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Title: **Long-term effects in the EXERDIET-HTA study: Supervised exercise training vs. physical activity advice**

Pablo Corres, MS, Sara Maldonado-Martín, Ph.D, Aitor MartinezAguirre-Betolaza, MS, Ilargi Gorostegi-Anduaga, MS, Iñaki Arratibel-Imaz, Ph.D, G. Rodrigo Aispuru, MS, Simon M. Fryer Ph.D

**Abstract**

**Purpose:** To determine whether improvements in cardiorespiratory fitness (CRF), blood pressure (BP) and body composition previously seen after a 16-week exercise intervention (POST) with hypocaloric diet, are maintained following six-months (6M) of unsupervised exercise time. **Methods:** Overweight/obese, physically inactive participants with primary hypertension (HTN) (n=190) were randomly assigned into an attention control group (physical activity recommendations) or one of three supervised exercise groups. After POST, all participants received diet and physical activity advice for the following 6M but no supervision. All anthropometric and physiological measurements were taken pre and post the 16-week supervised intervention period, as well as after 6M of no supervision. **Results:** After 6M: 1) body mass (BM) ( $\Delta=2.5\%$ ) and waist circumference ( $\Delta=1.8\%$ ) were higher ( $P<0.005$ ) than POST, but lower ( $P<0.005$ ) than pre-intervention (BM,  $\Delta=-5.1\%$ ; waist circumference,  $\Delta=-4.7\%$ ), with high-volume and high-intensity interval training group revealing a higher BM reduction ( $\Delta=-6.4\text{kg}$ ) compared to control group ( $\Delta=-3.5\text{kg}$ ); 2) BP variables were higher ( $P<0.001$ ) compared to POST with no change from pre-intervention; and 3) CRF was higher compared to pre-intervention ( $\Delta=17.1\%$ ,  $P<0.001$ ) but lower than POST ( $\Delta=-5.7\%$ ,  $P<0.001$ ). **Conclusions:** When an overweight/obese population with HTN attains significant improvements in cardiometabolic health POST intervention with diet restriction, there is a significant reduction following 6M when exercise and

diet supervision is removed, and only recommendations were applied. These results suggest the need for a regular, systematic and supervised diet and exercise programs to avoid subsequent declines in cardiometabolic health.

**Keywords:** obesity; blood pressure; cardiorespiratory fitness; body composition

The prevalence of primary hypertension (HTN) and overweight/obesity is considered an important public health issue in developed countries (Jensen et al., 2014; Mancia et al., 2013). Overall, 39% of adults were overweight in 2016, and 13% were obese (World Health Organization, 2018). Worryingly both HTN and overweight/obesity are two of the most common causes of premature death, yet they are modifiable cardiovascular risk factors (Authors/Task Force Members et al., 2016; Mancia et al., 2013). Consequently, lowering both blood pressure (BP) and body mass (BM) would likely result in a substantial improvements in cardiometabolic health (Authors/Task Force Members et al., 2016).

All international guidelines recommend appropriate lifestyle changes for the prevention and treatment of HTN and obesity (Jensen et al., 2014; Mancia et al., 2013). Interventions combining both exercise and diet have been shown to be effective for reducing BM, BP and increasing cardiorespiratory fitness (CRF) (Landsberg et al., 2013; Mancia et al., 2013). Recently, CRF (measured by peak oxygen uptake [ $\dot{V}O_{2peak}$ ]) has been recognized as an independent predictor of all-cause, and disease-specific mortality in a variety of different populations (Harber et al., 2017). As such CRF has an inverse relationship with cardiovascular disease risk factors such as dyslipidemia, obesity, diabetes mellitus, and HTN (Bakker, Sui, Brellenthin, & Lee, 2018; Myers et al., 2015). Consequently, people with HTN are advised to perform at least 30 min of moderate-intensity dynamic aerobic exercise 5-7 days per week (Mancia et al., 2013). However, alternative exercise options are available, including interval training which has previously shown to be a time efficient method for improving CRF in a population with HTN (Gorostegi-Anduaga, Corres, MartinezAguirre-Betolaza et al., 2018; Pescatello, MacDonald, Lamberti, & Johnson, 2015). In order for interval training to be

effective, the exercise program should be designed in a systematic and individualized manner by an exercise specialist, and Frequency, Intensity, Time and Type should be considered (*i.e.*, FITT principle) (Pescatello et al., 2015). Previous data from the EXERDIET-HTA study found that all groups (*i.e.*, diet and supervised aerobic exercise vs. diet and physical activity advice only), significantly improved body composition, BP and CRF following a 16-week intervention program, regardless exercise supervision, and independent of the FITT principle (*i.e.*, different volumes and exercise intensities). However, it was shown that the supervised exercise groups (*i.e.*, high volume and moderate-intensity continuous training [HV-MICT], HV and high-intensity interval training [HV-HIIT], and low volume-HIIT [LV-HIIT]) had significantly greater improvements in BM and CRF compared to a group which only had physical activity advice (Gorostegi-Anduaga et al., 2018).

