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A randomized controlled trial comparing home-based isometric handgrip exercise vs endurance training for blood pressure management

Short Title: Isometric handgrip versus aerobic training

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Abstract

Aerobic endurance exercise (AEX) is an effective treatment in the prevention and management of high blood pressure (BP). Growing evidence suggests potential benefits from isometric handgrip exercise (IHG), which may promote similar or even larger reductions in BP than AEX. We compared the effects of home-based AEX and home-based IHG on BP. Sixty healthy individuals (31 men, mean age 33.1 yrs, mean BP 126.9±1.6 mmHg/84.7±1.1 mmHg) were randomized to IHG, AEX or a control group. Both exercise interventions were performed in the home environment. The IHG group performed daily 4x2 minutes sustained grips at 30% of maximal volitional contraction. Participants in the AEX group were advised to perform at least 150 min/week of aerobic exercise at moderate intensity. Outcomes measurements were assessed at baseline and at eight weeks of follow-up. Compared to the control group, AEX resulted in a larger reduction in ambulatory BP; both AEX and IHG tended to induce larger reductions in office SBP and office DBP was significantly more reduced following AEX, but not IHG. Responses to training were not significantly different between both exercise interventions. Eight weeks of home-based AEX results in significant reductions in both ambulatory and office BP in healthy adults while IHG reduces only office BP.

Clinical trial registration: NCT02705911

Key words: blood pressure, handgrip exercise, training, endurance, randomized controlled trial.

Conflict of Interest: There are no conflicts of interest.

Introduction

Chronic elevation of blood pressure (BP) or hypertension (HTN) is a leading contributor to global disease burden and is directly responsible for as many as 7 million deaths annually, representing one of the biggest health problems worldwide with a significant societal and economic burden.¹ Systolic BP increases linearly with age resulting in an estimated lifetime risk of developing HTN of approximately 90%.^{2, 3} As a result, prevalence of HTN is expected to increase from 25 to 29% by 2025 due the aging of the population.² As a consequence strategies to prevent and treat high BP are a vital public health challenge. Aerobic endurance training at moderate intensity is a widely recommended component in the prevention and treatment of high BP.^{4, 5} Indeed, meta-analytic research clearly shows that individuals participating in an aerobic endurance exercise program experience significant reductions in both office (-3.5/-2.5 mmHg)⁶ and daytime ambulatory BP (-3.2/-2.7 mmHg).⁷

However, implementation, achievement and adherence to these exercise recommendations seems difficult, if not impossible, at the population level.⁸ Moreover, epidemiological data suggest that hypertensive individuals engage less into physically activity and hence are less likely to meet current physical activity recommendations than their normotensive counterparts.⁹ Most cited barriers to exercise include busy lifestyles (lack of time), lack of motivation and knowledge, logistics (costs), fear of injury and associated comorbidities.^{10, 11}

Isometric handgrip exercise training involves short periods of isometric contraction of lower arm muscles and seems to be a promising antihypertensive non-pharmacological tool which could counter many of these barriers. A growing number of research demonstrates that isometric exercise training elicits significant BP reductions both in normotensive, prehypertensive and medicated hypertensive individuals¹². Moreover, results from recent meta-analyses suggested that this type of low intensity isometric training might induce larger office BP reductions (range: -10.9 to -5.2 / -6.2 to -3.91 mmHg) compared to other modes of exercise.^{6, 13-15} However, at the conception of this research project, no direct comparison between isometric handgrip exercise and other modes of exercise had been performed. Furthermore, data on the effectiveness of isometric handgrip exercise to lower ambulatory BP were scant.^{16, 17} To date, studies involved supervised isometric handgrip training implying that patients had to visit the research facilities for 15 minutes of training usually three times per week. From a practical point of view, it is highly unlikely that patients will continue

doing so for longer-time periods. Home telemonitoring and telecoaching of physical activity has been proposed as a promising approach to support and provide individualized guidance from a distance to a wide variety of chronic diseases.¹⁸ As for now, to the best of our knowledge nobody has investigated the effectiveness of home-based isometric handgrip exercise with remote monitoring and telecoaching.

