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Original

ENTRENAMIENTO CONCURRENTE DE CORTA DURACIÓN REDUCE EL MÁXIMO, PERO NO EL PROMEDIO DEL GROSOR INTIMA-MEDIA CAROTÍDEA EN ADULTOS HIPERTENSOS.

SHORT-TERM OF CONCURRENT TRAINING DECREASES MAXIMUM BUT NOT AVERAGE CAROTID INTIMA-MEDIA THICKNESS IN HYPERTENSIVE ADULTS.

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RESUMEN

Antecedentes: El ejercicio físico previene la aterosclerosis y es una terapia para disfunción endotelial (EDys) e hipertensión (HTN), sin embargo, poco se sabe acerca del entrenamiento concurrente de corta duración ($CT_{HIIT+RT}$) en el grosor de la íntima-media carotídea promedio ($cIMT_{av}$) y máxima ($cIMT_{max}$) en adultos con HTN. **Objetivo**: Determinar los efectos de 6 semanas de $CT_{HIIT+RT}$ sobre $cIMT_{av}$ y $cIMT_{max}$ en adultos con HTN. Un objetivo secundario fue determinar los efectos de $CT_{HIIT+RT}$ sobre la presión arterial y composición corporal. **Métodos**: Ensayo clínico controlado aleatorizado en adultos distribuidos por categorización de presión arterial en grupos controles (no ejercicio) de HTA (CG-HTN, *n*=10), PA elevada (CG-Ele, *n*=10) y normotensos (CG-NT, *n*= 10) y en grupo experimental de ejercicio de HTN (EG-HTN), PA elevada (EG-Ele, *n*=10), y grupo normotenso (EG-NT, *n*=10). Los participantes se sometieron a 6 semanas de 10 min por sesión de $CT_{HIIT+RT}$ ($3 \cdot semana^{-1}$). Las variables $cIMT_{av}$, $cIMT_{max}$, presión sistólica/diastólica y la composición corporal fueron medidas. **Resultados:** Hubo disminuciones significativas pre-post en $cIMT_{max}$ en EG-HTN (Δ−0,10 cm, p<0,05) y en EG-Ele (Δ−0,30 cm, p<0,0001). Existió un reducción significativa de PAS en EG-HTN (Δ−19 mmHg), EG-Ele (Δ−11 mmHg) y EG-NT (Δ−8 mmHg, todos p<0,0001); PAD en EG-HTN (Δ−9 mmHg), EG-Ele (Δ−8 mmHg, ambos p<0,0001) y grupo EG-NT (Δ−4 mmHg, p<0,05); circunferencia de cintura en EG-HTN (Δ−4,3 cm, p<0,001) y EG-Ele (Δ−4,0 cm, p<0,05), grasa corporal en % en EG-HTN (Δ−1,9 %, p<0,05), y grasa corporal en kg EG-HTN (Δ−7,0 kg, p<0,05). **Conclusión:** Seis semanas de $CT_{HIIT+RT}$ reducen $cIMT_{max}$ pero no la $cIMT_{av}$ en adultos con HTN. Estos resultados mostraron una remisión adicional de la PAS/PAD en el grupo ejercicio con HTN y cambios beneficiosos en la composición corporal.

Palabras clave: Disfunción endotelial; Hipertensión arterial; Grosor íntima-media carotídea; Entrenamiento de ejercicio; Entrenamiento concurrente.

ABSTRACT

Background: Exercise training induces favourable changes in endothelial dysfunction (EDys) and improves hypertension (HTN); however, there is a scarcity of knowledge about short-term concurrent training using high-intensity interval and resistance training ($CT_{HIIT+RT}$) on both average ($cIMT_{av}$) and maximum ($cIMT_{max}$) carotid intima-media thickness. **Aim:** To determine the effects of six weeks of $CT_{HIIT+RT}$ on $cIMT_{av}$, and $cIMT_{max}$ in adults with HTN. A secondary aim was to determine the $CT_{HIIT+RT}$ effects on blood pressure and body composition. **Methods:** We conducted a randomized controlled clinical trial in adults distributed by blood pressure categorization to 6 groups: control (non-exercise) group of HTN (CG-HTN, *n*=10) elevated BP (CG-Ele, *n*=10), normotensive control group (CG-NT, *n*=10), and exercise HTN (EG-HTN, *n*=10), elevated BP (EG-Ele, *n*=10), or normotensive group (EG-NT, *n*=10). Participants underwent 6 weeks of 10 min per session of $CT_{HIIT+RT}$ ($3 \cdot week^{-1}$). Before and after training $cIMT_{av}$, and $cIMT_{max}$, systolic/diastolic (SBP/DBP) blood pressure and body composition outcomes were measured. **Results:** There were significant decreases from pre to post-test in $cIMT_{max}$ in EG-HTN (Δ−0,10 cm, p<0,05), and in EG-Ele group (Δ−0,30 cm, p<0,0001). Other significant modifications included reductions of SBP in EG-HTN (Δ−19 mmHg), EG-Ele (Δ−11 mmHg), and EG-NT group (Δ−8 mmHg, all p<0,0001); DBP in EG-HTN (Δ−9 mmHg), EG-Ele (Δ−8 mmHg, both p<0,0001), and EG-NT group (Δ−4 mmHg, p<0,05); waist circumference in EG-HTN (Δ−4,3 cm, p<0,001), and EG-Ele groups (Δ−4,0 cm, p<0,05), body fat in % EG-HTN (Δ−1,9 %, p<0,05), and body fat in kg in EG-HTN group (Δ−7,0 kg, p<0,05). **Conclusion:** Six weeks of $CT_{HIIT+RT}$ decreased $cIMT_{max}$ but not $cIMT_{av}$ in HTN adults. These results were displayed with additional SBP/DBP remission in the hypertensive participants, accompanied of reductions of body fat.

