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Diminuição da pressão arterial em idosos após o treinamento isométrico: o lactato desempenha um papel?

Blood pressure decrease in elderly after isometric training: does lactate play a role?

Reducir la presión arterial en personas mayores después del entrenamiento isométrico: ¿lo lactato tiene un papel?

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Resumo

Este estudo teve como objetivo investigar o efeito do treinamento isométrico de preensão manual (IPM) na redução da pressão arterial (PA) em idosos pré-hipertensivos e hipertensos, e o possível papel do equilíbrio do lactato e redox. Trinta e três idosos (75.3±1.3 anos) foram alocados no grupos: controle (GC,n=11), pré-hipertensos (GPH,n=10) e hipertensos (GH, n=12). O GPH e o GH realizaram um total de 8 séries de contrações bilaterias de 1- min com contração isómetrica voluntária (CVM) máxima de 30 %, cada uma separada por uma pausa de repouso de 1-min. O treinamento foi realizado por 8 semanas, 3 vezes por semana, em dias não consecutivos. A PA sistólica (PAS) e a frequencia cardíaca (FC) diminuíram no pós treinamento os níveis do GPH (-10 mm Hg; -5 bpm) e GH (-16 mm Hg; -9 bpm), respectivamente. A PA diastólica diminui apenas para GH (-9 mm Hg) (P<0,05). Além diso, as variáveis que mais apresentaram associação com a diminuição da PA foram a concentração capilar de lactato sanguíneo e a força muscular (P<0,05). Em resumo, o treinamento IPM pode ser prático para melhorar o estado clínico de pacientes pré-hipertensos e hipertensos, melhorando o controle da PA, a biodisponibilidade de óxido nítrico e o balanço redox. Mais estudos são necessários para elucidar as vias de concentração de lactato no fluxo sanguíneo durante o exercício.

Palavras-chave: Envelhecimento; Antioxidantes; Hemodinâmica; Hipertensão; Contração Isométrica.

Abstract

This study aimed to investigate the effect of isometric handgrip (IHG) training on the blood pressure (BP) reduction in prehypertensive and hypertensive elderly people, and the possible role of lactate and redox balance. Thirty-three older (75.3±1.3 years old) were allocated to a non-exercise control (CG, n=11), prehypertensive (PHG, n=10), and hypertensive (HG, n=12) groups. PHG and HG performed a total of 8 sets of 1-min bilateral contractions at 30% maximal voluntary isometric contraction, each separated by 1-minute rest-pause. IHG training was performed for 8-week, 3 times a week on non-consecutive days. Systolic BP (SBP) and heart rate (HR) decreased post-training on PHG (-10 mm Hg; -5 bpm) and HG (-16 mm Hg; -9 bpm), respectively. Diastolic BP (DBP) decreased for HG only (-9 mm Hg) ($P < 0.05$). In addition, the decrease in BP occurred in parallel to a better redox balance and increased bioavailability of nitric oxide in PHG and HG ($P < 0.05$). Also, the variables that most present association to SBP decrease were capillary blood lactate concentration and muscle strength ($P < 0.05$). In summary, IHG training may be practical in improving clinical status of prehypertensive and hypertensive patients, by improving BP control, NO- bioavailability and redox balance. Further studies are required to elucidate the pathways of lactate concentration in blood-flow during exercise.

Keywords: Aging; Antioxidants; Hemodynamics; Hypertension; Isometric Contraction.

Resumen

Este studio tuvo como obejtivo investigar el efecto del entrenamiento de la empuñadura isométrica (EEI) en la reducción de la presión arterial (PA) en las personas mayores prehipertensivas e hipertensas, y el possible papel del lactoto y el equilibrio redox. Treint y tres mayores (75.3±1.3 años) fueron asignados a un grupo control sin ejercicio (GC, n=11), prehipertensivo (GPH, n=10) e hipertensivo (GH, n=12). GPH y GH realizaron un total de 8 series de contracciones bilaterales de 1-min a una contracción isométrica voluntaria máxima del 30% cada una separada por una pause de descanso de 1-min. El entrenamiento de EEI se realize durante 8 semanas, 3 veces por semana en días no consecutives. La PA sistóltica (PAS) y la frequencia cardíaca (FC) disminuyeron después del entrenamiento con GPH (-10 mm Hg; - 5 bpm) y GH (-9 mm Hg) (P<0,05). Además, la disminución de la PA se produjo en paralelo a un major equilibrio redox y una major biodisponibilidad de óxido nítrico en GPH y GH (P<0,05). Además, las variables que presentan mayor associación con la dismución de SBP fueron la concentración de lactate en sangre capilar y la fuerza muscular (P<0,05). En resumen, el entrenamiento de EEI puede ser práctico para mejorar el estado clínico de pacientes prehipertensivos e hipertensos, al mejorar el control de la PA, la biodisponibilidad de NO y el equilibrio redox. Se requieren más estudios para dilucidar las vías de concentración de lactate en el flujo sanguíneo durante el ejercicio.

