómetro LODE Excalibur Sport (LODE, Groningen, Holanda).

La prueba comenzó con el ajuste de la bicicleta a la talla de cada participante (altura y retroceso del sillín y del manillar) y colocación de los instrumentos de medición: electrocardiograma (ECG) de 12 derivaciones, módulo de PA y pulsioximetría del ergómetro LODE-Excalibur Sport, mascarilla y sistema para la medición de variables ventilatorias y de intercambio de gases (monitor Ergo Card

Medi-soft S.S Bélgica. Ref. USM001 V1.0). La calibración de mezcla de gases con las concentraciones de oxígeno y dióxido de carbono se realizó antes de iniciar cada CPET. Se registraron variables en reposo, submáximas, pico y de recuperación para valorar la respuesta en las variables cardiorrespiratorias y hemodinámicas.

Tras explicar el funcionamiento de la prueba, se registraron las variables en reposo: FC, PA, $\dot{V}O_2$, ECG, saturación de oxígeno, y se inició el CPET que consistió en un protocolo en rampa con resistencia inicial de 40 vatios (W) que incrementaba un total de 10 W por minuto de forma continua (Tabla 4). La cadencia mínima que se debió mantener durante toda la prueba fue de 70 rpm. No hubo calentamiento previo.

Tabla 4. Características del protocolo del CPET en rampa sobre cicloergómetro.

Tiempo (min)	Potencia (W)
1	40
2	50
3	60
4	70
5	80
6	90
7	100
8	110
9	120
10	130
11	140
12	150
13	160
14	170
15	180
16	190
17	200
18	210
…	…

Se continuó registrando las variables submáximas hasta el final de la prueba: FC y percepción del esfuerzo (RPE) a través de la escala de Borg (6-20)[74] cada minuto, PA cada dos minutos, las variables ventilatorias y de intercambio de gases se monitorizaron respiración a respiración por un sistema de circuito abierto cada 30 segundos, y el ECG se monitorizó de forma constante. El CPET continuó hasta que no fuera capaz de mantener la potencia establecida, o se detuvo si se observaba una PAS > 250 mm Hg, o se mostraba cualquiera de los criterios de finalización de CPET presentados en la Guía práctica clínica de la Sociedad Española de Cardiología en pruebas de esfuerzo.[68] Se registraron los valores finales o pico de todas las variables: el valor más alto de $\dot{V}O_2$ alcanzado durante la prueba gradual de ejercicio se consideró $\dot{V}O_{2pico}$, al igual que en el resto de variables (FC_{pico}, RPE_{pico}, etc). Para asumir el logro del $\dot{V}O_{2pico}$ se tuvo en cuenta el cumplimiento de al menos dos de los siguientes criterios:[75]

- Meseta en el $\dot{V}O_2$ o en la FC con incremento de la potencia.
- Intercambio respiratorio (RER) > 1.10 (producción de dióxido de carbono dividido entre consumo de oxígeno, $\dot{V}CO_2 \cdot \dot{V}O_2^{-1}$).
- > 85 % FC máxima predicha (220-edad en hombres, 225-edad en mujeres).
- RPE > 18.

Una vez finalizada la prueba, se permaneció en el cicloergómetro durante 5 minutos para registrar las variables de recuperación, que se midieron en los minutos 1, 3 y 5.

Modified Shuttle Walk Test (MSWT)

El MSWT es un test progresivo de ida y vuelta a pie modificado a partir del ISWT.[42]

El MSWT tiene perfil de prueba pico, ya que se realiza EF de forma progresiva y gradual. La prueba se desarrolla caminando o corriendo, en una superficie llana de 10 m de longitud delimitada por un cono a 0.5 m de cada extremo que se debe rodear (Figura 3). El objetivo de la prueba es recorrer la mayor distancia posible, manteniendo el ritmo que marcan unas señales acústicas procedentes de una grabación.[43,76,77]

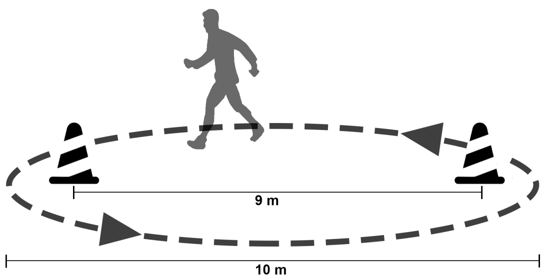

Figura 3. Esquema gráfico del MSWT.

La prueba consta de un máximo de 15 niveles, cada uno de 1 minuto. El primer nivel comienza a una velocidad de 0.5 $m \cdot s^{-1}$, y cada minuto o nivel aumenta 0.17 $m \cdot s^{-1}$. El primer nivel permite completar el recorrido de 10 m tres veces a 0.5 $m \cdot s^{-1}$, por lo que se recorren 30 m. El aumento progresivo de velocidad (0.17 $m \cdot s^{-1} \cdot min^{-1}$) permite que en cada nivel se puedan recorrer 10 m más que en el anterior, por lo que la distancia total máxima que se puede recorrer es de 1 500 m, si se llega a finalizar el nivel 15 de la prueba (Tabla 5). Cada señal acústica o pitido indica que se debe estar rodeando un cono, y se ha de llegar al cono opuesto con el pitido siguiente. Si el pitido es triple, significa que ha transcurrido un minuto y que se pasa al nivel siguiente, indicando que la velocidad va a aumentar. Las explicaciones fueron estandarizadas: “trate de caminar a un ritmo estable”, “trate de estar rodeando el cono al escuchar la señal acústica”, “si llega al cono antes de sonar la señal, espere a oírla para continuar”, “debe continuar caminando hasta que no pueda seguir el ritmo marcado, o hasta que sienta que no puede seguir por falta de aliento”.

Tabla 5. Características del protocolo del MSWT.

NIVEL	Velocidad ($m \cdot s^{-1}$)	Nº vueltas por nivel	Distancia del nivel (m)	Distancia acumulada al final del nivel (m)
1	0.50	3	30	30
2	0.67	4	40	70
3	0.83	5	50	120
4	1.00	6	60	189
5	1.17	7	70	250
6	1.33	8	80	330
7	1.50	9	90	420
8	1.67	10	100	520
9	1.83	11	110	630
10	2.00	12	120	750
11	2.17	13	130	880
12	2.33	14	140	1 020
13	2.50	15	150	1 170
14	2.67	16	160	1 330
15	2.83	17	170	1 500

La prueba finalizó al completar el nivel 15, o cuando se decidió parar voluntariamente, por imposibilidad de mantener el ritmo marcado. A quien no llegó al final de la prueba se le preguntó el porqué de su finalización; si el factor limitante fue fatiga central, fatiga de piernas u otros. También se dio por finalizada la prueba si presentaba cualquiera de los siguientes síntomas:[42,78]

- Falta de aire (disnea).
- Alcanzar el 85 % de la FC máxima predicha.
- Dolor en el pecho o sospecha de angina.
- Confusión mental o descoordinación.
- Mareo.
- Calambres en las piernas o fatiga muscular extrema en las piernas.

Antes de comenzar la prueba se registraron variables de reposo. En el transcurso del MSWT se registraron variables submáximas de FC justo antes de finalizar cada nivel o minuto, y al mismo tiempo, la RPE mediante la escala de Borg (6-20)[74]. Al dar la prueba por finalizada, se registraron variables pico de FC, PA y distancia total recorrida; y acto seguido, variables de recuperación durante cinco minutos.

3.4. Procedimiento

Después de diseñar el método del presente estudio de investigación y de recibir la aprobación por parte de los comités de ética correspondientes se procedió a publicitar el estudio en prensa escrita, radio y televisión locales, para reclutar como participantes potenciales a personas con HTA primaria, sobrepeso u obesidad, y hábitos de vida sedentarios. Se organizaron reuniones explicativas del proyecto, de forma grupal e individual, con el fin de dar más detalles y resolver dudas.

Todas las personas interesadas que después de haber sido informadas y conociendo la naturaleza del estudio decidieron participar, entregaron firmado un documento acreditando su consentimiento informado. A continuación fueron examinadas para comprobar si reunían los requisitos de acceso al estudio, descritos en el apartado *Participantes*, y si estaban exentas de los criterios de exclusión que se detallan en la Tabla 3. En el examen se comprobó si tenían sobrepeso u obesidad a través de valoración antropométrica, si obedecían a hábitos de vida sedentarios a través de la versión corta del IPAQ,[70] y se les realizó un ECG en reposo de 12 derivaciones para excluir la hipertrofia ventricular izquierda y otros predictores de evento CV. En una segunda cita fueron monitorizadas con MAPA que registraría la PA durante 24 horas.[11,36] Todas las pruebas previas a la inclusión fueron valoradas por el médico especialista en cardiología con el objetivo de estudiar su historial médico y decidir si eran elegibles o no para el proyecto, en función de los criterios establecidos. Las personas que reunieron los criterios fueron llamadas para realizar las pruebas de valoración y continuar con el procedimiento que se muestra de forma gráfica en la Figura 2.

Todas las pruebas de inclusión y valoración se realizaron antes de comenzar el periodo de intervención (PRE), y se repitieron una semana después de haber finalizado el mismo (POST), en tres citas distribuidas de la siguiente forma:

- 1.ª cita: mediciones antropométricas, cuestionario IPAQ y medicación (en la valoración PRE se aprovecharon los registros obtenidos en los exámenes de inclusión).
- 2.ª cita: registro de la PA ambulatoria con MAPA (en la valoración PRE se aprovecharon los registros obtenidos en los exámenes de inclusión).
- 3.ª cita: MSWT y CPET. Se pidió a las personas participantes acudir con ropa y calzado cómodos, habiendo realizado la última ingesta 3-4 horas antes de la hora citada, y sin olvidar tomar los fármacos que les hubieran sido prescritos; se registraron medicamentos y última comida. De forma previa al inicio de ambas pruebas se midieron PA y FC en

reposo (tensiómetro digital de brazo Omron M3 HEM-7200-E, Kyoto, Japón). Se dejaron al menos 30 minutos entre las dos pruebas de valoración de la CCR. Las condiciones del laboratorio se mantuvieron estables, con temperatura entre 19-22ºC, 40-50 % de humedad, y presión atmosférica de 706-710 mm Hg (estación meteorológica Sibelmed 511-570-003, Roselló, Barcelona, España).

Una vez realizadas las pruebas PRE, cada persona participante fue asignada de forma aleatoria a uno de los cuatro grupos de estudio. La aleatorización se realizó a través de un software informático estratificando por sexo, edad, PAS e IMC. Este proceso fue enmascarado para el personal médico que participó en el estudio.

Antes de comenzar la intervención, las personas participantes de todos los grupos recibieron un conjunto de elementos comunes estandarizados de práctica saludable por parte de uno de los investigadores del estudio siguiendo la Guía Europea de prevención CV en la práctica clínica:[79]

- Cambios en el estilo de vida y los beneficios que ello conlleva: tabaquismo, dieta saludable, AF y control de la masa corporal.
- Manejo o control de los factores de RCV: PA, colesterol, control glucémico.
- Tratamientos farmacológicos adecuados.

La intervención fue llevada a cabo en la misma facultad que las pruebas de valoración, durante 8, 12 o 16 semanas. Uno de los grupos sirvió como grupo control (CG), que aunque recibiera consejos de hábitos de vida saludables como los citados, no recibió intervención de EF supervisado (o AC, que además recibió tratamiento con dieta hipocalórica). Según recomienda la Guía Europea de prevención CV en su adaptación española del 2008 del Comité Español Interdisciplinario para la Prevención Cardiovascular,[79] se debe practicar un mínimo de 30 minutos al día de AF a intensidad moderada. Los demás grupos fueron grupos experimentales, que llevaron a cabo programas de EF supervisado de distinto tipo (MICT, HV-HIIT, LV-HIIT), con o sin intervención nutricional. Las personas participantes de los grupos experimentales recibieron los mismos consejos de hábitos de vida saludables que las del CG.

Programas de ejercicio físico supervisado

Fueron tres los programas de EF que se llevaron a cabo de forma supervisada por especialistas en EF, cada uno de ellos, a su vez, con distinta duración total de intervención (8-12-16 semanas), pero manteniendo un esquema similar. En todos los grupos experimentales se practicó dos sesiones no consecutivas de EF aeróbico a la semana, siendo una de ellas en bici estática, y la otra en cinta rodante. Las sesiones de EF comenzaron y finalizaron con la monitorización de la PA (tensiómetro oscilométrico digital de brazo Omron M3 HEM-7200-E, Kyoto, Japón), y se controló y ajustó la intensidad del entrenamiento mediante monitorización de la FC (pulsómetro Polar Electro, Kempele, Finlandia) y mediante RPE con la escala de Borg (6-20)[74].

Las sesiones de EF se dividieron en tres partes: calentamiento, parte principal y vuelta a la calma.

- *Calentamiento*: se hicieron ejercicios de movilidad articular amplia y de coordinación durante 10 minutos, con continuo movimiento de piernas, para facilitar el retorno venoso.
- *Parte principal*: el volumen de entrenamiento fue en progresión de 20 a 40-45 minutos a lo largo de las 8-12-16 semanas. El entrenamiento consistió en caminar-correr o pedalear alcanzando y manteniendo una determinada FC, para lo que se ajustaron tanto la velocidad como la pendiente de la cinta rodante, o la resistencia y cadencia en el bici estática, para conseguir la carga diseñada en el protocolo del proyecto.
- *Vuelta a la calma*: 10 minutos de ejercicios de fortalecimiento de la cintura pélvica (escuela de espalda) en suelo y estiramientos pasivos para asegurar una vuelta progresiva a los valores de reposo tanto de FC como de PA.

Las diferencias entre los grupos experimentales estuvieron en el tipo e intensidad del ejercicio CV que se practicó en la parte principal del entrenamiento (*i.e.* moderada o vigorosa) y consecuentemente, en el protocolo de realizarlo (*i.e.* continuo o interválico), así como en el volumen de las sesiones de entrenamiento (*i.e.* fijo o progresivo). En las Tablas 6, 7 y 8 se pueden observar los distintos protocolos de entrenamiento dentro de los programas de EF de 8, 12 y 16 semanas, respectivamente, con detalle de la progresión en volumen e intensidad, que se explican a continuación:

- MICT, del inglés *moderate-intensity continuous training*: grupo supervisado de EF aeróbico programado de modo continuo a intensidad moderada (valores de FC entre umbral ventilatorio 1 (UV_1) y umbral ventilatorio 2 (UV_2), o 50-75 % FC reserva, o 60-80 % FC pico. Borg = 11-13), y de larga duración (volumen de sesiones de entrenamiento en progresión, de 20 a 45 minutos).
- HIIT, del inglés *high-intensity interval training:* grupo supervisado de EF programado a diferentes intensidades (interválico), alternando vigorosas (valores de FC desde UV_2 y hasta FC pico, o 75-95 % FC reserva, o 85-95 % FC pico. Borg > 15) y moderadas (valores de FC entre UV_1 y UV_2, o 60-70 % FC reserva, o 65-75 % FC pico. Borg = 11-13). Hubo dos variantes dependientes del volumen de las sesiones de entrenamiento dentro del HIIT:
- HV-HIIT, del inglés *high-volume HIIT:* sesiones de entrenamiento de larga duración (volumen de sesiones de entrenamiento en progresión, de 20 a 45 minutos, igual que el MICT). A medida que la duración de las sesiones aumentaba, la cantidad de intervalos también fue en aumento.
- LV-HIIT, del inglés *low-volume HIIT:* sesiones de entrenamiento de corta duración (volumen de sesiones de entrenamiento de 20 minutos, no variables, inferior que el MICT y el HV-HIIT). Este grupo experimental se añadió a partir del ESTUDIO 3, por lo que solo se llevó a cabo en los programas con duración de 16 semanas.

Los protocolos de entrenamiento de cinta y bici fueron diferentes en los grupos HIIT:

- *Protocolo entrenamiento en cinta rodante*: se llevaron a cabo 5 minutos de calentamiento a intensidad moderada correspondiente al 50-60 % del $\dot{V}O_{2pico}$ (60-70 % FC reserva), antes de caminar o correr a intervalos de 4 minutos a intensidad vigorosa al 80-90 % $\dot{V}O_{2pico}$ (75-95 % FC reserva), seguidos de 3 minutos de recuperación a intensidad moderada o en reposo, y finalizando con 1-10 minutos a intensidad moderada. Se ejercitaron en las intensidades más bajas las primeras sesiones, antes de incrementar de forma progresiva hasta el límite superior.[63]

- *Protocolo entrenamiento en bici estática*: tras 10 minutos de calentamiento a intensidad moderada (60-70 % FC reserva), desarrollaron intervalos de 30 segundos a intensidad vigorosa (75-95 % FC reserva) intercalados con intervalos de recuperación de 60 segundos a intensidad moderada o en reposo, en función de la respuesta cardiaca en el periodo de recuperación. Las series se repitieron hasta finalizar el volumen correspondiente de entrenamiento, incluyendo al final un periodo de 4-10 minutos a intensidad moderada.[80]

Tabla 6. Características de los programas de entrenamiento supervisados con duración de 8 semanas.

Semana	MICT		HV-HIIT				
	Intensidad (% FC_{res})	Volumen (min)	Intensidad (% FC_{res})		Volumen (min)	Protocolos entrenamiento	
			Intervalo moderado	Intervalo vigoroso		Cinta	Bici
1-2	55-60	20	60	80	20	5’ Mod. + 2-4 x (4’ Vig. + 3’ Mod.) + 1-10’ Mod.	10’ Mod. + 4-13 x (30” Vig. + 60” Mod.) + 4-10’ Mod.
3-4	65	30	65	85	30		
5-6	70	35	70	90	35		
7-8	75	40	70	90	40		

FC_{res} = frecuencia cardiaca de reserva; HV-HIIT = entrenamiento interválico a intensidad vigorosa y volumen alto; MICT = entrenamiento continuo a intensidad moderada; Mod. = intensidad moderada; Vig. = intensidad vigorosa.

Tabla 7. Características de los programas de entrenamiento supervisados con duración de 12 semanas.

Semana	MICT		HV-HIIT				
	Intensidad (% FC_{res})	Volumen (min)	Intensidad (% FC_{res})		Volumen (min)	Protocolos entrenamiento	
			Intervalo moderado	Intervalo vigoroso		Cinta	Bici
1-2	50	20	60	80	20	5’ Mod. + 2-4 x (4’ Vig. + 3’ Mod.) + 1-10’ Mod.	10’ Mod. + 4-16 x (30” Vig. + 60” Mod.) + 4-10’ Mod.
3-4	60	25	60	80	25		
5-6	65	30	65	85	30		
7-8	70	35	65	85	35		
9-10	75	40	70	95	40		
11-12	75	45	70	95	45		

FC_{res} = frecuencia cardiaca de reserva; HV-HIIT = entrenamiento interválico a intensidad vigorosa y volumen alto; MICT = entrenamiento continuo a intensidad moderada; Mod. = intensidad moderada; Vig. = intensidad vigorosa.

Tabla 8. Características de los programas de entrenamiento supervisados con duración de 16 semanas.

<table>
<tr><th rowspan="3">Semana</th><th colspan="2">MICT</th><th colspan="2">HIIT</th><th colspan="3">HV-HIIT</th><th colspan="3">LV-HIIT</th></tr>
<tr><th rowspan="2">Intensidad (% FC_{res})</th><th rowspan="2">Volumen (min)</th><th colspan="2">Intensidad (% FC_{res})</th><th rowspan="2">Volumen (min)</th><th colspan="2">Protocolos entrenamiento</th><th rowspan="2">Volumen (min)</th><th colspan="2">Protocolos entrenamiento</th></tr>
<tr><th>Intervalo moderado</th><th>Intervalo vigoroso</th><th>Cinta</th><th>Bici</th><th>Cinta</th><th>Bici</th></tr>
<tr><td>1-2</td><td>50</td><td>20</td><td>60</td><td>80</td><td>20</td><td rowspan="7">5’ Mod.
+
2-4 x
(4’ Vig. + 3’ Mod.)
+
1-10’ Mod.</td><td rowspan="7">10’ Mod.
+
4-18 x
(30” Vig. + 60” Mod.)
+
4-10’ Mod.</td><td>20</td><td rowspan="7">5’ Mod.
+
2 x
(4’ Vig. + 3’ Mod.)
+
1-4’ Mod.</td><td rowspan="7">5-10’ Mod.
+
4-9 x
(30” Vig. + 60” Mod.)
+
4-10’ Mod.</td></tr>
<tr><td>3-4</td><td>60</td><td>25</td><td>60</td><td>80</td><td>25</td><td>20</td></tr>
<tr><td>5-6</td><td>65</td><td>30</td><td>65</td><td>85</td><td>30</td><td>20</td></tr>
<tr><td>7-8</td><td>70</td><td>35</td><td>65</td><td>85</td><td>35</td><td>20</td></tr>
<tr><td>9-10</td><td>75</td><td>40</td><td>70</td><td>95</td><td>40</td><td>20</td></tr>
<tr><td>11-12</td><td>75</td><td>45</td><td>70</td><td>95</td><td>45</td><td>20</td></tr>
<tr><td>13-16</td><td>75</td><td>45</td><td>70</td><td>95</td><td>45</td><td>20</td></tr>
</table>

FC_{res} = frecuencia cardiaca de reserva; HIIT = entrenamiento interválico a intensidad vigorosa (HV = volumen alto; LV = volumen bajo); MICT = entrenamiento continuo a intensidad moderada; Mod. = intensidad moderada; Vig. = intensidad vigorosa.

Capítulo 4.

Association between modified shuttle walk test and cardiorespiratory fitness in overweight/obese adults with primary hypertension: EXERDIET-HTA study.

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Journal of the American Society of Hypertension, 2017; 11(4) 186–195.
doi: 10.1016/j.jash.2017.01.008.

4. Association between modified shuttle walk test and cardiorespiratory fitness in overweight/obese adults with primary hypertension: EXERDIET-HTA study.

4.1. Abstract

Purpose: the aims of the study were: to evaluate the relationship between Modified Shuttle Walk Test (MSWT) with peak oxygen uptake ($\dot{V}O_{2peak}$) in overweight/obese people with primary hypertension (HTN), and to develop an equation for the MSWT to predict $\dot{V}O_{2peak}$. **Methods:** participants (*n* = 256, 53.9 ± 8.1 yr old) with HTN and overweight/obesity performed a cardiorespiratory exercise test to peak exertion on an upright bicycle ergometer using an incremental ramp protocol and the 15-level MSWT. The formula of Singh *et al.* was used as a template to predict $\dot{V}O_{2peak}$, and a new equation was generated from the measured $\dot{V}O_{2peak}$-MSWT relationship in this investigation. **Results:** the correlation between measured and predicted $\dot{V}O_{2peak}$ for Singh *et al.* equation was moderate ($r = 0.60$, $P < 0.001$) with a standard error of estimate (*SEE*) of 4.92 $mL \cdot kg^{-1} \cdot min^{-1}$; *SEE* % = 21 %. The correlation between MSWT and measured $\dot{V}O_{2peak}$, as well as for the new equation was strong ($r = 0.72$, $P < 0.001$) with a *SEE* of 4.35 $mL \cdot kg^{-1} \cdot min^{-1}$; *SEE* % = 19 %. **Conclusion:** these results indicate that MSWT does not accurately predict functional capacity in overweight/obese people with HTN and questions the validity of using this test to evaluate exercise intolerance. A more accurate determination from a new equation in the current study incorporating more variables from MSWT to estimate $\dot{V}O_{2peak}$ has been performed, but still results in substantial error.

Keywords: Peak oxygen uptake, field test, equation for estimation.

4.2. Introduction

The leading cause of noncommunicable diseases deaths is the cardiovascular disease (CVD). Hence, CVD prevention is the major goal of different organizations worldwide by improving the management of these diseases through professional education and research, and promoting healthy lifestyle.[6,49,81] Cardiovascular risk (CVR) factors such as overweight/obesity and primary hypertension (HTN) have been increasing substantially and often occur concurrently, leading to an exponential risk for CVD.[29] Therefore, in the management of overweight/obesity-related HTN a lifestyle change is imperative, particularly regular exercise[82] along with other lifestyle modification strategies.[10,29] Cardiorespiratory fitness (CRF) (*i.e.,* peak oxygen uptake, $\dot{V}O_{2peak}$) is a robust physiological marker of health risk and is now considered key vital sign.[34,75] Objective and direct measures of CRF, obtained from a cardiopulmonary exercise test (CPET), are essential for the assessment, clinical management and exercise programming of overweight/obesity and HTN patients.[6,10] However, the CPET is not widely available and is expensive. Cardiorespiratory fitness can be estimated using a variety of field tests,[42] but may not be valid in all populations and are heavily influenced by motivation and encouragement. Moreover, their simplicity results in limited physiological and symptoms assessment during exercise.[83] The Léger and Lambert shuttle field test is incremental and progressive, stressing the individual to a symptom limited maximal performance.[84] Singh *et al.* adapted the test and proposed an equation to assess functional capacity in patients with chronic obstructive pulmonary disease (COPD) using a 12-level protocol Incremental Shuttle Walk Test (ISWT).[42,85] This was further modified to a series of 15 levels by Bradley *et al.*[43,76] The 15-level Modified Shuttle Walk Test (MSWT) has important characteristics for functional capacity assessment in sedentary people with HTN [68,86,87] since it is based on incremental walking performance, a familiar activity to most people. Moreover the MSWT is simple to perform for both the patient and the test-operator and the equipment needed is minimal. The MSWT field test is suitable for all levels of function, as the first levels are very slow and it is difficult to reach the upper levels, allowing a peak response to be elicited.[88] Previous studies have assessed the association between the ISWT or MSWT and $\dot{V}O_{2peak}$ concluding that these field walk tests are “safe”, “objective”, “valid”, “reliable”, “effective” and “highly predictive” for the assessment of functional capacity in each of the populations examined (Table 9). To our knowledge, there have not been studies that have examined the relationship between the MSWT and $\dot{V}O_{2peak}$ in a cohort of overweight/obese population with diagnosed HTN. Therefore, the aims of the present study were: (1) to evaluate the relationship between MSWT and $\dot{V}O_{2peak}$ in overweight/obese people with HTN, and (2) to develop a new equation for the MSWT to predict $\dot{V}O_{2peak}$.

Table 9. Studies assessing validity of the ISWT or MSWT to predict $\dot{V}O_{2peak}$.

Source	Population	CPET	*n*	*r*	r^2	*P*
Singh *et al.*[85] 1994	Chronic airflow limitation	Treadmill	19	0.88	-	< 0.05
Elias *et al.*[89] 1997	COPD	Cycle ergometer	20	0.71	-	< 0.05
Keell *et al.*[90] 1998	Left ventricular dysfunction	Treadmill	50	0.84	0.70	< 0.001
Morales *et al.*[91] 1999	Chronic heart failure	Cycle ergometer	46	0.83	0.69	< 0.001
Bradley *et al.*[43] 1999	Cystic fibrosis	Treadmill	20	0.95	0.90	< 0.01
Green *et al.*[92] 2001	Heart failure	ISWT + AGA	7	0.83	-	< 0.05
Lewis *et al.*[88] 2001	Cardiomyopathy	Treadmill	25	0.73	-	< 0.001
Macsween *et al.*[93] 2001	Rheumatoid arthritis Cardiac rehabilitation	ISWT + AGA ISWT + AGA	10 10	0.31 0.05	0.10 0.03	< 0.05 < 0.05
Onorati *et al.*[94] 2003	COPD	Cycle ergometer	13	0.72	-	< 0.01
Satake *et al.*[95] 2003	Moderate COPD	Cycle ergometer	12	0.85	0.72	< 0.001
Turner *et al.*[96] 2004	COPD	Cycle ergometer	20	0.73	0.53	< 0.001
Fowler *et al.*[97] 2005	Coronary artery bypass surgery	Treadmill + 3 MSWT	39	0.79-0.87	-	< 0.05
Win *et al.*[98] 2006	Lung cancer	Treadmill	125	0.67	-	< 0.001
Campo *et al.*[99] 2006	COPD	Cycle ergometer	30	0.68	-	< 0.05
Pulz *et al.*[100] 2008	Chronic heart failure	Treadmill	63	0.79	-	< 0.001
Struthers *et al.*[101] 2008	General surgical patients	Cycle ergometer	50	-	0.57	< 0.001
Lopez-Campos *et al.*[102] 2008	Kyphoscoliosis	Cycle ergometer	24	0.67	-	< 0.001
Oliveira *et al.*[103] 2011	Pulmonary arterial hypertension	Treadmill	24	0.46	-	0.02
Stockton *et al.*[104] 2012	Thermal injury	Cycle ergometer	11	0.70	-	< 0.05
Dourado *et al.*[105] 2013	Healthy	ISWT + AGA	103	0.86	0.76	< 0.001
Mandic *et al.*[106] 2013	Coronary artery disease	Cycle ergometer	58	0.85	0.73	< 0.001
Costa *et al.*[107] 2014	Chagas heart disease	Cycle ergometer	35	0.59	-	< 0.001
de Boer *et al.*[108] 2014	Sarcoidosis	Cycle ergometer	33	0.87	-	< 0.001
de Camargo *et al.*[109] 2014	Noncystic fibrosis bronchiectasis	Cycle ergometer	75	0.72	-	< 0.05
Evans *et al.*[110] 2014	Obstructive sleep apnea	Treadmill	16	-	0.24	0.054
Mainguy *et al.*[111] 2014	Pulmonary arterial hypertension	ISWT + AGA	21	-	0.75	< 0.01
Irisawa *et al.*[112] 2014	Pulmonary arterial hypertension	Cycle ergometer	19	0.87	-	< 0.05
Granger *et al.*[113] 2015	Lung cancer	Cycle ergometer	20	0.61	-	0.007
Jurgensen *et al.*[114] 2015	Obese women	Treadmill	46	0.54	-	< 0.001
Neves *et al.*[115] 2015	Sedentary	Treadmill	12	0.70	0.41	0.001
Alves *et al.*[116] 2016	Chagas heart disease	Treadmill ISWT + AGA	32 32	0.46 0.87	- -	0.009 < 0.001
Jurgensen *et al.*[117] 2016	Obese women	Treadmill	40	-	0.67	< 0.05

ISWT = incremental shuttle walk test; MSWT = modified shuttle walk test; CPET = cardiopulmonary exercise test; AGA = ambulatory gas analyzer; *n* = sample size; *r* = Pearson's correlation coefficient; r^2 = coefficient of determination; COPD = chronic obstructive pulmonary disease.