Whilst short-term diet and physical activity interventions are important for the reduction of BM and improvement of cardiometabolic health, the main goal is a lifestyle based on long-standing behavioral patterns (*i.e.*, Dietary Approaches to Stop Hypertension [DASH] diet, and regular physical exercise) (Mancia et al., 2013; Authors/Task Force Members et al., 2016). No known longitudinal study has investigated the long-term effects of supervised training cessation or the persistence of changes in overweight/obese and hypertensive adults, who are receiving only diet and physical activity advice after an intervention period. Further, previous literature provides discordant data with respect to the type of exercise, periods of training, supervised training cessation, and population studied. Thus, while some investigations found that the exercise training induced-improvements were maintained after supervised training cessation period (Mora-Rodriguez et al., 2014; Tokmakidis et al.,

2014), other found significant reductions (Moker, Bateman, Kraus, & Pescatello, 2014; Volaklis, Douda, Kokkinos, & Tokmakidis, 2006). Given this discourse, the results cannot be applied to an overweight/obese population with HTN.

Therefore, the aim of this study was to determine whether the improvements in CRF, BP and body composition previously seen during both a 16-week supervised exercise training intervention, and a physical activity advice intervention with hypocaloric diet, are maintained following six-months (6M) of unsupervised time.

## **Methods**

### ***Research design***

Data from the current study is from the EXERDIET HTA study (multi-arm parallel, a randomized, single-blind controlled experimental trial, [www.clinicaltrials.gov](http://www.clinicaltrials.gov), number NCT02283047). This longitudinal data was collected between September 2013 and January 2018. While the current study will describe the methods, more specific details regarding the design, selection criteria and procedures associated with the EXERDIET-HTA study have been previously published (Maldonado-Martín et al., 2016). The Ethics Committee of The University of the Basque Country (UPV/EHU, CEISH/279/2014) and Clinical Investigation of Araba University Hospital (2015-030) approved the study design, protocols, and informed consent.

### ***Participants***

Two-hundred and twenty-four non-Hispanic white participants took part in the EXERDIET-HTA study, conducted in Vitoria-Gasteiz (Basque Country, Spain). Fifteen participants left the study during the intervention, and 19 more did not attend the 6M

assessment. Therefore, 190 participants (n=126 men and n=64 women, 54.3±7.3 yrs.) completed all three visits and are included in all analysis. A schematic representing the study design is presented in Figure 1. Participants were non-physically active, overweight or obese, with primary HTN. Hypertension was defined as systolic BP (SBP) of 140-179 mmHg and/or diastolic BP (DBP) of 90-109 mmHg, and/or under antihypertensive pharmacological treatment (Mancia et al., 2013). To ensure participants were non-physically active, the International Physical Activity Questionnaire (IPAQ) was used. For all other inclusion and exclusion criteria, please refer to the previously published study protocol (Maldonado-Martín et al., 2016).