Keywords: Endothelial dysfunction; Arterial hypertension; Carotid intima-media thickness; Exercise training; Concurrent training.

Journal of Sport and Health Research 2024, 16(2):279-292

INTRODUCTION

Atherosclerosis is the progressive reduction in arterial lumen caused by plaque accumulation in artery walls (Bentzon et al., 2014). The major risk posed by atherosclerosis is the potential thrombus formation and rupture, which may lead to major cardiovascular events such as myocardial infarction and stroke (Saba et al., 2019). Before atherosclerosis, individuals with risk factors develop an endothelial dysfunction (EDys) process, an inflammatory state of the endothelial cells that promotes a pro-thrombotic state of the intima (Restaino et al., 2016). As a common comorbidity, individuals with EDys have arterial hypertension (HTN), which is the elevated blood pressure condition of the artery (Whelton et al., 2018). Whether or not HTN precedes EDys or *vice-versa* is unclear. Recently, the American Heart Association (AHA) reported a worrying increase in several risk factors for cardiometabolic diseases (Tsao et al., 2023), increasing the need for new therapies for threatening both EDys and HTN.

Carotid intima-media thickness (cIMT) is a well-known marker of arterial wall health and can be measured with B-mode ultrasound imaging (Qu & Qu, 2015). Thus, using a standardized protocol (Mancia et al., 2017), it is possible to obtain both cIMT *average* ($cIMT_{av}$) and *maximum* ($cIMT_{max}$) using manual or automatic ultrasound configuration. cIMT is a subclinical marker of atherosclerosis and predicts major adverse cardiovascular events (Hodis et al., 1998; O'leary et al., 1999). However, there is a scarcity of information about the value that could represent each $cIMT_{av}$ or $cIMT_{max}$ in detecting the beneficial effects of non-pharmacological behavioural interventions such as exercise training on the artery wall.

Exercise training is promoted as a therapy for HTN and EDys conditions by relevant professional associations, including the American College of Sports Medicine (Garber et al., 2011; PESCATELLO et al., 2019), American Diabetes Association (Colberg et al., 2016), American Heart Association (Tsao et al., 2023), and expert panels (Mancia et al., 2013). Moderate-intensity continuous training (MICT, a continuum of exercise), resistance training (RT, consisting of voluntary concentric/eccentric muscle contractions using external loads), or both training modalities, termed concurrent training ($CT_{MICT+RT}$) have been reported to decrease $cIMT_{av}$ (Hetherington-Rauth et al., 2020; Kim et al., 2021; Tomoto et al., 2021). Additionally, high-intensity interval training (HIIT), defined as brief, usually cycling exercise intervals interspersed with recovery periods, has also been reported to decrease $cIMT_{av}$ (Hetherington-Rauth et al., 2020; Magalhães et al., 2019). However, an essential issue in the MICT, RT, or $CT_{MICT+RT}$ application is the prolonged duration of the exercise session (i.e., sessions >30 to ~45 min. hereafter), which limits their application in clinical contexts where the average time duration per patient in therapies are usually ~30 min·session with aims of cardiometabolic rehabilitation. Recent studies in healthy individuals have reported no changes in $cIMT_{av}$ after 12 weeks of MICT, HIIT, or RT (Au et al., 2020); however, long-term interventions of 52 weeks (Hetherington-Rauth et al., 2020) revealed a reduction in $cIMT_{av}$ in type 2 diabetes subjects who were non-responders to improve their cardiorespiratory fitness decreasing $cIMT_{av}$ from 0,74 to 0,71 mm (−0.03 mm) using $CT_{HIIT+RT}$ (HIIT: 60 sec cycling; 60 sec resting x 17 times, 79-90% heart rate reserve; RT: 10-12 repetitions [i.e., >60 min·session]) or $CT_{MICT+RT}$ (40-60% $VO_{2reserve}$; RT: 10-12 repetitions) protocols. Eight weeks of MICT (24 sessions of upper and lower limb cycling exercise at 50-85% of maximal power output, 20-45 min/session) by (Gelinas et al., 2017) reported no $cIMT_{av}$ changes in healthy, but in COPD subjects decreased from 0,79 to 0,77 mm (−0.02 mm). Interestingly, a common characteristic from these studies is that they are developed in older adults (~60 y), exercise sessions are longer (≥45 min/session), have reported only $cIMT_{av}$ but not $cIMT_{max}$, and no clear results can be obtained from exercise effects. Additionally, there is little evidence about the effects of short-term exercise modalities, including $CT_{HIIT+RT}$, but applied in time-efficient protocols (i.e., ≤30 min·session) in adults. One alarming point is that the last Chilean National Health Survey 2016-17 revealed that both physical inactivity (i.e., do not adhere to international physical activity guidelines) and obesity are sharply increased in ages ~40 years old, being of interest to study non-pharmacological interventions for populations of these characteristics. In addition, no clear volume-or-intensity dependence has been revealed, and in summary, it is not clear what exercise modality, and volume can improve $cIMT_{av}$ and $cIMT_{max}$. Thus, considering these different arguments of scientific and epidemiological necessity, and to acquire more evidence about exercise benefits in HTN patients on EDys and thus to prevent atherosclerosis, is that this study aimed to determine the effects of 6-weeks of $CT_{HIIT+RT}$ on $cIMT_{av}$, $cIMT_{max}$, blood pressure and body composition in adults with HTN. We hypothesized that $CT_{HIIT+RT}$ applying HIIT interval of ≤60 sec, and RT using exercise until muscle failure (i.e., ≤60 sec) in a short-term intervention would promote significant $cIMT_{av}$, or $cIMT_{max}$ in particularly those HTN patients.