We performed a randomized controlled clinical trial in healthy adults to 1) determine whether home-based IHG training with telemonitoring and telecoaching lowers office and ambulatory BP and 2) to evaluate whether BP responses to IHG are larger compared to home-based moderate intensity AEX. We hypothesized that both modalities would reduce BP in comparison with a non-exercise comparator group, and that IHG would result in a significantly larger reduction compared to AEX.

Methods

Study Design

The TeleRehabilitation for HYPertension (TRiHYP) study is an investigator-initiated randomized controlled parallel trial of eight weeks total duration designed to compare the BP lowering effect of home-based AEX with home-based IHG in healthy adults. The primary outcome was change in office BP, the secondary outcomes involved changes in ambulatory BP, exercise capacity, handgrip strength and anthropometric characteristics. Participants were randomized to AEX, IHG or a control comparator group using a computer-generated random number assignment program (www.randomization.com).

The Ethical Committee of the UZ - KU Leuven approved the study and all procedures are in line with the World Medical Association Declaration of Helsinki on ethics in medical research. This research project was registered on Clinical Trials (www.clinicaltrials.gov) under protocol number NCT02725911.

Recruitment and pre-inclusion screening of participants

Participants were recruited through advertisements between May 2015 and August 2016. After an initial screening by telephone or email, 122 potentially eligible individuals were invited for a screening visit. During this visit and following 15 minutes of seated rest, office BP was measured three times using an automated device (OMRON M6 Comfort,

Omron Healthcare, Kyoto, Japan). The mean value of the last two readings was used to confirm BP values, as defined in the eligibility criteria. This was followed by a maximal graded cardio-pulmonary exercise test (CPET) with gas analysis to exclude the presence of ischaemic heart diseases or clinical significant arrhythmia. Following CPET, maximal handgrip strength was measured by means of a JAMAR handgrip strength dynamometer (Lafayette Instrument, USA) using a standardized protocol.¹⁹

Eligibility criteria were: 1) sedentary (defined by the absence of regular intense exercise during the previous 3 months) healthy men or women; 2) aged 20-65 years old; 3) non-smokers, 4) resting office SBP ≤ 179 mmHg and DBP ≤ 109 mmHg and 5) not receiving any medication known to influence BP or BP lowering mechanisms. Subjects were excluded if they had any documented cardiovascular and/or pulmonary disease and/or presented with significant illness during the last six weeks or showed any signs of myocardial ischemia or severe ventricular arrhythmia during the screening exercise test. Further, persons with high to very high cardiovascular risk according to the European Society of Hypertension/European Society of Cardiology (ESH/ESC) risk stratification model were excluded because pharmacological treatment should be started promptly according to prevailing guidelines.⁴ All participants provided written informed consent prior to the screening test.

Interventions

Individuals randomized to one of the training groups were asked to exercise at home, using a telemonitoring system for eight weeks. An intervention duration of 8 weeks was chosen as this was the median duration of the isometric handgrip interventions to date.⁶ Weekly personalized feedback was provided by the research team to each individual participant by phone or e-mail. Participants in the IHG group were asked to daily perform 4 x 2 minutes bilateral contractions at 30% of maximal volitional contraction (MVC) with one minute of rest between contractions, using a standardized device (Zona Health®, Boise, USA). During the session, the participants received visual and auditory feedback to ensure compliance with the IHG protocol. They were requested to upload their data once a week to an online web application (<https://bpcharting.com>) to allow researchers to monitor their training data and provide them with feedback. The participants, randomized to the AEX group, were asked to perform at least 150 minutes of moderate aerobic exercise per week according to current guidelines for HTN management.⁴ Training heart rate (HR_{ex}) was determined by means of the formula of Karvonen: $HR_{ex} = HR_{rest} + [HR_{max} - HR_{rest}] * 40 -$