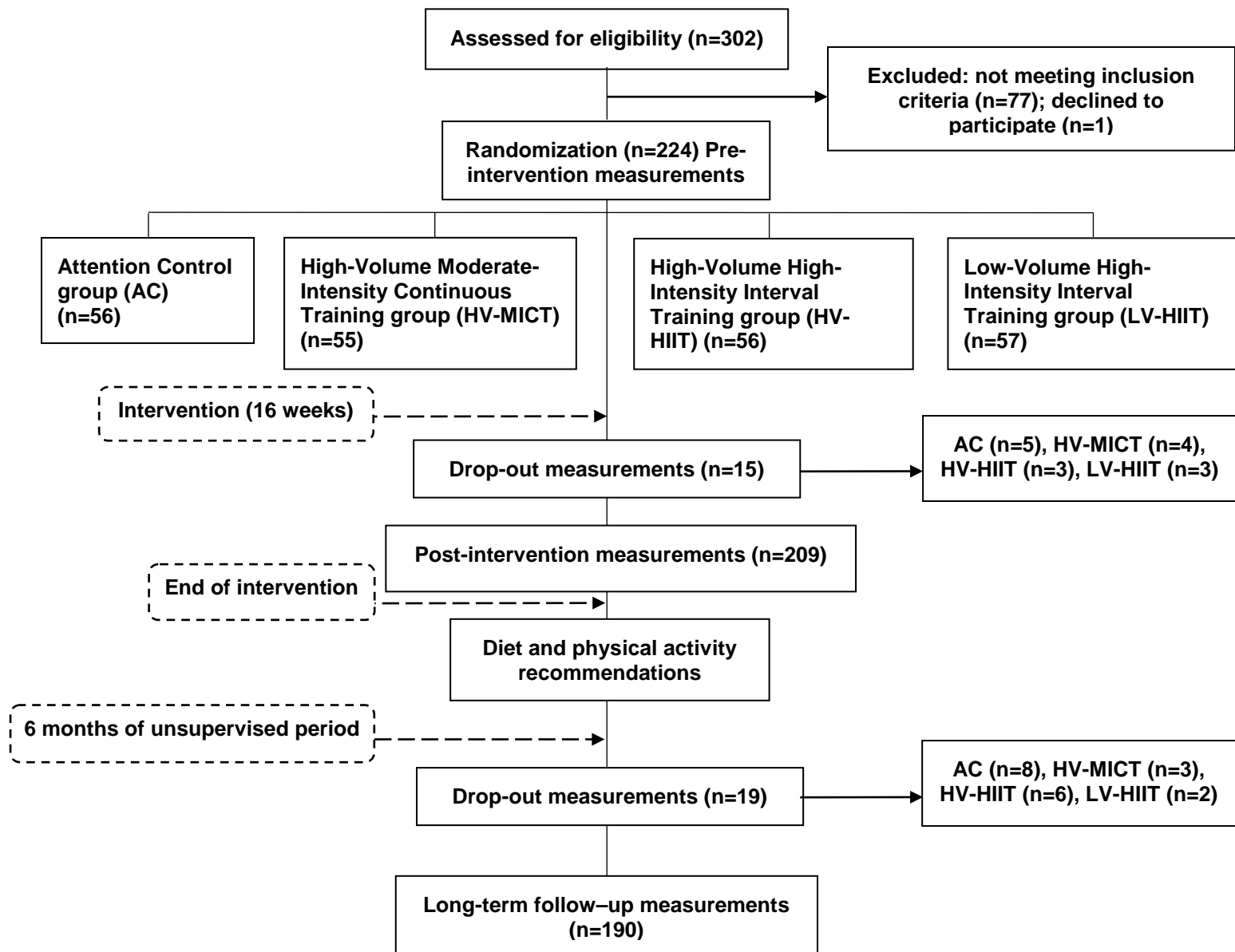


Figure 1. Flow diagram of the EXERDIET-HTA study from recruitment to the 6-month follow-up unsupervised period.

## ***Measurements***

### *Anthropometry and body composition*

Measurements were taken in accordance with guidelines from the International Society for the Advancement of Kinanthropometry. Stature, total BM, BM index (BMI), waist and hip circumferences, waist-to-hip ratio (WHR), fat-free mass (FFM), total body water and fat body mass (FBM) were recorded using a Tanita bio-impedance device (BF 350, Tokyo, Japan).

### *Blood pressure*

An ambulatory BP monitoring (ABPM) recorder (6100-Welch Allyn, New York, USA) was used during a 24-hour period. In accordance with the European guidelines (Mancia et al., 2013), measures were taken at 30 min intervals during the daytime and 60 min during night time. Participants self-disclosed their typical bedtime and wake up time, and this was used to define the automated 30 min and 60 min day/night time intervals (Maldonado-Martín et al., 2016). Mean BP (MBP) was calculated as  $[DBP + 0.333 \times (SBP - DBP)]$ .

### *Cardiorespiratory fitness*

Cardiorespiratory fitness ( $\dot{V}O_{2peak}$ ) was assessed using an electronically braked Lode Excalibur Sport Cycle Ergometer (Groningen, The Netherlands). The testing protocol maintained 70 rpm throughout and started at 40 W with gradual increments of 10 W every minute until volitional exhaustion occurred. For safety reasons, an electrocardiogram was used throughout the test. Expired gas analysis was collected using an Ergo CardMedi-soft S.S (Belgium Ref. USM001 V1.0) that was calibrated prior to each test. The test was considered 'true' in the presence of two or more of the

following criteria: 1) volitional fatigue (>18 on BORG scale), 2) peak respiratory exchange ratio of  $\geq 1.1$ , 3) achieving >85% of age predicted maximum heart rate, and 4) a plateau in oxygen uptake and/or heart rate (Mezzani et al., 2012). Blood pressure was measured every two minutes both during and following the cardiopulmonary exercise test. During the recovery period, participants remained on the bike for five minutes to monitor the electrocardiogram and BP. All other measurements have been previously published (Maldonado-Martín et al., 2016).

### ***Intervention***

After baseline measurements, participants were randomly allocated in one of the four intervention groups stratified by sex, systolic BP (SBP), BMI, and age using a time-blocked computerized randomization program. The four groups were attention control group (AC, participants were given physical activity advice only) and three supervised exercise groups: HV-MICT, HV-HIIT, and LV-HIIT, which trained two non-consecutive days under supervision by exercise specialists for a 16-week period. In addition, all participants received a hypocaloric diet. The advice for the AC group was to participate in at least 30 min of moderate-intensity aerobic exercise (walking, jogging, cycling or swimming) 5-7 days per week blended with some dynamic resistance exercises. (Maldonado-Martín et al., 2016) All the protocols for each group, including procedures and diet intervention have been previously published (Gorostegi-Anduaga et al., 2018; Maldonado-Martín et al., 2016).

### ***Six months post-intervention follow-up***

After the 16-week intervention (POST), all participants received diet and physical activity advice for the following 6M. Participants had no further supervised

intervention or attention from any of the research staff. Participants were also provided heart rate data for their current moderate and high exercise intensity domains to enable them to self-monitor. All the aforementioned anthropometric and physiological measurements for the study were taken before, POST, and 6M following the end of the intervention (Figure 1).