4.3. Material and methods

Study design

Baseline data from EXERDIET-HTA randomized controlled experimental trial were used for the purpose of this study. The design, selection criteria and procedures for the EXERDIET-HTA study have been previously detailed.[67] The study protocol was approved by The Ethics Committee of The University of the Basque Country (UPV/EHU, CEISH/279/2014) and the Ethics Committee of Clinical Investigation of Araba University Hospital (2015-030) (Clinical Trials.gov identifier, NCT02283047). All participants provided written informed consent prior to any data collection.

Participants

Non-Hispanic white participants with HTN and overweight/obesity were recruited from the cardiology services and local media. All participants (*n* = 256) that volunteered to take part in the present study were classified as overweight (body mass index, BMI ≥ 25) or obese (BMI ≥ 30)[49] and with diagnosed with stage 1 or 2 HTN, as defined with a systolic blood pressure (SBP) of 140-179 and/or a diastolic blood pressure (DBP) of 90-109 mm Hg or with antihypertensive pharmacological treatment (87.1 % of the participants).[10] Medication received by the participants included angiotensin-converting-enzyme inhibitors (36.8 %), angiotensin II receptor blockers (43.6 %), diuretics (32.1 %), calcium channel blockers (17.7 %), beta blockers (9.6 %), statins (12.9 %) and antiplatelets (3.9 %). Participants taking medication with beta-blockers were eligible only if the treatment allowed a peak cardiopulmonary test. Otherwise, the cardiologist will advise the most suitable pharmacological treatment.

Study parameters

Modified Shuttle Walk Test (MSWT). The fifteen-level MSWT consisted on walking/running up and down a 10-meter corridor at an incremental speed as previously described by Bradley *et al.*[43] A standardized explanation of the test was given to the patient before the test was conducted. Prior to commencing the test, with the participant in a seated position, baseline heart rate (HR) and blood pressure (BP) was recorded. A triple beep indicated the start of the test. The participant was instructed to walk/run to the opposite side/cone of the corridor every time a single beep sounded. If the participant reached the cone before the signal, they had to wait until the signal indicated they could proceed. The test was finished when; (a) the participant reached the end of level 15, (b) the participant was too breathless to maintain the required speed (dyspnea), (c) the participant was more than 0.5 m away from the cone when the beep sounded (allowed once), (d) the participant attained 85 % of the predicted maximum heart rate resulting from the formula [220-age], (e) or if the patient experienced chest pain or angina, dizziness, mental confusion or extreme muscle fatigue. Heart rate and Borg scale (6 to 20) were monitored throughout the test, and BP and HR will continue to be recorded five more minutes after completion of the test.[43,77]

Cardiorespiratory fitness (CRF)

Participants performed the CRF test after the MSWT with a minimum of 30 minute rest break prior in order to obtain stable resting HR and BP values. A CPET was used to asses $\dot{V}O_{2peak}$. Briefly, the test was performed on an electronically braked Lode Excalibur Sport Cycle Ergometer (Groningen, The Netherlands). Testing protocol was started with 40 W with gradual increments of 10 W every minute to exhaustion with continuous electrocardiogram monitoring and participants cycling at 70 rpm. Expired gas analysis was performed using a commercially available metabolic cart (Ergo CardMedi-soft S.S, Belgium Ref. USM001 V1.0) that was calibrated before each test with a standard gas of known concentration and volume. Breath by-breath data were measured continuously during exercise reported in 60 second averages. Blood pressure was measured every two minutes throughout the test and a self-reported Borg rating of perceived exertion (6 to 20) scale was recorded at the end of each stage. Peak oxygen uptake was defined as the highest oxygen uptake value attained toward the end of the test. Achievement of $\dot{V}O_{2peak}$ was assumed with the presence of two or more of the following criteria: (1) volitional fatigue (> 18 on BORG scale), (2) peak respiratory exchange ratio ($\dot{V}CO_2/\dot{V}O_2$) ≥ 1.1, (3) achieving > 85 % of age predicted maximum HR, and (4) failure of oxygen uptake and/or HR to increase with further increases in work rate.[67]

Predicted $\dot{V}O_{2peak}$ from MSWT

The following formula from Singh *et al.*[85] was used to predict $\dot{V}O_{2peak}$ in our cohort:

$\dot{V}O_{2peak}$ = [4.19 + (0.025 · ISWT distance in meters)].

A new equation was generated from the $\dot{V}O_{2peak}$-MSWT relationship assessed in the present study.

Previous studies search strategy and selection criteria

[This paragraph does not appear in the original publication due to a word limit]. The literature search was performed for studies published between June 1992 and August 2016 through the following electronic databases: PubMed, MEDLINE, Web of Science™ Core Collection, LILACS, PEDro, the Cochrane Library, ProQuest and Trip. The key terms used were "shuttle walk* test" and "modified shuttle test". The title and abstract of all articles were reviewed. Articles were considered relevant if validity of ISWT or MSWT in adult population was assessed with objective results of correlation between ISWT or MSWT and $\dot{V}O_{2peak}$ or $\dot{V}O_{2max}$. Only articles written in English, French, Portuguese or Spanish were included. Hand searches of the references of all relevant studies were also performed.

Statistical analysis

Statistical analyses were carried out with the SPSS Statistical software package (24^{th} edition). Descriptive statistics were performed on the baseline participants' characteristics. The differences and relationship between variables were evaluated using standard parametric tests, after appropriate assumptions were met. Intraclass correlation coefficients (*ICC*) with absolute agreement based on a two way mixed model with 95 % confidence intervals (*CI*) were calculated. Bland & Altman plots were constructed to evaluate the agreement of Singh *et al.* equation[85] to estimate $\dot{V}O_{2peak}$, compared to the measured $\dot{V}O_{2peak}$ values. Simple linear regression was used to analyze the relationship between the estimated and measured $\dot{V}O_{2peak}$. Forward stepwise linear regression was performed to test the effects of sex, age, body mass (BM), stature, BMI, waist-to-hip ratio, rest HR, MSWT peak HR and distance on $\dot{V}O_{2peak}$, and to determine which variables are the strongest predictors of $\dot{V}O_{2peak}$. Bland & Altman plots were also constructed to evaluate the relationship between the $\dot{V}O_{2peak}$ estimated from the new equation generated in the present study compared to the measured $\dot{V}O_{2peak}$ values. All values were expressed as mean and standard deviation (*SD*) unless otherwise stated. The level of significance (*P*-value) was set at 95 % (α = 0.05).

4.4. Results

Participants' characteristics

Physical characteristics of the study participants are shown in Table 10. Two hundred and fifty six participants [181 male (70.7 %) and 75 female (29.3 %)] aged 53.9 ± 8.1 years old met all the required criteria for inclusion in the study. In accordance with AHA/ACC/TOS guidelines for the Management of Overweight and Obesity in Adults, participants were classified as obese (BMI > 30 $kg{\cdot}m^{-2}$).[49] Exercise testing responses for peak exercise test are displayed in Table 11.

Agreement and reliability of Singh et al. equation for population of the study

Singh *et al.* equation-calculated mean $\dot{V}O_{2peak}$ was 25.4 ± 5.6 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$, which was statistically higher than the directly measured level on the CPET (22.9 ± 6.1 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$; $P < 0.001$). The relationship between measured and predicted $\dot{V}O_{2peak}$ was significant yet of moderate strength ($r = 0.60$), explaining 36 % of the variance ($r^2 = 0.36$; $P < 0.001$), and indicating 21 % of error in estimation (standard error of the estimate (*SEE*) = 4.92 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$; *SEE* % = 21 %). The *ICC* was 0.71 [95 % *CI* 0.56 to 0.80]. The Singh *et al.* equation showed a mean $\dot{V}O_{2peak}$ bias of -2.5 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ with limits of agreement from -13.1 to 8.2 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$. This indicates that using the equation proposed by Singh *et al.*, $\dot{V}O_{2peak}$ assessment of 95 % of patients would range from 13.1 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ less to 8.2 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ more than their experimental measure (Table 12, Figure 4).

New equation to estimate $\dot{V}O_{2peak}$

There was a strong significant correlation between MSWT and measured $\dot{V}O_{2peak}$ (r = 0.72, P < 0.001). In the equation proposed by Singh *et al.*, $\dot{V}O_{2peak}$ in COPD patients was calculated taking distance (m) in the ISWT test as the predictive variable. To potentially improve the prediction of $\dot{V}O_{2peak}$, the present investigation used forward stepwise regression, to identify other variables that may improve the prediction of $\dot{V}O_{2peak}$. In such procedure, variables are added sequentially to the regression as long as they significantly improve the predictive power of the model. The assumption of normality was met, as assessed by Q-Q Plots and Kolmogorov-Smirnov test. The multiple regression model significantly predicted $\dot{V}O_{2peak}$, $F(4, 251) = 69.255$, $P < 0.001$. There was significant strong level of association and a medium effect size, as indicated by r and adjusted r^2 values (Table 12). This model explained 51 % of variation, 30 % of *SD* and indicated 19 % of *SEE* for $\dot{V}O_{2peak}$. Sex, BM, Rest HR and distance (m) in the MSWT ($Distance_{MSWT}$) variables added statistically significantly to the prediction, P < 0.05. The equation generated in this study to calculate $\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$) from the MSWT is described by the following equation:

$$\dot{V}O_{2peak} = 34.94 + [0.008 \cdot Distance_{MSWT}] - [0.078 \cdot Rest\ HR] - [5.074 \cdot Sex] - [0.128 \cdot BM],$$

where sex is coded as Male = 0, Female = 1, $Distance_{MSWT}$ is measured in meters, and BM is measured in kg.

Table 10. Characteristics of the study population. Values are mean ± *SD* or percentage (%).

Variable	*n* = 256
Age (yr)	53.9 ± 8.1
Height (cm)	169.7 ± 9.5
BM (kg)	90.0 ± 15.4
BMI ($kg \cdot m^{-2}$)	31.2 ± 4.8
Waist (cm)	102.1 ± 10.7
Hip (cm)	108.3 ± 9.2
WHR (waist/hip)	0.9 ± 0.1
Rest HR (bpm)	78.7 ± 13.7
Rest SBP (mm Hg)	139.6 ± 16.5
Rest DBP (mm Hg)	90.0 ± 11.8
Antihypertensive medication (%)	87.1 %

BM = body mass; BMI = body mass index; WHR = waist-to-hip ratio; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure.

Table 11. Exercise testing peak values of the study population. Values are mean ± *SD*.

Variable	*n* = 256
Peak HR (bpm)	152.6 ± 15.9
Peak SBP (mm Hg)	212.4 ± 24.7
Peak DBP (mm Hg)	100.6 ± 18.5
Peak Power (W)	134.1 ± 38.9
Exercise Time (min)	11.2 ± 3.9
RER_{peak}	1.1 ± 0.1
$\dot{V}O_{2peak}$ ($L \cdot min^{-1}$)	2.0 ± 0.5
$\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	22.9 ± 6.1
MSWT (m)	847.6 ± 239.3
Peak HR in MSWT (bpm)	158.1 ± 18.5

HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; RER = respiratory exchange ratio; $\dot{V}O_{2peak}$ = peak oxygen uptake; MSWT = modified shuttle walk test.

Table 12. Differences and the relationships among $\dot{V}O_{2peak}$ values.

Variable	**Mean ±** ***SD***	***r***	***r^2***	**$r^2_{adjusted}$**	**%** ***SD***	***P*-value**	***SEE***	**%** ***SEE***
Measured $\dot{V}O_{2peak}$ (mL·kg^{-1}·min^{-1})	22.9 ± 6.1							
$\dot{V}O_{2peak}$ from Singh[85] predicted equation (mL·kg^{-1}·min^{-1})*	25.4 ± 5.6	0.60	0.36	0.36	19.9 %	0.001	4.92	21 %
$\dot{V}O_{2peak}$ from our predicted equation (mL·kg^{-1}·min^{-1})	22.7 ± 4.3	0.72	0.52	0.51	30.5 %	0.001	4.35	19 %

r = Pearson's correlation coefficient; r^2 = coefficient of determination; % *SD* = percent of *SD* explained; *SEE* = standard error; % *SEE* = percent of *SEE*; $\dot{V}O_{2peak}$ = peak oxygen uptake.* Significantly different from measured data (P < 0.05).

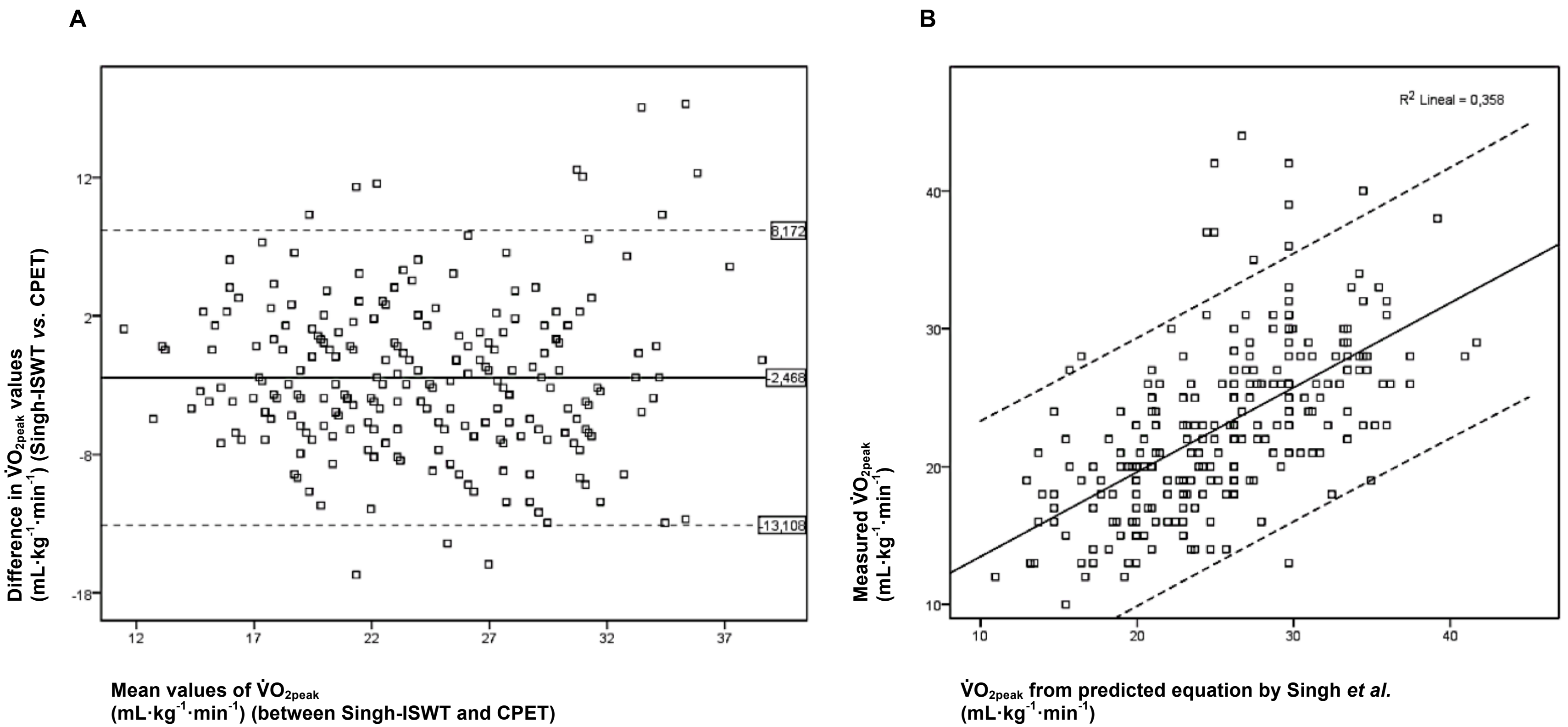

Figure 4.

A) Bland & Altman plot. Intra-individual differences in $\dot{V}O_{2peak}$ (calculated by Singh *et al.*[85] equation for ISWT *vs*. measured in CPET) plotted against intra-individual mean values of the two methods (Singh *et al.* equation for ISWT and CPET). The central line represents the mean of the intra-individual differences, and the flanking lines represent the 95 % limits of agreement.

B) Relationship between measured $\dot{V}O_{2peak}$ and $\dot{V}O_{2peak}$ values from the predicted equation by Singh *et al.*[85] The central line represents the linear regression line, and the flanking lines represent the 95 % individual prediction intervals.

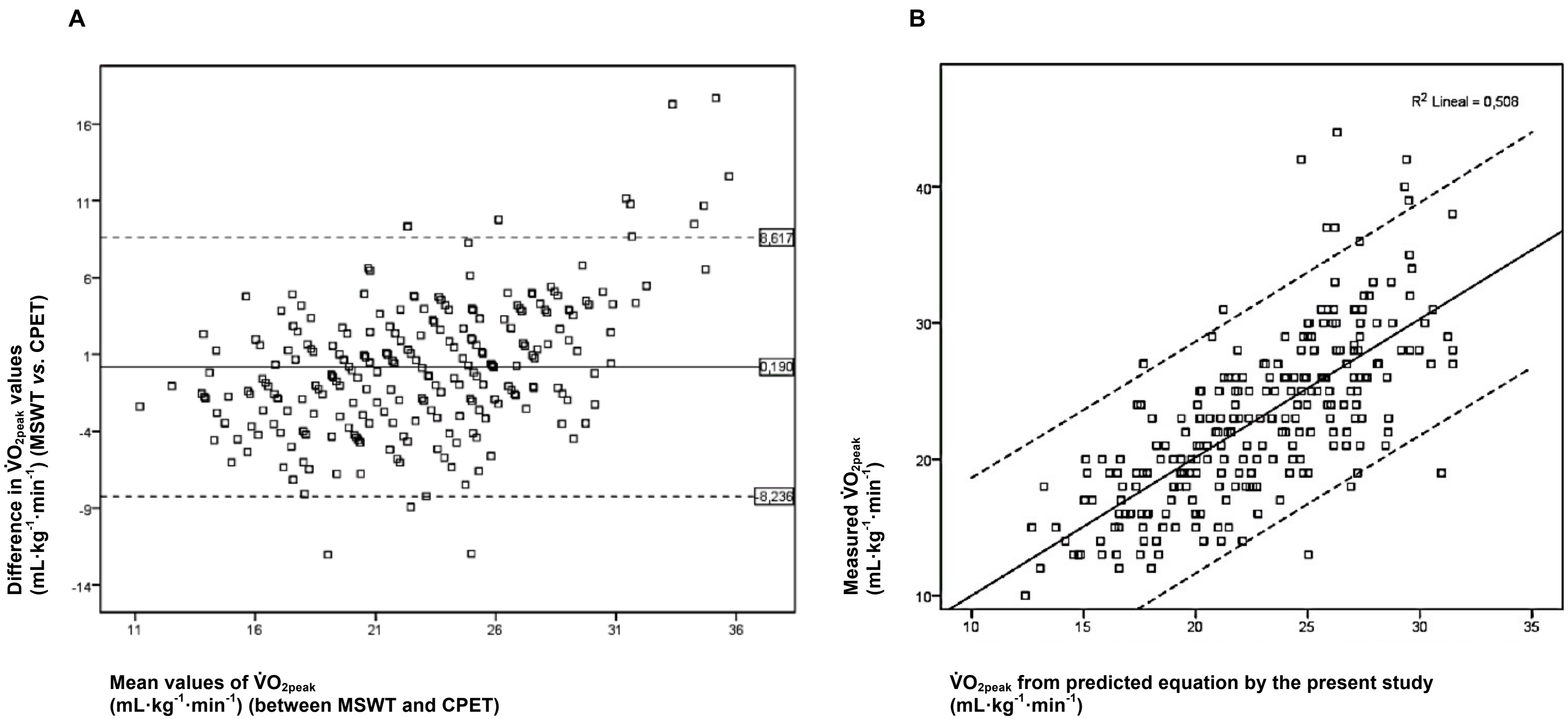

Figure 5.

A) Bland & Altman plot. Intra-individual differences in $\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$) between two exercise tests (MSWT vs. CPET) plotted against intra-individual mean values of the two exercise tests (MSWT and CPET). The central line represents the mean of the intra-individual differences, and the flanking lines represent the 95 % limits of agreement.

B) Relationship between measured $\dot{V}O_{2peak}$ and $\dot{V}O_{2peak}$ values from the predicted equation generated in the present study. The central line represents the linear regression line, and the flanking lines represent the 95 % individual prediction intervals.

The equation showed a significant proportional bias ($P < 0.001$) with a mean intra-individual difference of 0.2 $mL·kg^{-1}·min^{-1}$ (limits of agreement from -8.2 $mL·kg^{-1}·min^{-1}$ to 8.6 $mL·kg^{-1}·min^{-1}$). This indicates that using the new equation, $\dot{V}O_{2peak}$ assessment of 95 % of patients would range from 8.2 $mL·kg^{-1}·min^{-1}$ less to 8.6 $mL·kg^{-1}·min^{-1}$ more than their experimental measure. The $\dot{V}O_{2peak}$ predicted from the present study equation (22.7 ± 4.3 $mL·kg^{-1}·min^{-1}$) was not significantly different ($P = 0.48$) than the actual measured $\dot{V}O_{2peak}$ (22.9 ± 6.1 $mL·kg^{-1}·min^{-1}$). Figure 5.A illustrates the proportional bias previously mentioned, showing a linear trend between the mean and the difference of paired measurements.

Bland & Altman Plots show that the biggest and smallest individual means of $\dot{V}O_{2peak}$ between the two tests correspond with the biggest limits of agreement in a proportional basis (Figure 5).

4.5. Discussion

To our knowledge this is the first study to analyse the relationship between the MSWT and $\dot{V}O_{2peak}$ in a cohort of overweight/obese population diagnosed with HTN. Data from this study demonstrated that a new equation incorporating rest HR, sex, BM and distance from MSWT performs better than the Singh *et al.* equation to estimate $\dot{V}O_{2peak}$ for the studied population, yet still results in an error of estimate of 19 %. The participants that made up the sample of the present study had a mean $\dot{V}O_{2peak}$ of 22.9 ± 6.1 $mL·kg^{-1}·min^{-1}$, which is considered as poor functional capacity.[118] Singh *et al.* equation significantly overestimates $\dot{V}O_{2peak}$ (25.4 ± 5.9 $mL·kg^{-1}·min^{-1}$; $P < 0.001$) and 64 % of the prediction variability is not explained by this model (*i.e.,* the performance on the ISWT would explain just 36 % of the variance of the $\dot{V}O_{2peak}$ in the studied cohort). Moreover, the assessment of functional capacity would range in 21 $mL·kg^{-1}·min^{-1}$ around the mean bias which indicates there is too much variability when making decisions regarding disability, pharmacological therapy or exercise program design. Therefore, Singh *et al.* equation may be an appropriate equation for COPD population, but not for the assessment of functional capacity of overweight/obese individuals with HTN. The lack of accuracy might be because Singh *et al.* equation was generated for patients with chronic airways obstruction or COPD. In contrast to pulmonary[43,89,94-96,98,99,108,109,112,113] or cardiac[88,91,92,97,100,106] patients (Table 9), the performance of people with HTN is not usually limited by breathlessness, or exercise intolerance but by exhaustion, low fitness or high BP. Moreover, the participants in Singh *et al.* had much lower function capacity than those used in the present investigation (375 ± 137 m *vs*. 847 ± 239 m, respectively). Hence, a better estimation is necessary for the prediction and assessment of functional capacity by the MSWT in population with HTN and overweight/obesity. Thus, it appears be claimed that the MSWT provides a valid functional capacity assessment and greater predictive power compared to the *Singh et al*. model in overweight/obese HTN population. However, the new equation still only explains the 51 % of the variation in $\dot{V}O_{2peak}$, and substantial variability in estimation indicated by *SEE* (19 % probability of error) (Table 12). Recent studies have found similar strong significant correlations in estimation of $\dot{V}O_{2peak}$, through the ISWT and the MSWT, compared to the $\dot{V}O_{2peak}$ in healthy adults,[105] obese women,[114] and sedentary adult men[115] and have concluded that these field tests are appropriate alternatives to assess functional capacity. Nevertheless, all the reviewed studies present low statistical power due mainly to the small sample size, thus reducing the chance of detecting a true effect. It is well known that the true effect discovered by an underpowered study will exaggerate the estimation of the magnitude of that effect.[119] The present study presents a sample size of 256 overweight/obese participants diagnosed with HTN, which represents a much bigger sample compared to previous studies, with an actual statistical power of 0.95. On the other hand, the differences between correlation in the current study and correlation in the studies reported previously (Table 9) could be due to the fact that participants in this study were not affected by airflow limitation and because their functional capacity was only limited by their fitness and high BP. It seems that the two shuttle walk tests could be more appropriate for population with respiratory or heart disease, in which maximal distance (m) is statistically shorter than in HTN and overweight/obese population. Therefore, it could be that only patients with low CPET performance[118] would have an accurate estimation of $\dot{V}O_{2peak}$ by ISWT or MSWT. Thus, in the present study, trying to find a CRF threshold to explain the cases with higher error of estimation, different stratified regression analysis with subset CRF populations were performed (*i.e.,* $\dot{V}O_{2peak}$ < 20; 20-30; > 30 $mL \cdot kg^{-1} \cdot min^{-1}$). However, results of the full sample offered better regression model than the stratification into subsets.

On the other hand, the variability of the new equation indicated by a high *SEE* (19 % probability of error) questions the accuracy of using this approach to make an accurate prediction of functional capacity. It is very well known that functional capacity assessment based on $\dot{V}O_{2peak}$ and ventilatory gas exchange measures has good reliability, reproducibility and clinical utility as the exercise measurements are based on actual metabolic measures.[120] Thus, the CPET response includes and provides a full spectrum of objective indices to achieve integrated assessments of lung, cardiac and even muscle contributions to exercise performance.[120] The limitation of individual performance with CPET can be evaluated taking into account data from electrocardiogram (ECG), BP monitor, and/or gas analysis monitor to ensure that the termination criteria are fulfilled[68,121] to avoid CVR events during the test. In contrast, with ISWT and MSWT, there are no tools available to assess the performance other than RPE (Borg scale) and the formula to calculate the 85 % of the predicted maximum HR. To increase the safety of the ISWT and MSWT, additional equipment suitable for exercise test assessment, such as ambulatory BP monitor, ECG or gas analysis system. This equipment is expensive and makes the test more difficult to be administered. An important limitation in the use of ISWT and MSWT is that BP, the principal termination criterion of functional capacity assessment tests in population with HTN and obesity, cannot be addressed. Finally, knowing that exercise is recommended as a key lifestyle therapy for adults with HTN for the prevention, treatment, and control of BP by all international associations and committees,[122] exercise design should be tailored in a systematic and individualized way. Using MSWT as a reference test to this population could lead to substantial errors and potential risks. However, if the CPET is not available, exercise professionals could at least use the new equation generated in the present study that incorporates resting HR, sex, BM and distance from MSWT variables to estimate $\dot{V}O_{2peak}$ for overweight/obese people with HTN, but taking into account the error of estimation.

A potential limitation of this study is that experimental $\dot{V}O_{2peak}$ was measured during a CPET on a cycle ergometer, whereas the field test was performed with a walking test. The differences between testing modalities may have led to a lower prediction power, and higher probability of error in the prediction. Peak oxygen uptake is known to be up to 15-20 % higher when measured on a treadmill rather than on a cycle ergometer.[123] On the other hand, the increase in $\dot{V}O_2$ is more linear,[124] and it is easier to assess BP during on the cycle ergometer, which is an important criterion for CPET assessment in a HTN population.

4.6. Conclusions

The prediction of $\dot{V}O_{2peak}$ based on a new regression equation derived from the relationship between $\dot{V}O_{2peak}$ and MSWT results in an error of estimate of 19 %, calling into question the validity of using this test to evaluate exercise intolerance in people with HTN and obesity.

Consequently, when an accurate determination of functional capacity is required for diagnosis, clinical research, and exercise design, the direct measurements of $\dot{V}O_{2peak}$ is still preferred in obese population with diagnosed HTN.

Capítulo 5.

Validity of the modified shuttle walk test to assess cardiorespiratory fitness after exercise intervention in overweight/obese adults with primary hypertension.

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Clinical and Experimental Hypertension, 2018.
doi: 10.1080/10641963.2018.1481423.

5. Validity of the modified shuttle walk test to assess cardiorespiratory fitness after exercise intervention in overweight/obese adults with primary hypertension.

5.1. Abstract

Purpose: the study aimed to assess whether the Modified Shuttle Walk Test (MSWT) can detect changes in cardiorespiratory fitness (CRF) in overweight/obese people with hypertension (HTN) after an exercise intervention evaluating the equation presented in the previous research by Jurio-Iriarte *et al.* **Methods**: participants (*n* = 248) performed a peak cardiorespiratory exercise test (CPET) and MSWT before and after 16 weeks of different type of aerobic exercise intervention. The formula of Jurio-Iriarte *et al.* was used to predict peak oxygen uptake ($\dot{V}O_{2peak}$). **Results**: the correlation between measured and predicted $\dot{V}O_{2peak}$ was strong ($r = 0.76$, $P < 0.001$) with a standard error of estimate (*SEE*) of 4.9 $mL \cdot kg^{-1} \cdot min^{-1}$; *SEE %* = 17 %. The intraclass correlation coefficient indicates a moderate level of association and agreement (*ICC* = 0.69; *95 % CI* 0.34-0.82; $P < 0.001$) between the measured and predicted $\dot{V}O_{2peak}$. When analyzing obese participants alone (*n* = 128), MSWT equation was more accurate compared to the whole sample (*ICC* = 0.76; *95 % CI* 0.52-0.87). The relationship between the change of measured and predicted $\dot{V}O_{2peak}$ at follow-up was weak ($r = 0.42$, $P < 0.001$) with a 31 % *SEE,* and a low level of association and agreement (*ICC* = 0.31; *95 % CI* 0.06-0.49; $P < 0.001$). **Conclusions**: although MSWT does not accurately predict CRF in people with HTN after exercise intervention and questions its validity, the new equation may have practical application to estimate $\dot{V}O_{2peak}$ for obese people with HTN when CPET is not available.

Keywords: hypertension, obesity, field test, cardiopulmonary test, assessment, exercise design, sedentary.