60%. The Maximal Heart rate (HR_{max}) was obtained from the baseline CPET. For resting heart rate (HR_{rest}) we used baseline sitting HR. Participants in the AEX were instructed to wear a heart rate monitor (Garmin Forerunner 210 HRM) during each of their training sessions and were asked to weekly upload the recorded exercise data to an online web application (<https://connect.garmin.com/en-US/>) to allow the researcher to evaluate the volume and intensity of training. Participants enrolled in the control group were asked to continue with their daily routine and not to change anything in their physical activity behavior.

Exercise attendance and compliance

Weekly attendance and compliance with the training programs was recorded through online monitoring. Attendance was defined as % of weekly recommended duration (minutes) of aerobic exercise and % of total number of recommended isometric handgrip training sessions/week. The compliance was evaluated by the percentage of the time performed at the prescribed intensity for each of the intervention groups.

Outcome measurements

Individuals were evaluated at baseline and at the end of the 8-week period. At follow-up, measurements were performed within 120 hours after the intervention but at least 48 hours after the last exercise session. All measurements were performed between 8 AM – 12 AM in a quiet and temperature controlled room (18-23°C) by the same investigator (KG). To control for diurnal variation, measurements at baseline and 8 weeks of follow-up were performed at the same time of day for each individual. Measurements of office BP and anthropometrics were performed in fasting state and abstinence from caffeine for at least 12 hours.

Anthropometrics characteristics

Height (m) and weight (kg) were assessed using a wall-mounted stadiometer and a digital scale (Tefal PP6011) with patients barefoot and wearing light sportswear. Waist circumference was measured at the level of the umbilicus. Hip circumference was assessed at the widest portion of the buttocks. Both were measured a minimum of two times and the average of two measures that were within 5 mm was used for analysis. Body fat was measured using bioelectrical impedance methods (Omron BF 300; OMRON, Matoukasa Co. Ltd, Japan).

Office blood pressure

Office BP and HR were measured three times after 15 minutes of seated rest, with a validated automated device (OMRON M6 Comfort, Omron Healthcare, Kyoto, Japan at the left arm following the same procedures as described for the pre-screening evaluation. Accordingly, Topouchian et al.²⁰ showed that the Omron M6 fulfills the ESH International Protocol Revision 2010 requirements, and is therefore suitable for use by patients for BP measurements.

Exercise capacity and Maximal handgrip strength

A maximal graded exercise test until volitional fatigue was performed on a cycle ergometer (Siemens-Elema, Ergometrics 800S; Ergometrics; Bitz; Germany) using an individualized ergometer protocol (20W +20 W/min or 50W +25W/min). Twelve-lead ECG and gas exchange measurements were recorded continuously (Oxycon ProTM, CareFusion, Hoechberg, Germany). The ventilation, oxygen uptake (VO_2) and carbon dioxide production (VCO_2) were measured by the breath-by-breath gas exchange method. $\text{VO}_{2\text{peak}}$ was defined as the highest 30-s average of VO_2 obtained at the end of the test. Individual peak VO_2 results were compared with predicted reference values of Wasserman et al to determine percentage of predicted peak VO_2 .²¹

Ambulatory blood pressure

After completing the office measurements, individuals left the laboratory wearing on the left arm a validated ambulatory BP (ABP) device (Watch BP 03; Microlife, Widnau; Switzerland) (REF) for the next 24 hours. The ABP monitor was programmed to measure BP every 20 minutes. Subjects were instructed to stop any muscular activity and keep their arms still and extended during BP measurements. Further, they were asked to proceed with their normal daily activities and were asked to fill in an activity diary. Data from the ABP monitors were then downloaded to laboratory computers using the WatchBP 03 Analyzer software (Microlife, Widnau, Switzerland). Daytime and nighttime ABP were defined individually for each participant, according to their actual sleeping and awaking time, determined by means of the measures obtained from the SenseWear mini armband (Body Media Inc., Pittsburgh, PA, USA) that was worn simultaneously. The complete ABP data files were manually checked and invalid measurements were omitted. An erroneous value was defined as SBP lower than DBP, SBP >240 mmHg or <50 mmHg, or DBP >140 mmHg or <40mmHg. BP values were also deleted if SBP deviated ± 50 mmHg, or DBP deviated ± 20 mmHg from surrounding

values and could not be explained by changes in physical activity at that point in time. The ambulatory BP report of the participants should have at least one reading per hour to be included in the final analyses.