### ***Statistical analysis***

Descriptive statistics were calculated for all variables and presented as mean±SD unless otherwise stated. To determine normality, a Kolmogorov-Smirnov test was performed on all variables, and those with a skewed distribution were log transformed prior to any analysis. Repeated measures analysis of variance (ANOVA) was used to test the change in body composition, BP and CRF variables over time. Bonferroni post-hoc test was used to determine the level of significance when a significant main effect was found. From the repeated measures ANOVA, eta-squared ( $\eta^2$ ) was reported as a measure of effect size (ES). Analysis of covariance (ANCOVA) was performed to test the differences among groups in the delta score (differences between pre- vs. post-intervention and post-intervention vs. 6M follow-up); adjusting the analysis for age, sex and changes in BM (except for BM and BMI, that were adjusted by age and sex). Helmert contrast was used to compare the AC group vs. supervised exercise groups, and Bonferroni post-hoc test was used to determine the level of significance between groups when a significant main effect was found. All statistical analyses were performed using the Statistical Package for Social Science (SPSS) version 24.0. For all analysis, the alpha level of significance was set at  $P<0.05$ .

## Results

Baseline data (Gorostegi-Anduaga, Corres, Jurio-Iriarte et al., 2018) and the effects of the 16-week intervention (Gorostegi-Anduaga et al., 2018) from the EXERDIET-HTA study have been previously published.

Table 1 presents body composition, BP, and CRF data at baseline (pre-intervention), POST and after the 6M post-intervention period (long-term follow-up).

Table 1. Changes in mean  $\pm$  SD body composition, blood pressure and cardiorespiratory fitness at pre-intervention (PRE), immediately post-intervention (POST), and 6 months following supervised exercise cessation (6M).

	All (n=190)	Effect Size ( $\eta^2$ )	AC (n=43)	HV-MICT (n=48)	HV-HIIT (n=47)	LV-HIIT (n=52)	Time x group	<i>P</i> AC vs. EG PRE-6M	<i>P</i> groups PRE-6M	<i>P</i> AC vs. EG POST-6M	<i>P</i> groups POST-6M
Body mass (kg)											
PRE	90.7 $\pm$ 15.2	0.571	87.8 $\pm$ 13.3	93.2 $\pm$ 16.8	90.2 $\pm$ 16.9	91.2 $\pm$ 13.6	<b>0.029</b>	0.078	<b>0.034*</b>	0.953	0.297
POST	83.9 $\pm$ 14.2		82.2 $\pm$ 13.4	85.6 $\pm$ 15.6	82.4 $\pm$ 15.3	85.1 $\pm$ 12.7					
6M	86.0 $\pm$ 15.0*		84.3 $\pm$ 13.8*	88.2 $\pm$ 16.8*	83.4 $\pm$ 16.1*	87.4 $\pm$ 12.9*					
BMI (kg/m <sup>2</sup> )											
PRE	31.6 $\pm$ 4.0	0.572	30.9 $\pm$ 3.6	32.4 $\pm$ 4.6	31.1 $\pm$ 3.8	31.8 $\pm$ 4.1	<b>0.029</b>	0.083	<b>0.049</b>	0.839	0.287
POST	29.2 $\pm$ 3.9		28.9 $\pm$ 3.9	29.8 $\pm$ 4.1	28.5 $\pm$ 3.7	29.7 $\pm$ 3.9					
6M	30.0 $\pm$ 4.0*		29.7 $\pm$ 4.0*	30.6 $\pm$ 4.3*	29.0 $\pm$ 3.9*	30.5 $\pm$ 3.8*					
Waist (cm)											
PRE	102.6 $\pm$ 10.9	0.445	101.6 $\pm$ 10.2	104.9 $\pm$ 12.1	101.3 $\pm$ 12.1	102.5 $\pm$ 9.2	0.290	0.275	0.844	0.949	0.865
POST	96.1 $\pm$ 10.5		96.3 $\pm$ 10.3	97.8 $\pm$ 10.9	94.0 $\pm$ 12.1	96.1 $\pm$ 10.5					
6M	97.8 $\pm$ 11.0*		97.9 $\pm$ 10.2 <sup>x</sup>	99.6 $\pm$ 12.3 <sup>x</sup>	95.1 $\pm$ 11.9 <sup>x</sup>	98.4 $\pm$ 9.2*					
FFM (%)											
PRE	66.2 $\pm$ 7.8	0.252	66.6 $\pm$ 7.8	64.5 $\pm$ 8.3	67.3 $\pm$ 6.8	66.6 $\pm$ 8.0	0.202	0.978	0.554	0.454	0.455
POST	69.7 $\pm$ 8.1		69.2 $\pm$ 8.3	68.4 $\pm$ 8.1	71.4 $\pm$ 7.4	69.8 $\pm$ 8.4					
6M	68.2 $\pm$ 8.5*		68.1 $\pm$ 8.1 <sup>x</sup>	67.1 $\pm$ 8.0*	70.3 $\pm$ 7.4*	67.5 $\pm$ 10.0					
SBP (mmHg)											
PRE	135.1 $\pm$ 12.4	0.144	138.6 $\pm$ 13.2	133.5 $\pm$ 12.0	131.9 $\pm$ 11.0	136.0 $\pm$ 12.6	0.124	0.067	0.138	0.091	0.067
POST	128.0 $\pm$ 11.1		132.3 $\pm$ 14.0	125.6 $\pm$ 8.6	128.1 $\pm$ 10.1	126.6 $\pm$ 10.5					
6M	133.9 $\pm$ 12.5 <sup>§</sup>		135.2 $\pm$ 12.3	134.5 $\pm$ 12.8 <sup>§</sup>	130.9 $\pm$ 10.2	134.8 $\pm$ 13.9 <sup>§</sup>					
DBP (mmHg)											
PRE	78.0 $\pm$ 7.8	0.172	79.9 $\pm$ 7.7	75.2 $\pm$ 8.0	78.7 $\pm$ 7.1	78.4 $\pm$ 7.9	0.155	<b>0.042</b>	<b>0.037<sup>ψ</sup></b>	0.256	0.114
POST	73.7 $\pm$ 7.4		75.3 $\pm$ 8.1	71.6 $\pm$ 6.9	73.6 $\pm$ 7.4	73.6 $\pm$ 7.6					
6M	77.1 $\pm$ 8.0 <sup>§</sup>		77.6 $\pm$ 7.2	76.2 $\pm$ 9.1 <sup>§</sup>	76.4 $\pm$ 7.2	78.1 $\pm$ 8.3 <sup>§</sup>					