Palabras-clave: Enjecimiento; Antioxidantes; Hemodinámica; Hipertensión; Contracción Isométrica.

1. Introduction

Isometric handgrip (IHG) training performed has shown effective results in controlling blood pressure (BP) in elderly people (Millar, Bray, MacDonald, & McCartney, 2008; Souza et al., 2018), mainly in prehypertensive and hypertensive subjects (Millar et al., 2008; Millar, McGowan, Cornelissen, Araujo, & Swaine, 2014; Peters et al., 2006; Taylor, McCartney, Kamth, & Wiley, 2003). Yet, the mechanisms involved in the BP control in hypertensive individuals submitted to IHG training still are inconclusive (Farah et al., 2017; Millar et al., 2014).

Until now, it has been suggested that changes in the autonomic function (Taylor et al., 2003) and oxidative stress (Peters et al., 2006) may be mechanisms involved in BP control in hypertensive adults and older after IHG training. Currently it was demonstrated that oxidative stress has a crucial role in the pathogenesis of hypertension (Baradaran, Nasri, & Rafieian-Kopaei, 2014). It is well known that exercise positively alters the redox status of cells and tissues, possibly due to increased antioxidant defenses and nitric oxide (NO-) (de Sousa et al., 2017). However, specifically for isometric exercise, it was demonstrated that after an acute IHG session leading to BP reduction in hypertensive elderly people, no association was observed with NO- (Souza et al., 2018).

On the other hand, muscle contractions can elicit the release of metabolic mediators with vasodilatory effects, such as increased partial pressure of carbon dioxide potassium, adenosine, and lactate concentrations (Sarelius & Pohl, 2010). Lactate is considered a residual product of metabolism, but today is recognized as a multifaceted molecule, serving as fuel for different cells, with neuroprotective action, hormonal action, anti-aging, metaboreceptor stimulant and vasodilator (Devereux, Coleman, Wiles, & Swaine, 2012; Proia, Di Liegro, Schiera, Fricano, & Di Liegro, 2016). It can act as an important dilator of vascular smooth muscle, however the increase in blood lactate concentration does not seem to influence muscle blood flow, making it difficult to understand its role as a mediator of hyperemia in exercise, as well as its global effect on hemodynamics after a period of training (Lott et al., 2001).

In four weeks of isometric training on isokinetic dynamometer in normotensive young men, significant changes in blood lactate concentration accumulation and reductions in resting systolic BP were observed, in addition to an inverse correlation between lactate concentration and BP changes (Devereux et al., 2012). However, we still do not know whether IHG training has the same effect in hypertensive or prehypertensive elderly people with or without medication, as well as the isolated and combined role of different muscle contraction metabolites, such as NO-, redox balance equivalents and lactate. The hypothesis of this study was that IHG training would contribute for reducing BP and that both lactate concentration and redox balance changes could be associated with this phenomenon.

2. Methods

The study methodology characterized of an exploratory research, semi experimental study. In relashoship of a nature this study caracterized of a quantitative. That Characterized conformed Pereira et al. (2018).

Participants

Thirty-three elderly people (aged 75.3 ± 1.3 years; Table 1) sedentary with less than 2 h·wk-1 of physical activity volunteered to participate in this study. Everybody lived in a long-stay care institution for elderly people and had a controlled routine with predetermined schedules for sleeping, waking, and feeding. Participants were classified in prehypertensive and hypertensive individuals according to the 7th Brazilian Guideline of Arterial Hypertension (Malachias, 2016).

Experimental design

The participants were allocated based on a nonrandomized controlled trial: (a) 11 hypertensive individuals in non-exercise control group (CG); (b) 10 prehypertensive group (PHG); and (c) 12 elderly people in the hypertensive group (HG). The hypertensive individuals (CG and HG) received antihypertensive medication and had been hypertensive for 8.7 ± 1.3 years. The PHG group did not use any type of drug. PHG and HG performed the IHG training, while non-exercise CG maintained its usual activities for the same period. Individuals with a systolic BP (SBP) > 160 mm Hg or diastolic BP (DBP) > 100 mm Hg, osteoarticular problems, compromised auditory acuity, diabetes, obesity, cardiac arrhythmias, end-organ injury, peripheral arterial disease, myocardial infarction, stroke, coronary heart disease, heart failure, or a recent history of smoking, drug, or alcohol abuse were excluded. The study consisted of four phases: (i) physical assessment, application of a medical questionnaire, cardiovascular and biochemical measurements; (ii) familiarization with isometric exercise; (iii) maximal voluntary isometric contraction (MVIC) test; (iv) 8-week IHG training on nonconsecutive days. Before participating in the research project, each subject signed a written informed consent form. All methods and procedures were approved by the Human Research Ethics Committee of Catholic University of Brasilia, Federal District, Brazil (1.269.917), and all procedures were conducted in accordance with the Declaration of Helsinki.