To allow for the detection of differences in physical activity behavior on the day patients were wearing the ABP device, participants were requested to wear simultaneously a SenseWear® mini armband (Body Media Inc., Pittsburgh, PA, USA) on the upper posterior aspect of the right arm. The Sensewear is a wireless, noninvasive monitor that measures tri-axial accelerometry, galvanic skin response, heat flux, skin temperature and near body temperature to estimate minute-by-minute energy expenditure.²² They were instructed to continuously wear the devices during the 24h and only remove them during periods when they might get wet, such as taking a shower or swimming activity.

Statistical analysis

Statistical analyses were performed using SAS software version 9.4 (SAS Institute, Inc, Cary, North Caroline, USA). Assumptions of normality were assessed using the Shapiro-Wilk test. Baseline values and exercise adherence and compliance were compared between groups via one-way analysis of variance (ANOVA) or Chi-square tests for categorical variables. A paired-two-tailed t-test was used to test within-group difference in continuous variables. Between group differences in changes of the BP values from baseline and follow-up were compared by ANOVA, using Sheffé's correction for multiple testing. Continuous data were reported as mean $\pm$ standard error or mean (95% confidence intervals (CI)); categorical variables were reported as frequencies (%). A two-tailed p-value < 0.05 was considered statistically significant.

Results

Participant characteristics

A CONSORT flowchart of the trial is presented in Figure 1. After initial screening of 122 volunteers, 60 eligible participants were randomized in one of the three groups. Nine patients dropped out during the 8 week intervention of which, four in the AEX group (withdrew consent, n=3; lower back pain, n=1); two individuals of the control group (initiation of BP

medication, n=1; no time for follow-up measurements, n=1) and three participants of the IHG group (pregnant, n=1; withdrew consent n=2).

The general characteristics of the participants at entry are shown in Table 1. Overall, participants were slightly overweight with a mean office systolic BP of 127 mmHg (range 105 to 172 mmHg) and mean diastolic BP of 84.7 mmHg (range 62 to 109 mmHg). One of the included patient had hypertension.⁴ They had a normal average physical fitness for their age (% sedentary values $101.9\% \pm 2.7$).²¹ No differences could be observed for the baseline characteristics across the three groups ($p>0.05$ for all).

Primary outcome – blood pressure

As shown in figure 2, office SBP was lower after 8 weeks in AEX [-3.9 mmHg; (-8.3; +0.4); $p=0.07$] and IHG [-5.5 mmHg (-9.2;-1.7); $P<0.01$] compared to baseline with no change in the control group [+1.0 mmHg (-2.7;+4.7); $p>0.05$]. Changes in office SBP among participants in both intervention groups were borderline, but not significantly different from control group ($p=0.06$ for both). A significant reduction was also observed at 8 weeks of follow-up for office DBP following AEX [-4.4 mmHg (-7.5;-1.5)]; $p=0.006$), but not after IHG [-1.8mmHg (-5.3; +1.7); $p>0.05$]. Compared to the control group, reductions in office DBP were statistically significantly larger following AEX [-7.0 mmHg (-12.5;-1.5); $p<0.05$] but not following IHG [-4.3 mmHg (-9.7; +1.1); $p>0.05$]. Yet, no statistically significant differences were established between BP changes following AEX and IHG ($p>0.05$).