MBP (mmHg)											
PRE	97.0±8.4	0.172	99.5±8.8	94.6±8.2	96.4±7.6	97.6±8.6	0.157	<b>0.042</b>	0.074	0.136	0.066
POST	91.8±7.8		94.3±9.2	89.6±6.4	92.5±7.2	91.3±7.8					
6M	96.0±8.6 <sup>§</sup>		96.8±8.1	95.6±9.4 <sup>§</sup>	94.6±7.6	97.0±9.3 <sup>§</sup>					
$\dot{V}O_{2peak}$ (mL·kg <sup>-1</sup> ·min <sup>-1</sup> )											
PRE	22.8±5.5	0.353	24.6±6.6	21.8±5.1	22.5±5.0	22.8±5.3	<b>0.010</b>	0.191	0.426	0.098	0.299
POST	28.3±7.5		27.4±8.2	27.0±6.9	29.8±6.7	28.3±6.7					
6M	26.7±7.3*		27.0±6.9 <sup>x</sup>	25.2±6.2*	27.5±7.8*	27.2±8.0 <sup>x</sup>					
MET											
PRE	6.5±1.6	0.353	7.0±1.9	6.2±1.4	6.4±1.4	6.5±1.6	<b>0.018</b>	0.212	0.549	0.100	0.332
POST	8.1±2.2		7.8±2.4	7.7±2.0	8.5±2.3	8.2±1.9					
6M	7.6±2.1*		7.7±2.0 <sup>x</sup>	7.2±1.8*	7.9±2.2*	7.7±2.3 <sup>x</sup>					

AC: attention control group; HV: high volume; LV: low volume; MICT: moderate-intensity continuous training group; HIIT: high-intensity interval training group; EG: Exercise groups; BMI: body mass index; Waist: Waist circumference; FFM: fat-free mass; SBP: systolic blood pressure; DBP: diastolic blood pressure; MBP: mean blood pressure;  $\dot{V}O_{2peak}$ : peak oxygen uptake; MET: metabolic equivalent of task.

\* $P < 0.005$  between POST-6M and PRE-6M. <sup>x</sup> $P < 0.005$  between PRE-6M. <sup>§</sup> $P < 0.005$  between POST-6M. <sup>\*</sup> $P < 0.005$  AC and HV-HIIT. <sup>ψ</sup> $P < 0.005$  between AC and HV-MICT.

Repeated measures ANOVA and Bonferroni post-hoc analysis on all participants (irrespective of intervention group) found that BM ( $P<0.001$ , difference%,  $\Delta=-5.1\%$ , ES=0.57), BMI ( $P<0.001$ ,  $\Delta=-5.1\%$ , ES=0.57), and waist circumference ( $P<0.001$ ,  $\Delta=-4.7\%$ , ES=0.45) at 6M follow-up were all significantly reduced from pre-intervention. In addition, FFM ( $P<0.001$ ,  $\Delta=3.0\%$ , ES=0.25) at 6M follow-up was significantly higher than the pre-intervention. However, at 6M follow-up, BM ( $P<0.001$ ,  $\Delta=2.5\%$ ), BMI ( $P<0.001$ ,  $\Delta=2.7\%$ ) and waist circumference ( $P<0.001$ ,  $\Delta=1.8\%$ ) were significantly higher than immediately POST, and FFM ( $P<0.001$ ,  $\Delta=-2.2\%$ ) was significantly lower at immediately POST compared to 6M follow-up (Table1 and Figure 2D). The ANCOVA analysis revealed there were significant between-group differences in BM ( $P=0.034$ ) and BMI ( $P=0.049$ ). Post-hoc analysis revealed a higher BM reduction in the HV-HIIT group (pre-intervention vs. 6M follow-up,  $\Delta=-6.4\text{kg}$ , 95% confidence interval, CI=-8.1-4.7kg) compared to AC ( $\Delta=-3.5\text{kg}$ , 95% CI=-4.9-2.0kg) group (Table 1 and Figure 2A). No other significant between-group differences were detected in changes between pre-intervention vs. 6M follow-up and POST vs. 6M follow-up measures.