5.2. Introduction

Overweight/obesity and primary hypertension (HTN) are cardiovascular risk factors that continue to increase and augment the risk for cardiovascular disease.[29] Regular exercise along with other lifestyle modification strategies is imperative for effective management of overweight/obesity-related HTN.[10,29,82] Cardiorespiratory fitness (CRF) is considered a key vital sign and a robust physiological index of health risk.[34,75] Cardiorespiratory fitness is essential for the assessment, clinical management and exercise programming of individuals with overweight/obesity and HTN.[6,10] The cardiopulmonary exercise test (CPET) is used to objectively and directly measure peak oxygen uptake ($\dot{V}O_{2peak}$), which is considered the "gold standard" reference for the assessment of CRF and prescription of aerobic exercise intensity.[75]

The modified shuttle walk test (MSWT) is a low cost and easily administered field test[42,43,76] that can be used to estimate CRF. This test has been validated to predict $\dot{V}O_{2peak}$ in sedentary participants with overweight/obesity and HTN.[125] However, the ability of MSWT to assess the improvement in $\dot{V}O_{2peak}$ after an exercise intervention in the same cohort has not been evaluated. Consequently, it would be important to determine if the MSWT-measured overtime changes in $\dot{V}O_{2peak}$ were similar or proportional to the CPET-measured $\dot{V}O_{2peak}$. These findings would determine if the MSWT is a suitable tool as a follow-up assessment of CRF, when CPET is not available. Therefore, the aim of the present study was to evaluate the validity of the equation presented in previous study by Jurio-Iriarte *et al.*[125] after an exercise intervention in a cohort of overweight/obese population with HTN.

5.3. Material and methods

Participants

A total of 248 non-Hispanic white participants (174 men, 74 women) with stage 1 or 2 HTN[10] and overweight/obesity[49] volunteered to take part in the present study. The design, selection criteria (exclusion and inclusion criteria), and procedures for the EXERDIET-HTA study have been previously described.[67] Some of the exclusion criteria were to have secondary HTN, left ventricular hypertrophy, an uncrontrolled cardiovascular risk factor or diabetes mellitus more than 10 years since diagnosis, and other significant medical conditions.

Study design

Follow-up data from the EXERDIET-HTA randomized controlled experimental trial (Clinical Trials.gov identifier, NCT02283047) and a previous pilot study were used in this prospective study. The study protocol was approved by the Local Ethics Committees (UPV/EHU, CEISH/279/2014, and CEIC 2015-030), and also meets the ethical standards in sports and exercise science research.[126] All participants provided written informed consent prior to any data collection. Following baseline data collection, participants were randomly allocated to one of the four intervention groups (Figure 6): Attention Control (AC, with only physical activity recommendations); or three supervised exercise groups (Moderate-Intensity Continuous steady Training, MICT; High-Volume and High-Intensity Interval Training, alternating bursts of higher-intensity with lower-intensity activity, HV-HIIT, and Low-Volume, LV-HIIT). Each group was stratified by sex, systolic blood pressure, BMI and age. All measurements were performed at entry and after a 16-week intervention period.[67]

Procedures

Modified Shuttle Walk Test (MSWT). The fifteen-level MSWT consisted of walking up and down a 10-meter corridor at an incremental speed as previously described by Singh *et al.*[42] A standardized explanation of the test was given to the patient before the test was conducted.[43,77]

The equation used to calculate $\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$) from the MSWT is described by the Jurio-Iriarte *et al.*[125] equation:

$$\dot{V}O_{2peak} = 34.94 + [0.008 \cdot Distance_{MSWT}] - [0.078 \cdot Rest\ HR] - [5.074 \cdot Sex] - [0.128 \cdot BM],$$

where sex is coded as Male = 0, Female = 1, $Distance_{MSWT}$ is measured in meters, and BM is measured in kg.

Participants performed the CPET test after the MSWT with a minimum of 30-minute rest break to obtain stable resting HR and BP values. Briefly, the CPET was performed on an electronically braked Lode Excalibur Sport Cycle Ergometer (Groningen, The Netherlands). Testing protocol was started with 40 W with gradual increments of 10 W every minute at 70 rpm to exhaustion with continuous electrocardiogram monitoring. Expired gas analysis was performed using a commercially available metabolic cart (Ergo CardMedi-soft S.S, Belgium Ref. USM001 V1.0). $\dot{V}O_{2peak}$ was defined as the highest oxygen uptake value attained during the CPET.[67]

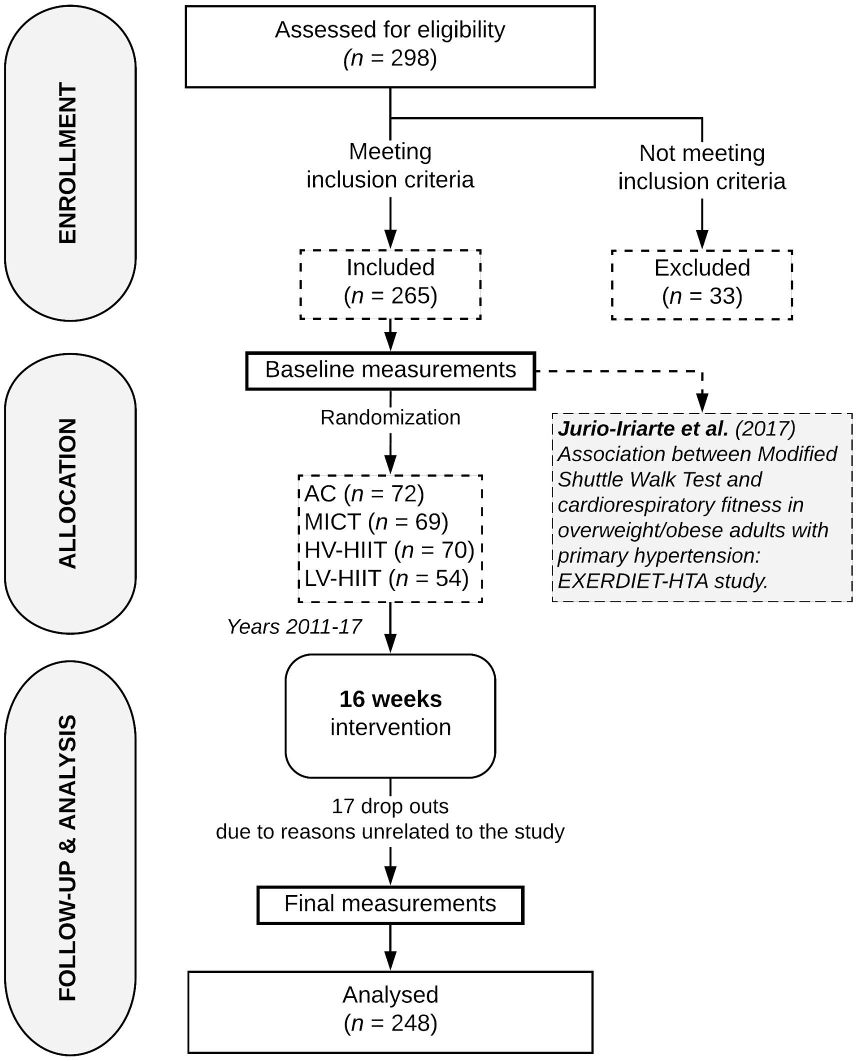

Figure 6. Flow-chart.

AC = attention-control group; MICT = moderate-intensity continuous training; HV-HIIT or LV-HIIT = high-intensity interval training of high/low-volume.

Exercise training intervention

The exercise program focused on improving cardiovascular endurance. Participants trained two days per week for 16 weeks under supervision. Each session started with a 10 minute warm-up period and ended with 10 minutes of cool-down. The main component of the training session consisted of aerobic exercises performed progressively in volume, duration, and intensity depending on the training group. Protocols of different aerobic programs have been previously published.[67] Briefly, The MICT group performed 45 minutes of aerobic exercise, whereas the HV-HIIT and LV-HIIT conducted 45 and 20 minutes, respectively. The intensity was individually tailored to each participant's HR at moderate or vigorous intensities, adjusting the speed and/or incline of the treadmill or the power and speed on the exercise-bike. The rationale of mixing stationary exercise-bike and treadmill was to avoid the orthopedic impact of two treadmill days and taking into account the nature of the HIIT program in overweight/obese participants. The HV-MICT group performed 45 minutes of continuous training at moderate intensity.

Statistical analysis

Statistical analyses were performed using the SPSS Statistical software package (24th edition). Descriptive statistics were performed on the participants' characteristics after the intervention. The differences and relationship between variables were evaluated using standard parametric tests after appropriate assumptions were met. Intraclass correlation coefficients (*ICC*) with an absolute agreement based on a two-way mixed model with 95 % confidence intervals (*CI*) were calculated. Bland & Altman plots were constructed to evaluate the agreement of Jurio-Iriarte *et al.* equation[125] of estimated $\dot{V}O_{2peak}$, compared to the measured $\dot{V}O_{2peak}$ values. Simple linear regression was used to analyze the relationship between the estimated and measured $\dot{V}O_{2peak}$. All values were expressed as mean and standard deviation (*SD*) unless otherwise stated. The level of statistical significance (*P*-value) was set at 95 % (α = 0.05). Power calculation was completed using G*Power 3 analysis program.[127] The required sample size was determined for a correlation bivariate normal model. It was determined that adequate power (0.90) to evaluate the relationships in the present investigation could be achieved with 92 people (α = 0.05).

5.4. Results

Participants' characteristics

Two hundred and forty-eight participants (174 men and 74 women) aged 54.0 ± 7.3 years old were followed until the end of the intervention (See Figure 6: Flow-chart). Physical and clinical characteristics of the study participants after a 16-week intervention period are shown in Table 13.

Table 13. Characteristics and exercise testing peak values of the study population after a 16-week intervention period. Values are mean ± *SD* or percentage (%).

Variable	***n* = 248 (174 ♂ 74 ♀)**
Age (yr)	54.0 ± 7.3
Height (cm)	169.7 ± 9.2
Body mass (kg)	84.6 ± 13.8
BMI ($kg \cdot m^{-2}$)	29.4 ± 4.3
Waist (cm)	96.7 ± 10.5
Hip (cm)	104.4 ± 8.2
WHR (waist/hip)	0.9 ± 0.1
Antihypertensive medication (%)	84.7 %
Rest HR (bpm)	70.9 ± 12.0
Rest SBP (mm Hg)	130.0 ± 13.9
Rest DBP (mm Hg)	82.9 ± 9.9
Peak HR (bpm)	154.5 ± 16.5
Peak SBP (mm Hg)	206.8 ± 23.9
Peak DBP (mm Hg)	96.8 ± 15.4
RER_{peak}	1.1 ± 0.1
$\dot{V}O_{2peak}$ ($L \cdot min^{-1}$)	2.4 ± 0.6
$\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	28.2 ± 7.6
Distance $_{MSWT}$ (m)	970.3 ± 255.7
Peak HR $_{MSWT}$ (bpm)	157.9 ± 16.9

♂ = male; ♀ = female; BMI = body mass index; WHR = waist-to-hip ratio; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; RER = respiratory exchange ratio; $\dot{V}O_{2peak}$ = peak oxygen uptake; MSWT = modified shuttle walk test.

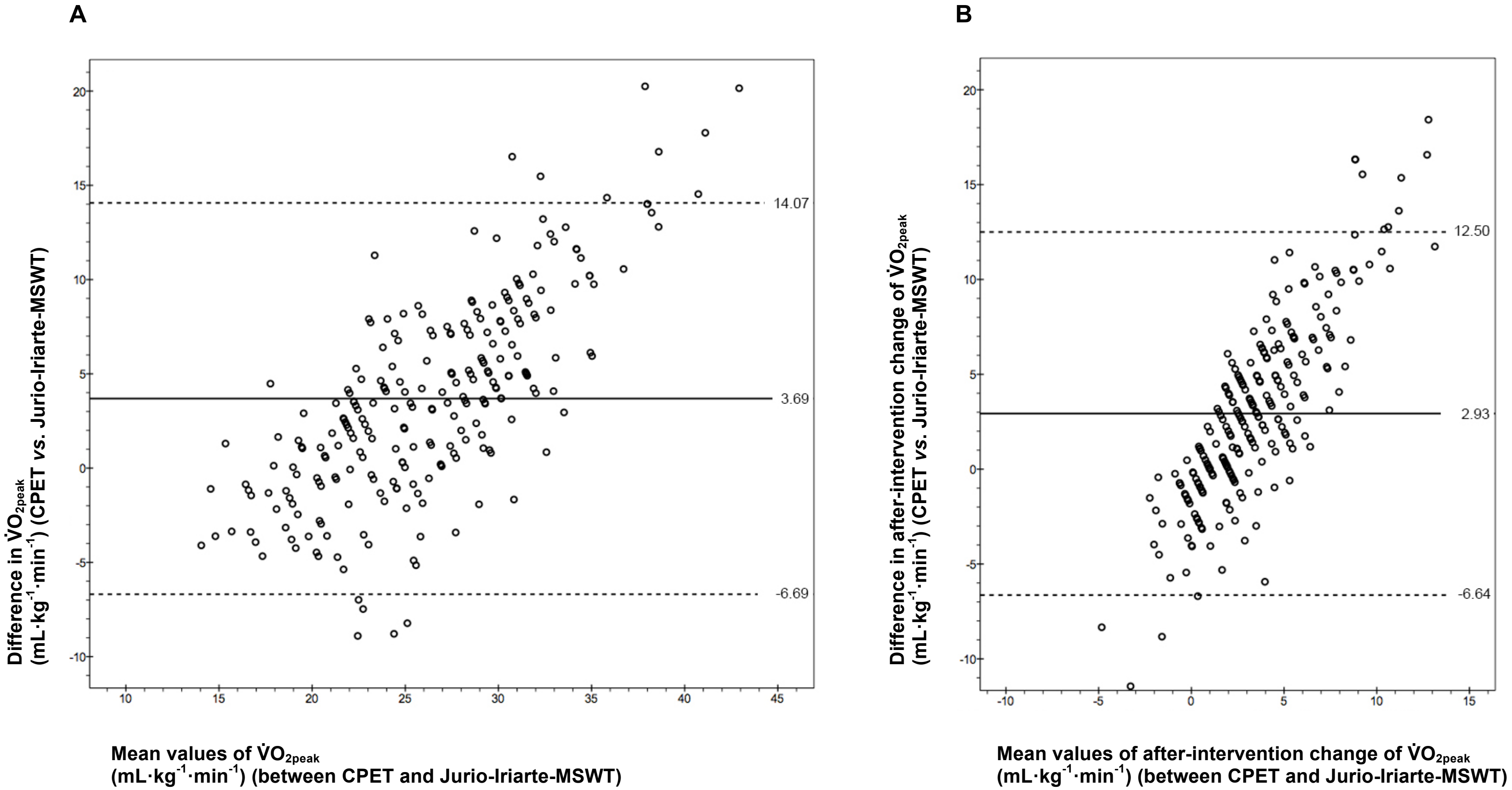

Figure 7. Bland & Altman plots.

A) Intraindividual difference in $\dot{V}O_{2peak}$ (calculated by Jurio-Iriarte *et al.*[125] equation for MSWT *vs*. measured in CPET) plotted against intraindividual mean values of the two methods (Jurio-Iriarte *et al.*[125] equation for MSWT and CPET).

B) Intraindividual difference in after-intervention change of $\dot{V}O_{2peak}$ (calculated by Jurio-Iriarte *et al.*[125] equation for MSWT *vs*. measured in CPET) plotted against intraindividual mean values of the two methods (Jurio-Iriarte *et al.*[125] equation for MSWT and CPET). The central line of the plots represents the mean of the intraindividual differences, and the flanking lines represent the 95 % limits of agreement.

Agreement and validity of Jurio-Iriarte et al. equation

Jurio-Iriarte *et al.*[125] equation-calculated mean $\dot{V}O_{2peak}$ for the whole sample after exercise intervention was 24.5 ± 3.9 $mL\cdot kg^{-1}\cdot min^{-1}$, which was statistically lower than the directly measured on the CPET (28.2 ± 7.6 $mL\cdot kg^{-1}\cdot min^{-1}$; $P < 0.001$) (Table 14). The relationship between measured and predicted $\dot{V}O_{2peak}$ was significant and strong ($r = 0.76$), explaining 58 % of the variance ($r^2 = 0.58$; $P < 0.001$), and indicating 17 % of error in estimation (standard error of the estimate, $SEE = 4.9$ $mL\cdot kg^{-1}\cdot min^{-1}$). The accuracy of the equation at follow-up was moderate,[128] as indicated by $ICC = 0.69$ (*95 % CI* 0.34 to 0.82) (Table 14). The Jurio-Iriarte *et al.* equation showed a mean $\dot{V}O_{2peak}$ bias of 3.7 $mL\cdot kg^{-1}\cdot min^{-1}$ with limits of agreement from -6.7 to 14.1 $mL\cdot kg^{-1}\cdot min^{-1}$. This indicates that using the equation proposed, $\dot{V}O_{2peak}$ assessment of 95 % of patients would range from 6.7 $mL\cdot kg^{-1}\cdot min^{-1}$ less to 14.1 $mL\cdot kg^{-1}\cdot min^{-1}$ more than their experimental measure (Figure 7.A). The tendency seen in Figure 7.A indicates that the higher the level of CPET $\dot{V}O_{2peak}$, the larger the difference between the measured and predicted value. Differences ≥ 10 $mL\cdot kg^{-1}\cdot min^{-1}$ were of those participants with highest CRF ($\dot{V}O_{2peak}$ > 33 $mL\cdot kg^{-1}\cdot min^{-1}$). These results were strengthened when analyzing obese (BMI ≥ 30) participants alone as the MSWT equation was more accurate in the 128 obese participants compared to the whole sample ($ICC = 0.76$; *95 % CI* 0.52-0.87).

A subset analysis showed that the relationship between measured and predicted $\dot{V}O_{2peak}$ and the *SEE* and *ICC* of different exercise intervention protocols was very similar to the analysis of the whole sample ($r^2_{adjusted}$ ranging from 0.49 to 0.60; *SEE* from 15 % to 20 %; *ICC* from 0.64 to 0.77). In most cases, the equation of Jurio-Iriarte *et al.*[125] significantly ($P < 0.001$) underestimated CRF.

The CPET measured fitness of the participants demonstrated a mean improvement of 4.9 ± 5.3 $mL\cdot kg^{-1}\cdot min^{-1}$ (22.7 %) after the intervention, which is significantly larger ($P < 0.001$) than the change calculated with the MSWT equation (1.9 ± 1.6 $mL\cdot kg^{-1}\cdot min^{-1}$; 9.1 %). The relationship between CPET and MSWT after-intervention absolute change of $\dot{V}O_{2peak}$ was significant but small ($r = 0.42$) explaining just 17 % of the variance ($r^2 = 0.17$; $P < 0.001$), and indicating 31 % *SEE* when assessing the determination of CRF with MSWT ($SEE = 1.5$ $mL\cdot kg^{-1}\cdot min^{-1}$). The validity of the equation to detect absolute changes in CRF after intervention was poor,[128] as indicated by $ICC = 0.31$ (*95 % CI* 0.06 to 0.49). In general, the validity of the equation to detect relative changes in CRF was also poor (Table 14). The Jurio-Iriarte *et al.* equation showed a change of $\dot{V}O_{2peak}$ mean bias of 2.9 $mL\cdot kg^{-1}\cdot min^{-1}$ with limits of agreement from -6.6 to 12.5 $mL\cdot kg^{-1}\cdot min^{-1}$ (Figure 7.B). This indicates that when using this prediction equation, the change in $\dot{V}O_{2peak}$ for 95 % of patients would range from 6.6 $mL\cdot kg^{-1}\cdot min^{-1}$ less to 12.5 $mL\cdot kg^{-1}\cdot min^{-1}$ more than their CPET measured $\dot{V}O_{2peak}$. The tendency shown in Figure 7.B indicates the larger the CRF improvement at follow-up, the greater difference *vs.* the MSWT calculated development.

Table 14. Validity of the MSWT to assess the development of CRF at follow-up in overweight/obesity people with hypertension (n = 248).

Variable	$\dot{V}O_{2peak}$ (mL·kg^{-1}·min^{-1})		r	r^2	$r^2_{adjusted}$	% *SD*	P_{value}	*SEE*	%*SEE*	*ICC* (95 % *CI*)
	CPET Measured	**Equation predicted**								
Follow-up	28.2 ± 7.6	24.5 ± 3.9	0.76	0.58	0.58	35.7 %	0.001	4.9	17 %	0.69 (0.34-0.82)
Absolute change	4.9 ± 5.3	1.9 ± 1.6	0.42	0.17	0.17	8.9 %	0.001	1.5	31 %	0.31 (0.06-0.49)
Relative change (%)	22.7 ± 23.9	9.1 ± 8.1	0.35	0.12	0.12	6.2 %	0.001			0.28 (0.04-0.46)

MSWT = modified shuttle walk test; CRF = cardiorespiratory fitness; $\dot{V}O_{2peak}$ = peak oxygen uptake; CPET = cardiopulmonary exercise test; *CI* = confidence intervals; *ICC* = intraclass correlation coefficient; *r* = Pearson's correlation coefficient; r^2 = coefficient of determination; % *SD* = percent of *SD* explained; *SEE* = standard error of estimation; % *SEE* = percent of *SEE*.

5.5. Discussion

To our knowledge, this is the first study to analyze the relationship between the MSWT and $\dot{V}O_{2peak}$ after a 16-week training intervention in a cohort of overweight/obese population diagnosed with HTN.

The previous study by Jurio-Iriarte *et al.*[125] demonstrated that a new equation incorporating sex, resting HR, BM and $distance_{MSWT}$ performs better than the Singh *et al.*[42] equation in estimating $\dot{V}O_{2peak}$ for sedentary and overweight/obese participants with HTN. However, assessment of CRF using this new equation still resulted in an *SEE* of 19 %, significantly underestimating CRF of the studied population.

In the present study that used an exercise intervention with different exercise protocols including an attention-control group (AC), the same equation was used to follow-up CRF of 248 participants. The participants that made up the sample of the present prospective study had a mean $\dot{V}O_{2peak}$ of 28.2 ± 7.6 $mL \cdot kg^{-1} \cdot min^{-1}$ (Table 13), which was 4.9 ± 5.3 $mL \cdot kg^{-1} \cdot min^{-1}$ higher than at baseline (23.4 ± 6.2 $mL \cdot kg^{-1} \cdot min^{-1}$). Thus, the CRF of the sample improved from poor to average.[118] As well as at baseline, Jurio-Iriarte *et al.* equation underestimated $\dot{V}O_{2peak}$ of the same participants at follow-up, with a mean difference of 3.7 ± 5.3 $mL \cdot kg^{-1} \cdot min^{-1}$ less than the direct CPET measurement.

Although the MSWT provides a valid functional capacity assessment with good predictive power, 42 % of the prediction variability was not explained by the model at follow-up (*i.e.,* the performance on the MSWT explained 58 % of the variance of the $\dot{V}O_{2peak}$ in the studied cohort, $r^2 = 0.58$) (Table 14). Similar to other recent studies,[105,114,115] the MSWT appears to be a valid tool for the assessment of CRF. However, variability in estimation at follow-up testing (17 % probability of error) questions the use of this approach to accurately predict CRF.

The Jurio-Iriarte *et al.* equation would be a valuable equation if it were sensitive to CRF changes after exercise intervention (*i.e.,* able to detect proportional changes to the experimental magnitude). In this respect, we found that absolute and relative improvement of $\dot{V}O_{2peak}$ was significantly different ($P < 0.001$) and not proportional ($r = 0.42$; $r^2 = 0.17$; $ICC = 0.31$), with a difference of 2.93 ± 4.88 $mL \cdot kg^{-1} \cdot min^{-1}$ (13.7 %) between the CPET measurements and MSWT prediction (Table 14). Taking the aforementioned into account, it appears that in general the MSWT does not accurately detect the change in CRF, as it underestimates the improvements of $\dot{V}O_2$ (Figure 7.B).

Other studies analyzing populations affected by airflow limitation and very limited functional capacity (pulmonary or cardiac disability) have reported much higher correlations between $\dot{V}O_{2peak}$ and MSWT than reported in the present study (see in Jurio-Iriarte *et al.*[125], Table 9). Fitness and high BP only limit the CRF of the population in the current investigation, which is likely the explanation for the differences in the observed correlations.

The main finding of the present investigation was that the validity of the MSWT-estimated $\dot{V}O_{2peak}$ was moderate ($ICC = 0.69$) compared to the measured value, but would be considered weak if the *95 % CI*

(0.34-0.82) is taken into account,[128] indicating a lower bound of 0.34. This may be caused by the values of participants with the highest CRF whose $\dot{V}O_{2peak}$ prediction are further away from the mean value of the sample (Table 14). The assessment of CRF at baseline ranged in 21 $mL \cdot kg^{-1} \cdot min^{-1}$ and in 19 $mL \cdot kg^{-1} \cdot min^{-1}$ at follow-up around the mean bias with a tendency related to the difference between measured and predicted $\dot{V}O_{2peak}$ (Bland & Altman plots, Figure 7.A and 7.B, respectively). Thus, the participants with higher functional capacity (*i.e.,* higher CRF) demonstrated the larger error with predicting of $\dot{V}O_{2peak}$ (≥ 10 $mL \cdot kg^{-1} \cdot min^{-1}$ of difference), minimizing the achievements of the participants that had the most improvement (Figure 7.B). Therefore, these findings indicate there is too much variability when predicting $\dot{V}O_{2peak}$ from the MSWT in situations (disability, pharmacological therapy or exercise programming) when an accurate determination of CRF is critical. The improvement of CRF at follow-up (from 22.9 ± 6.1 to 28.2 ± 7.6 $mL \cdot kg^{-1} \cdot min^{-1}$) affected the prediction of $\dot{V}O_{2peak}$, mostly of the highest values. In this respect, we found that obese (n = 128) participants' CRF (BMI ≥ 30) was more accurately determined by the MSWT equation than the non-obese participants (*ICC* = 0.76; *95 % CI* 0.52-0.87), which could be of interest for this sub-population with HTN. These findings have two important implications: (1) taking into account the error of estimation, the MSWT may have a practical application to estimate $\dot{V}O_{2peak}$ for obese people with HTN through the equation generated by Jurio-Iriarte *et al.*[125], mainly with more deconditioned participants and when CPET is no available, and (2) when CRF is necessary to be accurately measured, the CPET (*i.e.,* $\dot{V}O_{2peak}$) continues being the "gold standard".

5.6. Conclusions

In summary, the findings of this study do not fully support the validity of the equation presented in the previous research by Jurio-Iriarte *et al.* Although predicting $\dot{V}O_{2peak}$ from Jurio-Iriarte *et al.* equation using MSWT results in substantial variability after exercise intervention, the new equation may still have practical value in estimating $\dot{V}O_{2peak}$ for obese people with HTN when CPET is not available.

Perspective

Although the MSWT has been previously validated to predict $\dot{V}O_{2peak}$ in sedentary and overweight/obese participants with HTN.[125] The ability of this field test to assess the improvement in CRF after an exercise intervention in the same cohort has not been evaluated. Due to the large variability of the new equation, the results of the present study justify the practical use of this easy and cost-effective test on studied population only when CPET is not available. On the other hand, findings of this study cannot be extrapolated to other different population than sedentary and overweight/obese individuals with HTN. Therefore, more investigations should be conducted to research the validity of MSWT to estimate CRF in different populations.

Capítulo 6.

Effects of different exercise training programmes on cardiorespiratory fitness in overweight/obese adults with hypertension: a pilot study.

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Health Promotion Practice, 2018.
doi: 10.1177/1524839918774310.

6. Effects of different exercise training programmes on cardiorespiratory fitness in overweight/obese adults with hypertension: a pilot study.

6.1. Abstract

Purpose: the goal of the study was to compare the effects of two supervised aerobic exercise programmes (moderate-intensity continuous training, MICT *vs.* high-intensity interval training, HIIT) after 8-, 12- and 16-week intervention periods on cardiorespiratory fitness (CRF) in overweight/obese adults diagnosed with hypertension (HTN). **Methods:** participants ($n = 64$) were divided into three intervention cohorts (control group 'CG', MICT, and HIIT) and each of these in turn, into three intervention length cohorts (8, 12 and 16 weeks). Supervised groups exercised twice a week. **Results**: there were no statistical changes in post-intervention periods in CG ($g < 0.1$). CRF as assessed by peak oxygen uptake ($mL \cdot kg^{-1} \cdot min^{-1}$) increased ($P < 0.001$) in exercise groups (MICT, 3.8 ± 3.3, $g = 0.6$; HIIT, 4.2 ± 4.7, $g = 0.7$). The effect of exercise interventions compared with CG was substantial ($P < 0.02$; $g > 0.8$) and mostly consequence of HIIT-related effects. The improvements on CRF occurred after 12 and 16 weeks in exercise interventions, rather than in the 8-week group or CG, where Hedges' *g* index indicated small effect. **Conclusion:** this study may suggest that both MICT and HIIT exert cardioprotector effects on HTN in the overweight/obese population. However, short-term training duration (< 12 weeks) does not seem to improve CRF, and HIIT intervention might generate higher aerobic capacity, which seems to grow as intervention lengthens.

Keywords: cardiovascular disease, chronic disease, obesity, physical activity/exercise, training.

6.2. Introduction

Hypertension (HTN) is a significant risk factor for cardiovascular diseases (CVD), which are the top global risk causes of morbidity and mortality.[129] Therefore, it is necessary a treatment to reduce avoidable risk factors and consequently the high rate of mortality due to CVD.[8] It has been shown that people with HTN are generally also overweight or obese, and physically inactive,[34] being those factors additive regarding cardiovascular risk (CVR).[35] A relatively small increase in cardiorespiratory fitness (CRF) substantially reduces CVR, and this risk declines progressively with increasing aerobic capacity. Thus, unfit individuals have twice the risk of mortality regardless of body mass index (BMI).[54] An increase in exercise within an exhaustive change of lifestyle (*i.e.*, salt restriction, moderation of alcohol consumption, high consumption of vegetables and fruit and low-fat diet, total body mass reduction and smoking cessation) is recommended to prevent, treat and control HTN,[10] as exercise is associated with antihypertensive benefits.[122] On the other hand, there is no agreement about the optimal dose of *F*requency of exercise (number of sessions per week), *I*ntensity (how hard an individual works during exercise), *T*ime or Length (how long each session lasts), and *T*ype of exercise (*FITT* principle) to obtain the greatest health benefit.[130] Compared with moderate-intensity continuous training (MICT, continuous steady training), high-intensity interval training (HIIT, intermittent exercise alternating bursts of higher intensity with lower-intensity activity) aerobic exercise typically results in a higher CRF increase in less time and produces greater metabolic changes.[131] However, the effect of HIIT on both office and ambulatory blood pressure (BP) appears to be medication dependent with untreated hypertensive individuals displaying more significant decreases compared with their treated counterparts, who could present normalized resting BP and less adaptation to exercise.[131] Previous investigations have studied the effects of 10 [63], 12 [56,62,132,133], 15 [134], 16 [135,136], 20 [137] and 24 [138] weeks of HIIT intervention on BP and some of them on CRF. Nevertheless, it is not known if effects occur with less than 12-week interventions (*i.e.,* a short-term impact) on the CRF of overweight/obese adults with HTN. The evidence mentioned above suggests that for this population, 8 weeks of HIIT intervention may offer CRF adaptations that MICT may not. The aim of the present study was, therefore, to compare the effects of two different aerobic exercise programmes (MICT *vs.* HIIT) after 8-, 12- and 16-week intervention periods on the CRF of overweight/obese adult population diagnosed with HTN.