METHODS

Participants and study design

We conducted a randomized controlled clinical trial in which seventy-five volunteers were initially invited to participate in an exercise training intervention of 6 weeks of $CT_{HIIT+RT}$. Participants were enrolled through different media (phone calls, WhatsApp). All participants received a personal interview, were screened on blood pressure, and were classified as normotensive, elevated blood pressure, or HTN, following standard international guidelines (Whelton et al., 2018). The study was conducted from September 2022 to February 2023 and was ascribed to clinical trials.gov NCT05710653. The study was conducted by the Declaration of Helsinki and approved by the Institutional Review Board of the Bioethical Committee of Universidad Andres Bello (Approval 026/2022 of September 22nd). Informed consent was obtained from all subjects involved in the study.

Eligibility criteria were as follows: *a*) individuals with blood pressure in normal, elevated (Ele), or HTN condition (independent of being treated or untreated with hypotensive pharmacotherapy), following the AHA categorization (Whelton et al., 2018), *b*) individuals with body mass index (BMI) in normal, overweight, or obesity [BMI ≥18,5 and <40 kg/m^2]), and *c*) additional risk factors as hyperglycemic or type 2 diabetes mellitus (T2DM, treated with pharmacotherapy), and *d*) residence in the neighbourhood near of the University community. Exclusion criteria were: *a*) individuals with abnormal electrocardiogram, established cardiovascular disease, or heart disease; *b*) uncontrolled HTN (SBP ≥169 mmHg, DBP >95 mmHg); *c*) T2DM associated with comorbidities; ulcers, nephropathies, muscle-or osteoarthrosis, *d*) individuals consuming drugs for weight loss treatment or individuals participating in any other exercise therapy (or within the past three months). The sample size for the study was determined by SBP changes reported from a previous exercise training study (Alvarez et al., 2023). Thus, we used G*Power software (3.1.9.7, Germany), where (*n*=10) subjects per group were determined as a minimum (*i.e.*, with 'moderate' effect size [ES]) using a statistical power of ≥80% and an alpha error of 5% (p<0,05). Thus, we needed (*n*=60) volunteers (ten subjects per group). All participants provided their written informed consent, and the study protocol was conducted according to the Declaration of Helsinki and was approved by the Ethics Committee of Universidad Andres Bello, Chile (Approval N° 026/2022).

Initially, Eighty-five (*n*=85) participants were contacted and twenty-five (*n*=25) were excluded for not fulfilling the inclusion criteria. Thus sixty volunteers were allocated (1:1 ratio) to six study groups as follows: to a control group of HTN (CG-HTN, *n*=10, SBP/DBP 145±7/87±10), Ele (CG-Ele, *n*=10, SBP/DBP 125±3/84±8), normotensive control group (CG-NT, *n*=10, SBP/DBP 109±7/74±9 mmHg), or to the experimental group of HTN (EG-HTN, SBP/DBP, *n*=10, 142±12/89±12), EG-Ele (EG-Ele, *n*=10, SBP/DBP 123±2/82±10), or normotensive training group (EG-NT, *n*=10, SBP/DBP 111±8/75±5 mmHg). Study design can be seen in (**Figure 1)**.

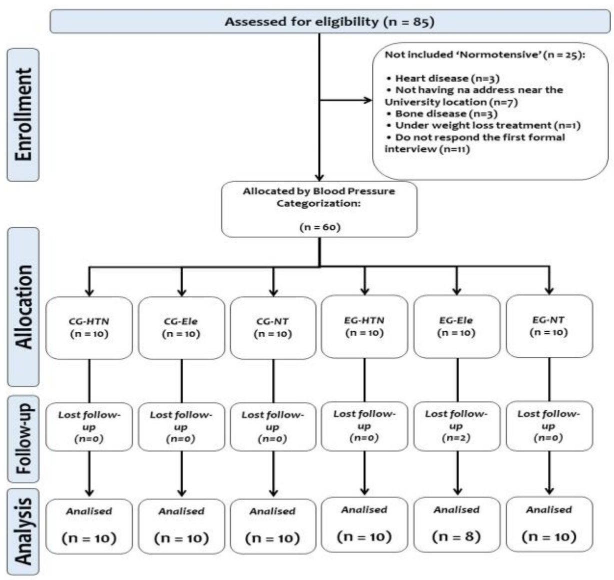

Figure 2. Study design.

Journal of Sport and Health Research 2024, 16(2):279-292

Average and maximum carotid intima-media thickness

To measure $cIMT_{av}$ and $cIMT_{max}$, all patients remained supine on a stretcher for at least 20 minutes. After this, an ultrasound probe (General Electric Medical Systems, Model LOGIQ-E PRO, Milwaukee, USA) using a 7−12 MHz linear-array transducer was placed in the longitudinal carotid for measuring the cIMT was used (Coll & Feinstein, 2008). Patients were instructed to turn their heads slightly to the left side. The carotid bulb was identified, and a B-mode image was obtained for the longitudinal right orientation of the common carotid artery, in which both $cIMT_{av}$ and $cIMT_{max}$ were obtained automatically (Coll & Feinstein, 2008). The scan was focused on 1 cm from the bifurcation on the far wall of the common carotid artery. Measurements were recorded at the end-diastolic stage, and the mean value of three wall measurements of the cIMT of each side was used for further analysis (Coll & Feinstein, 2008). A cIMT value of ≥0,9 mm was considered pathological (Mancia et al., 2013).