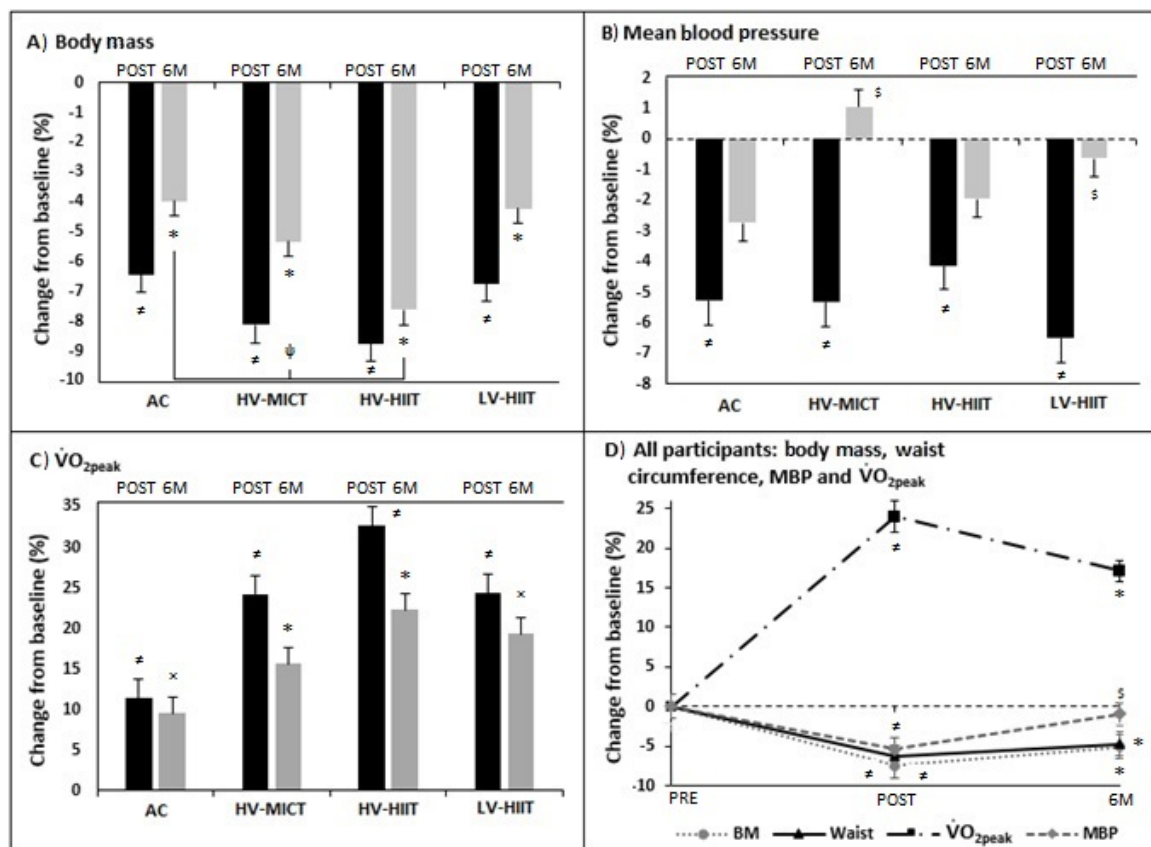


Figure 2. Percentage change from pre-intervention in percentages of body mass (BM, A), mean blood pressure (MBP, B) and peak oxygen uptake ( $\dot{V}O_{2peak}$ , C) displayed as group. Change from baseline of the whole sample in percentages of body mass, MBP, waist circumference (Waist) and  $\dot{V}O_{2peak}$  (D). PRE: pre-intervention measurements. POST: post-intervention measurements. 6M: long-term six months follow-up measurements. AC: attention control group; HV: high volume; LV: low volume; MICT: moderate-intensity continuous training group; HIIT: high-intensity interval training group.  
 \*  $P < 0.005$  between POST-PRE. \*  $P < 0.005$  between 6M-POST and 6M-PRE. \*  $P < 0.005$  between 6M-PRE. \$  $P < 0.005$  between 6M-POST.  $\psi$   $P < 0.005$  AC and HV-HIIT in change between PRE-6M.