6.3. Material and methods

Study design

This work is a pilot study before the EXERDIET-HTA (Trial Registration: NCT02283047) randomised single-blind controlled experimental trial.[67] The Ethics Committee of The University of the Basque Country (UPV/EHU, CEISH/279/2014) approved the study protocol. All participants provided written informed consent before any data collection. After baseline measurements, participants were randomly assigned to the control group (CG), or two supervised exercise groups (MICT or HIIT). All in all, participants were randomised into nine groups (*i.e.,* 8-weeks CG, 8-weeks MICT, 8-weeks HIIT, 12-weeks CG, and so on) (Figure 8).

Participants

Non-Hispanic white sedentary (those who did not comply with the *"Global Recommendations on Physical Activity for Health"* by the World Health Organization) participants (*n* = 70) that volunteered to take part in the present study classified as overweight (BMI ≥ 25) or obese (BMI ≥ 30)[49] and diagnosed with stage 1 or 2 HTN. A systolic blood pressure (SBP) of 140-179 and/or a diastolic blood pressure (DBP) of 90-109 mm Hg and/or under antihypertensive pharmacological treatment.[10] The exclusion and inclusion criteria for the study have been published previously.[67]

Measurements

The measurements used in the protocol were taken before and after each intervention period (8-, 12- and 16-weeks). The post-intervention test was scheduled the following week after finishing the intervention period, and it was single-blind by the medical doctor, with no information regarding the intervention group of each participant.

The fifteen-level Modified Shuttle Walk Test (MSWT) consisted in walking/running up and down a 10-meter corridor at an incremental speed as previously described.[43,77]

A CardioPulmonary Exercise Test (CPET*)* was used to objectively assess aerobic capacity after the MSWT with a minimum prior 30-minute rest break to obtain stable resting heart rate (HR) and BP values. The test was performed briefly on an electronically braked Lode Excalibur Sport Cycle Ergometer (Groningen, The Netherlands). The testing protocol was started at 40 W with gradual increments of 10 W every minute to exhaustion with continuous electrocardiogram monitoring and participants cycling at 70 rpm. The expired gas analysis was performed using a commercially available metabolic cart (Ergo CardMedi-soft S.S, Belgium Ref. USM001 V1.0) that was calibrated before each test with a standard gas of known concentration and volume. The BP was measured at rest before starting the test, every two minutes throughout the test and during the recovery period. Borg rating of perceived exertion (RPE) (6 to 20) scale was self-reported at the end of each stage. Peak oxygen uptake ($\dot{V}O_{2peak}$) was defined as the highest oxygen uptake value attained towards the end of the test and reflected peak aerobic capacity. Achievement of $\dot{V}O_{2peak}$ criteria have been described previously.[75] After completion of the test, participants remained on the bike five more minutes for recovery with electrocardiogram and BP monitoring. Absolute and relative indications for terminating the exercise test were taken into account.[121]

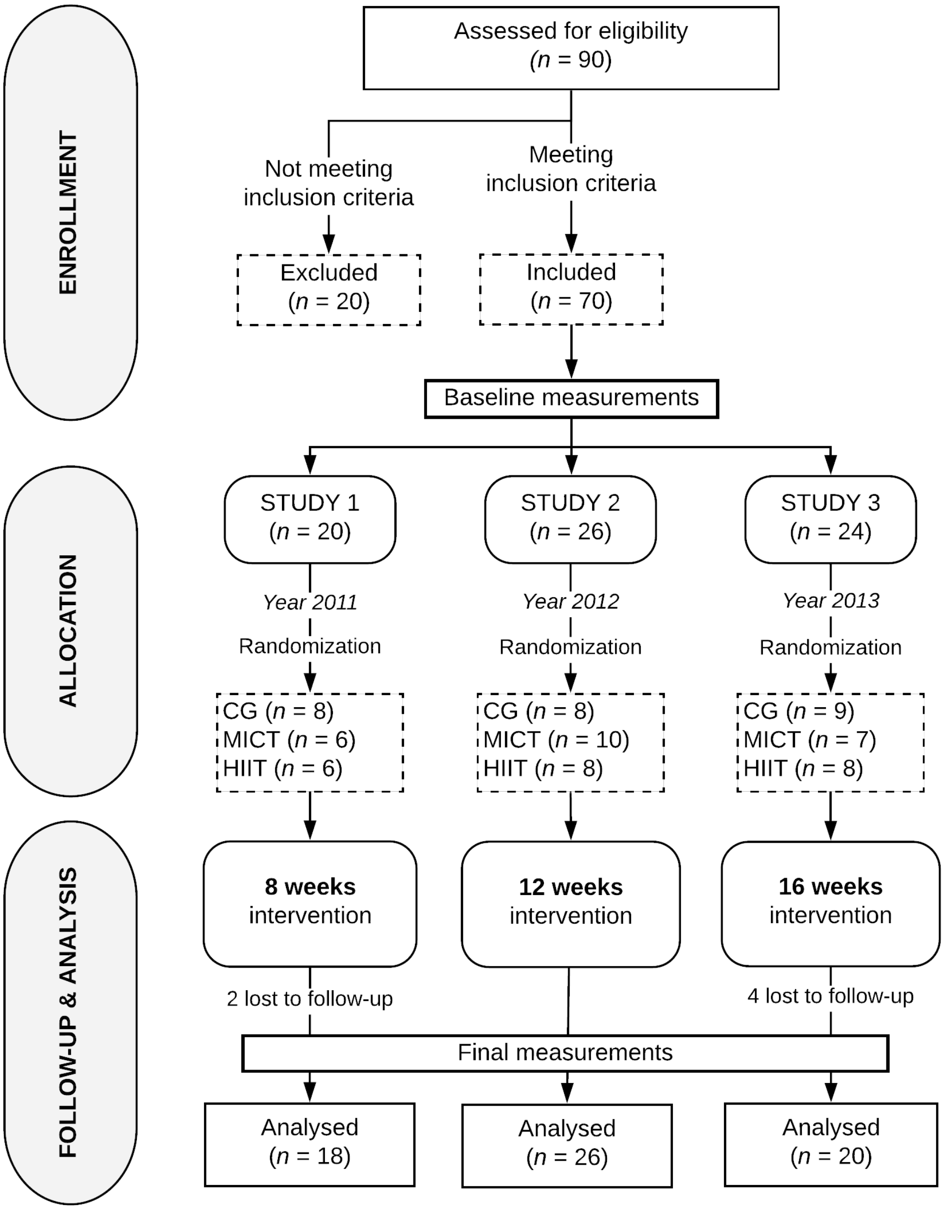

Figure 8. Planned flow diagram of the pilot study from recruitment to the end of intervention.

CG = control group; MICT = moderate-intensity continuous training; HIIT = high-intensity interval training.

Anthropometry measurements which were taken to assess body composition included stature (SECA 213), total body mass (BM) (SECA 869), BMI and waist and hip circumferences (SECA 200) to calculate waist-to-hip ratio (WHR). All measurements were taken following guidelines from the International Society for the Advancement of Kinanthropometry.[72]

Intervention

Even though we requested participants continue with their regular physical activity patterns outside the study protocol, prior to the intervention period they received advice regarding a healthy lifestyle (*i.e.,* nutrition and physical activity general recommendations) regarding guidelines for the management of arterial hypertension[10] to maintain ethical procedures.

The exercise groups received supervised exercise intervention for 45 minutes, twice a week. Both intensity and training volume increased progressively during the intervention period in the same range for the two groups: MICT group performed HR values at 50-75 % of HR reserve with steady continuous exercise;[75] HIIT group, interval training alternating high (76-95 % of HR reserve) and moderate (50-75 % of HR reserve) intensities at different exercise protocols depending on the type of exercise (*i.e.,* treadmill or bike).[75]

All the exercise sessions started and finished with BP monitoring. The training intensity was controlled by an HR monitor (Polar Electro, Kempele, Finland) and through the RPE using the original Borg scale (6-20 points). Each session included a 5-10 minute warm-up and a 10 minute cool-down period. The central portion of the training session consisted of 45 minutes of aerobic exercise (*i.e.,* one day of the week on the treadmill, and the second one on the bike, both using BH Fitness equipment ™). The participants exercised at the lower HR intensity limit for the first two weeks (only one week for the 8-week programme) of the training period before progressively increasing the HR intensity towards the upper limit. The rationale of mixing bike and treadmill was to avoid the osteoarticular impact of two days on the treadmill, bearing in mind the intensity of the HIIT programme. The intensity was individually tailored to HR at moderate or vigorous efforts, adjusting the speed and angle of the treadmill or the power and speed on the bike, to reach the planned target HR.

High-intensity interval training protocol on the treadmill was carried out with 5 minute warm-up period at moderate intensity, before walking two intervals of 4 minutes at high intensity for the first two weeks, increasing, afterwards, to four intervals of 4 minutes in the following weeks (*i.e.,* 16 minutes of total high-intensity volume on the treadmill). Between the high-intensity intervals, the participants did 3 minutes of walking at moderate intensity. The training session ended with a 1-4 minute cool-down period at moderate-intensity.[63]

High-intensity interval training protocol on the bike consisted of a 10 minute warm-up period. After that, participants cycled for 30 seconds at high intensity followed by 60 seconds at moderate intensity. Four repetitions (1 rep = 30 s high intensity followed by 60 s moderate intensity) were initially performed and increased, afterwards, to 18 repetitions. The training session ended with a 5-10 minute cool-down period at moderate-intensity.[80] The total high-intensity volume on the bike was 9 minutes.

Statistical analysis

Statistical analyses were carried out with the SPSS Statistical software package (24th edition). The required sample size was determined for the primary outcome variable (SBP). It was identified that adequate power (0.80) to evaluate differences in our design consisting of four experimental groups would be achieved with 164 people (41 each group, $\alpha = 0.05$, effect size $f = 0.27$).[67] Therefore, as the sample size was too small to have adequate power for statistical significance for anything smaller than very large effects, the current report is considered a pilot study, and we evaluated effect sizes for each outcome variable.[139] Hedges' *g* (*g*) was used as the index of effect size for within and between comparisons of two groups (*i.e.*, Pre *vs*. Post-intervention; after-intervention change in CG *vs.* exercise groups). A *g* index of 0.2 was considered small effect, 0.5 medium and 0.8 large.[140] Cohen's *f* (*f*) was used to assess training effects across the different intervention groups (CG, MICT, HIIT) and different length of training programmes (8-, 12-, 16-weeks). When we compared more than two interventions, an *f* index of 0.1 was considered small effect, 0.25 medium and 0.4 large.[141] Baseline and follow-up values of all the independent variables expressed are as the mean and standard deviation (*SD*).

When doing within and between comparisons without subsets in lengths of intervention (*i.e.,* taking all lengths of each type of intervention together: *All*), the sample size was big enough to evaluate statistical significance. The paired-samples Student's *t*-test compared the baseline, and follow-up mean values of all the independent variables. Analysis of covariance (ANCOVA) was used to assess training effects across the different intervention groups. Post-intervention outcome selected as a dependent variable and PRE-intervention outcome as a covariate. We performed Bonferroni post hoc comparisons, and Helmert contrasts were performed. The level of significance (*P* or *P*-value) set at 95 % ($\alpha = 0.05$).

6.4. Results

Seventy participants met all the required criteria for inclusion in the study. There were six drop-outs (8.6 %) for reasons unrelated to the study (Figure 8). Thus, 64 participants [48 male (75 %) and 16 female (25 %)] aged 55.9 ± 8.5 years old completed the intervention. Fifty-eight (90 %) participants were taking anti-hypertensive medication. Table 15 shows the participants' baseline characteristics. At baseline there were no between-group differences in any of the studied variables (*i.e*., BM, $Distance_{MSWT}$, $Distance_{CPET}$, $Workload_{CPET}$, $\dot{V}O_{2peak}$, MET_{peak}).

Table 16 shows the effect of different types of intervention without subsets of differing lengths or durations of intervention: CG reduced BM ($P < 0.001$; $g = 0.1$) and had small changes in exercise groups ($P > 0.05$; $g < 0.03$). Total distance walked/run in the MSWT ($Distance_{MSWT}$) increased 45.0 ± 59.3 m after the MICT ($P < 0.001$; $g = 0.3$) and 63.3 ± 73.4 m after the HIIT ($P = 0.02$; $g = 0.5$), and total distance ridden in the CPET ($Distance_{CPET}$) increased ($P < 0.001$) 0.5 ± 0.3 km after the MICT ($g = 0.4$) and 0.7 ± 0.4 km after the HIIT ($g = 0.6$). Workload increased ($P < 0.001$) 20.4 ± 15.2 W in MICT ($g = 0.5$) and 30.5 ± 15.6 W in HIIT ($g = 0.7$). The MICT increased ($P < 0.001$) the absolute $\dot{V}O_{2peak}$ 0.3 ± 0.2 $L \cdot min^{-1}$ ($g = 0.6$) and 0.3 ± 0.4 $L \cdot min^{-1}$ in HIIT ($g = 0.5$), and relative $\dot{V}O_{2peak}$ increased ($P < 0.001$) 3.8 ± 3.3 $mL \cdot kg^{-1} \cdot min^{-1}$ after MICT ($g = 0.6$) and 4.2 ± 4.7 $mL \cdot kg^{-1} \cdot min^{-1}$ after HIIT ($g = 0.7$) (Figure 9: All). We found similar improvements in the Metabolic Equivalent of Task (MET), which increased ($P < 0.001$) 1.2 ± 1.1 after MICT ($g = 0.7$) and 1.1 ± 1.3 after HIIT ($g = 0.6$). Moreover, we found the change after intervention to be statistically significant in most analysed parameters; the effect size of MICT and HIIT interventions was medium in CRF variables ($\dot{V}O_{2peak}$ and MET) and also medium size in $Distance_{CPET}$ and workload of HIIT intervention. Changes after intervention period in CG were not statistically significant, and the effect size of those changes was considered very small ($g < 0.1$).

The effect of exercise interventions (*i.e.*, MICT and HIIT) compared with CG was substantial and statistically significant ($P < 0.02$; $g > 0.8$) for all variables. However, for $Distance_{MSWT}$ a medium-sized effect was observed ($P = 0.01$; $g = 0.7$) and small changes in BM were not significant ($P > 0.05$; $g = 0.4$) (Table 16: Helmert contrast). Those large effects were mostly the consequence of HIIT-related effects, as indicated by Cohen’s *f* index and Bonferroni post hoc comparisons (Table 16).

Table 16 *(All)* shows that the 8-week intervention effect is small or medium. Thus, the previously related improvements occurred in the 12- and 16-week MICT and HIIT interventions; rather than in the 8-week interventions or CG, where the gain effect was small, as indicated by Hedges' *g* index. Cohen’s *f* index also indicated a medium or large effect of intervention-length in all measured parameters, due to the more significant effects of 12- and 16-week interventions. Body mass was reduced in CG and in the longest exercise interventions, while it increased after shorter exercise interventions, showing large differences between the gain of BM after short interventions and the longer ones or CG (Figure 9).

Table 15. Baseline characteristics of the study population. Data are expressed as mean ± *SD*, or frequency (%).

Variable	***n* = 64**	
Sex	48 (75 %) ♂	16 (25 %) ♀
Age (years)	55.9 ± 8.5	
BM (kg)	81.9 ± 13.1	
BMI ($kg \cdot m^{-2}$)	27.9 ± 3.4	
Waist circumference (cm)	99.7 ± 7.4 ♂	85.7 ± 11.3 ♀
Hip circumference (cm)	102.7 ± 5.3 ♂	103.1 ± 8.1 ♀
WHR	0.97 ± 0.05 ♂	0.83 ± 0.06 ♀
Rest SBP (mm Hg)	134.8 ± 16.1	
Rest DBP (mm Hg)	89.9 ± 8.8	
Peak SBP (mm Hg)	205.8 ± 26.9	
Peak DBP (mm Hg)	94.1 ± 14.8	
$\dot{V}O_{2peak}$ ($L \cdot min^{-1}$)	2.1 ± 0.6	
$\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	25.7 ± 7.3	
RER_{peak}	1.1 ± 0.1	
Workload (W)	135.9 ± 42.1	
MET_{peak}	7.3 ± 2.1	
$Distance_{CPET}$ (km)	2.1 ± 1.0	
Medication	58 (90 %)	
– ACEI	20 (31 %)	
– ARB	28 (44 %)	
– Diuretics	13 (20 %)	
– CCB	13 (20 %)	
– BB	9 (14 %)	
– Statins	11 (17 %)	
– Hypoglycemic Agents	3 (5 %)	
– Antiplatelets	1 (2 %)	
– Anticoagulants	2 (3 %)	

BM = body mass; BMI = body mass index; WHR = waist-to-hip ratio; CPET = cardiopulmonary exercise test; $\dot{V}O_{2peak}$ = peak oxygen uptake; RER = respiratory exchange ratio; MET = metabolic equivalent of task; SBP = systolic blood pressure; DBP = diastolic blood pressure; ACEI = angiotensin-converting-enzyme inhibitors; ARB = angiotensin receptor blockers; CCB = calcium channel blockers; BB = beta blockers.

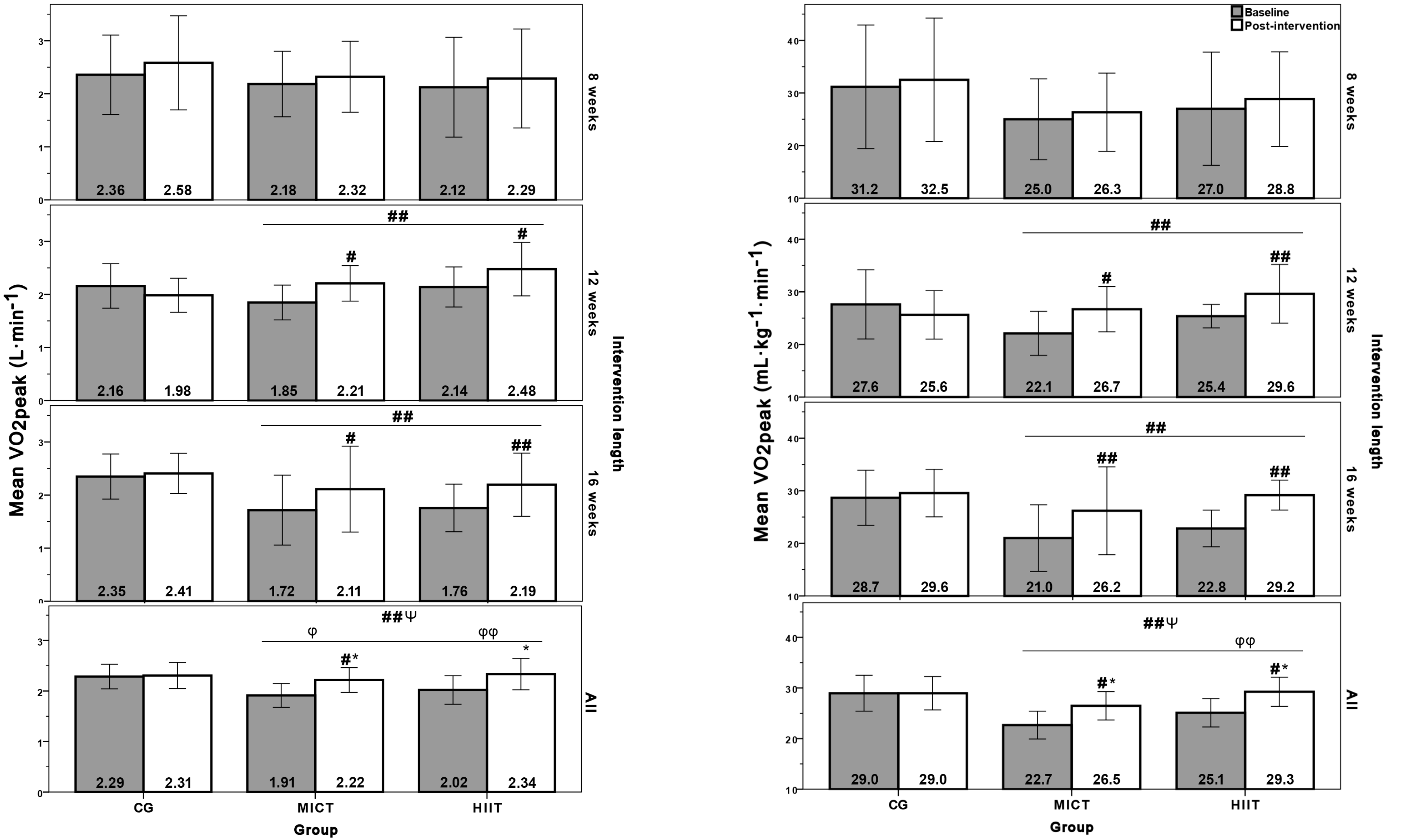

Figure 9. Evolution of $\dot{V}O_{2peak}$ after intervention periods.

Values are Mean ± *SD.* Error bars at 95 % *CI*. Medium *(#)* and large *(##)* effects within and between interventions are indicated. Statistically significant differences (*P* < 0.05) are expressed as: * = pre- *vs*. post-intervention; φ = CG *vs*. MICT; φφ = CG *vs*. HIIT; **Ψ** = CG *vs*. exercise groups.

Table 16. Comparison between after-intervention effects of different types and lengths of exercise-training.

Variable	CG: 8 weeks (*n* = 6); 12 weeks (*n* = 8); 16 weeks (*n* = 9); All (*n* = 23)			Hedges' *g* (PRE-POST)	Cohen's *f* (length of intervention)	MICT: 8 weeks (*n* = 6); 12 weeks (*n* = 10); 16 weeks (*n* = 5); All (*n* = 21)			Hedges' *g* (PRE-POST)	Cohen's *f* (length of intervention)	HIIT: 8 weeks (*n* = 6); 12 weeks (*n* = 8); 16 weeks (*n* = 6); All (*n* = 20)			Hedges' *g* (PRE-POST)	Cohen's *f* (length of intervention)	Comparison between effects of types of intervention (ANCOVA): Cohen's *f* (CG *vs* MICT *vs* HIIT)	Bonferroni	Hedges' *g* (CG *vs* exercise groups)	Helmert
Body Mass (kg)	80.5 ± 8.9	↙	79.5 ± 9.9	0.095		88.5 ± 19.7	↗	89.0 ± 18.0	0.023		76.9 ± 9.4	↗	77.3 ± 9.6	0.036		0.592	-	0.927	-
	79.5 ± 10.0	↙	78.0 ± 9.5	0.145	0.280	84.0 ± 8.9	↙	83.1 ± 8.4	0.106	0.559	84.1 ± 17.9	↗	85.1 ± 18.7	0.048	0.565	0.567	-	0.664	-
	82.7 ± 9.6	↙	82.2 ± 9.8	0.053		82.7 ± 19.9	↙	81.7 ± 20.2	0.045		76.5 ± 16.0	↙	75.0 ± 15.8	0.085		0.277	-	0.466	-
	81.0 ± 9.3	↙	80.0 ± 9.4 *	0.104	-	85.0 ± 14.7	↙	84.4 ± 14.3	0.038	-	79.7 ± 14.9	=	79.7 ± 15.5	0.003	-	0.248		0.408	
$Distance_{MSWT}$ (m)	865.0 ± 224.8	↗	898.3 ± 194.4	0.146		863.3 ± 183.5	↗	908.3 ± 138.9	0.255		865.0 ± 123.6	↗	928.3 ± 103.6	0.513		0.299	-	0.340	-
	826.3 ± 236.9	↗	833.8 ± 244.9	0.029	0.193	817.0 ± 247.3	↗	877.0 ± 195.3	0.258	0.495	906.3 ± 175.9	↗	946.3 ± 137.2	0.240	0.516	0.344	-	0.532	-
	1028.9 ± 209.4	↗	1036.7 ± 175.7	0.038		936.0 ± 328.1	↗	1020.0 ± 289.1	0.245		936.7 ± 171.9	↗	1048.3 ± 163.6	0.614		0.530	-	1.011	-
	915.7 ± 232.7	↗	930.0 ± 217.3	0.063	-	858.6 ± 244.6	↗	920.0 ± 205.3 *	0.267	-	903.0 ± 155.0	↗	971.5 ± 139.8 *	0.455	-	0.334	φφ	0.654	Ψ
$Distance_{CPET}$ (km)	2.6 ± 1.2	↗	2.8 ± 1.5	0.126		2.5 ± 1.1	↗	2.8 ± 1.1	0.221		2.2 ± 1.4	↗	2.8 ± 1.6	0.334		0.465	-	0.528	-
	2.2 ± 0.6	↗	2.4 ± 0.8	0.163	0.157	1.7 ± 0.8	↗	2.2 ± 0.8	0.600	0.456	2.0 ± 0.4	↗	2.7 ± 0.8	1.058	0.364	0.748	-	1.256	-
	2.6 ± 1.0	↗	2.7 ± 1.2	0.047		1.4 ± 1.3	↗	2.1 ± 1.5	0.430		1.7 ± 1.0	↗	2.5 ± 1.4	0.551		0.974	-	1.319	-
	2.5 ± 0.9	↗	2.6 ± 1.1	0.104	-	1.9 ± 1.0	↗	2.4 ± 1.1 *	0.441	-	2.0 ± 0.9	↗	2.7 ± 1.2 *	0.612	-	0.647	φ φφ	1.106	Ψ
$Workload_{CPET}$ (Watt)	160.8 ± 47.4	↗	161.3 ± 51.5	0.009		155.2 ± 46.3	↗	163.0 ± 44.4	0.159		137.8 ± 57.9	↗	159.0 ± 58.7	0.335		0.686	-	0.951	-
	142.8 ± 28.9	↗	146.8 ± 36.4	0.115	0.160	118.6 ± 33.9	↗	141.3 ± 31.8	0.661	0.617	130.9 ± 22.1	↗	161.0 ± 29.9	1.084	0.530	0.929	-	1.728	-
	152.9 ± 37.2	↗	156.3 ± 40.5	0.084		107.2 ± 51.4	↗	138.0 ± 60.4	0.496		115.0 ± 50.4	↗	155.2 ± 48.2	0.752		1.103	-	2.068	-
	151.4 ± 36.5	↗	154.3 ± 40.7	0.073	-	126.3 ± 44.2	↗	146.7 ± 42.3 *	0.462	-	128.2 ± 42.6	↗	158.7 ± 43.1 *	0.697	-	0.771	φ φφ	1.498	Ψ
$\dot{V}O_{2peak}$ ($L \cdot min^{-1}$)	2.4 ± 0.7	↗	2.6 ± 0.8	0.266		2.2 ± 0.6	↗	2.3 ± 0.6	0.206		2.1 ± 0.9	↗	2.3 ± 0.9	0.171		0.119	-	0.190	-
	2.2 ± 0.5	↙	2.0 ± 0.4	0.370	0.630	1.8 ± 0.5	↗	2.2 ± 0.5	0.744	0.484	2.1 ± 0.5	↗	2.5 ± 0.6	0.595	0.311	0.883	-	1.844	-
	2.3 ± 0.6	↗	2.4 ± 0.5	0.107		1.7 ± 0.5	↗	2.1 ± 0.7	0.602		1.8 ± 0.4	↗	2.2 ± 0.6	0.806		0.752	-	1.628	-
	2.3 ± 0.6	↗	2.3 ± 0.6	0.034	-	1.9 ± 0.5	↗	2.2 ± 0.5 *	0.574	-	2.0 ± 0.6	↗	2.3 ± 0.7 *	0.482	-	0.408	φ φφ	0.928	Ψ
$\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	31.2 ± 11.2	↗	32.5 ± 11.2	0.110		25.0 ± 7.3	↗	26.3 ± 7.1	0.171		27.0 ± 10.3	↗	28.8 ± 8.6	0.179		0.123	-	0.041	-
	27.6 ± 7.9	↙	25.6 ± 5.5	0.278	0.433	22.1 ± 5.9	↗	26.7 ± 6.0	0.742	0.522	25.4 ± 2.7	↗	29.6 ± 6.7	0.790	0.335	0.711	-	1.633	-
	28.7 ± 6.8	↗	29.6 ± 5.9	0.133		21.0 ± 5.1	↗	26.2 ± 6.7	0.787		22.8 ± 3.3	↗	29.2 ± 2.7	1.931		0.755	-	1.795	-
	29.0 ± 8.2	=	29.0 ± 7.6	0.009	-	22.7 ± 6.0	↗	26.5 ± 6.2 *	0.613	-	25.1 ± 6.0	↗	29.3 ± 6.1 *	0.672	-	0.332	φφ	0.898	Ψ
MET_{peak}	8.9 ± 3.2	↗	9.3 ± 3.2	0.116		7.2 ± 2.0	↗	7.53 ± 2.0	0.161		7.7 ± 2.9	↗	8.1 ± 2.6	0.140		0.123	-	0.009	-
	7.9 ± 2.2	↙	7.3 ± 1.6	0.297	0.451	6.2 ± 1.7	↗	7.63 ± 1.7	0.755	0.472	7.3 ± 0.7	↗	8.5 ± 1.9	0.787	0.362	0.688	-	1.625	-
	8.2 ± 2.0	↗	8.4 ± 1.7	0.115		6.0 ± 1.4	↗	7.50 ± 1.9	0.802		6.6 ± 1.0	↗	8.3 ± 0.7	1.891		0.810	-	1.921	-
	8.3 ± 2.3	=	8.3 ± 2.2	0.009	-	6.4 ± 1.7	↗	7.6 ± 1.7 *	0.642	-	7.2 ± 1.7	↗	8.3 ± 1.8 *	0.661	-	0.319	φφ	0.895	Ψ

CG = control group; MICT = moderate-intensity continuous training; HIIT = high-intensity interval training; MSWT = modified shuttle walk test; CPET = cardiopulmonary exercise test; $\dot{V}O_{2peak}$ = peak oxygen uptake; MET = metabolic equivalent of task. Data are expressed as mean ± *SD* values before and after intervention period. Effect size between PRE-POST design is expressed by Hedges' *g*. Effect size between after intervention effects of different length and type interventions is expressed by Cohen's *f*. Effect size between CG and exercise groups is expressed by Hedges' *g*. Statistically significant differences ($P < 0.05$) are expressed as: ***** = pre- *vs*. post-intervention; φ = CG *vs*. MICT; φφ = CG *vs*. HIIT; Ψ = CG *vs*. exercise groups; **-** = not calculated.