Blood pressure measurement

In resting position for 10 minutes, SBP and DBP were measured on each participant. Blood pressure values were classified following the AHA guideline as follows: normotensive SBP/DBP less than 120/80 mmHg, elevated blood pressure (Ele) as SBP/DBP between 120-129/80 mmHg, and stage 1 HTN as SBP/DBP between 130-139/80-89 mmHg, and stage 2 HTN as SBP/DBP greater than or equal to 140/90 mmHg (Whelton et al., 2018). Thus, blood pressure was measured at baseline, three weeks, and six weeks of $CT_{HIIT+RT}$. The readings were taken twice using an automatic monitor (OMRON™, model HEM 7114) with a pneumatic cuff positioned on the left arm using at least 1 minute of resting period between measurements. From SBP and DBP data, pulse pressure (PP) and mean arterial pressure (MAP) were recorded and used for analysis.

Body composition

Weight, fat and muscle mass percentage (%) and the resting metabolic rate (RMR) were determined by a bioelectrical impedance meter analyzer (model HEM 7114™, OMRON Healthcare Inc., Lake Forest, IL, USA) in stand conditions for 30 seconds with subjects without shoes, socks and metal devices as watches or jewellery, as previous studies (Alvarez et al., 2017). Additionally, we calculated body fat (kg) and fat-free mass (kg). Height (m) was measured using a stadiometer (Health o Meter™ Professional, Sunbeam Products, Inc., Chicago, IL, USA), and waist circumference (cm) was measured in duplicate after an exhalation using an inextensible tape (Hoechstmass™, Sulzbach, Germany). BMI was calculated using weight and height values, and the degree of obesity was categorized based on standard criteria as underweight, normal, overweight, or obesity [37].

Concurrent training

The exercise program included HIIT cycling (5 min) (Impulse™, model PS 300, Sparta, Chile) plus RT (5 min), completing 10 min of exercise, but including all rest periods between exercise intervals for recovery (i.e., ~20 min), each $CT_{HIIT+RT}$ exercise session was of 30 min duration. For the HIIT stage, all subjects developed 60 s cycling (x 5 times) at a vigorous intensity (80-100% heart rate peak), interspersed with 120 s or less resting time to reach target HR (≤70% of HR_{peak}). None of the subjects started a new interval if they did not complete this recovery parameter, ensuring a good exercise performance. For the following 5 min of RT**,** participants performed three exercises (coupled concentric/eccentric exercises): biceps curl (x 2 sets), shoulder press (x 2 times), and back exercise (x 1 time) during 60 seconds at a high exercise tolerance (~20 to 50% of 1RM) following the American College of Sports Medicine (Thompson et al., 2021). After each exercise, a 60-second resting period was started to get a Rated of perceived exertion (RPE) of 1-3 subjective (1-10) modified Borg's scale to start the next exercise time. The study protocol is presented in (**Figure 2)**.

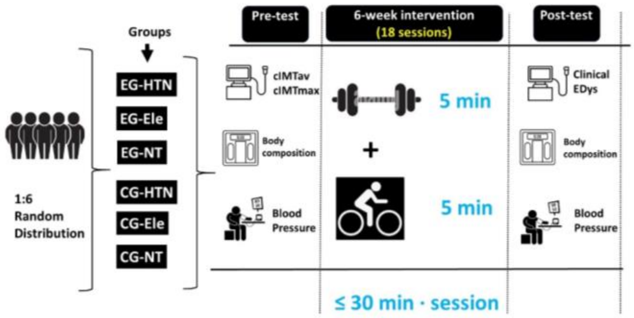

Figure 2. Study protocol. The figure describes randomization (1:6), control and experimental groups, pre-and post-test measurements, and intervention period.

Statistical analyses

Data are presented as the mean ± standard error (SE) in Table 1 and as deviation (SD) in the figures. The normality and homoscedasticity assumptions were tested by the Shapiro-Wilk and Levene's (*F*) tests, respectively. The Wilcoxon sign rank test was used for non-parametric data (BMI, fat, and muscle mass). One-way analysis of variance (ANOVA) was used to compare baseline data groups. A repeated measure two-way ANOVA was carried out to identify training-induced changes (groups x time). When an *F* value was significant, Sidack's *post hoc* test was applied to establish group comparisons at pre-and post-test. A trend analysis [*p*trend] was applied to test the potential (linear) tendency to increase or decrease a particular primary/secondary outcome through blood pressure categories. Statistical analyses were performed using Prism 8.0 software (Graph Pad, San Diego, CA, USA). The alpha level was fixed at ($p \leq 0.05$) for all statistical significance.

RESULTS

Baseline characteristics

Significant differences were detected in weight between EG-HTN vs. EG-NT and EG-Ele vs. EG-NT exercise groups. Moreover, significant differences in BMI between EG-HTN *vs*. EG-NT were found (Table 1).

Body composition

Significant changes were detected between pre to post-test in RMR in EG-HTN (Δ+321,3±178,9 kcal *p*<0,0001, Figure 3A), and EG-Ele groups (Δ+93,0±95,2 kcal, *p*<0,05, Figure 3A), waist circumference in EG-HTN (Δ−4,3±0.3 cm, *p*<0,001, Figure 3B), and EG-Ele groups (Δ−3.9±0.7 cm, *p*<0,05, Figure 3B), body fat in % EG-HTN group (Δ−1,9±0,2 %, *p*<0,05, Figure 3C), and body fat in kg in EG-HTN group (Δ−7,0±2,2 kg, *p*<0,05, Figure 3D).

Table 1. Baseline characteristics of different blood pressure adult groups, participants of 6-weeks of concurrent training of HIIT plus RT.