Outcome measures

Subjects did not perform any physical activity for at least 24 h before the evaluations and avoided caffeine. All data were collected in a long-stay care institution for elderly people, located in Brasilia, Brazil.

Anthropometry

Body mass and height were measured before and after training period, according to the World Health Organization guidelines (Chalmers et al., 1999). Body composition was determined using an adipometer Lange skinfold caliper (Beta Technology, Santa Cruz, CA, USA) using the Durnin and Womersley skinfolds protocol (Durnin & Womersley, 1974) and the Siri equation (Siri, 1961).

Hemodynamic measurement

The SBP, DBP and heart rate (HR) were measured in pre-training, during IHG and immediately after each session to ensure that it remained within safe limits (160/100 mm Hg) (Pickering et al., 2005), maintaining at least 10-min at rest in the seated position. The oscillometric method with validated equipment (Microlife®, 3A-BP 1PC, Switzerland) was used according to the recommendations of the American Heart Association (Pickering et al., 2005). Mean blood pressure (MBP) was calculated as Moraes et al. (Moraes et al., 2012). The double product (DP) was defined as the product of SBP (mmHg) and HR (bpm). Pulse pressure (PP) was calculated SBP - DBP.

Biochemical dosages

A volume of 5 mL venous blood (EDTA, BD Vacutainer®, IL, USA) sample was collected on resting pre and 48 hours after the last training session, at 06:00 AM, with 12 hours of fasting. After collection, venous blood samples were immediately processed in a refrigerated centrifuge to obtain blood plasma (4ºC for 15 minutes at 1500 rpm). All the biochemical analyses were performed at Molecular Biology of Exercise Laboratory of Catholic University of Brasilia.

Resting Blood lactate

The concentration of lactate (mmol · L-1) in the blood was determined in 25µl of capillary blood collected from the distal part of the thumb. Samples were deposited in a plastic tube (Eppendorf®, Berlin, Germany) with 50µl of 1% sodium fluoride, and stored at -80°C for further analysis on an electrochemical biochemical analyzer (YSI 2700 Select, Yellow Springs, OH, USA). The intraassay coefficient of variation was ≤ 10%.

Antioxidant parameter

Total antioxidant capacity (mM) was measured with a Trolox-equivalent assay kit (QuantiChrom® BioAssay Systems, CA, USA). The principle of the antioxidant assay is formation of a ferryl myoglobin radical from metmyoglobin and hydrogen peroxide, which oxides the ABTS (2,2’-azino-bis (3-ethilbenzthiazoline-6-sulfonic acid) to produce a radical cation, ABTS•+, a soluble chromogen that is green in color and was determined spectrophotometrically at 405 nm. The intraassay coefficient of variation was 20%.

Lipid peroxidation

The calorimetrical method for the test of lipoperoxidation by thiobarbituric acid reactive substances (TBARS; nmol.mL-1) was based in the reaction between the trichloroacetic acid (TCA) 17.5%, thiobarbituric acid (TBA) 0.6% and the plasma sample that form a rosy chromogen compound. After homogenization, the samples were kept in a water bath for 20 minutes at 95°C. The reaction was interrupted with the immersion of the microtubes in ice and the addition of TCA 70%, and another incubation for 20 minutes at room temperature. After centrifugation (3000 rpm for 15 minutes), the supernatant was removed and put in new microtubes and read by spectrophotometry at 534 nm. The concentration of lipid peroxidation products was calculated using the molar extinction coefficient equivalent for malondialdehyde (MDA-equivalent = 0,156 nmol · mL-1). The intraassay coefficient of variation was 7%.

Nitric oxide

NO- bioavailability was measured by plasma nitrite (NO2-; μM) according the description of the Griess Reagent System Kit (Promega Corporation, Madison, USA). One means to investigate NO- formation is to measure NO2-, which is one of two primary, stable and nonvolatile breakdown products of NO-. This assay relies on a diazotization reaction that was originally described by Griess (Griess, 1879). The absorbance was measured in a plate reader with 490 nm filter. The intraassay coefficient of variation was ≤ 10%.

Maximal voluntary isometric contraction

Participants completed 2 weeks of familiarization on handgrip exercise prior to the MVIC. A hydraulic handgrip dynamometer Jamar™® (Sammons Preston, IL, USA) was used to determine the isometric strength; three trials were performed on each hand, and the highest result was recorded (Crosby & Wehbé, 1994; Frederiksen et al., 2006). The positioning of the volunteers while performing the test followed the recommendation of the American Society of Hands Therapists (Fess, 1981). The MVIC test was held before, during (load adjustment every two weeks) and after the training period.