6.5. Discussion

The present study evaluated the effects of different structured, formal and supervised physical exercise training programmes in the CRF of overweight/obese adult population diagnosed with HTN, after 8-, 12- and 16-week intervention periods, and compared them with a CG. The main findings showed that only participants who performed two days per week of supervised training modes (MICT and HIIT) statistically increased CRF. There was also a superior tendency effect from HIIT, and we found that "short-term" exercise intervention (8 weeks) with MICT or HIIT was not enough to increase CRF in overweight/obese people diagnosed with HTN.

Sixty-four participants divided into three cohorts subject to kind of intervention (CG, MICT, and HIIT) and each one into three other cohorts subject to intervention length (8, 12 and 16 weeks) are not enough to reach any generalisable conclusion related to the effects of exercise intervention based on different combinations of *FITT* principle's components in the CRF markers of overweight/obese patients with HTN. Consequently, the authors of the manuscript suggest considering this study a pilot study. However, taking into account the estimated effect sizes with such a small sample per group we do find these initial tendencies promising.

European guidelines for the management of arterial HTN[10] recommend lifestyle changes for reducing and controlling BP and BM, including calorie-restricted diet and regular physical exercise. In fact, previous investigations[142] had shown better control of BP and BM when dual treatment was applied. The present pilot study was designed to evaluate only CRF after different exercise programmes, without diet intervention (only some basic recommendations but with no control or supervision). Therefore, although out of the scope of the current work, the small and irregular changes showed in BM, may confirm the requirement of diet as a key component along with exercise intervention to achieve BM loss in overweight/obese people with HTN.[49]

Even though it recognises that exercise reduces CVD risk, how much of it is needed and the intensity that provides optimal cardiovascular protection are two questions for which there are still no definitive answers.[34] In this study, both supervised exercise training interventions provided significant improvements on the different variables measured at the CPET (distance, workload, $\dot{V}O_{2peak}$, MET). It is noteworthy that each 1-MET higher CRF is associated with considerable (10-25 %) improvement in survival.[37] It might state, therefore, that comparing MET_{peak} values before *vs*. after the intervention, in the present study, MICT (6.4 *vs.* 7.6) and HIIT (7.2 *vs.* 8.3) exercise programmes were effective regarding reduction of CVR (Table 16). Furthermore, it is well known that the bigger the amount of activity or intensity, the higher gain in CRF.[37] Thus, in this study, although the effect of both exercise interventions compared with CG was significant for all variables, the large improvement in CRF was mostly the consequence of HIIT (Cohen's *f* index and Bonferroni post hoc comparisons, Table 16). In this sense, the two groups were equated with regard to the total amount of work but not intensity, which leads to a more considerable energy expenditure in HIIT group and points out high aerobic intensity as a critical factor for increasing aerobic capacity in this population. These results are in line with previous ones in coronary artery disease,[63] hypertensive population [56,131], and recent reviews with different populations [143-145] showing the beneficial effects of HIIT on cardiometabolic health markers.

Taking into account the evidence mentioned above, it may hypothesise that a short-term HIIT intervention (*i.e.,* eight weeks) might offer better CRF adaptations compared with MICT in this population. However, in the present study, there was a tendency towards bigger improvements as the intervention became longer and more intense (Table 16, *All*). At least 12 weeks seem to be necessary to obtain large improvements in physical fitness with either of both exercise programmes performed; thus, the longer the intervention was, the larger the beneficial effect it had (Figure 9). Results from the present study reveal that at the end of 8 weeks of training participants presented no statistical increases in CRF (MICT, $\Delta \dot{V}O_{2peak}$ = 5 %, Hedges' g = 0.171; HIIT, $\Delta \dot{V}O_{2peak}$ = 6.2 %, Hedges' g = 0.179, Table 16, *All*) compared with the pre-intervention period, similar to CG. However, after 12- (MICT, $\Delta \dot{V}O_{2peak}$ = 17 %, Hedges' g = 0.742; HIIT, $\Delta \dot{V}O_{2peak}$ = 14 %, Hedges' g = 0.790, Table 16, *All*) and 16 weeks of training (MICT, $\Delta \dot{V}O_{2peak}$ = 19 %, Hedges' g = 0.787; HIIT, $\Delta \dot{V}O_{2peak}$ = 22 %, Hedges' g = 1.931, Table 16, *All*) participants presented medium and large effects with a tendency of better results as the intervention lengthens (*i.e.,* 16 weeks *vs.* 12 weeks) (Figure 9). These findings are in line with a recent systematic review and meta-analysis[144] examining HIIT and cardiometabolic health markers. It establishes the ability of this procedure (at least 12 weeks of HIIT) with clinical applications in overweight/obese population that need to improve their aerobic fitness via increasing mitochondrial density, stroke volume, and skeletal muscle diffusive capacity, showing larger improvements in aerobic capacity by longer training periods.

It is known that CRF is a potentially stronger predictor of mortality than established risk factors such as smoking, HTN, high cholesterol, and type 2 diabetes mellitus[37] and that those fitter individuals who are overweight/obese are not automatically at a higher risk for all-cause mortality.[54] Therefore, this pilot study has shown the positive effect of different exercise interventions on overweight/obese people with HTN allowing this population to carry out HIIT.

Finally, and regarding the "*F*requency" of exercise, most professional committees recommend exercising on most, if not all, days of the week.[130] In the present study, with only two days per week of supervised exercise, an essential improvement on CRF was shown in both exercise groups (Figure 9). Thus, it might be that regular and individualised exercise, supervised and controlled by exercise professionals, will lead individuals to carry out the actual moderate and high exercise intensities achieving greater improvements than in unsupervised protocols. However, taking into account the post-exercise hypotension effect and the urgent need for increasing caloric expenditure and CRF in this population,[130] two days of supervised HIIT exercise along with other physical activities at lower intensities the other five days of the week could be the best option.

Limitations of the study

We should consider several limitations of the study. First, a bigger sample size is recommended to evaluate the effects of different kinds of exercise on BP, body composition and CRF. Second, we describe the effects of 8, 12 and 16 weeks in duration. Therefore, although it seems that an intervention length of less than 12 weeks does not offer the same beneficial adaptations as ≥ 12 weeks, we do not know the effects in between (9, 10 or 11 weeks). Finally, we required participants to continue with their normal physical activity patterns outside the study protocol; however, though all of them were sedentary at the beginning of the study, we did not control whether participants performed other daily physical activities.

6.6. Conclusions

This study indicates that both MICT and HIIT, in the form of 2-weekly bouts, exert cardioprotector effects on HTN in overweight/obese population. Furthermore, short-term training duration (< 12 weeks) may not improve CRF, and HIIT intervention might generate higher aerobic capacity, which seems to improve as intervention lengthens (> 12 weeks). The components of *FITT* principle for the assessment of exercise treatment to HTN and overweight/obese individuals need further research to reach generalisable results that will resolve the recommendations of exercise training in this population. The practical implications of this study indicate that a complete lifestyle treatment (diet plus exercise) is required to have a better control of BP, body composition and CRF, and that exercise treatment should include different types of training modes (MICT and HIIT).

Capítulo 7.

Conclusiones

7. CONCLUSIONES

- La validez del MSWT y la ecuación creada para predecir el $\dot{V}O_{2pico}$ y evaluar la intolerancia al EF de personas con HTA primaria y sobrepeso u obesidad es cuestionable, debido al error de estimación que se asume, tanto si se realiza antes como después de una intervención de EF con o sin intervención nutricional.
- Es preferible realizar la medición del $\dot{V}O_{2pico}$ de forma directa a través del CPET, para determinar la capacidad funcional de forma precisa, y realizar el diagnóstico, investigación, diseño de EF y seguimiento de personas con HTA primaria y sobrepeso u obesidad.
- Cuando no haya posibilidad de realizar CPET, el MSWT y la ecuación predictora de $\dot{V}O_{2pico}$ podría resultar válida para estimar la CCR de personas con HTA primaria y sobrepeso u obesidad.
- Los programas MICT y HIIT de al menos 12 semanas entrenando dos días a la semana brindan efecto cardioprotector en personas con HTA primaria y sobrepeso u obesidad.
- HIIT es el programa de EF que mayores mejoras genera en la capacidad aeróbica, y resulta en mayor beneficio cuanto más duradera es la aplicación del programa.
- Se necesita más investigación que permita llegar a conclusiones generalizables en cuanto a los componentes de la carga de entrenamiento definidos con el principio *FITT* y sus efectos en la salud de personas con HTA primaria y sobrepeso u obesidad, para diseñar programas de EF combinándolos adecuadamente.
- Se recomienda un tratamiento con cambio completo del estilo de vida (EF + dieta) para tener un mejor control de la PA, composición corporal y CCR.
- Los programas de EF deberían incluir diferentes tipos de entrenamiento aeróbico, como MICT y HIIT.

Capítulo 8.

Límites del trabajo y propuestas de futuro

8. LIMITACIONES DEL TRABAJO Y PROPUESTAS DE FUTURO

Una limitación potencial en este estudio es que el $\dot{V}O_{2pico}$ experimental fue medido en un CPET en cicloergómetro, mientras que se comprobó su asociación con variables obtenidas en el MSWT, que es un test de campo caminando o corriendo. La diferencia entre las actividades en las que se realizaron las mediciones podría haber influido resultando en un poder de estimación menor, y aumentando la probabilidad de error a través de la ecuación creada. Otros autores han observado que en cinta rodante se obtienen registros de $\dot{V}O_{2pico}$ 15-20 % mayores que en cicloergómetro[123], y este CPET se asemeja más al test de campo investigado, por lo que este estudio podría haber valorado realizar el CPET en cinta; tal decisión habría traído consigo otra serie de perjuicios, como que el aumento de $\dot{V}O_2$ sea menos lineal[124], o que resulte complicado medir la PA durante el CPET (no pudiéndose hacer a través de instrumental automático como en el cicloergómetro) que es un importante criterio de evaluación de los CPET en la población de estudio.

A la hora de crear una ecuación de estimación del $\dot{V}O_{2pico}$, se tuvieron en cuenta los datos de todas las personas participantes. La creación de la ecuación se podría haber realizado con una muestra de participantes menor, reservando la parte restante para la validación de la ecuación creada, con personas distintas que pertenecen a la misma población. Lo mismo cabría proponer para la validación del MSWT y la ecuación después de haber participado en una intervención de EF.

Las personas participantes conocieron la existencia de distintos grupos de intervención, las características generales de cada uno, y a cuál de ellos fueron asignadas, por lo que no eran ciegas en cuanto al experimento, como tampoco lo fueron los especialistas en EF que supervisaron las sesiones de entrenamiento. El personal investigador y médico que hizo el registro de las pruebas sí fue ciego a la asignación de participantes a los correspondientes grupos de intervención. Se podría conseguir un doble-ciego no informando de la existencia de distintos tipos de EF, y organizando las sesiones de EF por grupos de intervención, para que las expectativas sobre las distintas intervenciones no influyeran en los resultados de quienes participan en ellas; este cambio supondría mayor dificultad de organización, y probablemente la muestra de participantes disminuiría por menor disponibilidad horaria.

Teniendo en cuenta que se dieron recomendaciones generales de estilo de vida, sería interesante conocer si el mero hecho de hacer a las personas participantes conocedoras de tales recomendaciones puede influir de forma significativa en sus costumbres y consecuentemente en su salud. Al tratarse de personas sedentarias, no se hizo seguimiento regular de posibles cambios en el estilo de vida, como dieta, AF fuera del programa de intervención, u otros, excepto en los estudios que implementaron intervención nutricional, por lo que, podría cuestionarse si los efectos observados fueron consecuencia de la intervención, o de los posibles cambios en el estilo de vida. Añadir los cambios en el estilo de vida a las variables de observación haría el proceso de análisis y discusión más complejo, y resultaría más difícil lograr uno de los objetivos de esta investigación, que es identificar la intervención con EF más adecuada para personas con HTA primaria y sobrepeso u obesidad. Teniendo lo anterior en consideración, sería preferible para el interés investigador que los estilos de vida no variasen fuera del programa de intervención. Por otro lado, y desde un punto de vista ético, siempre conviene mejorar los hábitos y estilos de vida, hacia los más saludables para cada persona por lo que resultaría éticamente incorrecto no dar a conocer las recomendaciones sobre estilos de vida saludables.

Organizar sub-estudios que comparen los mismos programas de EF pero de duraciones distintas hace que la muestra total del proyecto de investigación se distribuya entre muchos grupos y quede disipada. Para próximas investigaciones, sería conveniente optar por las intervenciones de mayor duración, y hacer controles de las variables de estudio en diferentes momentos además de al principio y al final de la intervención; en el caso este proyecto se harían a las 8 y 12 semanas. De este modo la muestra en cada uno de los tipos y duraciones de intervención sería mucho mayor, permitiendo sacar conclusiones generalizables en todos los casos.

Debido al reducido número de mujeres que han participado en el estudio, no se puede estimar los efectos de cada tipo de EF dependiendo del sexo.

Sería interesante observar y comparar el efecto del desentrenamiento en los distintos grupos de intervención, para comprobar cómo resulta la ausencia del estímulo de entrenamiento. Este aspecto se implementó en los estudios de 16 semanas de duración.

El presente estudio se llevó a cabo con personas sedentarias con HTA primaria y sobrepeso u obesidad, por lo que los hallazgos no se deben extrapolar a poblaciones distintas. Para conocer si el MSWT es un método adecuado y con utilidad práctica, o determinar que combinación de los principios *FITT* es la más adecuada para distintas situaciones clínicas o distintas poblaciones, se debería realizar experimentos con las mismas.

Capítulo 9.

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Capítulo 10.

Anexos y publicaciones

10. ANEXOS

10.1. Anexo 1. Indicadores de calidad

Los indicadores de calidad de los artículos publicados, según *Journal Citation Reports* (JCR) y el *Cite Score* de Scopus en el año 2016 son los siguientes:

Revista	ISSN	País	Categoría	JCR		Scopus	
				JCR	Cuartil	Cite score	Cuartil
JASH	1933-1711	EEUU	Enfermedad vascular periférica	3.067	2	2.22	1
CEH	1064-1963	EEUU	Enfermedad vascular periférica	1.116	4	1.08	2
HPP	1524-8399	EEUU	Temática variada	-	-	1.29	1

CEH = Clinical and Experimental Hypertension; EEUU = Estados Unidos de América; HPP = Health Promotion Practice; ISSN = international standard serial number; JASH = Journal of the American Society of Hypertension; JCR = Journal Citation Reports.

10.2. Anexo 2. Publicaciones en formato original

- Association between modified shuttle walk test and cardiorespiratory fitness in overweight/obese adults with primary hypertension: EXERDIET-HTA study (*p*. 135).
- Validity of the modified shuttle walk test to assess cardiorespiratory fitness after exercise intervention in overweight/obese adults with primary hypertension (*p*. 145).
- Effects of different exercise training programmes on cardiorespiratory fitness in overweight/obese adults with hypertension: a pilot study (*p*. 151).

Journal of the American Society of Hypertension 11(4) (2017) 186–195

Research Article

Association between Modified Shuttle Walk Test and cardiorespiratory fitness in overweight/obese adults with primary hypertension: EXERDIET-HTA study

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Manuscript received October 16, 2016 and accepted January 27, 2017

Abstract

The aims of the study were to evaluate the relationship between Modified Shuttle Walk Test (MSWT) with peak oxygen uptake ($\dot{V}O_{2peak}$) in overweight/obese people with primary hypertension (HTN) and to develop an equation for the MSWT to predict $\dot{V}O_{2peak}$. Participants (N = 256, 53.9 ± 8.1 years old) with HTN and overweight/obesity performed a cardiorespiratory exercise test to peak exertion on an upright bicycle ergometer using an incremental ramp protocol and the 15-level MSWT. The formula of Singh et al was used as a template to predict $\dot{V}O_{2peak}$, and a new equation was generated from the measured $\dot{V}O_{2peak}$-MSWT relationship in this investigation.
The correlation between measured and predicted $\dot{V}O_{2peak}$ for Singh et al equation was moderate ($r = 0.60$, $P < .001$) with a standard error of the estimate (SEE) of 4.92 mL·kg^{-1} minute^{-1}, SEE% = 21%. The correlation between MSWT and measured $\dot{V}O_{2peak}$ as well as for the new equation was strong ($r = 0.72$, $P < .001$) with a SEE of 4.35 mL·kg^{-1} minute^{-1}, SEE % = 19%. These results indicate that MSWT does not accurately predict functional capacity in overweight/obese people with HTN and questions the validity of using this test to evaluate exercise intolerance. A more accurate determination from a new equation in the current study incorporating more variables from MSWT to estimate $\dot{V}O_{2peak}$ has been performed but still results in substantial error. J Am Soc Hypertens 2017;11(4):186–195. © 2017 American Society of Hypertension. All rights reserved.

Keywords: Equation for estimation; field test; peak oxygen uptake.

Introduction

The leading cause of noncommunicable disease deaths is the cardiovascular disease (CVD). Hence, CVD prevention is the major goal of different organizations worldwide by improving the management of these diseases through professional education and research and promoting healthy lifestyle.[1–3] Cardiovascular risk factors such as overweight/obesity and primary hypertension (HTN) have been increasing substantially and often occur concurrently, leading to an exponential risk for CVD.[4] Therefore, in the management of overweight/obesity-related HTN, a lifestyle change is imperative, particularly regular exercise[5] along with other lifestyle modification strategies.[4,6] Cardiorespiratory fitness

Conflict of interest: The authors declare that there is no conflict of interest.

The study was supported by the University of the Basque Country (GIU14/21 and EHU14/08) and by the Government of the Basque Country (SAIOTEK, SAI12/217).

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http://dx.doi.org/10.1016/j.jash.2017.01.008

(CRF) (ie, peak oxygen uptake, [$\dot{V}O_{2peak}$]) is a robust physiological marker of health risk and is now considered key vital sign.[7,8] Objective and direct measures of CRF, obtained from a cardiopulmonary exercise test (CPET), are essential for the assessment, clinical management, and exercise programming of overweight/obesity and HTN patients.[1,6] However, the CPET is not widely available and is expensive. CRF can be estimated using a variety of field tests[9] but may not be valid in all populations and are heavily influenced by motivation and encouragement. Moreover, their simplicity results in limited physiological and symptoms assessment during exercise.[10] The Léger and Lambert shuttle field test is incremental and progressive, stressing the individual to a symptom limited maximal performance.[11] Singh et al adapted the test and proposed an equation to assess functional capacity in patients with chronic obstructive pulmonary disease (COPD) using a 12-level protocol Incremental Shuttle Walk Test (ISWT).[9,12] This was further modified to a series of 15 levels by Bradley et al.[13,14] The 15-level Modified Shuttle Walk Test (MSWT) has important characteristics for functional capacity assessment in sedentary people with HTN[15–17] since it is based on incremental walking performance, a familiar activity to most people. Moreover, the MSWT is simple to perform for both the patient and the test operator, and the equipment needed is minimal. The MSWT field test is suitable for all levels of function, as the first levels are very slow and it is difficult to reach the upper levels, allowing a peak response to be elicited.[18] Previous studies have assessed the association between the ISWT or MSWT and $\dot{V}O_{2peak}$ concluding that these field walk tests are "safe," "objective," "valid," "reliable," "effective," and "highly predictive" for the assessment of functional capacity in each of the populations examined (Table 1). To our knowledge, there have not been studies that have examined the relationship between the MSWT and $\dot{V}O_{2peak}$ in a cohort of overweight/obese population with diagnosed HTN. Therefore, the aims of the present study were: (1) to evaluate the relationship between MSWT and $\dot{V}O_{2peak}$ in overweight/obese people with HTN and (2) to develop a new equation for the MSWT to predict $\dot{V}O_{2peak}$.

Material and Methods

Study Design

Baseline data from EXERDIET-HTA randomized controlled experimental trial were used for the purpose of this study. The design, selection criteria, and procedures for the EXERDIET-HTA study have been previously detailed.[47] The study protocol was approved by The Ethics Committee of The University of the Basque Country (UPV/EHU, CEISH/279/2014) and the Ethics Committee of Clinical Investigation of Araba University Hospital (2015-030) (ClinicalTrials.gov identifier, NCT02283047). All participants provided written informed consent prior to any data collection.

Participants

Non-Hispanic white participants with HTN and overweight/obesity were recruited from the cardiology services and local media. All participants (N = 256) that volunteered to take part in the present study were classified as overweight (body mass index [BMI] ≥ 25) or obese (BMI ≥ 30)[3] and with diagnosed with Stage 1 or 2 HTN, as defined with a systolic blood pressure (SBP) of 140–179 and/or a diastolic blood pressure (DBP) of 90–109 mm Hg or with antihypertensive pharmacologic treatment (87.1% of the participants).[6] Medication received by the participants included angiotensin-converting enzyme inhibitors (36.8%), angiotensin II receptor blockers (43.6%), diuretics (32.1%), calcium channel blockers (17.7%), beta blockers (9.6%), statins (12.9%), and antiplatelets (3.9%). Participants taking medication with beta blockers were eligible only if the treatment allowed a peak cardiopulmonary test. Otherwise, the cardiologist will advise the most suitable pharmacologic treatment.

Study Parameters

Modified Shuttle Walk Test

The 15-level MSWT consisted on walking/running up and down a 10-meter corridor at an incremental speed as previously described by Bradley et al.[13] A standardized explanation of the test was given to the patient before the test was conducted. Prior to commencing the test, with the participant in a seated position, baseline heart rate (HR) and blood pressure (BP) was recorded. A triple beep indicated the start of the test. The participant was instructed to walk/run to the opposite side/cone of the corridor every time a single beep sounded. If the participant reached the cone before the signal, they had to wait until the signal indicated they could proceed. The test was finished when; (1) the participant reached the end of level 15, (2) the participant was too breathless to maintain the required speed (dyspnea), (3) the participant was more than 0.5 m away from the cone when the beep sounded (allowed once), (4) the participant attained 85% of the predicted maximum HR resulting from the formula [220 − age], or (5) if the patient experienced chest pain or angina, dizziness, mental confusion, or extreme muscle fatigue. HR and Borg scale (6–20) were monitored throughout the test, and BP and HR will continue to be recorded 5 more minutes after completion of the test.[13,48]

Cardiorespiratory Fitness

Participants performed the CRF test after the MSWT with a minimum of 30-minute rest break prior in order to obtain stable resting HR and BP values. A CPET was used to asses $\dot{V}O_{2peak}$. Briefly, the test was performed on an electronically braked Lode Excalibur Sport Cycle Ergometer (Groningen, the Netherlands). Testing protocol was started with 40 W with gradual increments of 10 W

Table 1
Studies assessing validity of the ISWT or MSWT to predict VO_{2peak}

Source	Population	CPET	*N*	*r*	r^2	*P*
Singh et al[12] 1994	Chronic airflow limitation	Treadmill	19	0.88	—	<.05
Elias et al[19] 1997	COPD	Cycle ergometer	20	0.71	—	<.05
Keell et al[20] 1998	Left ventricular dysfunction	Treadmill	50	0.84	0.70	<.001
Morales et al[21] 1999	Chronic heart failure	Cycle ergometer	46	0.83	0.69	<.001
Bradley et al[13] 1999	Cystic fibrosis	Treadmill	20	0.95	0.90	<.01
Green et al[22] 2001	Heart failure	ISWT + AGA	7	0.83	—	<.05
Lewis et al[18] 2001	Cardiomyopathy	Treadmill	25	0.73	—	<.001
Macsween et al[23] 2001	Rheumatoid arthritis	ISWT + AGA	10	0.31	0.10	<.05
	Cardiac rehabilitation	ISWT + AGA	10	0.05	0.03	<.05
Onorati et al[24] 2003	COPD	Cycle ergometer	13	0.72	—	<.01
Satake et al[25] 2003	Moderate COPD	Cycle ergometer	12	0.85	0.72	<.001
Turner et al[26] 2004	COPD	Cycle ergometer	20	0.73	0.53	<.001
Fowler et al[27] 2005	Coronary artery bypass surgery	Treadmill +3 MSWT	39	0.79–0.87	—	<.05
Win et al[28] 2006	Lung cancer	Treadmill	125	0.67	—	<.001
Campo et al[29] 2006	COPD	Cycle ergometer	30	0.68	—	<.05
Pulz et al[30] 2008	Chronic heart failure	Treadmill	63	0.79	—	<.001
Struthers et al[31] 2008	General surgical patients	Cycle ergometer	50	—	0.57	<.001
Lopez-Campos et al[32] 2008	Kyphoscoliosis	Cycle ergometer	24	0.67	—	<.001
Oliveira et al[33] 2011	Pulmonary arterial hypertension	Treadmill	24	0.46	—	.02
Stockton et al[34] 2012	Thermal injury	Cycle ergometer	11	0.7	—	<.05
Dourado et al[35] 2013	Healthy	ISWT + AGA	103	0.86	0.76	<.001
Mandic et al[36] 2013	Coronary artery disease	Cycle ergometer	58	0.85	0.73	<.001
Costa et al[37] 2014	Chagas heart disease	Cycle ergometer	35	0.59	—	<.001
de Boer et al[38] 2014	Sarcoidosis	Cycle ergometer	33	0.87	—	<.001
de Camargo et al[39] 2014	Noncystic fibrosis bronchiectasis	Cycle ergometer	75	0.72	—	<.05
Evans et al[40] 2014	Obstructive sleep apnea	Treadmill	16	—	0.24	.054
Mainguy et al[41] 2014	Pulmonary arterial hypertension	ISWT + AGA	21	—	0.75	<.01
Irisawa et al[42] 2014	Pulmonary arterial hypertension	Cycle ergometer	19	0.87	—	<.05
Granger et al[43] 2015	Lung cancer	Cycle ergometer	20	0.61	—	.007
Jurgensen et al[44] 2015	Obese women	Treadmill	46	0.54	—	<.001
Neves et al[45] 2015	Sedentary	Treadmill	12	0.70	0.41	.001
Alves et al[46] 2016	Chagas heart disease	Treadmill	32	0.46	—	.009
		ISWT + AGA	32	0.87	—	<.001
Jurgensen et al[56] 2016	Obese women	Treadmill	40	—	0.67	<.05

AGA, ambulatory gas analyzer; COPD, chronic obstructive pulmonary disease; CPET, cardiopulmonary exercise test; ISWT, Incremental Shuttle Walk Test; MSWT, Modified Shuttle Walk Test; *n*, sample size; *r*, Pearson's correlation coefficient; r^2, coefficient of determination; $\dot{V}O_{2peak}$, peak oxygen uptake.

every minute to exhaustion with continuous electrocardiogram monitoring and participants cycling at 70 rpm. Expired gas analysis was performed using a commercially available metabolic cart (Ergo CardMedi-soft S.S, Belgium Ref. USM001 V1.0) that was calibrated before each test with a standard gas of known concentration and volume. Breath-by-breath data were measured continuously during exercise reported in 60-second averages. BP was measured every 2 minutes throughout the test, and a self-reported Borg rating of perceived exertion (6–20) scale was recorded at the end of each stage. $\dot{V}O_{2peak}$ was defined as the highest oxygen uptake value attained toward the end of the test. Achievement of $\dot{V}O_{2peak}$ was assumed with the presence of two or more of the following criteria: (1) volitional fatigue (>18 on BORG scale), (2) peak respiratory exchange ratio ($\dot{V}CO_2/\dot{V}O_2$) $\geq$1.1, (3) achieving >85% of age predicted maximum HR, and (4) failure of oxygen uptake and/or HR to increase with further increases in work rate.[47]

Predicted $\dot{V}O_{2peak}$ From MSWT

The following formula from Singh et al[12] was used to predict $\dot{V}O_{2peak}$ in our cohort.

$$\dot{V}O_{2peak} = [4.19 + (0.025 \text{ x ISWT distance in meters})]$$

A new equation was generated from the $\dot{V}O_{2peak}$-MSWT relationship assessed in the present study.

Statistical Analysis

Statistical analyses were carried out with the SPSS Statistical software package (24th edition). Descriptive statistics were performed on the baseline participants' characteristics. The differences and relationship between variables were evaluated using standard parametric tests, after appropriate assumptions were met. Intraclass correlation coefficients with absolute agreement based on a two-way mixed model with 95% confidence intervals were calculated. Bland and Altman plots were constructed to evaluate the agreement of Singh et al equation[12] to estimate $\dot{V}O_{2peak}$, compared to the measured $\dot{V}O_{2peak}$ values. Simple linear regression was used to analyze the relationship between the estimated and measured $\dot{V}O_{2peak}$. Forward stepwise linear regression was performed to test the effects of sex, age, body mass, stature, BMI, waist-to-hip ratio, rest HR, MSWT peak HR, and distance on $\dot{V}O_{2peak}$ and to determine which variables are the strongest predictors of $\dot{V}O_{2peak}$. Bland and Altman plots were also constructed to evaluate the relationship between the $\dot{V}O_{2peak}$ estimated from the new equation generated in the present study compared to the measured $\dot{V}O_{2peak}$ values. All values were expressed as mean and standard deviation unless otherwise stated. The level of significance (*P* value) was set at 95% ($\alpha = 0.05$).

Results

Participants' Characteristics

Physical characteristics of the study participants are shown in Table 2. Two hundred fifty-six participants (181 male [70.7%] and 75 female [29.3%]) aged 53.9 ± 8.1 years old met all the required criteria for inclusion in the study. In accordance with AHA/ACC/TOS guidelines for the Management of Overweight and Obesity in Adults, participants were classified as obese (BMI > 30 kg/m^2).[3] Exercise testing responses for peak exercise test are displayed in Table 3.

Agreement and Reliability of Singh et al Equation for Population of the Study

Sing et al equation-calculated mean $\dot{V}O_{2peak}$ was 25.4 ± 5.6 mL·kg^{-1} minute^{-1}, which was statistically higher than the directly measured level on the CPET (22.9 ± 6.1 mL·kg^{-1} minute^{-1}; $P < .001$). The relationship between measured and predicted $\dot{V}O_{2peak}$ was significant yet of moderate strength ($r = 0.60$), explaining 36% of the variance ($r^2 = 0.36$; $P < .001$), and indicating 21% of error in estimation (standard error of the estimate [SEE] = 4.92 mL·kg^{-1} minute^{-1}; SEE% = 21%). The intraclass correlation coefficient was 0.71 (95% confidence interval 0.56–0.80). The Singh et al equation showed a mean $\dot{V}O_{2peak}$ bias of −2.5 mL·kg^{-1} minute^{-1} with limits of agreement from −13.1 to 8.2 mL·kg^{-1} minute^{-1}. This indicates that using the equation proposed by Singh et al, $\dot{V}O_{2peak}$ assessment of 95% of patients would range from 13.1 mL·kg^{-1} minute^{-1} less to 8.2 mL·kg^{-1} minute^{-1} more than their experimental measure (Table 4, Figure 1).