Outcomes	Time	CG-HTN[a]	CG-Ele[b]	CG-NT[c]	EG-HTN[d]	EG-Ele[e]	EG-NT[f]	$F_{()}$, ANOVA, R^2 (ES)
(*n* =)		10	10	10	10	8	10	
Anthropometric								
Age (y)	Pre	44,8±12,8	34,2±11,2	36,3±13,8	44,5±9,9	50,3±14,8	41,9±16,5	$F_{(1,83)}$, p=0,123, R^2 0,15
Height (m)	Pre	1,66±0,10	1,64±0,11	1,61±0,06	1,70±0,11	1,63±0,07	1,59±0,07	$F_{(2,10)}$, p=0,079, R^2 0,16
Weight (kg)	Pre	77,9±14,3	83,4±12,9	67,7±7,4	86,9±16,5[f]	76,5±16,0[f]	66,3±10,1	$F_{(3,94)}$, **p=0,004**, R^2 0,27
BMI (kg·m²)	Pre	28,4±5,0	31,2±4,2	26,0±2,3	30,3±4,1[f]	28,5±4,2	26,2±2,8	$F_{(2,96)}$, **p=0,020**, R^2 0,22
Obesity prevalence								
Normoweight (*n* = / %)	Pre	3 (30,0)	1 (10,0)	4 (40,0)	1 (10,0)	1 (12,5)	3 (30,0)	
	Post	2 (20,0)	1 (10,0)	4 (40,0)	1 (10,0)	1 (12,5)	4 (40,0)	
Overweight (*n* = / %)	Pre	4 (40,0)	2 (20,0)	6 (60,0)	3 (30,0)	4 (50,0)	6 (60,0)	
	Post	5 (50,0)	3 (30,0)	6 (60,0)	2 (20,0)	4 (50,0)	6 (60,0)	
Obesity (*n* = / %)	Pre	3 (30,0)	7 (70,0)	0 (0)	6 (60,0)	3 (37,5)	1 (10,0)	
	Post	3 (30,0)	6 (60,0)	0 (0)	7 (70,0)	3 (37,5)	0 (0)	
Hypertension prevalence								
Hypertensive (*n* = / %)	Pre	10 (100)	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	
	Post	10 (100)	1 (10,0)	0 (0)	3 (30,0)	0 (0)	0 (0)	
Elevated BP (*n* = / %)	Pre	0 (0)	10 (100)	0 (0)	0 (0)	8 (100)	0 (0)	
	Post	0 (0)	8 (80,0)	0 (0)	4 (40,0)	1 (12,5)	0 (0)	
Normotensive (*n* = / %)	Pre	0 (0)	0 (0)	10 (100)	0 (0)	0 (0)	10 (100)	
	Post	0 (0)	1 (10,0)	10 (100)	3 (30,0)	7 (87,5)	10 (100)	

Data are shown as mean and ±standard deviation. Groups are described as; (CG-HTN) Control group hypertensive. (CG-Ele) Control group elevated BP. (CG-NT) Control group normotensive. (EG-HTN) experimental hypertensive group. (EG-Ele) Experimental elevated BP. (EG-NT) Experimental normotensive group. Outcomes are described as; (BMI) Body mass index. (WC) Waist circumference. (SMM) Skeletal muscle mass. (f) Denotes significant differences vs. EG-NT group at $p<0.05$ by Sidak's *post hoc*. Bold values denote significant interaction-group at $p<0.05$.

Journal of Sport and Health Research 2024, 16(2):279-292

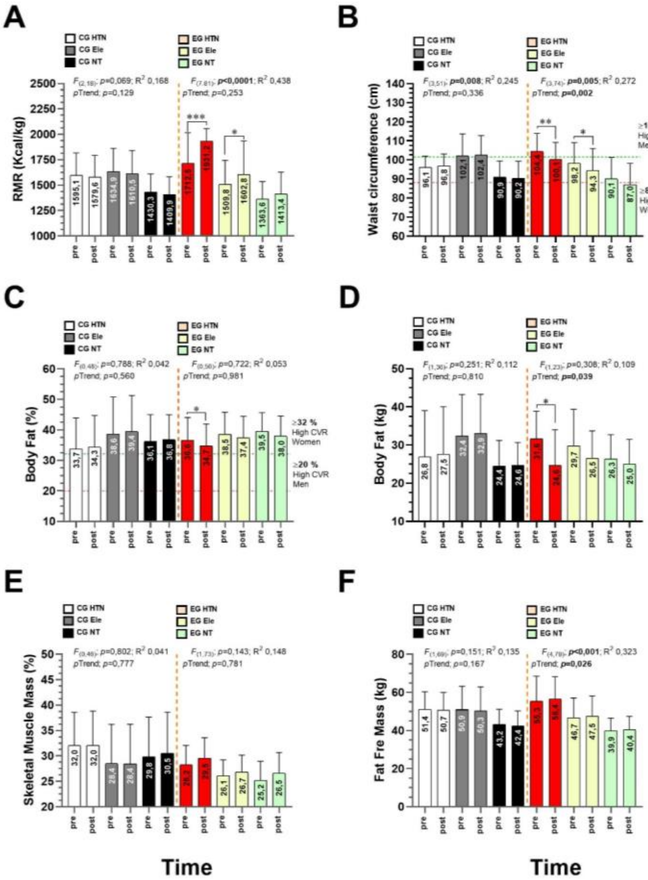

Figure 3. Body composition resting metabolic rate (A), waist circumference (B), body fat percentage (C), body fat in kg (D), skeletal muscle mass (E), and fat-free mass (F) in hypertensive, elevated blood pressure and normotensive participants of 6-weeks of concurrent training of HIIT+RT ($CT_{HIIT+RT}$). **Groups are described as;** hypertension exercise (EG-HTN *n*=10, or hypertensive control group (CG-HTN, *n*=10), elevated blood pressure exercise (EG-Ele *n*=10), or Ele control group (CG-Ele, *n*=10), and exercise normotensive control (EG-NT, *n*=10), or normotensive control group (CG-NT, *n*=10). Within-group comparisons; (*) Denotes significant differences between pre *vs*. post at *p*<0.05. (**) Denotes significant differences between pre *vs*. post at *p*<0.01. (***) Denotes significant differences between pre *vs*. post at *p*<0.0001.