Isometric handgrip training

IHG training was performed during an 8-week period, three times a week on nonconsecutive days. The sessions were held in the afternoon between 02:00 and 05:00 PM. The volunteers underwent 24 sessions of IHG (Jamar™® Sammons Preston, IL, USA), completing a total of 8 sets of 1-minute contractions at 30% MVIC and 1-minute rest-pause, with 4 sets in each hand, alternately, based on the program described in a previous study (Souza et al., 2018). Volunteers were also instructed to avoid the Valsalva maneuver during the isometric exercise, following ACSM guidelines (Pescatello et al., 2004). The sessions

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were supervised by an exercise physiologist and four students of physical education that instructing the volunteers during the exercise.

Statistical analysis

The alpha adopted was 0.05 and the values were expressed as mean and standard error of the mean. Shapiro-Wilk and Levene tests were used to verify the normality and homoscedasticity of the data, respectively, only glucose, lactate, TBARS and Trolox present normality. To compare the hemodynamic response to eight weeks of IHT, we perform the area under the curve (AUC) from the 1st to the 8th week. After calculated, the AUC was compared using ordinary one-way ANOVA followed by Tuckey's post roc. To perform the multiple comparisons between groups over time (group vs. time) to Gaussian variables, it was used the Two-Way ANOVA, with post hoc Least Significant Difference (LSD). For the non-Gaussian variables, we applied the Kruskal-Wallis test followed by Dunn's multiple comparison. Pearson's correlation was used to verify the associations of the study. We performed a backward elimination stepwise multiple regression to determine if we could identify the sequence of variables that could explain blood pressure decrease (Δ NO, Δ lactate, Δ Trolox/TBARS ratio and Δ MVIC relative to lean mass and Δ body mass), at each step, the variable that is the least significant is removed. This process continues until no nonsignificant variables remain. These analyses were performed with the Statistical Package of Social Sciences (SPSS) version 20.0 (IBM Inc., Chicago, IL, USA), and GraphPad Prism 6.0 (GraphPad Software, CA, USA). The effect size considers the values for partial eta squared small (0.01 to 0.05), medium (0.06 to 0.13) and large (≥0.14) effect. The post-hoc power analysis was applied and a significance power > 0.95 was verified, considering an alpha error of 0.05, effect size 0.40 (high) and partial eta squared of 0.20. The sample power was calculated by the software G*Power 3.1.9.2. 9 (IL, USA).

3. Results

The general characteristics of the elderly people are presented in Table 1. There was no intercurrence during the sessions. All participants joined IHG training, completing an average of 88.8% [variance 75% to 95%] of the exercise sessions (~ 21 sessions) during the 8-week period. There was no statistical difference between the groups for the anthropometrics variables ($P > 0.05$). The mean values of hemodynamic variables (Table 1) found in pre-training were not statistically different between groups (*P* > 0.05), however, there was a decrease in PHG and HG group in relation to CG (*P* < 0.05).

Table 1. Anthropometric and hemodynamic variables of participants.

Variables	CG (n = 11)		PHG (n = 10)		HG (n = 12)	
Sex (male/female)	5 / 6		6 / 4		7 / 5	
Age (yrs)	77.7 ± 1.9		74.2 ± 3.2		74.1 ± 1.6	
Hypertension time (yrs)	7.4 ± 1.2		-----		9.5 ± 2.1	
Anthropometric measures						
	Pre	Post	Pre	Post	Pre	Post
Body mass (kg)	63.8 ± 3.9	65.1 ± 3.8	67.9 ± 3.8	69.3 ± 3.8	68.8 ± 3.3	69.3 ± 3.2
Body fat (%)	28.9 ± 2.7	30.9 ± 2.1 †	29.5 ± 2.3	29.9 ± 2.3	28.5 ± 2.9	28.3 ± 3.1
Fat mass (kg)	18.8 ± 2.3	20.4 ± 2.1 †	19.8 ± 1.8	20.6 ± 1.7	20.1 ± 2.4	20.0 ± 2.4
Lean mass (kg)	44.9 ± 2.6	44.7 ± 2.5	48.0 ± 3.3	48.7 ± 3.3	48.7 ± 2.4	49.3 ± 2.5
Hemodynamic measures						
	Pre	Post	Pre	Post	Pre	Post
SBP (mm Hg)	126 ± 5.3	133 ± 3.6	125 ± 2.9	115 ± 2.7 *,†	128 ± 5.4	112 ± 2.8 *,†
DBP (mm Hg)	75 ± 1.4	79 ± 2.2	75 ± 2.3	72 ± 2.0 *	77 ± 4.1	68 ± 2.0 *,†
MAP (mm Hg)	92 ± 7.7	97.1 ± 7.3	92 ± 5.0	86 ± 5.5 *,†	94 ± 14.2	82 ± 7.0 *,†
HR (bpm)	79 ± 1.9	83 ± 3.0 †	77 ± 2.4	72 ± 1.8 *,†	80 ± 3.1	71 ± 2.8 *,†
Number of medications (%)						
Adrenergic inhibitor	0		NA		3 (25%)	
ACE inhibitor	0		NA		3 (25%)	
ARB	9 (81.8%)		NA		2 (16.6%)	
Diuretics	1 (9.1%)		NA		0	
Combination	1 (9.1%)		NA		4 (33.3%)	