Repeated measures ANOVA and Bonferroni post-hoc analysis found that there was no significant change from pre-intervention to 6M follow-up for SBP, DBP, and MBP ( $P > 0.05$ ) in all participants irrespective of the intervention group. However, SBP ( $\Delta = 4.6\%$ ,  $ES = 0.14$ ), DBP ( $\Delta = 4.6\%$ ,  $ES = 0.17$ ) and MBP ( $\Delta = 4.6\%$ ,  $ES = 0.17$ ) were higher ( $P < 0.001$ ) at 6M follow-up compared to immediately POST (Table 1 and Figure 2D). According to CRF,  $\dot{V}O_{2peak}$  ( $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ ) and MET were higher at 6M follow-up compared to pre-intervention ( $\Delta = 17.1\%$ ,  $P < 0.001$ ,  $ES = 0.35$ ) and lower than

immediately POST ( $\Delta=-5.7\%$ ,  $P<0.001$ , Table 1 and Figure 2D). Helmert contrast revealed there were significant between group differences (pre-intervention vs. 6M follow-up, AC vs. exercise groups) in DBP ( $P=0.042$ ) and MBP ( $P=0.042$ ), with AC group having the smallest decline in DBP and MBP compared to exercise groups at 6M follow-up when compared with pre-intervention. Further, Bonferroni post-hoc analysis showed pre-intervention vs. 6M follow-up differences ( $P=0.037$ ) between AC ( $\Delta=-2.4\text{mmHg}$ , 95% CI=-5.3-0.6mmHg) and HV-MICT in DBP ( $\Delta=1.0\text{mmHg}$ , 95% CI=-1.9-3.9mmHg) resulting the change lower for the AC group. No other significant between group differences were observed in any other variables (Table 1 and Figure 2B/2C).

## Discussion

The effects of different aerobic exercise programs conducted twice a week in conjunction with a hypocaloric DASH diet have been previously analyzed (Gorostegi-Anduaga et al., 2018). The authors reported that the intervention was an optimal non-pharmacological tool in the management of risk factors in overweight/obese, non-physically active individuals with HTN. Thus, after the 16 weeks intervention, body composition, BP, and CRF significantly improved in all groups (*i.e.*, supervised exercise, and physical activity advice). In addition, the study revealed between-group differences; the supervised exercise group was better than the AC group for reducing BM and improving CRF. However, there were no between-group differences in BP (Gorostegi-Anduaga et al., 2018).

In the present study, the focus was to analyze the effects of withdrawing exercise supervision for 6M post following the 16-week intervention period. In addition, a secondary aim was to determine any potential differences between the 16-

week intervention groups (supervised exercise training vs. physical activity advice). The main findings of the current study were: 1) the intervention induced-benefits in body composition and CRF were not maintained after 6M of physical activity advice, but they were still significantly better than those seen pre-intervention. However, the significant improvement in BP returned to baseline following 6M supervision cessation; 2) although a favorable effect by HV-HIIT exercise-induced in BM compared to AC group was found after 6M follow-up, there were no other significant between-group differences following the removal of exercise and diet supervision.

Long-term detraining syndrome or exercise training cessation is a clinical state arising when individuals involved in a systematic, supervised, designed exercise program suddenly stop their regular physical activity for more than four weeks. As such, the physiological consequences of an insufficient training stimulus to maintain training-induced adaptations will be presented (Mujika & Padilla, 2000a; Mujika & Padilla, 2000b). In the current study, the removal of supervised exercise training followed by 6M of only physical activity advice resulted in a worsening of the positive adaptations, which were previously achieved during the supervised 16-week intervention in the all groups (supervised exercise, and physical activity advice only group). After this withdrawal, both body composition (*i.e.*, BM,  $\Delta=2.5\%$ ; BMI,  $\Delta=2.7\%$ ; waist circumference,  $\Delta=1.8\%$ ; and FFM,  $\Delta=-2.2\%$ ) and CRF ( $\Delta=-5.7\%$ ) significantly worsened. However, it should be noted that they remained significantly better than values seen at baseline (Table 1). Our findings are in line with previous studies with other 'at risk' populations (*i.e.*, coronary artery disease patients, overweight polycystic ovary syndrome, and women with parental HTN, adults with metabolic syndrome, healthy men, and women with Type II Diabetes), using different types of exercise,

duration of intervention, and detraining periods (*i.e.*, four weeks to four months) (Mora-Rodriguez et al., 2014; Orio et al., 2008; St-Amand et al., 2012; Theodorou et al., 2016; Tokmakidis, Spassis, & Volaklis, 2008; Tokmakidis et al., 2014; Volaklis et al., 2006).