Blood pressure

Significant changes were detected between pre to post-changes at six weeks of intervention in SBP in EG-HTN (135±14 to 116±4 mmHg, *p*<0,0001, Figure 4A), EG-Ele groups (127±6 to 116±4 mmHg, *p*<0,0001, Figure 4C), and EG-NT group (118±7 to 110±13 mmHg, *p*<0,0001, Figure 4E). Similarly, significant differences were detected between pre to post-test intervention in DBP in EG-HTN (85±10 to 76±4 mmHg, *p*<0,0001, Figure 4B), EG-Ele group (87±9 to 79±7 mmHg, *p*<0,0001, Figure 4D), and EG-NT group (77±6 to 73±12 mmHg, *p*<0,05, Figure 4F).

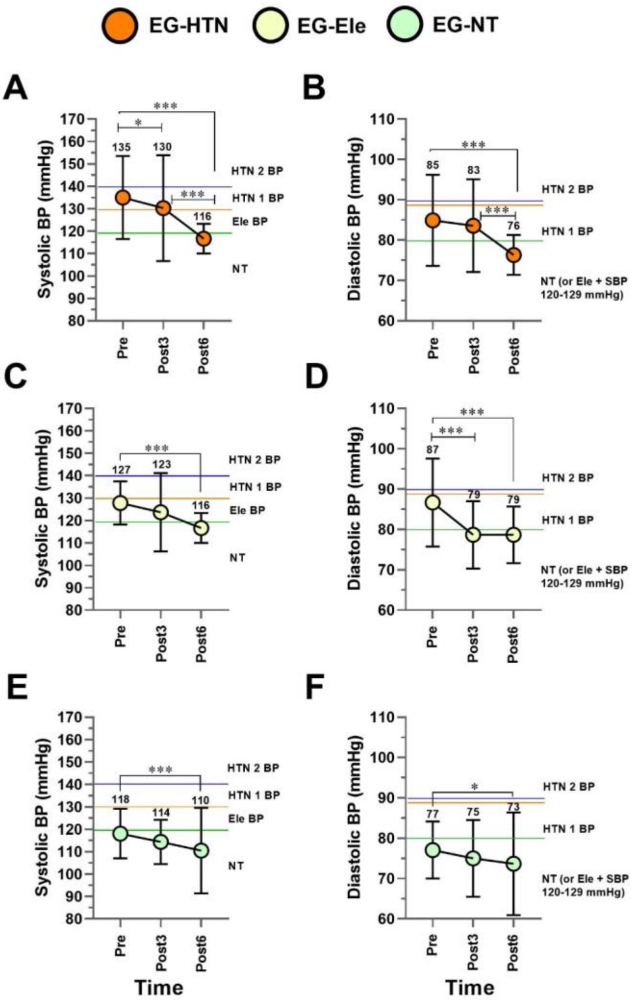

Figure 4. Systolic (A, C, E), and diastolic (B, D, F) blood pressure measurement, in hypertensive (A,B), elevated blood pressure (C, D) and normotensive adults (E, F) participants of 6-weeks of concurrent training of HIIT+RT ($CT_{HIIT+RT}$). **Groups are described as;** hypertension exercise (EG-HTN, elevated blood pressure exercise (EG-Ele), and exercise normotensive (EG-NT). Within-group comparisons; (*) Denotes significant differences between pre *vs*. post-test at *p*<0.05. (***) Denotes significant differences between pre *vs*. post-test at *p*<0.0001.

Carotid intima media thickness

There were significant changes from pre to post-test intervention in $cIMT_{max}$ in EG-HTN (0,87±0,34 to 0,77±0,25 cm, *p*<0,05, Figure 5B), and in EG-Ele group (0,99±0,42 to 0,69±0,12 cm, *p*<0,0001, Figure 5B).