Date are presented as mean ± *SD*. CG, control group; PHG, prehypertensive group; HG, hypertensive group; SBP, systolic blood pressure; DBP, diastolic blood pressure; MAP, mean arterial pressure; HR, heart rate; ACE, angiotensin-converting-enzyme; ARB, type 1 angiotensin II receptor blockers; NA, not applicable; * *P* < 0.05 CG *vs*. PHG and/or HG (between group); † *P* < 0.05 (within group). *Source: Authors.*

Table 2 shows the values of the voluntary isometric contraction of both members of the studied groups. In addition, we can also see the basic values performed in three attempts. There was also no difference, in pre-training, between right and left handgrip strength (*P* > 0.05) (Table 2). Handgrip muscle strength was higher in post-training compared to pre-training in both trained groups, while the CG (non-exercise) decreased muscle strength after 8 weeks. The workload was adjusted every two weeks and increased significantly over baseline in both groups submitted to the IHG training ($P > 0.05$).

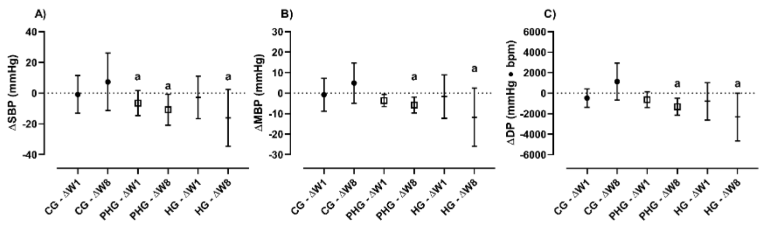
Table 2. Neuromuscular variables of participants.

Variables	CG (n = 11)	PHG (n = 10)	HG (n = 12)
MVIC relative (kgf • LM^{-1}) - pre R	0.47 ± 0,03	0.47 ± 0,03	0.44 ± 0,03
MVIC relative (kgf • LM^{-1}) - post R	0.42 ± 0.03 †	0.52 ± 0.04 *†	0.51 ± 0.03 †
MVIC relative (kgf • LM^{-1}) - pre L	0.43 ± 0.02	0.42 ± 0.03	0.43 ± 0.04
MVIC relative (kgf • LM^{-1}) - post L	0.38 ± 0.03 †	0.48 ± 0.03 *†	0.50 ± 0.03 *†
Workload (kgf • min)			
Baseline	NA	52.8 ± 4.6	51.0 ± 4.5
1st adjustment	NA	58.4 ± 4.9 ‡	55.3 ± 4.2 ‡
2nd adjustment	NA	60.0 ± 4.8 ‡	59.3 ± 4.3 ‡
3rd adjustment	NA	63.2 ± 4.5 ‡	62.3 ± 4.0 ‡

Date are presented as mean ± *SD*. CG, control group; PHG, prehypertensive group; HG, hypertensive group; MVIC, maximal voluntary isometric contraction; BM, body mass; BMI, body mass index; LM, lean mass; R, right hand; L, right hand. * $P < 0.05$ CG *vs*. PHG and/or HG (between group); † $P < 0.05$ (within group); ‡ $P < 0.05$ (within group *vs*. baseline). *Source: Authors.*

Figure 1 displayed the values of hemodynamic variables deltas: delta systolic blood pressure (ΔSBP) delta mean blood pressure (ΔMBP) and delta double product (ΔDP). The groups studied at week 1(pre) and week 8(post) over the intervention period. According to the results found both PHG and HG groups presented a decrease in SBP, MBP and DP based on the delta for the IHT period ($P < 0.05$) (Figure 1).

Figure 1. Delta of systolic blood pressure (ΔSBP) Δ mean blood pressure (ΔMBP) and Δ double product (ΔDP)



ΔW1: delta of the 1st week (1st week – baseline); ΔW8 delta of the 8th week (8th week – baseline); CG: control group; PHG: prehypertensive group; HG: hypertensive group. a $p < 0.05$ *vs* CG – ΔW8. *Source: Authors*.