Table 2 presents the within and between group differences in ABP of 46 patients with valid measurements. Reductions in ABP were significantly larger after AEX compared to control ($p<0.05$). No statistically significant differences were observed between AEX and IHG ($p>0.05$ for all). No significant within and between effects could be observed for nighttime BP. Physical activity behavior (steps, total EE and physical activity intensity) on ABP monitoring days was similar between groups and on the day of baseline and follow-up measurement ($p>0.05$ for all).

Secondary outcomes - anthropometrics, exercise capacity and handgrip strength

Within and between group differences for the secondary outcomes are shown in table 3. As can be judged from the RER, participants from all three groups performed a similar maximal

effort during the CPET at baseline and follow-up. At 8 weeks following the intervention, participants in the AEX improved their aerobic exercise capacity more than the CON group [+5.4, 95% CL 1.5 to 9.2) ml/min/kg; $p < 0.05$]. Changes in exercise capacity among participants in the IHG group were not different from the control group ($p > 0.05$). All participants showed a significant increase in handgrip strength from pre- to post intervention ($p < 0.05$ for all). No significant differences in gains in handgrip strength were established among participants in the three groups ($p > 0.05$). There was a tendency ($p = 0.08$) towards weight reduction from baseline to follow-up in participants of AEX, although not significantly different from the control group ($p > 0.05$).

Compliance and adherence

Overall, the compliance to prescribed intensity during exercise was 93.4% (range 82.4% to 100%) in AEX and 91% (range 89% to 93%) in IHG. Attendance, defined as the % of participation to weekly prescribed session for IHG decreased over time from 96% during the first week [median number of sessions 7 (range 6-7)] to 63% during the last week [median 6 (range 0-7 sessions)]. Four patients in the IHG group did less than three sessions weekly in the last two weeks. Attendance to AEX 72.8% or 110 minutes/week (range 58.8% to 88.2%).

Discussion

The present study is the first large randomized trial evaluating the effect of home-based IHG with remote monitoring and telecoaching on office and ambulatory BP; and comparing home-based IHG to home-based AEX in healthy adults. The main finding was that eight weeks of home-based AEX, but not IHG with telemonitoring guidance promoted significant reductions in day-time ambulatory BP and office DBP, compared to the control group. Yet, no statistically significant differences in BP responses could be observed between both exercise interventions.

Our results did not fully confirm our working hypotheses of 1) significant reductions in office BP following IHG and AEX in comparison to a comparator control group and 2) superior effect of IHG compared to AEX. The first hypothesis was based on a growing body of evidence demonstrating that isometric exercise has the potential to become a valuable new non-pharmacological tool in the management of blood pressure^{6, 13, 23} Much of this evidence

however came from small studies evaluating the effect of isometric handgrip exercise on office BP.^{6, 24} Although we observed a tendency for larger reduction in office SBP following IHG compared to control, this did not reach statistical significance ($p=0.06$). As such our results contrast somewhat with the earlier small pilot studies that reported highly significant larger BP reductions in favor of IHG, but are in line with two recently published randomized controlled trials who found no difference between sham and isometric handgrip exercise.^{23, 25} Nevertheless, although not statistically significant, it could be argued that the observed reduction in SBP of -4.5 mmHg in comparison to control group is clinically relevant. That is, a 2 mmHg reduction of office SBP has been shown to result in a 6% reduction in stroke mortality and a 4% reduction in mortality attributable to coronary heart disease; the reductions amount to 14 and 9%, respectively, for 5 mmHg decrease of SBP.³

Our second hypothesis was based on the only meta-analytic study comparing the effect of different modes of exercise and showing significantly larger reductions in office BP following IHG compared to aerobic endurance or dynamic resistance training.⁶ However, at the conception of our trial, no study had made a direct comparison between aerobic endurance training and isometric handgrip exercise. No significant differences were found among the office BP responses of both interventions, although office DBP was only significantly reduced after AEX. This concurs with a recently published randomized controlled trial of Pagonas et al.²⁵ who randomly allocated 75 hypertensive patients to isometric handgrip exercise, a sham control group or aerobic endurance training. They found a significant reduction of -10 mmHg ($p=0.03$)/ -3 mmHg ($p=0.18$) in office SBP/DBP following 12 weeks of aerobic endurance training, though no change following IHG. Yet, BP responses between both their intervention groups were also not significantly different.