Journal of Sport and Health Research 2024, 16(2):279-292

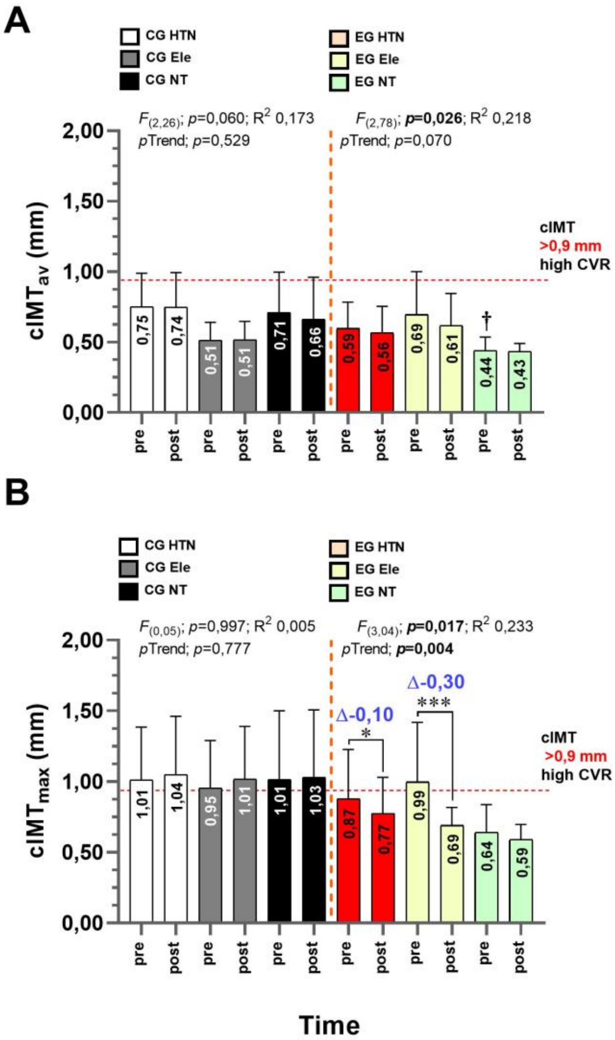

Figure 5. Vascular measurement of carotid intima-media thickness in average (A), and maximum carotid intima-media thickness (B), in hypertensive, elevated blood pressure and normotensive adult participants of 6 weeks of concurrent training of HIIT+RT ($CT_{HIIT+RT}$). **Groups are described as;** hypertension exercise (EG-HTN, or hypertensive control group (CG-HTN), elevated blood pressure exercise (EG-Ele), or Ele control group (CG-Ele), and exercise normotensive control (EG-NT), or normotensive control group (CG-NT). Within-group comparisons; (Δ) Denotes delta changes pre-post in mm. (*) Denotes significant differences between pre *vs*. post-test at p<0.05. (***) Denotes significant differences between pre *vs*. post-test at p<0.0001.

Figure 6 shows the protocol of measurement of $cIMT_{av}$ and $cIMT_{max}$, as well as the results obtained from the ultrasound by B-mode image capture.

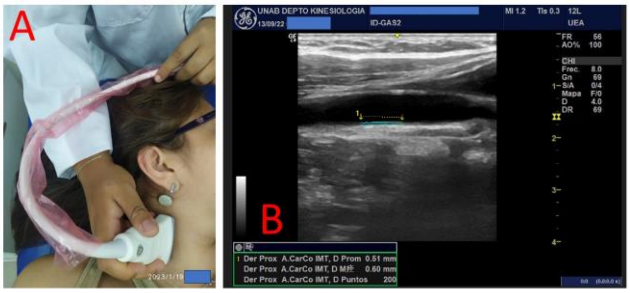

Figure 6. Representative image of the $cIMT_{av}$ and $cIMT_{max}$ measured by the automatic option with B-mode of an ultrasound machine.

DISCUSSION

The main findings of this study were that *i*) 6-week $CT_{HIIT+RT}$ decreased $cIMT_{max}$ but not $cIMT_{av}$ in adults with HTN and elevated blood pressure (Figure 5B), where in *average* data *ii*) the $CT_{HIIT+RT}$ regime promoted HTN remission (Figure 3), and beneficial body composition changes by body fat % and body fat in kg decrease in HTN group (Figure 4C-D).

There is a scarcity of studies reporting vascular measurements with exercise training intervention and a handful of studies performed in HTN populations. Previously, (Nichols et al., 2020) reported that eight weeks of MICT did not decrease $cIMT_{av}$. After 12 weeks of $CT_{MICT+RT}$ in middle-aged women with obesity, (Kim et al., 2021) reported that the participants decreased $cIMT_{av}$ from $0{,}61 \pm 0{,}13$ to $0{,}58 \pm 0{,}12$ mm after training (Δ−0.03 mm). Thus, these interesting results were associated with decreased waist circumference ($r = 0{,}41$) and increased peak oxygen consumption of participants ($r = -0{,}53$). Also recently, a novel study from (Au et al., 2020) reported the effects of 12 weeks of MICT, HIIT, or RT, showing no significant changes in the $cIMT_{av}$ of healthy men by including data from retrospective studies. (Au et al., 2020) analyzed statistically the $cIMT_{av}$ data from two previous studies in which men performed 12 weeks of MICT (n=9), HIIT (n=7), and RT (in higher-repetition [n=15] or lower-repetition RT [n=15]). We speculate that the healthy normotensive condition of this literature study of Au et al., in comparison with our present HTN sample (control and experimental), reveals a high variability in the effects of these exercise modalities (i.e., MICT, HIIT, or RT alone) in comparison of our HTN or other disease condition (Au et al., 2020). Our present study detected that only $cIMT_{max}$ was significantly decreased, but not $cIMT_{av}$

(Figure 5B). We speculate that the HTN condition of the participants had more endothelium commitment (i.e., damage), where this condition would potentially permit the detection of more sensitivity changes at the level of the $cIMT_{max}$ but not precisely $cIMT_{av}$). Long-term exercise training interventions have also revealed $cIMT_{av}$ decreases in T2DM patients (Hetherington-Rauth et al., 2020), but this study included adults with T2DM diagnosed, and the $cIMT_{av}$ decreases were correlated with cardiorespiratory fitness (i.e., VO_{2peak}) of those responders to exercise. However, common clinical interventions using exercise as medicine are usually standardized under ≤12 weeks of duration, being long-term studies challenging to implement in clinical contexts. Other potential mechanisms underlying our results could be originated from implicate molecular/cellular adaptations. It is well-known that physical inactivity is related with more inflammation such as adhesion molecule-1 (ICAM-1), and vascular cell adhesion molecule-1 (VCAM-1) (Nadar et al., 2004). Similarly, Is has been described an increase in the vasoconstrictors agents such as endothelin-1 (ET-1), that overall could be reduced in their action with the $CT_{HIIT+RT}$ exercise intervention. However, we do not measured these outcomes, it has been well dilucidated that different exercise modalities increase the nitric oxide synthase enzyme activity (NOs), and thus the nitric oxide availability (NO) (Ferroni et al., 2006), which is an essential vasoprotective gas associated with the shear stress in the endothelial wall associated with exercise.