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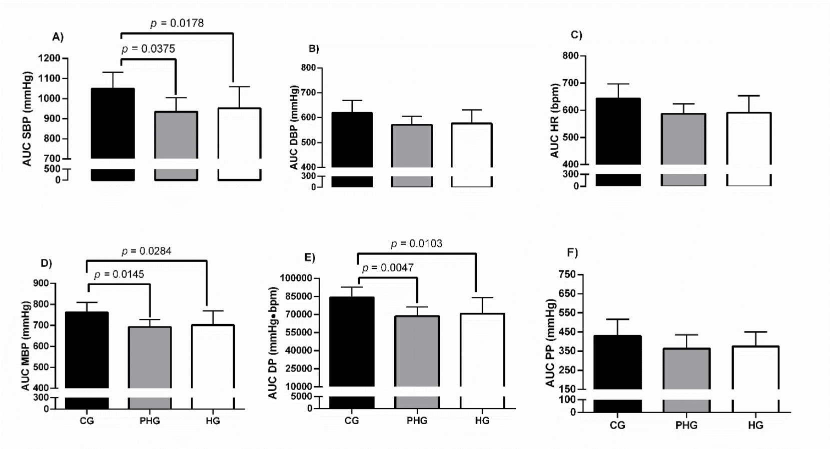
We can see that, in Figure 2, the values of the AUC of the variables are presented for the systolic blood pressure (SBP) (A), diastolic blood pressure (DBP) (B) and heart rate (HR) (C), mean blood pressure (MBP) , double product (DP), pulse pressure (PP) after 8 weeks of IHG Furthermore, the decrease of SBP, MBP and DP between week one and week eight was higher in both training groups described as deltas in Figure 2.

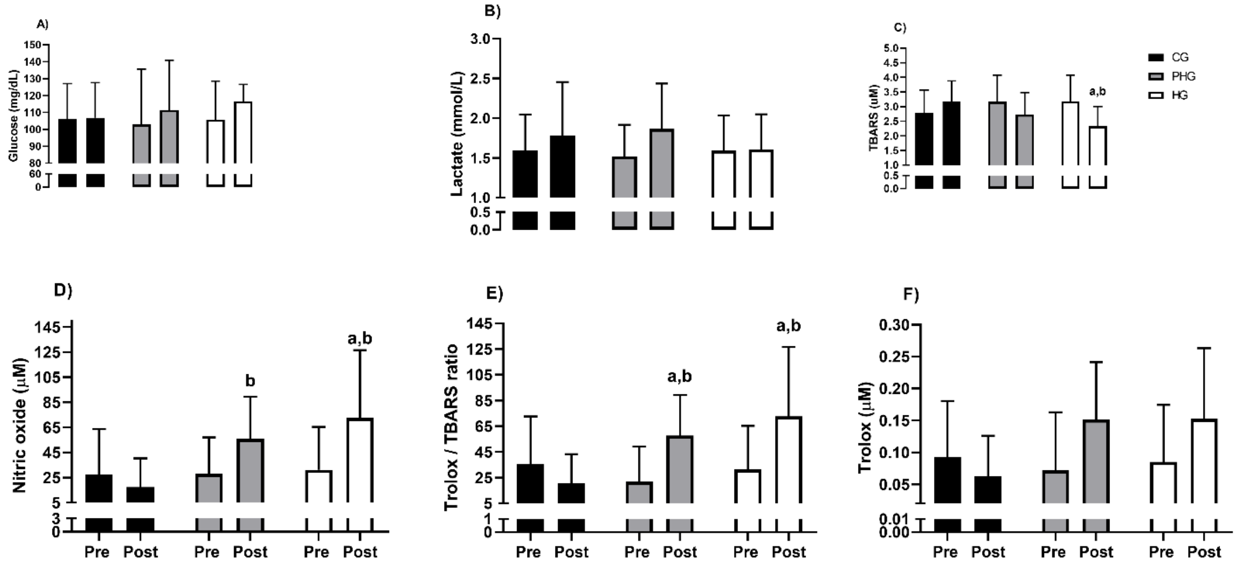
Figure 2. Area under the curve of SBP, DBP, MBP, DP e PP.



Area under the curve of Systolic blood pressure (SBP) (A), diastolic blood pressure (DBP) (B) and heart rate (HR) (C), mean blood pressure (MBP) , double product (DP), pulse pressure (PP) after 8 weeks of IHG. Data are presented as means ± SD. CG: control group; PHG: pre-hypertensive group; HG: hypertensive group. *Source: Authors.*

Figure 3 presents the values of the Glucose (A), lactate (B), TBARS (C), Nitric oxide (D), Trolox/TBARS ratio (E) and Trolox (F) pre- and post- intervention for 8 weeks. The mean values of the biochemical parameters found in pre-training were similar between groups ($P > 0.05$). It was observed a decrease in TBARS in relation to pre-training and CG. Higher values of nitric oxide were found in PHG and HG in relation to pre-training.However, only HG presented an increase of nitric oxide in relation to baseline ($P < 0.05$). Also, both training groups increased Trolox/TBARS ratio in relation to baseline and CG ($P < 0.05$) (Figure 3). There was no change in Trolox throughout the study ($P > 0.05$).