From a clinical perspective, ambulatory BP is more important. Today, ambulatory BP is the recommended standard for the diagnosis of true hypertension and accurate assessment of cardiovascular risk in all adults.²⁶ The prognostic value of ambulatory BP has been shown to be superior to office BP²⁷; and ambulatory BP monitoring is a valuable tool for follow-up of BP lowering treatments. To date, results on effectiveness of IHG training on ambulatory BP have not been in agreement with results on office BP. In a population of 25 medicated hypertensive individuals (mean BP 116mmHg/64mmHg), Stiller-Moldovan et al.¹⁷ found no effect of 8 weeks of isometric exercise training performed at 30% of MVC on ambulatory BP. In line, Pagonas et al.²⁵ also showed no reduction in ambulatory BP following IHG in a hypertensive population. Our study confirms these results in a population of non-medicated

normotensive and prehypertensive individuals. Two recently published studies^{16, 25} have compared the BP lowering effect of both exercise interventions, i.e. isometric handgrip exercise and aerobic endurance training, on ambulatory BP. In a pilot non-randomized controlled trial involving 11 prehypertensive obese patients, Ash et al^{16, 25} reported a significant reduction in daytime ABP following AEX, which was significantly larger compared to IHG. In addition, they found no effect of AEX on nighttime BP, whereas IHG seemed to increase nighttime DBP. Pagonas et al²⁵ made a similar observation demonstrating significant greater benefits for daytime and nighttime SBP after AEX compared to isometric handgrip or sham isometric training. As such, our results add further evidence for the fact that isometric handgrip exercise is not superior to aerobic endurance training for decreasing ABP.

Further, it should be acknowledged that the benefits of aerobic endurance training go beyond BP reductions. We observed a significantly larger increase in exercise capacity following 8 weeks of home-based aerobic endurance training whereas no change was observed following IHG. Peak exercise capacity is widely known to be an independent predictor of mortality in healthy adults and patients with hypertension.²⁸ Therefore we believe that AEX should remain a number one recommendation in the prevention and treatment of high BP and that strategies for increasing uptake and adherence to a physically active lifestyle should remain a focus in healthcare policies. IHG could be a useful tool for lowering BP in specific groups of individuals for which AEX is less feasible due to for instance high age and/or comorbidities, even though further research in this population seems warranted.

This study comes with its limitations. First of all, attendance to isometric handgrip training showed a clear decline over time. Individuals included in our sample were rather young and healthy and reported that this isometric handgrip exercises was not that attractive, was quite boring and did not really feel like exercising for them likely explaining the decrease in adherence. As such, our results cannot be generalized to the overall hypertensive population. Further large well-controlled studies including older and less mobile individuals are needed to confirm our findings. Therefore, it is also likely that if our participants would have adhered better to the exercise prescription we would have seen a larger reduction. Secondly, only baseline and follow-up ABP monitoring from 46 out of 60 participants were valid for inclusion in the analysis, which might have reduced statistical power for this outcome of our study. Finally, we included a rather young normotensive population, so generalizability to older or hypertensive patients needs caution.

Conclusions

Eight weeks of home-based aerobic endurance exercise, but not isometric handgrip exercise training results in a significant reduction in office and ambulatory daytime BP. Isometric handgrip exercise is not superior to aerobic endurance training to reduce BP in young, healthy adults.

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Summary Table

What is known about topic?

- Isometric exercise might be superior compared to aerobic endurance training to reduce BP
- Further studies are warranted to expand the limited data on whether isometric handgrip training might be superior to aerobic endurance exercise to lower BP

What this study adds?