In the body composition outcomes, we observed significant body fat decreases in % and kg (Figure 3C-D), and waist circumference decreases in both EG-HTN and EG-Ele (WC) (Figure 3B). Regarding these results, after two weeks of HIIT (Whyte et al., 2010), a decrease of Δ−2,4 cm in waist circumference was found. By contrast, after 16 weeks of HIIT, we found a decrease of Δ−4,1 cm in waist circumference. Sixteen weeks of HIIT in HTN adults reported significant body mass Δ −2,7 kg, body fat % Δ−1,3%), displayed with additional SBP decreases of Δ−8,7 mmHg (Delgado-Floody et al., 2020).
Regarding blood pressure reductions, previous literature has reported other similar relevant results. For example, (Olea et al., 2017), after eight weeks of HIIT exercise (3 sessions per week, 1 min cycling, 2 min rest x 10 times), reported a decrease of SBP Δ−17 mmHg in HTN adults. Similarly, eight weeks of $CT_{MICT+RT}$ (3 sessions per week) reported decreases in SBP Δ−5.1 and DBP Δ−3,9 mmHg in offspring of HTN parents (Songcharern et al., 2022). After ten weeks of $CT_{MICT+RT}$ (20 min RT by exercise machines of 15 repetitions at 60-70% of 1RM plus 20 min of MICT by treadmill) in HTN patients, there was reported a decrease in SBP of Δ−5,0 mmHg (Matias et al., 2020). A recent meta-analysis of RT in HTN patients, including 77 studies and (*n*=646) participants, revealed that interventions of >7 weeks decrease SBP Δ−4,7 and DBP Δ−3,5 mmHg (Igarashi, 2023). From here, the present $CT_{HIIT+RT}$ protocol of 10 min of exercise per session (~30 min·session) of time-investment reduced SBP in Δ−19 in EG-HTN and DBP in Δ−9 mmHg, where in average date, the categorization in both outcomes was changed from HTN to NT categorization following the AHA guidelines for blood pressure diagnosed, promoting thus HTN remission (Figure 3AB). We think that these results are not new because Cade *et al.* in 1984 (Cade et al., 1984) reported that (n=24) HTN subjects treated under hypotensive therapy decrease SBP Δ−22 and DBP Δ−18 mmHg after the application of 12 weeks of MICT (walking 2 miles·day), being regulated (i.e., retired) the baseline pharmacotherapy at the final of the exercise intervention period. Some of the mechanisms by which exercise decreases blood pressure include a reduction in vascular peripheral resistance (Wilkins et al., 2004), an increase in nitric oxide (Augeri et al., 2009), a decrease in vasoconstrictors as endothelin 1 (Maeda et al., 2001), an increase in shear stress (Restaino et al., 2016), a decrease in sympathetic nervous activity (Halliwill, 2001), and skeletal muscle mass angiogenesis (Fernandes et al., 2012). It was reported that a minimum of ~2 mmHg SBP reduction in HTN adults was associated with a 10% decrease in brain vascular accidents and a 7% reduction in cardiovascular disease (Lewington et al., 2002), having our SBP (Δ−19), and DBP (Δ−11 mmHg) reductions in the EG-HTN group, clinical implications.

We also report that our $CT_{HIIT+RT}$ exercise program promotes HTN remission in average data. For example, the EG-HTN group started with (*n*=10) subjects classified as hypertensive. However, after the intervention, only (*n*=3) subjects were classified in this category, being (*n*=4) categorized as elevated blood pressure, and notably (*n*=3) subjects classified as normotensive (Table 1). More notably, our results also showed that from (*n*=8) subjects classified as elevated BP in EG-Ele group, after the intervention, only one subject (*n*=1) maintained an elevated BP condition, being the other (*n*=7) subjects categorized in the normotensive condition. Although previous studies have also reported HTN remission (Cade et al., 1984; Cano-Montoya, Álvarez, et al., 2016; Cano-Montoya, Ramírez-Campillo, et al., 2016; Delgado-Floody et al., 2020; Olea et al., 2017), however, none of these studies reports vascular parameters of EDys that permit us to know how blood pressure normalization from HTN subjects is translated to the arteries changes (i.e., structurally), as by reporting both $cIMT_{av}$ and $cIMT_{max}$ in the present study.

Strengths and limitations

The present study is not far from limitations. First, we estimated body fat and muscle mass by body composition by electrical BIA equipment with lower precision than other more robust equipment such as plethysmography or dual X absorptiometry energy; however, the equipment has been used in previous studies. Second, we included a middle-term measurement on the blood pressure subjects of the experimental EG-HTN, EG-Ele, and EG-NT, but not from other outcomes nor the control groups; however, it was of our hypothesis to not have expectations/modifications in blood SBP/DBP, or carotid changes at 3-week post-intervention. The strength of our study is that it is the first study that reports both $cIMT_{av}$ and $cIMT_{max}$ and body composition outcomes in a short-term exercise intervention in HTN or elevated blood pressure population, which represents a valuable advance in the clarification of the exercise effects in populations cardiovascular risk factors. In addition, we proposed (based on our previous research experience in the exercise sciences) a time-efficient $CT_{HIIT+RT}$ exercise program for HTN adults looking for their practical feasibility to be applied in clinical context interventions (i.e., with a time of ≤30 min·session), that similarly, we believe it represents a worthwhile tool to be considered.

CONCLUSIONS

Six weeks of $CT_{HIIT+RT}$ decreased $cIMT_{max}$ but not $cIMT_{av}$ in HTN adults. These results were displayed with additional cases of hypertensive remission in the experimental HTN group and beneficial body composition changes.

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