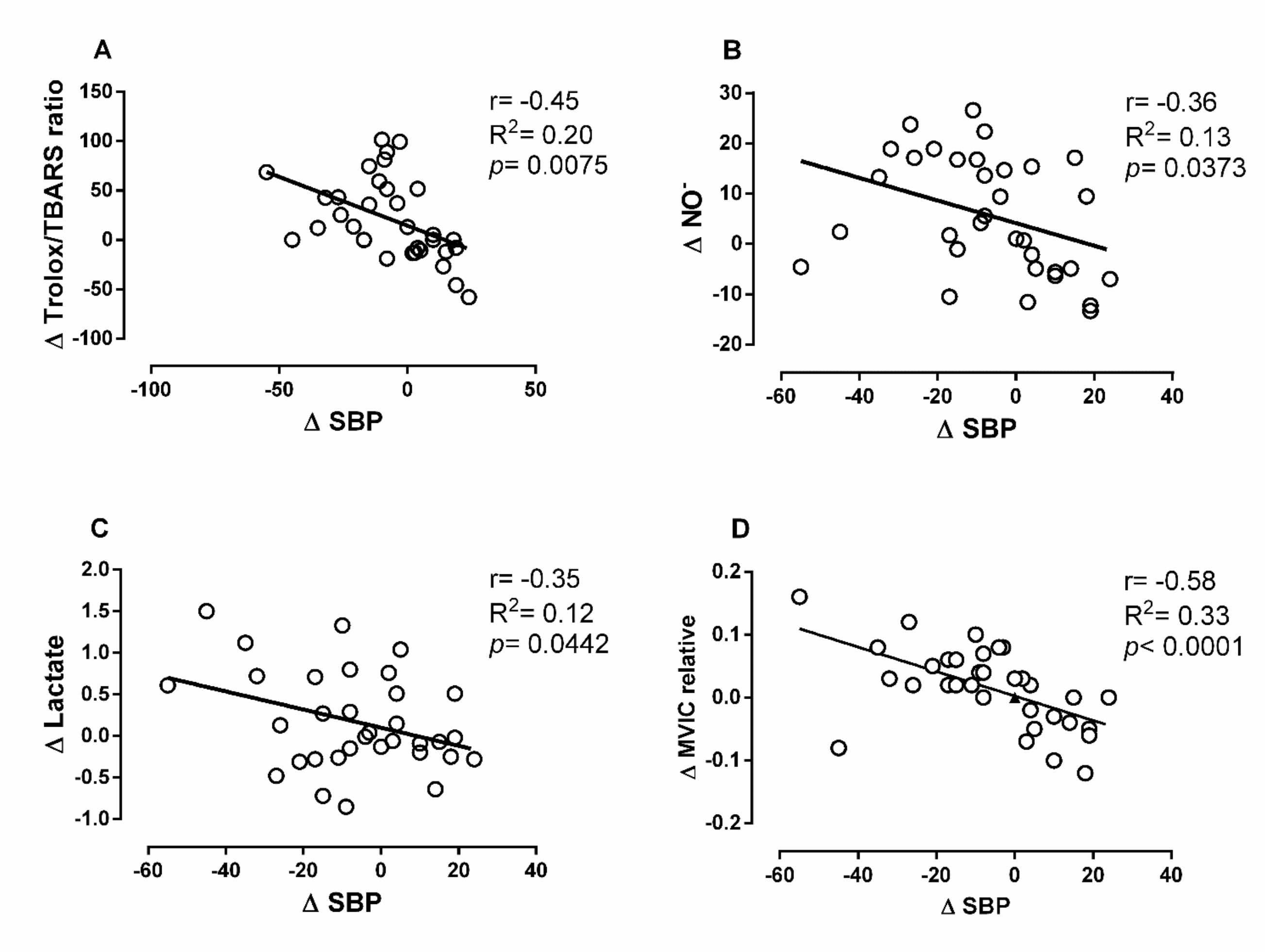
Figure 3. Glucose, TBARS, NO, Trolox/TBARS, Trolox



Glucose (A), lactate (B), TBARS (C), Nitric oxide (D), Trolox/TBARS ratio (E) and Trolox (F) pre- and post-IHG. Data are presented as means ± SD. TBARS: thiobarbituric reactive species; CG: control group, PHG: prehypertensive group, HG: hypertensive group. a $p < 0.05$ vs. pre-training (within group); b $p < 0.05$ vs. CG (between group), c $p < 0.05$ *vs* pre - PHG . *Source: Authors.*

We analyzed a correlation of Δ SBP with the Δ Trolox/TBARS ratio (A), Δ nitric oxide (B) , Δ lactate (C) and Δ MVIC relative as show in figure 4. There were significant associations between the Δ SBP with the Δ Trolox/TBARS ratio ($P = 0.0075$), Δ NO- ($P = 0.0373$), Δ lactate ($P = 0.0442$) Δ MVIC ($P < 0.0001$). Data presented in Figure 4.

Figure 4. Correlation of Δ SBP with the Δ Trolox/TBARS ratio (A), Δ nitric oxide (B) , Δ lactate (C) and Δ MVIC relative



Δ SBP with the Δ Trolox/TBARS ratio (A), Δ nitric oxide (B), Δ lactate (C) and Δ MVIC relative. TBARS: thiobarbituric reactive species, MVIC: maximum voluntary isometric contraction. *Source: Authors.*

Was applied an analysis of backward elimination stepwise multiple regression with Δ lactate, Δ Trolox / TBARS ratio, Δ MVIC relative (kgf • LM-1) Δ nitric oxide and Δ body mass using Δ SBP as dependent variable. As observed in Table 3, the variables presenting significant associations with the decrease in BP were lactate and muscle strength ($P < 0.05$).