Another interesting finding of the present investigation was that HV-HIIT caused a greater reduction (6M follow-up vs. pre-intervention,  $P=0.034$ ) in BM ( $\Delta=-6.4$  kg) compared to AC group ( $\Delta=-3.5$  kg) after 6M of no supervision (Table 1, Figure 2A). As such, our data helps to confirm that enhanced energy expenditure elicited by HV and moderate-to-high intensity exercise training, is related to long-term BM loss maintenance (Donnelly et al., 2009). Previous studies have supported this and have shown that HIIT is an effective stimulus for reducing body fat in those individuals with obesity (Batacan, Duncan, Dalbo, Tucker, & Fenning, 2017; Ouerghi et al., 2017). The possible mechanisms behind HIIT-induced fat loss include 1) a more elevated catecholamine response, and 2) an increased excess post-exercise oxygen consumption leading to an increase in fat oxidation (Boutcher, 2011; LaForgia, Withers, & Gore, 2006). With respect to our study, it is important to note that the removal of supervised exercise training for 6M, did not lead to a complete loss of CRF assessed by  $\dot{V}O_{2peak}$  ( $\Delta=18\%$  comparing follow-up vs. pre-intervention) in any of the intervention groups as shown in Figure 2. In addition, it is well known that each 1-MET increment in CRF is associated with a ~13-15% lower risk of all-cause and cardiovascular mortality (Harber et al., 2017). Thus, comparing 6M follow-up to pre-intervention data only the supervised exercise groups in the intervention period preserved >1MET compared to baseline (AC=0.7, HV-MICT=1, HV-HIIT=1.5, LV-HIIT=1.2) (Table 1). Although adherence

with the 16-week exercise intervention was very high in the supervised-exercise groups, 6M later only 51% of all participants were engaged in physical activity >2 times per week and implementing the recommendations (unpublished data from the EXERDIET-HTA study). This suggests that supervised exercise is needed to potentially achieve optimal results.

In accordance with previous research (Abdelaal & Mohamad, 2015) after removing exercise supervision for 6M, BP returned to pre-intervention values, but it was significantly higher compared to POST, as shown in Table 1. This finding is of importance given that BP is a robust and sensitive clinical marker associated with changes in BM (Neter, Stam, Kok, Grobbee, & Geleijnse, 2003) due to an increase in visceral adiposity (in the present study, at follow-up BM  $\Delta$ =2.5%; and waist circumference  $\Delta$ =1.8% compared to post-intervention,  $P<0.005$ ). It is possible that a range of physiological factors and biological pathways, such as physical compression of the kidneys by fat, over activation of the renin-angiotensin-aldosterone system, and increased sympathetic nervous system activity, will be involved in the increased BP response seen in the current study (Hall, do Carmo, da Silva, Wang, & Hall, 2015). Even though there is enough evidence reporting the efficacy of the DASH diet, BM loss, and exercise in lowering BP (Blumenthal et al., 2010; Gorostegi-Anduaga et al., 2018), the adherence to DASH diet seems difficult to follow by individuals with HTN, and even lower DASH accordance is shown in those with obesity (Kim & Andrade, 2016). Therefore, in this population, an optimal training FITT and supervised exercise together with close dietetic supervision are needed to particularly optimize the BP-lowering capacities of exercise and diet (Hinderliter et al., 2014; Pescatello et al., 2015).

The authors feel that to interpret findings from the current study; it is essential to consider both the strengths and limitations. The main aim of the study was to assess the effects of supervised exercise cessation 6M following a 16-week supervised exercise and dietary intervention. Whilst the design of the study is appropriate, the lack of exercise supervision could have led to inter-individual differences, which could be masked with quantitative data techniques. Future studies should look to use mixed-methods to help interpret reasons behind the reported changes. Although efforts were done to assess all post-intervention participants, 19 individuals do not perform the 6M follow-up tests (nine from the AC group), that may have affected the between-group differences in BP values favoring AC group and the lack of differences with exercise supervised groups in body composition and CRF. Further, dietary intake was self-reported through questionnaires at pre-intervention, but it was not assessed at follow-up, which hinders the knowledge regarding the adherence to DASH diet.

In conclusion, when overweight/obese individuals with HTN attains significant improvements in cardiometabolic health following 16-week supervised-exercise intervention with diet restriction, there is a significant reduction following 6M when the exercise and diet supervision is removed, and only recommendations were applied. These results suggest the need for a regular, systematic and supervised diet and exercise programs to avoid subsequent declines in cardiometabolic health. Future research needs to determine whether long-term exercise and diet supervision can maintain improvements in cardiometabolic health.

## **What does this article add?**

The recommended lifestyle measures for reducing BP and BM management include regular physical exercise (*i.e.*, at least 30 min of moderate-intensity dynamic aerobic exercise on 5-7 days per week, and also aerobic interval training). In order to be effective, the exercise has to be designed in a systematic and individualized manner in terms of the frequency, intensity, time, and type (FITT principle). However, there is a lack of evidence regarding the impact of well-designed but only advised vs. adequately powered and supervised exercise. Although these effects have been evaluated in other populations, the present study is a well-designed, high-quality randomized clinical trial, and the first to examine the exercise intervention effects, based on FITT recommendations for people with overweight/obesity and HTN, and to evaluate the long-term effects of supervised training cessation, who are receiving only diet and physical activity advice after an intervention period.

To our knowledge, the consensus in the FITT of the recommended exercise prescription and design for this population will not present optimum health-related results if the exercise program is not closely supervised by exercise professionals. Supervision and not only physical activity advice is necessary to monitor all the acute responses and chronic adaptations to training and when appropriate, to modify the FITT exercise design, accordingly.

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