- Only aerobic endurance exercise results in significant reductions in office DBP and ambulatory BP compared to a control group
- Yet, BP changes following aerobic endurance exercise and isometric handgrip exercise are clinically relevant and similar
- Eight weeks of home-based aerobic endurance exercise, but not isometric handgrip exercise training results in a significant reduction in office and ambulatory daytime BP

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Legends to Figures

Figure 1: Flow chart of the study

Figure 2: Changes in office systolic and diastolic BP from pre- to postintervention. Data are presented as mean (SE) * $P < 0.05$ different from control.

Table 1. Baseline characteristics of the overall study population and by intervention

	Overall	AEX	IHG	CONTROL	p-between groups
N	60	22	22	16	
Men	31 (51.7%)	14 (63.6%)	10 (45.5%)	7 (43.8%)	0.36
Age (years)	33.1±1.3	32.9±2.1	33.1±2.1	33.4±3.0	0.98
Anthropometrics					
Weight (kg)	78.1±2.0	81.8±4.0	78.6±3.2	72.4±8.7	0.18
Height (cm)	172.1±1.0	173.2±1.8	171.4±7.5	171.7±1.7	0.72
BMI (kg/m ²)	26.3±0.5	27.1±1.0	26.8±1.0	24.6±0.7	0.22
Office Blood Pressure					
SBP (mmHg)	126.9±1.6	125.8±2.4	125.2±1.9	130.6±4.5	0.39
DBP (mmHg)	84.7±1.1	85.4±1.5	84.6±1.3	84.0±3.1	0.88
Resting heart rate (bpm)	75.9±1.4	76.5±2.5	76.0±2.4	74.9±2.9	0.92
Exercise Capacity					
VO ₂ peak (ml.min ⁻¹)	2509.3±88.5	2600.4±143.0	2365.3±159.3	2573.1±158.7	0.48
VO ₂ peak (ml.kg ⁻¹ .min ⁻¹)	32.5±0.98	32.3±1.5	30.4±1.7	35.3±1.6	0.15
Peak heart rate (bpm)	177.0±2.0	181.0±3.4	174.6±3.8	174.5±3.0	0.33

Data are expressed as mean ± SE or number (%).

Abbreviations: BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; VO₂peak, peak oxygen uptake

Table 2. Change in ambulatory blood pressure from pre- to post intervention.

	Group	N	Baseline	8 weeks Follow-up	Within Interventions Changes (%CL)	Between Interventions Changes vs. Control Group (%CL)	P-ANOVA
Day-time SBP (mmHg)	AEX	14	120.6±2.6	117.3±3.0 *	-3.3 (-6.3, -0.27)*	-6.9 (-13,-0.81)†	0.02
	IHG	18	120.0±1.9	119.1±1.7	-0.85 (-4.2,+2.4)	-4.4 (-10.2,+1.3)	
	CON	14	116.9±3.0	120.5±2.7	3.6 (-0.4,+7.6)	NA	
Day-time DBP (mmHg)	AEX	14	76.7±1.9†	74.1±1.9	-2.6 (-5.2,+0.04)**	-4.8 (-8.4,-1.1)†	0.03
	IHG	18	75.3±1.5†	74.3±1.1	-0.93 (-3.6,+1.7)	-3.3 (-6.7,+0.2)	
	CON	14	70.3±2.5	72.7±2.1	2.4 (-0.46,+5.2)	NA	
Night-time SBP (mmHg)	AEX	14	103.0±1.9	100.1±3.0	-2.8 (-7.1; +1.4)	-3.9 (-11.5,+3.6)	0.30
	IHG	16	104.8±1.4	105.8±1.4	0.9(-2.9; +4.8)	-0.2 (-7.6,+7.27)	
	CON	11	104.0±2.3	105.1±3.0	1.1 (-3.8;+6.0)	NA	
Night-time DBP (mmHg)	AEX	14	60.5±1.05	58.6±1.9	-1.8 (-5.6,+1.9)	-2.3 (-8.6,+4.1)	0.50
	IHG	16	60.5±1.5	61.1±1.0	0.6 (-2.3, +3.6)	0.14 (-6.2,+6.5)	
	CON	11	58.6±2.6	59.0±2.8	0.5 (-4.0,+5.0)	NA	

Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; AE, aerobic endurance exercise; IHG, isometric handgrip; CON, control group. *P<0.05 vs. baseline; **P=0.053 vs baseline; †P<0.05 vs. control group

Table 3. Change in anthropometrics, exercise capacity and handgrip strength from pre- to post intervention.

	Group	N	Baseline	8 weeks Follow-up	Within Interventions Changes (%CL)	Between Interventions Changes vs. Control Group (%CL)	P-Interaction
Weight (kg)	AEX	18	81.0±3.9	79.4±3.5	-1.5 (-3.3;+0.25)	-1.6 (-4.3,+1.1)	0.33
	IHG	19	77.2±3.3	76.6±3.1	-0.6 (-2.0;+0.7)	-0.7 (-3.4,+1.9)	
	CON	14	74.2±3.5	74.3±3.2	0.06 (-1.3;+1.4)	NA	
Waist (cm)	AEX	18	93.1±3.5	92.0±3.1	-1.4 (-3.3,+0.4)	-1.4 (-3.7,+0.8)	0.44
	IHG	19	89.8±2.7	88.7±2.6	-1.0 (-2.4,+0.4)	-1.0 (-3.2,+1.2)	
	CON	14	84.0±2.7	83.8±2.6	0.0 (-1.4,+1.5)	NA	
Hip (cm)	AEX	18	103.9±2.3	97.8±5.5	-1.9 (-3.8,+0.1)	-2.8 (-4.9,-0.8)	0.30
	IHG	19	107.4±2.1	106.8±2.0	-0.6 (-1.8,+0.5)	-1.6 (-3.6,+0.4)	
	CON	14	104.1±2.0	105.6±1.8	1.0 (-0.3,+2.3)	NA	
Fat mass %	AEX	16	24.4±1.8	24.5±1.6	+0.1(-1.1;+1.3)	-0.1 (-2.2;+2.4)	0.70
	IHG	17	25.5±2.0	25.0±1.9	-0.4(-1.7;+0.8)	-0.6(-2.9;+1.6)	
	CON	9	21.1±2.0	21.3±2.3	+0.2(-0.7;+1.14)	NA	
VO ₂ peak (ml/min/kg)	AEX	15	32.3±1.6	36.3±1.5	+4.0 (+2.6;+5.3)*	5.4 (1.5; 9.2)*	0.044
	IHG	14	31.8±2.1	32.7±1.8	+0.89 (-2.0,+3.9)	2.3(-1.5;+6.2)	
	CON	10	35.8±1.9	34.4±2.1	-1.4 (-3.8;+1.01)	NA	
Handgrip Strength (kg)	AEX	13	39.2±3.2	42.9±3.2	+3.6 (+0.2;+7.2)*	-0.25 (-5.0;+4.5)	0.80
	IHG	16	34.1±2.7	36.7±2.5	+2.7 (+0.8;+4.6)*	+0.76 (-3.8;+5.3)	
	CON	9	40.2±4.6	43.7±4.7	+3.4 (+1.6;+5.3)*	NA	
Peak RER	AEX	15	1.14±0.02	1.16±0.01	0.01 (-0.05,+0.09)	0.004 (-0.1,+0.1)	0.96
	IHG	14	1.13±0.01	1.15±0.01	0.05 (-0.02,+0.10)	-0.07 (-0.21,+0.07)	
	CON	10	1.15±0.01	1.16±0.01	0.01 (-0.06,+0.04)	NA	

VO₂ peak, peak oxygen uptake; peak RER, peak respiratory exchange ratio. *P<0.05

Figure 1