New Equation to Estimate $\dot{V}O_{2peak}$

There was a strong significant correlation between MSWT and measured $\dot{V}O_{2peak}$ ($r = 0.72$, $P < .001$). In the equation proposed by Singh et al, $\dot{V}O_{2peak}$ in COPD patients was calculated taking distance (m) in the ISWT test as the predictive variable. To potentially improve the prediction of $\dot{V}O_{2peak}$, the present investigation used forward stepwise regression, to identify other variables that may improve the prediction of $\dot{V}O_{2peak}$. In such procedure, variables are added sequentially to the regression as long as they significantly improve the predictive power of the model. The assumption

Table 2
Characteristics of the study population

Variable	N = 256
Age (y)	53.9 ± 8.1
Height (cm)	169.7 ± 9.5
Body mass (kg)	90.0 ± 15.4
BMI (kg·m^{-2})	31.2 ± 4.8
Waist (cm)	102.1 ± 10.7
Hip (cm)	108.3 ± 9.2
WHR (waist/hip)	0.9 ± 0.1
Rest HR (bpm)	78.7 ± 13.7
Rest SBP (mm Hg)	139.6 ± 16.5
Rest DBP (mm Hg)	90.0 ± 11.8
Antihypertensive medication (%)	87.1%

BMI, body mass index; DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure; SD, standard deviation; WHR, waist hip ratio.
Values are mean ± SD or percentage (%).

Table 3
Exercise testing peak values of the study population

Variable	N = 256
Peak HR (bpm)	152.6 ± 15.9
Peak SBP (mm Hg)	212.4 ± 24.7
Peak DBP (mm Hg)	100.6 ± 18.5
Peak power (W)	134.1 ± 38.9
Exercise time (min)	11.2 ± 3.9
RER_{peak}	1.1 ± 0.1
$\dot{V}O_{2peak}$ (L·min^{-1})	2.0 ± 0.5
$\dot{V}O_{2peak}$ (mL·kg^{-1} min^{-1})	22.9 ± 6.1
MSWT (m)	847.6 ± 239.3
Peak HR in MSWT (bpm)	158.1 ± 18.5

DBP, diastolic blood pressure; HR, heart rate; MSWT, Modified Shuttle Walk Test; RER, respiratory exchange ratio; SBP, systolic blood pressure; SD, standard deviation; $\dot{V}O_{2peak}$, peak oxygen uptake.
Values are mean ± SD.

Table 4
Differences and the relationships among $\dot{V}O_{2peak}$ values

Variable	Mean ± SD	r	r^2	$r^2_{adjusted}$	SD %	P Value	SEE	SEE %
Measured $\dot{V}O_{2peak}$ (mL·kg^{-1} min^{-1})	22.9 ± 6.1							
$\dot{V}O_{2peak}$ from Singh et al[12] predicted equation(mL·kg^{-1} min^{-1})*	25.4 ± 5.6	0.60	0.36	0.36	19.9	.001	4.92	21
$\dot{V}O_{2peak}$ from our predicted equation (mL·kg^{-1} min^{-1})	22.7 ± 4.3	0.72	0.52	0.51	30.5	.001	4.35	19

r, Pearson correlation coefficient; r^2, coefficient of determination; SD, standard deviation; SD %, percent of SD explained; SEE, standard error; SEE %, percent of SEE; $\dot{V}O_{2peak}$, peak oxygen uptake.
* Significantly different from measured data ($P < .05$).

of normality was met as assessed by Q–Q Plots and Kolmogorov–Smirnov test. The multiple regression model significantly predicted $\dot{V}O_{2peak}$, $F(4, 251) = 69.255$, $P < .001$. There was significant strong level of association and a medium effect size, as indicated by r and adjusted r^2 values (Table 4). This model explained 51% of variation, 30% of standard deviation, and indicated 19% of SEE for $\dot{V}O_{2peak}$. Sex, BM, rest HR, and distance (m) in the MSWT ($Distance_{MSWT}$) variables added statistically significantly to the prediction, $P < .05$. The equation generated in this study to calculate $\dot{V}O_{2peak}$ (mL·kg^{-1} minute^{-1}) from the MSWT is described by the following equation:

$$\dot{V}O_{2peak} = 34.94 + [0.008 \cdot Distance_{MSWT}] - [0.078 \cdot RestHR] - [5.074 \cdot Sex] - [0.128 \cdot BM],$$

where sex is coded as male = 0 and female = 1, $Distance_{MSWT}$ is measured in meters, and body mass is measured in kg. The equation showed a significant proportional bias ($P < .001$) with a mean intraindividual difference of 0.2 mL·kg^{-1} minute^{-1} (limits of agreement from −8.2 mL·kg^{-1} minute^{-1} to 8.6 mL·kg^{-1} minute^{-1}). This indicates that using the new equation, $\dot{V}O_{2peak}$ assessment of 95% of patients would range from 8.2 mL·kg^{-1} minute^{-1} less to 8.6 mL·kg^{-1} minute^{-1} more than their experimental measure. The $\dot{V}O_{2peak}$ predicted from the present study equation (22.7 ± 4.3 mL·kg^{-1} minute^{-1}) was not significantly different ($P = .48$) than the actual measured $\dot{V}O_{2peak}$ (22.9 ± 6.1 mL·kg^{-1} minute^{-1}). Figure 2A illustrates the proportional bias previously mentioned, showing a linear trend between the mean and the difference of paired measurements.

Bland–Altman plots show that the biggest and smallest individual means of $\dot{V}O_{2peak}$ between the two tests

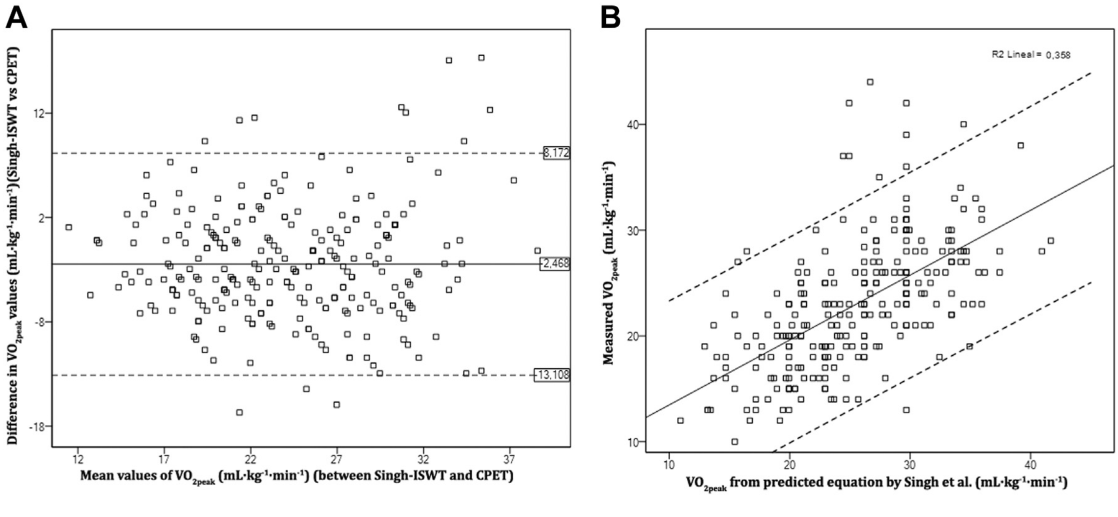

Figure 1. (A) Bland and Altman plot. Intraindividual difference in VO_{2peak} (calculated by Singh et al equation[12] for ISWT vs measured in CPET) plotted against intraindividual mean values of the two methods (Singh et al equation for ISWT and CPET). The central line represents the mean of the intraindividual differences, and the flanking lines represent the 95% limits of agreement. (B) Relationship between measured VO_{2peak} and VO_{2peak} values from the predicted equation by Singh et al. (1). The central line represents the linear regression line, and the flanking lines represent the 95% individual prediction intervals. CPET, cardiopulmonary exercise test; ISWT, Incremental Shuttle Walk Test; $\dot{V}O_{2peak}$, peak oxygen uptake.

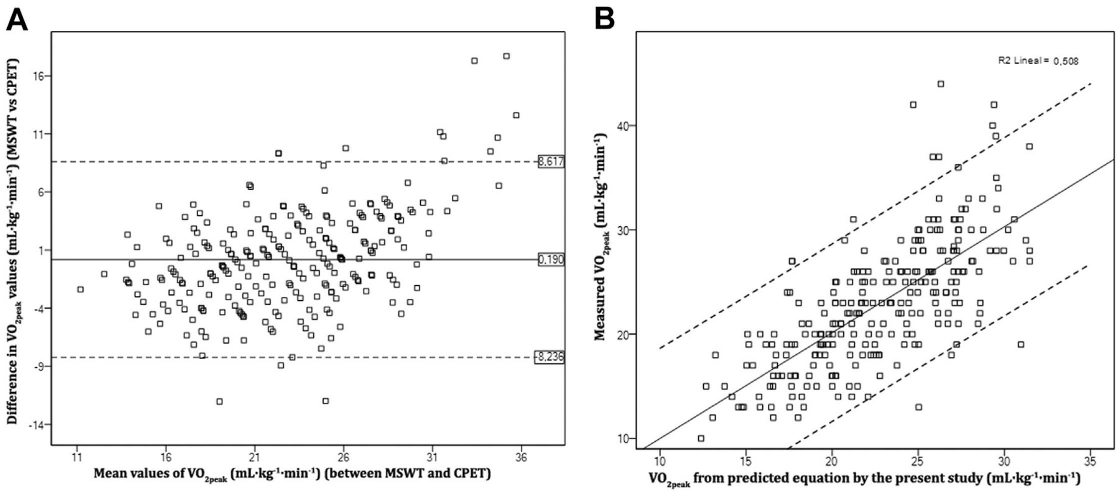

Figure 2. (A) Bland and Altman plot. Intraindividual difference in VO_{2peak} (mL·kg^{-1} minute^{-1}) between two exercise tests (MSWT vs. CPET) plotted against intraindividual mean values of the exercise tests (MSWT and CPET). The central line represents the mean of the intraindividual differences, and the flanking lines represent the 95% limits of agreement. (B) Relationship between measured VO_{2peak} and VO_{2peak} values from the predicted equation generated in the present study. The central line represents the linear regression line, and the flanking lines represent the 95% individual prediction intervals. CPET, cardiopulmonary exercise test; ISWT, Incremental Shuttle Walk Test; $\dot{V}O_{2peak}$, peak oxygen uptake.

correspond with the biggest limits of agreement in a proportional basis (Figure 2).

Discussion

To our knowledge, this is the first study to analyze the relationship between the MSWT and $\dot{V}O_{2peak}$ in a cohort of overweight/obese population diagnosed with HTN. Data from this study demonstrated that a new equation incorporating rest HR, sex, BM, and distance from MSWT performs better than the Singh et al equation to estimate $\dot{V}O_{2peak}$ for the studied population yet still results in an error of estimate of 19%. The participants that made up the sample of the present study had a mean $\dot{V}O_{2peak}$ of 22.9 ± 6.1 mL·kg^{-1} minute^{-1}, which is considered as poor functional capacity.[49] Singh et al equation significantly overestimates $\dot{V}O_{2peak}$ (25.4 ± 5.9 mL·kg^{-1} minute^{-1}; $P < .001$), and 64% of the prediction variability is not explained by this model (ie, the performance on the ISWT would explain just 36% of the variance of the $\dot{V}O_{2peak}$ in the studied cohort). Moreover, the assessment of functional capacity would range in 21 mL·kg^{-1} minute^{-1} around the mean bias which indicates there is too much variability when making decisions regarding disability, pharmacologic therapy, or exercise program design. Therefore, Singh et al equation may be an appropriate equation for COPD population but not for the assessment of functional capacity of overweight/obese individuals with HTN. The lack of accuracy might be because Singh et al equation was generated for patients with chronic airways obstruction or COPD. In contrast to pulmonary[13,19,24–26,28,29,38,39,42,43] or cardiac[18,21,22,27,30,36] patients (Table 1), the performance of people with HTN is not usually limited by breathlessness, or exercise intolerance but by exhaustion, low fitness, or high BP. Moreover, the participants in Singh et al had much lower function capacity than those used in the present investigation (375 m ± 137 m vs. 847 m ± 239 m, respectively). Hence, a better estimation is necessary for the prediction and assessment of functional capacity by the MSWT in population with HTN and overweight/obesity. Thus, it appears be claimed that the MSWT provides a valid functional capacity assessment and greater predictive power compared to the Singh et al model in overweight/obese HTN population. However, the new equation still only explains the 51% of the variation in $\dot{V}O_{2peak}$, and substantial variability in estimation indicated by SEE (19% probability of error) (Table 4). Recent studies have found similar strong significant correlations in estimation of $\dot{V}O_{2peak}$, through the ISWT and the MSWT, compared to the $\dot{V}O_{2peak}$ in healthy adults,[35] obese women,[44] and sedentary adult men[45] and have concluded that these field tests are appropriate alternatives to assess functional capacity. Nevertheless, all the reviewed studies present low statistical power due mainly to the small sample size, thus reducing the chance of detecting a true effect. It is well known that the true effect discovered by an underpowered study will exaggerate the estimation of the magnitude of that effect.[50] The present study presents a sample size of 256 overweight/obese participants diagnosed with HTN, which represents a much bigger sample compared to previous studies, with an actual statistical power of 0.95. On the other hand, the differences between correlation in the current study and correlation in the studies reported previously (Table 1) could be due to the fact that participants in this study were not affected by airflow limitation and because their functional capacity was only limited by their fitness and high BP. It seems that the two shuttle walk tests could be more appropriate for population with respiratory or heart disease, in which maximal distance (m) is statistically shorter than in HTN and overweight/obese population. Therefore, it could be that only patients with low CPET performance[49] would have an accurate estimation of $\dot{V}O_{2peak}$ by ISWT or MSWT. Thus, in the present study, trying to find a CRF threshold to explain the cases with higher error of estimation, different stratified regression analysis with subset CRF populations was performed (ie, $\dot{V}O_{2peak} < 20$; 20–30; >30 $mL \cdot kg^{-1}$ $minute^{-1}$). However, results of the full sample offered better regression model than the stratification into subsets.

On the other hand, the variability of the new equation indicated by a high SEE (19% probability of error) questions the accuracy of using this approach to make an accurate prediction of functional capacity. It is very well known that functional capacity assessment based on $\dot{V}O_{2peak}$ and ventilatory gas exchange measures has good reliability, reproducibility, and clinical utility as the exercise measurements are based on actual metabolic measures.[51] Thus, the CPET response includes and provides a full spectrum of objective indices to achieve integrated assessments of lung, cardiac, and even muscle contributions to exercise performance.[51] The limitation of individual performance with CPET can be evaluated taking into account data from ECG, BP monitor, and/or gas analysis monitor to ensure that the termination criteria are fulfilled[17,52] to avoid cardiovascular risk events during the test. In contrast, with ISWT and MSWT, there are no tools available to assess the performance other than RPE (Borg scale) and the formula to calculate the 85% of the predicted maximum HR. To increase the safety of the MSWT, additional equipment suitable for exercise test assessment would be necessary, such as ambulatory BM monitor, ECG or gas analysis system. This equipment is expensive and makes the test more difficult to be administered. An important limitation in the use of ISWT and MSWT is that BP, the principal termination criterion of functional capacity assessment tests in population with HTN and obesity, cannot be addressed. Finally, knowing that exercise is recommended as a key lifestyle therapy for adults with HTN for the prevention, treatment, and control of BP by all international associations and committees,[53] exercise design should be tailored in a systematic and individualized way. Using MSWT as a reference test to this population could lead to substantial errors and potential risks. However, if the CPET is not available, exercise professionals could at least use the new equation generated in the present study that incorporates resting HR, sex, BM, and distance from MSWT variables to estimate $\dot{V}O_{2peak}$ for overweight/obese people with HTN but taking into account the error of estimation.

A potential limitation of this study is that experimental $\dot{V}O_{2peak}$ was measured during a CPET on a cycle ergometer, whereas the field test was performed with a walking test. The differences between testing modalities may have led to a lower prediction power and higher probability of error in the prediction. $\dot{V}O_{2peak}$ is known to be up to 15%–20% higher when measured on a treadmill rather than on a cycle ergometer.[54] On the other hand, the increase in VO_2 is more linear,[55] and it is easier to assess BP during on the cycle ergometer, which is an important criterion for CPET assessment in a HTN population.

Conclusions

The prediction of $\dot{V}O_{2peak}$ based on a new regression equation derived from the relationship between $\dot{V}O_{2peak}$ and MSWT results in an error of estimate of 19%, calling into question the validity of using this test to evaluate exercise intolerance in people with HTN and obesity.

Consequently, when an accurate determination of functional capacity is required for diagnosis, clinical research, and exercise design, the direct measurements of $\dot{V}O_{2peak}$ are still preferred in obese population with diagnosed HTN.

Acknowledgments

Our special thanks to Ignacio Camacho-Azkargorta, the cardiologist who begin to move forward this project and Laura Vicente-Martín, the Master degree student, for her initial data analysis.

Author contributions: B.J.-I. and S.M.-M. contributed to the conception, design, acquisition, analysis of the study. I.G.-A., G.R.A., J.P.-A. contributed to acquisition of data. B.J.-I., P.H.B., and S.M.-M. drafted the manuscript. All the authors critically reviewed the manuscript, gave final approval, and agree to be accountable of all aspects of work ensuring integrity and accuracy.

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CLINICAL AND EXPERIMENTAL HYPERTENSION
https://doi.org/10.1080/10641963.2018.1481423

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Validity of the modified shuttle walk test to assess cardiorespiratory fitness after exercise intervention in overweight/obese adults with primary hypertension

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ABSTRACT

The study aimed to assess whether the Modified Shuttle Walk Test (MSWT) can detect changes in cardiorespiratory fitness (CRF) in overweight/obese people with hypertension (HTN) after an exercise intervention evaluating the equation presented in the previous research by Jurio-Iriarte *et al.* Participants (N= 248) performed a peak cardiorespiratory exercise test (CPET) and MSWT before and after 16-weeks of different types of aerobic exercise intervention. The formula of Jurio-Iriarte *et al.* was used to predict peak oxygen uptake ($\dot{V}O_{2peak}$). The correlation between measured and predicted $\dot{V}O_{2peak}$ was strong (r= 0.76, P< 0.001) with a standard error of estimate (*SEE*) of 4.9 mL·kg^{-1}·min^{-1}; *SEE%*= 17%. The intraclass correlation coefficient indicates a moderate level of association and agreement (*ICC*= 0.69; *95% CI* 0.34–0.82; P< 0.001) between the measured and predicted $\dot{V}O_{2peak}$. When analyzing obese participants alone (N= 128), MSWT equation was more accurate compared to the whole sample (*ICC*= 0.76; *95% CI* 0.52–0.87). The relationship between the change of measured and predicted $\dot{V}O_{2peak}$ at follow-up was weak (r= 0.42, P< 0.001) with a 31% *SEE*, and a low level of association and agreement (*ICC*= 0.31; *95% CI* 0.06–0.49; P< 0.001). In conclusion, although MSWT does not accurately predict CRF in people with HTN after exercise intervention and questions its validity, the new equation may have practical application to estimate $\dot{V}O_{2peak}$ for obese people with HTN when CPET is not available.

Abbreviations: AC: Attention Control; BM: Body Mass; BP: Blood Pressure; CI: Confidence Interval; CRF: Cardiorespiratory Fitness; CPET: Cardiopulmonary Exercise Test; HTN: Primary Hypertension; HR: Heart Rate; HV-HIIT: High-Volume and High-Intensity Interval Training; ICC: Intraclass Correlation Coefficient; LV-HIIT: Low-Volume and High-Intensity Interval Training; MICT: Moderate-intensity continuous training; MSWT: Modified Shuttle Walk Test; SD: Standard Deviation; SEE: Standard Error of Estimate; $\dot{V}O_{2peak}$: Peak Oxygen Uptake.

ARTICLE HISTORY
Received 28 March 2018
Revised 24 April 2018
Accepted 1 May 2018

KEYWORDS
Hypertension; obesity; field test; cardiopulmonary test; assessment; exercise design; sedentary

Introduction

Overweight/obesity and primary hypertension (HTN) are cardiovascular risk factors that continue to increase and augment the risk for cardiovascular disease (1). Regular exercise along with other lifestyle modification strategies is imperative for effective management of overweight/obesity-related HTN (1–3). Cardiorespiratory fitness (CRF) is considered a key vital sign and a robust physiological index of health risk (4,5). Cardiorespiratory fitness is essential for the assessment, clinical management and exercise programming of individuals with overweight/obesity and HTN (2,6). The cardiopulmonary exercise test (CPET) is used to objectively and directly measure peak oxygen uptake ($\dot{V}O_{2peak}$), which is considered the "gold standard" reference for the assessment of CRF and prescription of aerobic exercise intensity (5).

The modified shuttle walk test (MSWT) is a low cost and easily administered field test (7–9) that can be used to estimate CRF. This test has been validated to predict $\dot{V}O_{2peak}$ in sedentary participants with overweight/obesity and HTN (10). However, the ability of MSWT to assess the improvement in $\dot{V}O_{2peak}$ after an exercise intervention in the same cohort has not been evaluated. Consequently, it would be important to determine if the MSWT-measured overtime changes in $\dot{V}O_{2peak}$ were similar or proportional to the CPET-measured $\dot{V}O_{2peak}$. These findings would determine if the MSWT is a suitable tool for a follow-up assessment of CRF when CPET is not available. Therefore, the aim of the present study was to evaluate the validity of the equation presented in the previous study by Jurio-Iriarte *et al.* (10) after an exercise intervention in a cohort of overweight/obese population with HTN.

Methods

Participants

A total of 248 non-Hispanic white participants (174 men, 74 women) with stage 1 or 2 HTN (2) and overweight/obesity (11) volunteered to take part in the present study. The design, selection criteria (exclusion and inclusion criteria), and procedures for the EXERDIET-HTA study have been previously described (12). Some exclusion criteria were to have secondary HTN, left ventricular hypertrophy, an uncontrolled cardiovascular risk

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Trial Registration: NCT02283047

factor or diabetes mellitus more than 10 years since diagnosis, and other significant medical conditions.

Study design

Follow-up data from the EXERDIET-HTA randomized controlled experimental trial (Clinical Trials.gov identifier, NCT02283047) and a previous pilot study were used in this prospective study. The study protocol was approved by the Local Ethics Committees (UPV/EHU, CEISH/279/2014, and CEIC 2015–030), and also meets the ethical standards in sports and exercise science research (13). All participants provided written informed consent prior to any data collection. Following baseline data collection, participants were randomly allocated to one of the four intervention groups (Figure 1): Attention Control (AC, with only physical activity recommendations); or three supervised exercise groups (Moderate-Intensity Continuous steady Training, MICT; High-Volume and High-Intensity Interval Training, alternating bursts of higher-intensity with lower-intensity activity, HV-HIIT, and Low-Volume, LV-HIIT). Each group was stratified by sex, systolic blood pressure, Body mass (BM) index and age. All measurements were performed at entry and after 16-weeks intervention period (12).

Procedures

Modified shuttle walk test (MSWT)

The fifteen-level MSWT consisted of walking up and down a 10-m corridor at an incremental speed as previously described by Singh *et al.* (7) A standardized explanation of the test was given to the patient before the test was conducted (8,14).

The equation used to calculate $\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$) from the MSWT is described by the Jurio-Iriarte *et al.* equation (10):

$$\dot{V}O_{2peak} = 34.94 + [0.008 \cdot Distance_{MSWT}] - [0.078 \cdot RestHR] - [5.074 \cdot Sex] - [0.128 \cdot BM],$$

where sex is coded as Male = 0, Female = 1, $Distance_{MSWT}$ is measured in meters, and BM is measured in kg.

Participants performed the CPET test after the MSWT with a minimum of 30-min rest break to obtain stable resting HR and BP values. Briefly, the CPET was performed on an electronically braked Lode Excalibur Sport Cycle Ergometer (Groningen, The Netherlands). The testing protocol was started with 40 W with gradual increments of 10 W every minute at 70 rpm to exhaustion with continuous electrocardiogram monitoring. The expired gas analysis was performed using a commercially available metabolic cart (Ergo CardMedi-soft S.S, Belgium Ref. USM001 V1.0). $\dot{V}O_{2peak}$ was defined as the highest oxygen uptake value attained during the CPET (12).

Exercise training intervention

The exercise program focused on improving cardiovascular endurance. Participants trained two days per week for 16 weeks under supervision. Each session started with 10 min of the warm-up period and ended with 10 min of cool-down. The main component of the training session consisted of aerobic exercises performed progressively in volume, duration, and intensity depending on the training group. Protocols of different aerobic programs have been previously published (12). Briefly, The MICT group performed a 45 min aerobic exercise, whereas the HV-HIIT and LV-HIIT conducted 45 and 20 min, respectively.

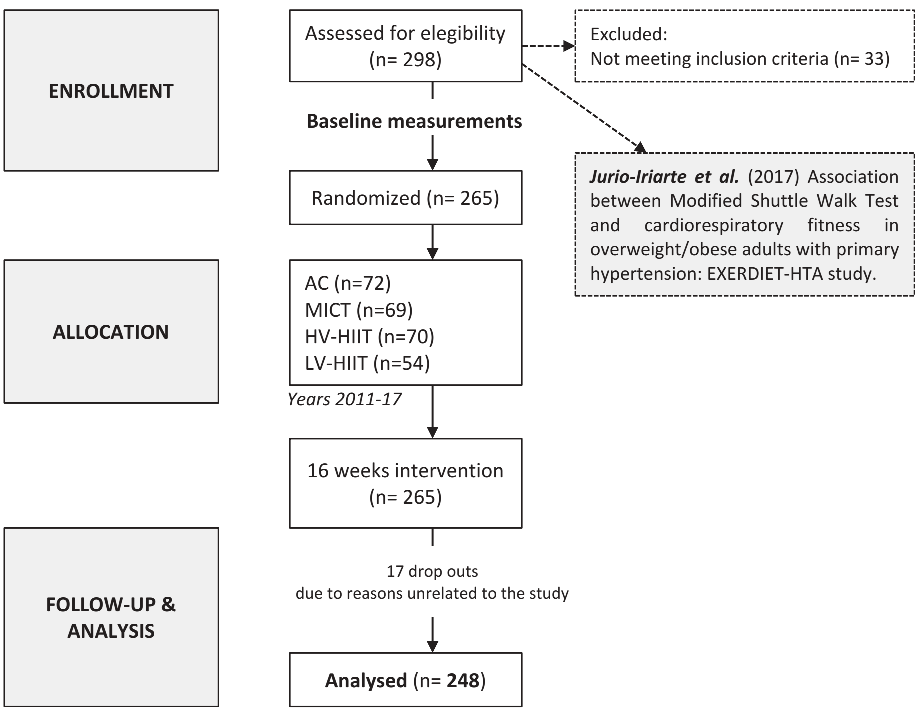

Figure 1. Flow-chart. AC, attention/control group; MICT, moderate-intensity continuous training; HV-HIIT or LV-HIIT, high-intensity interval training of high/low-volume.

The intensity was individually tailored to each participant's HR at moderate or vigorous intensities, adjusting the speed and/or incline of the treadmill or the power and speed on the exercise bike. The rationale of mixing stationary exercise-bike and treadmill was to avoid the orthopedic impact of two treadmill days and taking into account the nature of the HIIT program in overweight/obese participants. The HV-MICT group performed 45 min continuous training at moderate intensity.

Statistical analysis

Statistical analyses were performed using the SPSS Statistical software package (24th edition). Descriptive statistics were performed on the participants' characteristics after the intervention. The differences and relationship between variables were evaluated using standard parametric tests after appropriate assumptions were met. Intraclass correlation coefficients (*ICC*) with an absolute agreement based on a two-way mixed model with 95% confidence intervals (*CI*) were calculated. Bland-Altman plots were constructed to evaluate the agreement of Jurio-Iriarte *et al.* equation (10) of estimated $\dot{V}O_{2peak}$, compared to the measured $\dot{V}O_{2peak}$ values. Simple linear regression was used to analyze the relationship between the estimated and measured $\dot{V}O_{2peak}$. All values were expressed as the mean and standard deviation (SD) unless otherwise stated. The level of statistical significance (*P*-value) was set at 95% (α = 0.05). Power calculation was completed using G*Power 3 analysis program (15). The required sample size was determined for a correlation bivariate normal model. It was determined that adequate power (0.90) to evaluate the relationships in the present investigation could be achieved with 92 people (α = 0.05).

Results

Participants' characteristics

Two hundred and forty-eight participants (174 men and 74 women) aged 54.0 ± 7.3 years old were followed—until the end of the intervention (See Figure 1: Flow-chart). Physical and clinical characteristics of the study participants after 16-weeks intervention period are shown in Table 1.

Table 1. Characteristics and exercise testing peak values of the study population after 16-weeks intervention period. Values are mean±SD or percentage (%).

Variable	N = 248 (174♂ 74♀)
Age (yr)	54.0 ± 7.3
Height (cm)	169.7 ± 9.2
Body mass (kg)	84.6 ± 13.8
BMI (kg·m^{-2})	29.4 ± 4.3
Waist (cm)	96.7 ± 10.5
Hip (cm)	104.4 ± 8.2
WHR (waist/hip)	0.9 ± 0.1
Antihypertensive medication (%)	84.7%
Rest HR (bpm)	70.9 ± 12.0
Rest SBP (mmHg)	130.0 ± 13.9
Rest DBP (mmHg)	82.9 ± 9.9
Peak HR (bpm)	154.5 ± 16.5
Peak SBP (mmHg)	206.8 ± 23.9
Peak DBP (mmHg)	96.8 ± 15.4
RER_{peak}	1.1 ± 0.1
VO_{2peak} (L·min^{-1})	2.4 ± 0.6
VO_{2peak} (mL·kg^{-1}·min^{-1})	28.2 ± 7.6
Distance $_{MSWT}$ (m)	970.3 ± 255.7
Peak HR $_{MSWT}$ (bpm)	157.9 ± 16.9

♂, male; ♀, female; BMI, Body Mass Index; WHR, Waist-Hip Ratio; HR, Heart Rate; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; RER, Respiratory Exchange Ratio; VO_{2peak}, Peak Oxygen Uptake; MSWT, Modified Shuttle Walk Test.

Agreement and validity of jurio-Iriarte* et al. *equation.

Jurio-Iriarte *et al.* (10) equation-calculated mean $\dot{V}O_{2peak}$ for the whole sample after exercise intervention was 24.5 ± 3.9 mL·kg^{-1}·min^{-1}, which was statistically lower than the directly measured on the CPET (28.2 ± 7.6 mL·kg^{-1}·min^{-1}; *P*< 0.001) (Table 2). The relationship between measured and predicted $\dot{V}O_{2peak}$ was significant and strong (*r*= 0.76), explaining 58% of the variance (r^2= 0.58; *P*< 0.001), and indicating 17% of error in estimation (standard error of the estimate, *SEE*= 4.9 mL·kg^{-1}·min^{-1}). The accuracy of the equation at follow-up was moderate (16), as indicated by *ICC*= 0.69 (*95% CI* 0.34 to 0.82) (Table 2). The Jurio-Iriarte *et al.* equation showed a mean $\dot{V}O_{2peak}$ bias of 3.7 mL·kg^{-1}·min^{-1} with limits of agreement from −6.7 to 14.1 mL·kg^{-1}·min^{-1}. This indicates that using the equation proposed, $\dot{V}O_{2peak}$ assessment of 95% of patients would range from 6.7 mL·kg^{-1}·min^{-1} less to 14.1 mL·kg^{-1}·min^{-1} more than their experimental measure (Figure 2(a)). The tendency seen in Figure 2(a) indicates that the higher the level of CPET $\dot{V}O_{2peak}$, the larger the difference between the measured and predicted value. Differences ≥10 mL·kg^{-1}·min^{-1} were of those participants with the highest CRF ($\dot{V}O_{2peak}$>33 mL·kg^{-1}·min^{-1}). These results were strengthened when analyzing obese (BM Index≥30) participants alone as the MSWT equation was more accurate in the 128 obese participants compared to the whole sample (*ICC*= 0.76; *95% CI* 0.52–0.87).

A subset analysis showed that the relationship between measured and predicted $\dot{V}O_{2peak}$ and the *SEE* and *ICC* of different exercise intervention protocols was very similar to the analysis of the whole sample ($r^2_{adjusted}$ ranging from 0.49 to 0.60; *SEE* from 15% to 20%; *ICC* from 0.64 to 0.77). In most cases, the equation of Jurio-Iriarte *et al.* (10) significantly (*P*< 0.001) underestimated CRF.

The CPET measured fitness of the participants demonstrated a mean improvement of 4.9 ± 5.3 mL·kg^{-1}·min^{-1} (22.7%) after

Table 2. Validity of the MSWT to assess the development of CRF at follow-up in overweight/obesity people with hypertension (*N*= 248).

	$\dot{V}O_{2peak}$ (mL·kg^{-1}·min^{-1})									
Variable	CPET Measured	Equation predicted	*r*	r^2	$r^2_{adjusted}$	*%SD*	*P Value*	*SEE*	*%SEE*	*ICC (95% CI)*
Follow-up	28.2 ± 7.6	24.5 ± 3.9	0.76	0.58	0.58	35.7%	0.001	4.9	17%	0.69 (0.34–0.82)
Absolute change	4.9 ± 5.3	1.9 ± 1.6	0.42	0.17	0.17	8.9%	0.001	1.5	31%	0.31 (0.06–0.49)
Relative change (%)	22.7 ± 23.9	9.1 ± 8.1	0.35	0.12	0.12	6.2%	0.001			0.28 (0.04–0.46)

MSWT: Modified Shuttle Walk Test; CRF: Cardiorespiratory Fitness; $\dot{V}O_{2peak}$: peak oxygen uptake; CPET: cardiopulmonary exercise test.
CI = confidence intervals; ICC = Intraclass correlation coefficient; r = Pearson correlation coefficient; r^2 = coefficient of determination; %SD = Percent of SD explained; SEE = Standard Error of Estimation; %SEE = Percent of SEE.

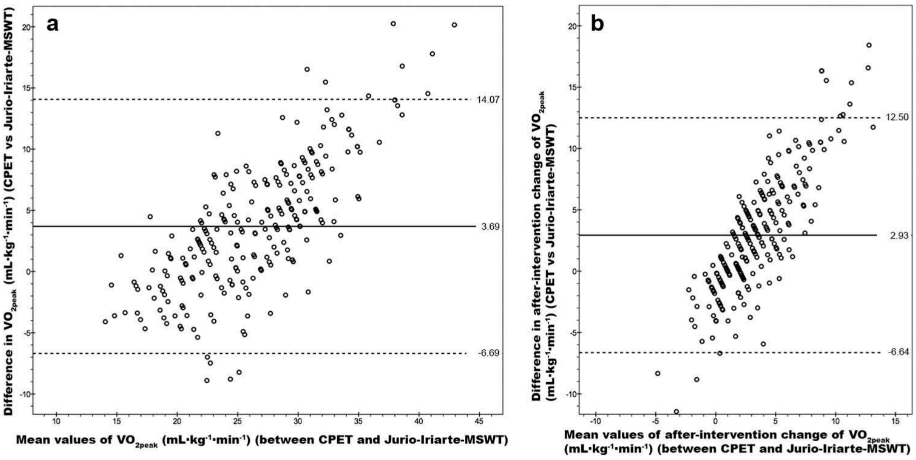

Figure 2. Bland-Altman plots. (a) Intraindividual difference in $\dot{V}O_{2peak}$ (calculated by Jurio-Iriarte *et al.* equation (10) for MSWT vs. measured in CPET) plotted against intraindividual mean values of the two methods (Jurio-Iriarte *et al.* equation (10) for MSWT and CPET). (b) Intraindividual difference in after-intervention change of $\dot{V}O_{2peak}$ (calculated by Jurio-Iriarte *et al.* equation (10) for MSWT vs. measured in CPET) plotted against intraindividual mean values of the two methods (Jurio-Iriarte *et al.* equation (10) for MSWT and CPET). The central line of the plots represents the mean of the intraindividual differences, and the flanking lines represent the 95% limits of agreement.

the intervention, which is significantly larger ($P< 0.001$) than the change calculated with the MSWT equation (1.9 ± 1.6 mL·kg^{-1}·min^{-1}; 9.1%). The relationship between CPET and MSWT after-intervention absolute change of $\dot{V}O_{2peak}$ was significant but small ($r= 0.42$) explaining just 17% of the variance ($r^2= 0.17$; $P< 0.001$), and indicating 31% *SEE* when assessing the determination of CRF with MSWT (*SEE*= 1.5 mL·kg^{-1}·min^{-1}). The validity of the equation to detect absolute changes in CRF after the intervention was poor (16), as indicated by *ICC*= 0.31 (*95% CI* 0.06 to 0.49). In general, the validity of the equation to detect relative changes in CRF was also poor (Table 2). The Jurio-Iriarte *et al.* equation showed a change of $\dot{V}O_{2peak}$ mean bias of 2.9 mL·kg^{-1}·min^{-1} with limits of agreement from −6.6 to 12.5 mL·kg^{-1}·min^{-1} (Figure 2(b)). This indicates that when using this prediction equation, the change in $\dot{V}O_{2peak}$ for 95% of patients would range from 6.6 mL·kg^{-1}·min^{-1} less to 12.5 mL·kg^{-1}·min^{-1} more than their CPET measured $\dot{V}O_{2peak}$. The tendency shown in Figure 2(b) indicates the larger the CRF improvement at follow-up, the greater difference *vs.* the MSWT calculated development.

Discussion

To our knowledge, this is the first study to analyze the relationship between the MSWT and $\dot{V}O_{2peak}$ after 16-week intervention training in a cohort of overweight/obese population diagnosed with HTN.

The previous study by Jurio-Iriarte *et al.* (10) demonstrated that a new equation incorporating sex, resting HR, BM, and $distance_{MSWT}$ performs better than the Singh *et al.* equation (7) in estimating $\dot{V}O_{2peak}$ for sedentary and overweight/obese participants with HTN. However, assessment of CRF using this new equation still resulted in an *SEE* of 19%, significantly underestimating CRF of the studied population.

In the present study that used an exercise intervention with different exercise protocols including a control group (AC), the same equation was used to follow-up CRF of 248 participants. The participants that made up the sample of the present prospective study had a mean $\dot{V}O_{2peak}$ of 28.2 ± 7.6 mL·kg^{-1}·min^{-1} (Table 1), which was 4.9 ± 5.3 mL·kg^{-1}·min^{-1} higher than at baseline (23.4 ± 6.2 mL·kg^{-1}·min^{-1}). Thus, the CRF of the sample improved from poor to average (17). As well as at baseline, Jurio-Iriarte *et al.* equation underestimated $\dot{V}O_{2peak}$ of the same participants at follow-up, with a mean difference of 3.7 ± 5.3 mL·kg^{-1}·min^{-1} less than the direct CPET measurement.

Although the MSWT provides a valid functional capacity assessment with good predictive power, 42% of the prediction variability was not explained by the model at follow-up (*i.e.*, the performance on the MSWT explained 58% of the variance of the $\dot{V}O_{2peak}$ in the studied cohort, $r^2= 0.58$) (Table 2). Similar to other recent studies (18–20), the MSWT appears to be a valid tool for the assessment of CRF. However, variability in estimation at follow-up testing (17% probability of error) questions the use of this approach to accurately predict CRF.

The Jurio-Iriarte *et al.* equation would be a valuable equation if it were sensitive to CRF changes after exercise intervention (*i.e.*, able to detect proportional changes to the experimental magnitude). In this respect, we found that absolute and relative improvement of $\dot{V}O_{2peak}$ was significantly different ($P< 0.001$) and not proportional ($r= 0.42$; $r^2= 0.17$; *ICC*= 0.31), with a difference of 2.93 ± 4.88 mL·kg^{-1}·min^{-1} (13.7%) between the CPET measurements and MSWT prediction (Table 2). Taking the aforementioned into account, it appears that in general, the MSWT does not accurately detect the change in CRF, as it underestimates the improvements of $\dot{V}O_2$ (Figure 2(b)).

Other studies analyzing populations affected by airflow limitation and very limited functional capacity (pulmonary or cardiac disability) have reported much higher correlations between $\dot{V}O_{2peak}$ and MSWT than reported in the present study (see in Jurio-Iriarte *et al.* (10), Table 2). Fitness and high BP only limit the CRF of the population in the current investigation, which is likely the explanation for the differences in the observed correlations.

The main finding of the present investigation was that the validity of the MSWT-estimated $\dot{V}O_{2peak}$ was moderate (*ICC*= 0.69) compared to the measured value, but would be considered weak if the *95% CI* (0.34–0.82) is taken into account (16), indicating a lower bound of 0.34. This may be caused by the values of participants with the highest CRF whose $\dot{V}O_{2peak}$ prediction is further away from the mean value of the sample (Table 2). The assessment of CRF at baseline ranged in 21 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ and in 19 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ at follow-up around the mean bias with a tendency related to the difference between measured and predicted $\dot{V}O_{2peak}$ (Bland-Altman plots, Figures 2(a) and 2(b), respectively). Thus, the participants with higher functional capacity (*i.e.*, higher CRF) demonstrated the larger error with predicting of $\dot{V}O_{2peak}$ (≥10 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$ of difference), minimizing the achievements of the participants that had the most improvement (Figure 2(b)). Therefore, these findings indicate there is too much variability when predicting $\dot{V}O_{2peak}$ from the MSWT in situations (disability, pharmacological therapy or exercise programming) when an accurate determination of CRF is critical. The improvement of CRF at follow-up (from 22.9 ± 6.1 to 28.2 ± 7.6 $mL{\cdot}kg^{-1}{\cdot}min^{-1}$) affected the prediction of $\dot{V}O_{2peak}$, mostly of the highest values. In this respect, we found that obese (*N*= 128) participants' CRF (BM Index≥30) was more accurately determined by the MSWT equation than the non-obese participants (*ICC*= 0.76; *95% CI* 0.52–0.87), which could be of interest for this sub-population with HTN. These findings have two important implications: 1) taking into account the error of estimation, the MSWT may have a practical application to estimate $\dot{V}O_{2peak}$ for obese people with HTN through the equation generated by Jurio-Iriarte *et al.* (10), mainly with more deconditioned participants and when CPET is no available, and 2) when CRF is necessary to be accurately measured, the CPET (*i.e.*, $\dot{V}O_{2peak}$) continues being the "gold standard".

Conclusion

In summary, the findings of this study do not fully support the validity of the equation presented in the previous research by Jurio-Iriarte *et al.* Although predicting $\dot{V}O_{2peak}$ from Jurio-Iriarte *et al.* equation using MSWT results in substantial variability after exercise intervention, the new equation may still have practical value in estimating $\dot{V}O_{2peak}$ for obese people with HTN when CPET is not available.

Perspective

Although the MSWT has been previously validated to predict $\dot{V}O_{2peak}$ in sedentary and overweight/obese participants with HTN (10). The ability of this field test to assess the improvement in CRF after an exercise intervention in the same cohort has not been evaluated. Due to the large variability of the new equation, the results of the present study justify the practical use of this easy and cost-effective test on studied population only when CPET is not available. On the other hand, findings of this study cannot be extrapolated to other different population than sedentary and overweight/obese individuals with HTN. Therefore, more investigations should be conducted to research the validity of MSWT to estimate CRF in different populations.

Acknowledgments

Our special thanks to Javier Pérez-Asenjo and Rodrigo Aispuru for their medical assessment and support, and Exercycle S.L. (BH Fitness Company) for the machines donated to conduct the exercise intervention. Last but not least to all undergraduate students who collaborated in this project (2011-2017 academic years).

Conflicts of interest

None

Funding

The Government of the Basque Country (SAIOTEK, SAI12/217) supported the study and to IGA, PC and AMAB with predoctoral grants.

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Effects of Different Exercise Training Programs on Cardiorespiratory Fitness in Overweight/Obese Adults With Hypertension: A Pilot Study

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The goal of the study was to compare the effects of two supervised aerobic exercise programs (moderate-intensity continuous training [MICT] vs. high-intensity interval training [HIIT]) after 8-, 12-, and 16-week intervention periods on cardiorespiratory fitness (CRF) in overweight/obese adults diagnosed with hypertension. Participants (N = 64) were divided into three intervention cohorts (control group [CG], MICT, and HIIT) and each of these, in turn, into three intervention length cohorts (8, 12, and 16 weeks). Supervised groups exercised twice a week. There were no statistical changes in postintervention periods in CG (g < 0.1). CRF as assessed by peak oxygen uptake (mL kg^{-1}·min^{-1}) increased (p < .001) in exercise groups (MICT, 3.8 ± 3.3, g = 0.6; HIIT, 4.2 ± 4.7, g = 0.7). The effect of exercise interventions compared with CG was substantial (p < .02, g > .8) and mostly consequence of HIIT-related effects. The improvements on CRF occurred after 12 and 16 weeks in exercise interventions, rather than in the 8-week group or CG, where Hedges's g index indicated small effect. This study may suggest that both MICT and HIIT exert cardioprotector effects on hypertension in the overweight/obese population. However, short-term training duration (<12 weeks) does not seem to improve CRF, and HIIT intervention might generate higher aerobic capacity, which seems to grow as intervention lengthens.

Keywords: *cardiovascular disease; chronic disease; obesity; physical activity/exercise; training*

Health Promotion Practice
Month XXXX Vol. XX , No. (X) 1–11
DOI: 10.1177/1524839918774310

INTRODUCTION

Hypertension (HTN) is a significant risk factor for cardiovascular diseases (CVDs), and both are the top global risk causes of morbidity and mortality (Ford, 2011). Therefore, it is necessary a treatment to reduce avoidable risk factors and consequently the high rate of mortality due to CVD (Perk et al., 2012). It has been shown that people with HTN are generally also overweight or obese and physically inactive (Despres, 2016), being those factors additive regarding cardiovascular risk (CVR; Thomas et al., 2001). A relatively small increase in cardiorespiratory fitness (CRF) substantially reduces CVR, and this risk declines progressively with increasing aerobic capacity. Thus, unfit individuals have twice the risk of mortality regardless of body mass index (BMI; Barry et al., 2014). An increase in

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Authors' Note: *Our special thanks to Ignacio Camacho-Azkargorta, the cardiologist who began to move this project forward. Also thanks to the Department of Physical Education and Sport and Faculty of Physical Activity and Sport Sciences (University of the Basque Country, UPV/EHU) for believing in our project and providing the material and facilities to start with, and to BH Fitness Company for donating the machines to conduct the exercise interventions. Last but not least, thank you to all the undergraduate students who collaborated in this pilot study (academic years 2010-2013). The study was supported by the Government of the Basque Country (SAIOTEK, SAI12/217).*
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exercise within an exhaustive change of lifestyle (i.e., salt restriction, moderation of alcohol consumption, high consumption of vegetables and fruit, low-fat diet, total body mass reduction, and smoking cessation) is recommended to prevent, treat, and control HTN (Mancia et al., 2013), as exercise is associated with antihypertensive benefits (Pescatello, MacDonald, Ash, et al., 2015). On the other hand, there is no agreement about the optimal dose of *F*requency of exercise (number of sessions per week), *I*ntensity (how hard an individual works during exercise), *T*ime or length (how long each session lasts), and *T*ype of exercise (*FITT* principle) to obtain the greatest health benefit (Pescatello, MacDonald, Lamberti, & Johnson, 2015). Compared with moderate-intensity continuous training (MICT, continuous steady training), high-intensity interval training (HIIT, intermittent exercise alternating bursts of higher intensity with lower intensity activity), aerobic exercise typically results in a higher CRF increase in less time and produces greater metabolic changes (Boutcher & Boutcher, 2017). However, the effect of HIIT on both office and ambulatory blood pressure (BP) appears to be medication dependent with untreated hypertensive individuals displaying more significant decreases compared with their treated counterparts, who could present normalized resting BP and less adaptation to exercise (Boutcher & Boutcher, 2017). Previous investigations have studied the effects of 10 (Rognmo, Hetland, Helgerud, Hoff, & Slordahl, 2004), 12 (Gunjal, Shinde, Kazi, & Khatri, 2013; Molmen-Hansen et al., 2012; Parpa, Michaelides, & Brown, 2009; Wisloff et al., 2007), 15 (Mohr et al., 2014), 16 (Guimaraes et al., 2010; Warburton et al., 2005), 20 (Nemoto, Gen-no, Masuki, Okazaki, & Nose, 2007), and 24 (Moholdt et al., 2009) weeks of HIIT intervention on BP and some of them on CRF. Nevertheless, it is not known if effects occur with less than 12-week interventions (i.e., a short-term impact) on the CRF of overweight/obese adults with HTN. The evidence mentioned above suggests that for this population, 8 weeks of HIIT intervention may offer CRF adaptations that MICT may not. The aim of the present study was, therefore, to compare the effects of two different aerobic exercise programs (MICT vs. HIIT) after 8-, 12-, and 16-week intervention periods on the CRF of overweight/obese adult population diagnosed with HTN.

METHOD

Study Design

This work is a pilot study before the EXERDIET-HTA (Trial Registration: NCT02283047) randomized single-blind controlled experimental trial (Maldonado-Martín et al., 2016). The ethics committee of the University of the Basque Country (UPV/EHU, CEISH/279/2014) approved the study protocol. All participants provided written informed consent before any data collection. After baseline measurements, participants were randomly assigned to the control group (CG), or two supervised exercise groups (MICT or HIIT). All in all, participants were randomized into nine groups (i.e., 8-week CG, 8-week MICT, 8-week HIIT, 12-week CG, etc.; Figure 1).

Participants

Non-Hispanic White sedentary (those who did not comply with the “Global Recommendations on Physical Activity for Health” by the World Health Organization) participants (N = 70) who volunteered to take part in the present study classified as overweight (BMI ≥ 25) or obese (BMI ≥ 30; Jensen et al., 2014) and were diagnosed with Stage 1 or 2 HTN, had a systolic blood pressure (SBP) of 140 to 179 mmHg and/or a diastolic blood pressure (DBP) of 90 to 109 mmHg, and/or were under antihypertensive pharmacological treatment (Mancia et al., 2013). The exclusion and inclusion criteria for the study have been published previously (Maldonado-Martín et al., 2016).

Measurements

The measurements used in the protocol were taken before and after each intervention period (8, 12, and 16 weeks). The postintervention test was scheduled the following week after finishing the intervention period, and it was single-blind by the medical doctor, with no information regarding the intervention group of each participant.

The 15-level modified shuttle walk test (MSWT) consisted in walking/running up and down a 10-meter corridor at an incremental speed as previously described (Bradley, Howard, Wallace, & Elborn, 1999; Hanson, Taylor, & McBurney, 2016).

A cardiopulmonary exercise test (CPET) was used to objectively assess aerobic capacity after the MSWT with a minimum prior 30-minute rest break to obtain stable resting heart rate (HR) and BP values. The test was performed briefly on an electronically braked Lode Excalibur Sport Cycle Ergometer (Groningen, The Netherlands). The testing protocol was started at 40 W with gradual increments of 10 W every minute to exhaustion with continuous electrocardiogram monitoring and participants cycling at 70 rpm. The expired gas analysis was performed using a commercially

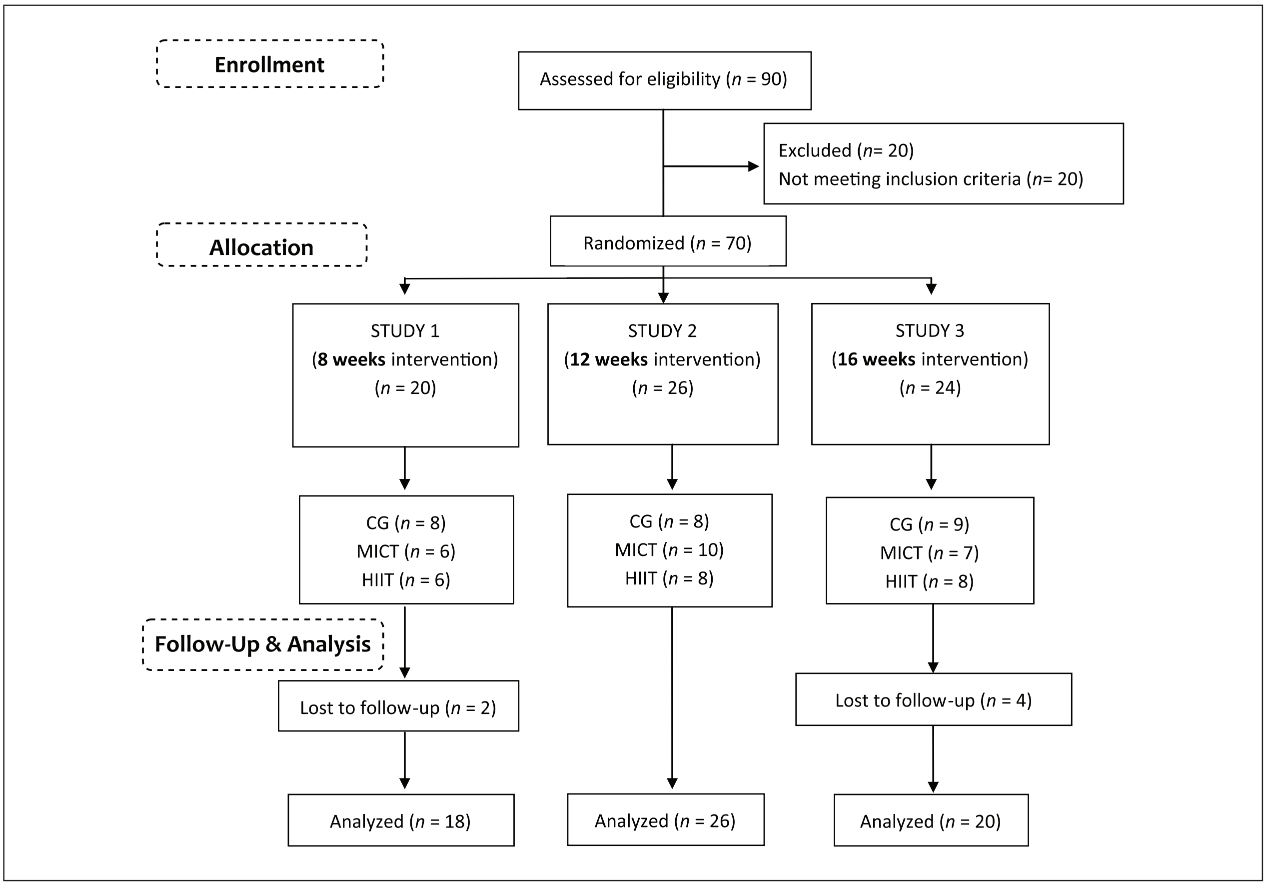

FIGURE 1 Planned Flow Diagram of the Pilot Study From Recruitment to the End of Intervention
NOTE: CG = control group; MICT = moderate-intensity continuous training; HIIT = high-intensity interval training.

available metabolic cart (Ergo CardMedi-soft S.S, Belgium Ref. USM001 V1.0) that was calibrated before each test with a standard gas of known concentration and volume. The BP was measured at rest before starting the test, every 2 minutes throughout the test, and during the recovery period. Borg rating of perceived exertion (RPE; 6-20) scale was self-reported at the end of each stage. Peak oxygen uptake ($\dot{V}O_{2peak}$) was defined as the highest oxygen uptake value attained toward the end of the test and reflected peak aerobic capacity. Achievement of $\dot{V}O_{2peak}$ criteria have been described previously (Mezzani et al., 2012). After completion of the test, participants remained on the bike 5 more minutes for recovery with electrocardiogram and BP monitoring. Absolute and relative indications for terminating the exercise test were taken into account (Task Force of the Italian Working Group on Cardiac Rehabilitation and Prevention et al., 2006).

Anthropometry measurements that were taken to assess body composition included stature (SECA 213), total body mass (BM; SECA 869), BMI, and waist and hip circumferences (SECA 200) to calculate waist-to-hip ratio. All measurements were taken following guidelines from the International Society for the Advancement of Kinanthropometry (Norton et al., 1996).

Intervention

Even though we requested that participants continue with their regular physical activity patterns outside the study protocol, prior to the intervention period they received advice regarding a healthy lifestyle (i.e., nutrition and physical activity general recommendations) regarding guidelines for the management of arterial HTN (Mancia et al., 2013) to maintain ethical procedures.

The exercise groups received supervised exercise intervention for 45 minutes, twice a week. Both intensity and training volume increased progressively during the intervention period in the same range for the two groups: MICT group performed HR values at 50% to 75% of HR reserve with steady continuous exercise (Mezzani et al., 2012); HIIT group, interval training alternating high (76% to 95% of HR reserve) and moderate (50% to 75% of HR reserve) intensities at different exercise protocols depending on the type of exercise (i.e., treadmill or bike; Mezzani et al., 2012).

All the exercise sessions started and finished with BP monitoring. The training intensity was controlled by an HR monitor (Polar Electro, Kempele, Finland) and through the RPE using the original Borg scale (6-20 points). Each session included a 5 to 10 minute warm-up and a 10-minute cool-down period. The central portion of the training session consisted of 45 minutes aerobic exercise (i.e., one day of the week on the treadmill, and the second one on the bike, both using BH Fitness equipment™). The participants exercised at the lower HR intensity limit for the first 2 weeks (only 1 week for the 8-week program) of the training period before progressively increasing the HR intensity toward the upper limit. The rationale of mixing bike and treadmill was to avoid the osteoarticular impact of 2 days on the treadmill, bearing in mind the intensity of the HIIT program. The intensity was individually tailored to HR at moderate or vigorous efforts, adjusting the speed and angle of the treadmill or the power and speed on the bike, to reach the planned target HR.

High-Intensity Interval Training Protocol on the Treadmill. This was carried out with a 5-minute warm-up period at moderate intensity, before walking two intervals of 4 minutes at high intensity for the first 2 weeks, increasing, afterward, to four intervals of 4 minutes in the following weeks (i.e., 16 minutes of total high-intensity volume on the treadmill). Between the high-intensity intervals, the participants did 3 minutes of walking at moderate intensity. The training session ended with a 1- to 4-minute cool-down period at moderate intensity (Rognmo et al., 2004).

High-Intensity Interval Training Protocol on the Bike. This consisted of a 10-minute warm-up period. After that, participants cycled for 30 seconds at high intensity followed by 60 seconds at moderate intensity. Four repetitions (1 rep = 30 seconds high intensity followed by 60 seconds moderate intensity) were initially performed and increased, afterward, to 18 repetitions. The training session ended with a 5 to 10 min cool-down period at moderate intensity (Haykowsky, Taylor, Kim, & Tymchak, 2009). The total high-intensity volume on the bike was 9 minutes.

Statistical Analysis

Statistical analyses were carried out with the SPSS statistical software package (24th ed.). The required sample size was determined for the primary outcome variable (SBP). It was identified that adequate power (0.80) to evaluate differences in our design consisting of four experimental groups would be achieved with 164 people (41 each group, $\alpha = .05$, effect size $f = 0.27$; Maldonado-Martín et al., 2016). Therefore, as the sample size was too small to have adequate power for statistical significance for anything smaller than very large effects, the current report is considered a pilot study, and we evaluated effect sizes for each outcome variable (Lakens, 2013). Hedges's *g* was used as the index of effect size for within and between comparisons of two groups (i.e., pre- vs. postintervention; after-intervention change in CG vs. exercise groups). A *g* index of 0.2 was considered small effect, 0.5 medium and 0.8 large (Hedges & Olkin, 1985). Cohen's *f* was used to assess training effects across the different intervention groups (CG, MICT, HIIT) and different length of training programs (8, 12, 16 weeks). When we compared more than two interventions, an *f* index of 0.1 was considered small effect, 0.25 medium, and 0.4 large (Cohen, 1977). Baseline and follow-up values of all the independent variables are expressed as the mean and standard deviation.

When doing within and between comparisons without subsets in lengths of intervention (i.e., taking all lengths of each type of intervention together: All), the sample size was big enough to evaluate statistical significance. The paired-samples Student's *t* test compared the baseline and follow-up mean values of all the independent variables. Analysis of covariance was used to assess training effects across the different intervention groups. Postintervention outcome selected as a dependent variable and pre-intervention outcome as a covariate. We performed Bonferroni post hoc comparisons, and Helmert contrasts. The level of significance (p) set at 95% ($\alpha = .05$).

RESULTS

Seventy participants met all the required criteria for inclusion in the study. There were six dropouts (8.6%) for reasons unrelated to the study (Figure 1). Thus, 64 participants (48 male, 75%; 16 female, 25%) aged 55.9 ± 8.5 years completed the intervention. Fifty-eight (90%) participants were taking antihypertensive medication. Table 1 shows the participants' baseline characteristics. At baseline there were no between-group differences in any of the studied variables (i.e., BM, $Distance_{MSWT}$, $Distance_{CPET}$, $Workload_{CPET}$, $\dot{V}O_{2peak}$, MET_{peak}).

Table 2 shows the effect of different types of intervention without subsets of differing lengths or durations of intervention: CG reduced BM ($p < .001$, $g = 0.1$) and had small changes in exercise groups ($p > .05$, $g < 0.03$). Total distance walked/run in the MSWT ($Distance_{MSWT}$) increased 45.0 ± 59.3 m after the MICT ($p < .001$, $g = 0.3$) and 63.3 ± 73.4 m after the HIIT ($p = .02$, $g = 0.5$), and total distance ridden in the CPET ($Distance_{CPET}$) increased ($p < .001$) 0.5 ± 0.3 km after the MICT ($g = 0.4$) and 0.7 ± 0.4 km after the HIIT ($g = 0.6$). Workload increased ($p < .001$) 20.4 ± 15.2 W in MICT ($g = 0.5$) and 30.5 ± 15.6 W in HIIT ($g = 0.7$). The MICT increased ($p < .001$) the absolute $\dot{V}O_{2peak}$ 0.3±0.2 $L \cdot min^{-1}$ ($g = 0.6$) and 0.3 ± 0.4 $L \cdot min^{-1}$ in HIIT ($g = 0.5$), and relative $\dot{V}O_{2peak}$ increased ($p < .001$) 3.8 ± 3.3 $mL \cdot kg^{-1} \cdot min^{-1}$ after MICT ($g = 0.6$) and 4.2 ± 4.7 $mL \cdot kg^{-1} \cdot min^{-1}$ after HIIT ($g = 0.7$; Figure 2: All). We found similar improvements in the metabolic equivalent of task (MET), which increased ($p < .001$) 1.2 ± 1.1 after MICT ($g = 0.7$) and 1.1 ± 1.3 after HIIT ($g = 0.6$). Moreover, we found the change after intervention to be statistically significant in most analyzed parameters; the effect size of MICT and HIIT interventions was medium in CRF variables ($\dot{V}O_{2peak}$ and MET) and also medium size in $Distance_{CPET}$ and workload of HIIT intervention. Changes after intervention period in CG were not statistically significant, and the effect size of those changes was considered very small ($g < 0.1$).

The effect of exercise interventions (i.e., MICT and HIIT) compared with CG was substantial and statistically significant ($p < .02$; $g > 0.8$) for all variables. However, for $Distance_{MSWT}$ a medium-sized effect was observed ($p = .01$, $g = 0.7$) and small changes in BM were not significant ($p > .05$, $g = 0.4$; Table 2: Helmert contrast). Those large effects were mostly the consequence of HIIT-related effects, as indicated by Cohen's *f* index and Bonferroni post hoc comparisons (Table 2).

Table 2 (All) shows that the 8-week intervention effect is small or medium. Thus, the previously related improvements occurred in the 12- and 16-week MICT and HIIT interventions rather than in the 8-week interventions or CG, where the gain effect was small, as indicated by Hedges's *g* index. Cohen's *f* index also indicated a medium or large effect of intervention length in all measured parameters, due to the more significant effects of 12- and 16-week interventions. Body mass was reduced in CG and in the longest exercise interventions, while it increased after shorter exercise interventions, showing large differences between the gain of BM after short interventions and the longer ones or CG (Figure 2).

TABLE 1
Baseline Characteristics of the Study Population ($n = 64$)

Characteristics	M ± SD *or Frequency (%)*
Sex	48 (75%)♂; 16 (25%)♀
Age (years)	55.9 ± 8.5
BM (kg)	81.9 ± 13.1
BMI ($kg \cdot m^{-2}$)	27.9 ± 3.4
Waist circumference (cm)	99.7 ± 7.4♂; 85.7 ± 11.3♀
Hip circumference (cm)	102.7 ± 5.3♂; 103.1 ± 8.1♀
WHR	0.97 ± 0.05♂; 0.83 ± 0.06♀
Rest SBP (mmHg)	134.8 ± 16.1
Rest DBP (mmHg)	89.9 ± 8.8
Peak SBP (mmHg)	205.8 ± 26.9
Peak DBP (mmHg)	94.1 ± 14.8
$\dot{V}O_{2peak}$ ($L \cdot min^{-1}$)	2.1 ± 0.6
$\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	25.7 ± 7.3
RER_{peak}	1.1 ± 0.1
Workload (W)	135.9 ± 42.1
MET_{peak}	7.3 ± 2.1
$Distance_{CPET}$ (km)	2.1 ± 1.0
Medication	58 (90)
ACEIs	20 (31)
ARBs	28 (44)
Diuretics	13 (20)
CCBs	13 (20)
BBs	9 (14)
Statins	11 (17)
Hypoglycemic agents	3 (5)
Antiplatelets	1 (2)
Anticoagulants	2 (3)

NOTE: BM = body mass; BMI = body mass index; WHR = waist-to-hip ratio; SBP = systolic blood pressure; DBP = diastolic blood pressure; $\dot{V}O_{2peak}$ = peak oxygen uptake; RER = respiratory exchange ratio; MET = metabolic equivalent of task; CPET = cardiopulmonary exercise test; ACEI = angiotensin-converting-enzyme inhibitor; ARB = angiotensin receptor blocker; CCB = calcium channel blocker; BB = beta blocker.

DISCUSSION

The present study evaluated the effects of different structured, formal, and supervised physical exercise training programs in the CRF of overweight/obese adult population diagnosed with HTN, after 8-, 12-, and 16-week intervention periods, and compared them

TABLE 2
Comparison Between After-Intervention Effects of Different Types and Lengths of Exercise-Training

Variable	CG: 8 Weeks (n = 6), 12 Weeks (n = 8), 16 Weeks (n = 9), All (n = 23)			CG: Hedges'g (Pre–Post)	CG: Cohen's f (Length of Intervention)	MICT: 8 Weeks (n = 6), 12 Weeks (n = 10), 16 Weeks (n = 5), All (n = 21)			MICT: Hedges's g (Pre–Post)	MICT: Cohen's f (Length of Intervention)	HIIT: 8 Weeks (n = 6), 12 Weeks (n = 8), 16 Weeks (n = 6), All (n = 20)			HIIT: Hedges's g (Pre–Post)	HIIT: Cohen's f (Length of Intervention)	Comparison Between Effects of Types of Intervention (ANCOVA): Cohen's f (CG vs. MICT vs. HIIT)	Bonferroni (CG vs. MICT vs. HIIT)	Hedges's g (CG vs. Exercise Groups)	Helmert (CG vs. Exercise Groups)
Body mass (kg)	80.5 ± 8.9	↙	79.5 ± 9.9	0.095	0.280	88.5 ± 19.7	↗	89.0 ± 18.0	0.023	0.559	76.9 ± 9.4	↗	77.3 ± 9.6	0.036	0.565	0.592	—	0.927	—
	79.5 ± 10.0	↙	78.0 ± 9.5	0.145		84.0 ± 8.9	↙	83.1 ± 8.4	0.106		84.1 ± 17.9	↗	85.1 ± 18.7	0.048		0.567	—	0.664	—
	82.7 ± 9.6	↙	82.2 ± 9.8	0.053		82.7 ± 19.9	↙	81.7 ± 20.2	0.045		76.5 ± 16.0	↙	75.0 ± 15.8	0.085		0.277	—	0.466	—
	81.0 ± 9.3	↙	80.0 ± 9.4*	0.104	—	85.0 ± 14.7	↙	84.4 ± 14.3	0.038	—	79.7 ± 14.9	=	79.7 ± 15.5	0.003	—	0.248	—	0.408	—
$Distance_{MSWT}$ (m)	865.0 ± 224.8	↗	898.3 ± 194.4	0.146	0.193	863.3 ± 183.5	↗	908.3 ± 138.9	0.255	0.495	865.0 ± 123.6	↗	928.3 ± 103.6	0.513	0.516	0.299	—	0.340	—
	826.3 ± 236.9	↗	833.8 ± 244.9	0.029		817.0 ± 247.3	↗	877.0 ± 195.3	0.258		906.3 ± 175.9	↗	946.3 ± 137.2	0.240		0.344	—	0.532	—
	1028.9 ± 209.4	↗	1036.7 ± 175.7	0.038		936.0 ± 328.1	↗	1020.0 ± 289.1	0.245		936.7 ± 171.9	↗	1048.3 ± 163.6	0.614		0.530	—	1.011	—
	915.7 ± 232.7	↗	930.0 ± 217.3	0.063	—	858.6 ± 244.6	↗	920.0 ± 205.3*	0.267	—	903.0 ± 155.0	↗	971.5 ± 139.8*	0.455	—	0.334	φφ	0.654	Ψ
$Distance_{CPET}$ (km)	2.6 ± 1.2	↗	2.8 ± 1.5	0.126	0.157	2.5 ± 1.1	↗	2.8 ± 1.1	0.221	0.456	2.2 ± 1.4	↗	2.8 ± 1.6	0.334	0.364	0.465	—	0.528	—
	2.2 ± 0.6	↗	2.4 ± 0.8	0.163		1.7 ± 0.8	↗	2.2 ± 0.8	0.600		2.0 ± 0.4	↗	2.7 ± 0.8	1.058		0.748	—	1.256	—
	2.6 ± 1.0	↗	2.7 ± 1.2	0.047		1.4 ± 1.3	↗	2.1 ± 1.5	0.430		1.7 ± 1.0	↗	2.5 ± 1.4	0.551		0.974	—	1.319	—
	2.5 ± 0.9	↗	2.6 ± 1.1	0.104	—	1.9 ± 1.0	↗	2.4 ± 1.1*	0.441	—	2.0 ± 0.9	↗	2.7 ± 1.2*	0.612	—	0.647	φ φφ	1.106	Ψ
$Workload_{CPET}$ (watt)	160.8 ± 47.4	↗	161.3 ± 51.5	0.009	0.160	155.2 ± 46.3	↗	163.0 ± 44.4	0.159	0.617	137.8 ± 57.9	↗	159.0 ± 58.7	0.335	0.530	0.686	—	0.951	—
	142.8 ± 28.9	↗	146.8 ± 36.4	0.115		118.6 ± 33.9	↗	141.3 ± 31.8	0.661		130.9 ± 22.1	↗	161.0 ± 29.9	1.084		0.929	—	1.728	—
	152.9 ± 37.2	↗	156.3 ± 40.5	0.084		107.2 ± 51.4	↗	138.0 ± 60.4	0.496		115.0 ± 50.4	↗	155.2 ± 48.2	0.752		1.103	—	2.068	—
	151.4 ± 36.5	↗	154.3 ± 40.7	0.073	—	126.3 ± 44.2	↗	146.7 ± 42.3*	0.462	—	128.2 ± 42.6	↗	158.7 ± 43.1*	0.697	—	0.771	φ φφ	1.498	Ψ
$\dot{V}O_{2peak}$ ($L \cdot min^{-1}$)	2.4 ± 0.7	↗	2.6 ± 0.8	0.266	0.630	2.2 ± 0.6	↗	2.3 ± 0.6	0.206	0.484	2.1 ± 0.9	↗	2.3 ± 0.9	0.171	0.311	0.119	—	0.190	—
	2.2 ± 0.5	↙	2.0 ± 0.4	0.370		1.8 ± 0.5	↗	2.2 ± 0.5	0.744		2.1 ± 0.5	↗	2.5 ± 0.6	0.595		0.883	—	1.844	—
	2.3 ± 0.6	↗	2.4 ± 0.5	0.107		1.7 ± 0.5	↗	2.1 ± 0.7	0.602		1.8 ± 0.4	↗	2.2 ± 0.6	0.806		0.752	—	1.628	—
	2.3 ± 0.6	↗	2.3 ± 0.6	0.034	—	1.9 ± 0.5	↗	2.2 ± 0.5*	0.574	—	2.0 ± 0.6	↗	2.3 ± 0.7*	0.482	—	0.408	φ φφ	0.928	Ψ
$\dot{V}O_{2peak}$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	31.2 ± 11.2	↗	32.5 ± 11.2	0.110	0.433	25.0 ± 7.3	↗	26.3 ± 7.1	0.171	0.522	27.0 ± 10.3	↗	28.8 ± 8.6	0.179	0.335	0.123	—	0.041	—
	27.6 ± 7.9	↙	25.6 ± 5.5	0.278		22.1 ± 5.9	↗	26.7 ± 6.0	0.742		25.4 ± 2.7	↗	29.6 ± 6.7	0.790		0.711	—	1.633	—
	28.7 ± 6.8	↗	29.6 ± 5.9	0.133		21.0 ± 5.1	↗	26.2 ± 6.7	0.787		22.8 ± 3.3	↗	29.2 ± 2.7	1.931		0.755	—	1.795	—
	29.0 ± 8.2	=	29.0 ± 7.6	0.009	—	22.7 ± 6.0	↗	26.5 ± 6.2*	0.613	—	25.1 ± 6.0	↗	29.3 ± 6.1*	0.672	—	0.332	φφ	0.898	Ψ
MET_{peak}	8.9 ± 3.2	↗	9.3 ± 3.2	0.116	0.451	7.2 ± 2.0	↗	7.53 ± 2.0	0.161	0.472	7.7 ± 2.9	↗	8.1 ± 2.6	0.140	0.362	0.123	—	0.009	—
	7.9 ± 2.2	↙	7.3 ± 1.6	0.297		6.2 ± 1.7	↗	7.63 ± 1.7	0.755		7.3 ± 0.7	↗	8.5 ± 1.9	0.787		0.688	—	1.625	—
	8.2 ± 2.0	↗	8.4 ± 1.7	0.115		6.0 ± 1.4	↗	7.50 ± 1.9	0.802		6.6 ± 1.0	↗	8.3 ± 0.7	1.891		0.810	—	1.921	—
	8.3 ± 2.3	=	8.3 ± 2.2	0.009	—	6.4 ± 1.7	↗	7.6 ± 1.7*	0.642	—	7.2 ± 1.7	↗	8.3 ± 1.8*	0.661	—	0.319	φφ	0.895	Ψ

NOTE: ANCOVA = analysis of covariance; CG = control group; MICT = moderate-intensity continuous group; HIIT = high-intensity interval training; MSWT = modified shuttle walk test; CPET = cardiopulmonary exercise test; $\dot{V}O_{2peak}$ = peak oxygen uptake; MET = metabolic equivalent of task. Data are expressed as *M* ± *SD* values before and after intervention period. Effect size between pre–post design is expressed by Hedges's *g*. Effect size between after intervention effects of different length and type interventions is expressed by Cohen's *f*. Effect size between CG and exercise groups is expressed by Hedges's *g*. Statistically significant differences ($p < .05$) are expressed as: * (pre vs. postintervention); φ (CG vs. MICT); φφ (CG vs. HIIT); Ψ (CG vs. exercise groups); — (not calculated).

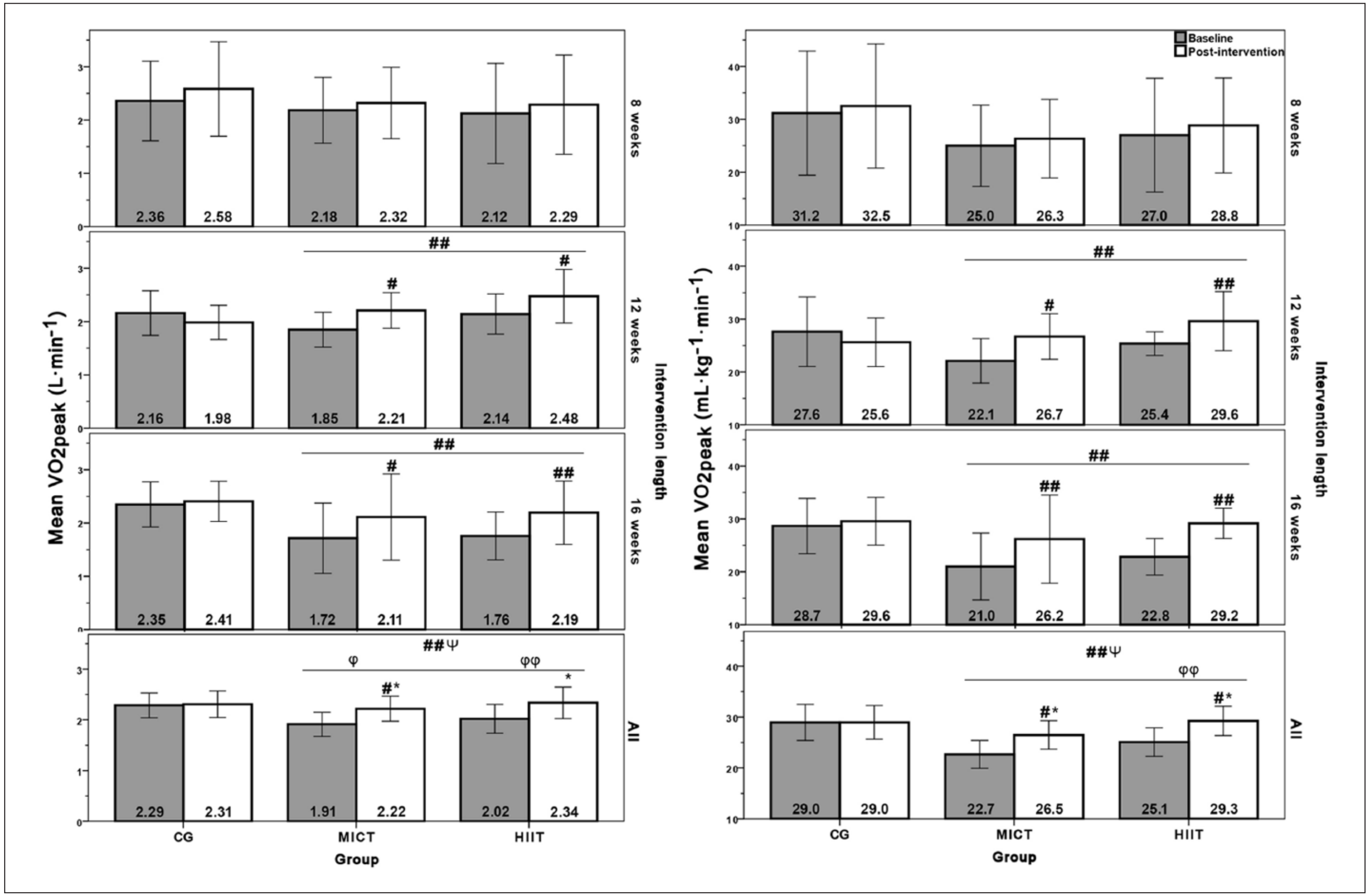

FIGURE 2 Evolution of $\dot{V}O_{2peak}$ After Intervention Periods

NOTE: Values are *M* ± *SD*. $\dot{V}O_{2peak}$ = peak oxygen uptake. CG = control group; MICT = moderate-intensity continuous training; HIIT = high-intensity interval training. Error bars at 95% confidence interval. Medium (#) and large (##) effects within and between interventions are indicated. Statistically significant differences ($p < .05$) are expressed as follows: * (pre vs. postintervention); φ (CG vs. MICT); φφ (CG vs. HIIT); Ψ (CG vs. exercise groups).

with a CG. The main findings showed that only participants who performed 2 days per week of supervised training modes (MICT and HIIT) statistically increased CRF. There was also a superior tendency effect from HIIT, and we found that "short-term" exercise intervention (8 weeks) with MICT or HIIT was not enough to increase CRF in overweight/obese people diagnosed with HTN.

Sixty-four participants divided into three cohorts subject to kind of intervention (CG, MICT, and HIIT) and each one into three other cohorts subject to intervention length (8, 12, and 16 weeks) are not enough to reach any generalisable conclusion related to the effects of exercise intervention based on different combinations of FITT principles in the CRF markers of overweight/obese patients with HTN. Consequently, the authors of the article suggest considering this study a pilot study. However, taking into account the estimated effect sizes with such a small sample per group we do find these initial tendencies promising.

European guidelines for the management of arterial HTN (Mancia et al., 2013) recommend lifestyle changes for reducing and controlling BP and BM, including calorie-restricted diet and regular physical exercise. In fact, previous investigations (Blumenthal et al., 2010) had shown better control of BP and BM when dual treatment was applied. The present pilot study was designed to evaluate only CRF after different exercise programs, without diet intervention (only some basic recommendations but with no control or supervision). Therefore, although out of the scope of the current work, the small and irregular changes showed in BM may confirm the requirement of diet as a key component along with exercise intervention to achieve BM loss in overweight/obese people with HTN (Jensen et al., 2014).

Even though it recognises that exercise reduces CVD risk, how much of it is needed and the intensity that provides optimal cardiovascular protection are two questions for which there are still no definitive answers (Despres, 2016). In this study, both supervised exercise training interventions provided significant improvements on the different variables measured at the CPET (distance, workload, $\dot{V}O_{2peak}$, MET). It is noteworthy that each 1-MET higher CRF is associated with considerable (10% to 25%) improvement in survival (Ross et al., 2016). It might state, therefore, that comparing MET_{peak} values before versus after the intervention, in the present study, MICT (6.4 vs. 7.6) and HIIT (7.2 vs. 8.3) exercise programs were effective regarding reduction of CVR (Table 2). Furthermore, it is well known that the bigger the amount of activity or intensity, the higher gain in CRF (Ross et al., 2016). Thus, in this study, although the effect of both exercise interventions compared with CG was significant for all variables, the large improvement in CRF was mostly the consequence of HIIT (Cohen's *f* index and Bonferroni post hoc comparisons; Table 2). In this sense, the two groups were equated with regard to the total amount of work but not intensity, which leads to a more considerable energy expenditure in HIIT group and points out high aerobic intensity as a critical factor for increasing aerobic capacity in this population. These results are in line with previous ones in coronary artery disease (Rognmo et al., 2004) and hypertensive population (Boutcher & Boutcher, 2017; Molmen-Hansen et al., 2012) and with recent reviews in different populations (Batacan, Duncan, Dalbo, Tucker, & Fenning, 2017; Karlsen, Aamot, Haykowsky, & Rognmo, 2017; Kessler, Sisson, & Short, 2012) showing the beneficial effects of HIIT on cardiometabolic health markers.

Taking into account the evidence mentioned above, it may hypothesise that a short-term HIIT intervention (i.e., 8 weeks) might offer better CRF adaptations compared with MICT in this population. However, in the present study, there was a tendency toward bigger improvements as the intervention became longer and more intense (Table 2, All). At least 12 weeks seem to be necessary to obtain large improvements in physical fitness with either of both exercise programs performed; thus, the longer the intervention was, the larger the beneficial effect it had (Figure 2). Results from the present study reveal that at the end of 8 weeks of training participants presented no statistical increases in CRF (MICT, $\Delta\dot{V}O_{2peak}$ = 5%, Hedges's g = 0.171; HIIT, $\Delta\dot{V}OO_{2peak}$ = 6.2%, Hedges's g = 0.179; Table 2, All) compared with the preintervention period, similar to CG. However, after 12-weeks (MICT, $\Delta\dot{V}O_{2peak}$ = 17%, Hedges's g = 0.742; HIIT, $\Delta\dot{V}O_{2peak}$ = 14%, Hedges's g = 0;790, Table 2, All) and 16 weeks of training (MICT, $\Delta\dot{V}O_{2peak}$ = 19%, Hedges's g = 0.787; HIIT, $\Delta\dot{V}O_{2peak}$ = 22%, Hedges's g = 1.931; Table 2, All) participants presented medium and large effects that tended toward better results as the intervention lengthens (i.e., 16 weeks vs. 12 weeks; Figure 2). These findings are in line with a recent systematic review and meta-analysis (Batacan et al., 2017) examining HIIT and cardiometabolic health markers. It establishes the ability of this procedure (at least 12 weeks of HIIT) with clinical applications in overweight/obese population that need to improve their aerobic fitness via increasing mitochondrial density, stroke volume, and skeletal muscle diffusive capacity, showing larger improvements in aerobic capacity by longer training periods.

It is known that CRF is a potentially stronger predictor of mortality than established risk factors such as smoking, HTN, high cholesterol, and type 2 diabetes mellitus (Ross et al., 2016) and that those fitter individuals who are overweight/obese are not automatically at a higher risk for all-cause mortality (Barry et al., 2014). Therefore, this pilot study has shown the positive effect of different exercise interventions on overweight/obese people with HTN allowing this population to carry out HIIT.

Finally, and regarding the "*F*requency" of exercise, most professional committees recommend exercising on most, if not all, days of the week (Pescatello, MacDonald, Lamberti, et al., 2015). In the present study, with only two days per week of supervised exercise, an essential improvement on CRF was shown in both exercise groups (Figure 2). Thus, it might be that regular and individualised exercise, supervised and controlled by exercise professionals, will lead individuals to carry out the actual moderate and high exercise intensities achieving greater improvements than in unsupervised protocols. However, taking into account the postexercise hypotension effect and the urgent need for increasing caloric expenditure and CRF in this population (Pescatello, MacDonald, Lamberti, et al., 2015), 2 days of supervised HIIT exercise along with other physical activities at lower intensities the other 5 days of the week could be the best option.

Limitations of the Study

We should consider several limitations of the study. First, a bigger sample size is recommended to evaluate the effects of different kinds of exercise on BP, body composition and CRF. Second, we describe the effects of 8, 12, and 16 weeks in duration. Therefore, although it seems that an intervention length of less than 12 weeks does not offer the same beneficial adaptations as ≥12 weeks, we do not know the effects in-between (9, 10, or 11 weeks). Finally, we required participants to continue with their normal physical activity patterns outside the study protocol; however, though all of them were sedentary at the beginning of the study, we did not control whether participants performed other daily physical activities.

Conclusions

This study indicates that both MICT and HIIT, in the form of 2-weekly bouts, exert cardioprotector effects on HTN in overweight/obese population. Furthermore, short-term training duration (<12 weeks) may not improve CRF, and HIIT intervention might generate higher aerobic capacity, which seems to improve as intervention lengthens (>12 weeks). The components of FITT principle for the assessment of exercise treatment to HTN and overweight/obese individuals need further research to reach generalisable results that will resolve the recommendations of exercise training in this population. The practical implications of this study indicate that a complete lifestyle treatment (diet plus exercise) is required to have a better control of BP, body composition, and CRF and that exercise treatment should include different types of training modes (MICT and HIIT).

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10.3. Anexo 3. Publicaciones relacionadas con la tesis

En revistas internacionales

- Maldonado-Martín S, Gorostegi-Anduaga I, Aispuru GR, Illera-Villas M, Jurio-Iriarte B, Francisco-Terreros S, Pérez-Asenjo J. Effects of different aerobic exercise programs with nutritional intervention in primary hypertensive and overweight/obese adults: EXERDIET-HTA controlled trial. *J Clin Trials.* 2016;6(1). doi:10.4172/2167-0870.1000252.

- Gorostegi-Anduaga I, Corres P, Jurio-Iriarte B, Martínez-Aguirre A, Pérez-Asenjo J, Aispuru GR, Arenaza L, Romaratezabala E, Arratibel-Imaz I, Mujika I, Francisco-Terreros S, Maldonado-Martín S. Clinical, physical, physiological, and dietary patterns of obese and sedentary adults with primary hypertension characterized by sex and cardiorespiratory fitness: EXERDIET-HTA study. *Clin Exp Hypertens.* 2018;40(2):141-149. doi:10.1080/10641963.2017.1346111.

Comunicaciones presentadas en congresos

- Maldonado-Martin S, Jurio-Iriarte B, Camacho-Azkargorta I. Effects on blood pressure and cardiorespiratory condition of an 8-week exercise programme of differing intensities in hypertensive patients: pilot study. EuroPRevent: the EACPR annual meeting - Universal approach to preventive cardiology; 18-20 de abril, 2013; Roma, Italia.

- Maldonado-Martin S, Jurio-Iriarte B, Camacho-Azkargorta I. Effects of 8 and 12 weeks of high-intensity aerobic interval training *vs.* moderate exercise on blood pressure and cardiorespiratory condition in hypertensive patients: a randomized controlled trial. EuroPRevent: the EACPR annual meeting - Global cardiovascular health; 8-10 de mayo, 2014; Amsterdam, Holanda.

- Maldonado-Martin S, Jurio-Iriarte B, Labayen I, Gorostegi-Anduaga I, Illera-Villas M, Medrano-Echeverria M, Pérez-Asenjo J. Effects of high-intensity aerobic interval training *vs.* moderate exercise on body mass, blood pressure and cardiorespiratory condition in hypertensive patients with diet *vs.* no diet. 25th European Meeting on Hypertension and Cardiovascular Protection; 12-15 de junio, 2015; Milán, Italia.

- Jurio-Iriarte B, Gorostegi-Anduaga I, Aispuru GR, Corres P, Perez-Asenjo J, Martinez-Aguirre A, Brubaker PH, Maldonado-Martin S. Association between modified shuttle walk test and cardiorespiratory fitness in overweight/obese adults with primary hypertension: EXERDIET-HTA study. EuroPRevent: European Congress on Preventive Cardiology - Innovations in preventive cardiology; 6-8 de abril, 2017; Málaga, España.

- Gorostegi-Anduaga I, Aispuru GR, Corres P, Perez-Asenjo J, Martinez-Aguirre A, Jurio-Iriarte B, Maldonado-Martin S. Assessment of cardiovascular risk and vascular age in overweight/obese adults with primary hypertension: EXERDIET-HTA study. EuroPRevent: European Congress on Preventive Cardiology - Innovations in preventive cardiology; 6-8 de abril, 2017; Málaga, España.

- Maldonado-Martin S, Gorostegi-Anduaga I, Aispuru GR, Corres P, Jurio-Iriarte B, Martinez-Aguirre A, Fryer SM, Mujika I, Perez-Asenjo J. Association of nocturnal blood pressure dipping with cardiorespiratory fitness and body mass index in overweight/obese adults with primary hypertension: EXERDIET-HTA study. EuroPRevent: European Congress on Preventive Cardiology - Innovations in preventive cardiology; 6-8 de abril, 2017; Málaga, España.

- Corres P, Gorostegi-Anduaga I, Fryer SM, Jurio-Iriarte B, Martinez-Aguirre A, Arratibel-Imaz I, Perez-Asenjo J, Maldonado-Martin S. Is cardiorespiratory fitness independently associated with biochemical profile in overweight/obese adults with primary hypertension? EXERDIET-HTA study. EuroPRevent: European Congress on Preventive Cardiology - Evidence based cardiovascular prevention. A lifelong endeavour; 19-21 de abril, 2018; Liubliana, Eslovenia.

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