Table 3- Backward elimination stepwise multiple regression using Δ SBP as dependent variable.

In	Variable	Standard Coefficient	Standard error	T-value	*p*-value
Yes	**Δ Lactate**	-10.48	4.60	-2.28	**0.03**
Yes	**Δ Trolox/TBARS ratio**	-0.10	0.09	-1.16	0.25
Yes	**Δ MVIC relative (kgf • LM^{-1})**	-120.72	53.62	-2.25	**0.03**
Yes	**Δ Nitric oxide**	-0.07	0.28	-0.25	0.80
Yes	**Δ Body mass**	0.12	1.08	0.11	0.91
R^2-multiple = 0.6808 / R^2 = 0.4636 / R^2- adjusted = 0.3642					
Body mass eliminated					
Yes	**Δ Lactate**	-10.47	4.52	-2.32	**0.03**
Yes	**Δ Trolox/TBARS ratio**	-0.10	0.08	-1.24	0.23
Yes	**Δ MVIC relative (kgf • LM^{-1})**	-120.40	52.60	-2.29	**0.03**
Yes	**Δ Nitric oxide**	-0.07	0.27	-0.24	0.81
No	Δ Body mass	-	-	-	-
R^2-multiple = 0.6807 / R^2 = 0.4633 / R^2- adjusted = 0.3867					
Nitric oxide eliminated					
Yes	**Δ Lactate**	-10.50	4.44	-2.36	**0.03**
Yes	**Δ Trolox/TBARS ratio**	-0.11	0.08	-1.40	0.17
Yes	**Δ MVIC relative (kgf • LM^{-1})**	-124.11	49.43	-2.51	**0.02**
No	Δ Nitric oxide	-	-	-	-
No	Δ Body mass	-	-	-	-
R^2-multiple = 0.6799 / R^2 = 0.4622 / R^2- adjusted = 0.4066					
Trolox/TBARS ratio eliminated					
Yes	**Δ Lactate**	-9.84	4.49	-2.19	0.04
No	Δ Trolox/TBARS ratio	-	-	-	-
Yes	**Δ MVIC relative (kgf • LM^{-1})**	-163.68	41.24	-3.97	0.00
No	Δ Nitric oxide	-	-	-	-
No	Δ Body mass	-	-	-	-
R^2-multiple = 0.6525 / R^2 = 0.4258 / R^2- adjusted = 0.3875					

MVIC: maximal voluntary isometric contraction. *Source: Authors.*

4. Discussion and Final Considerations

The current findings support the potential effect of IHG training as a non-pharmacological strategy to improve hemodynamics in prehypertensive and hypertensive subjects. In parallel, IHG training promoted an increase in plasmatic NO- and improve redox balance. Also, among the number of variants that could promote BP decrease, lactate concentration and muscle strength seem to most explain this phenomenon.

Clearly, muscle-derived metabolites are formed during exercise, some of them, usually have potential vasodilatation signaling which contributes to exercise hyperemia (Sarelius & Pohl, 2010). Due to the difficult in quantitate the respective contribution of each metabolite in vasodilatation, some studies debate which substances are involved in the regulation of human blood-flow (Mortensen & Saltin, 2014; Nawab et al., 1984; Saltin, Rådegran, Koskolou, & Roach, 1998). Among a number of vasoactive substances, we highlight lactate as an important mediator of vasodilatation (Nawab et al., 1984). It is suggested that lactate stimulate NO synthase and subsequent activation of guanylyl cyclase which will trigger the opening of ATP-sensitive potassium channels of vasodilation (Hein, Xu, & Kuo, 2006). In this regard, the present study adds information regarding the role of lactate in blood flow stimulated by IHG training, which is the variable that most explain BP decrease in both prehypertensive and hypertensive patients. Moreover, Devereux et al (Devereux et al., 2012), suggests that higher levels of anaerobiosis may promote the training-induced reduction in BP which might be linked to increased lactate.

Isometric muscle contraction induces ischemia-reperfusion in the adjacent region (Gaffney, Sjøgaard, & Saltin, 1990), which promotes an increase in the production of free radicals. It is important to induce intracellular adaptations in the antioxidant defense. This can be observed in the work of Peters et al (Peters et al., 2006) in which they demonstrated that the IHG at 50% of MVIC reducing the production of free radicals after 6 weeks of training. Similar results were found in the present study, however we applied IHG training at 30% of MVIC, demonstrated that even in lower intensities, IHG training can induce systemic and molecular benefits.

It is well known that IHG training reduces BP in hypertensive subjects (Gaffney et al., 1990; Millar et al., 2008; Millar et al., 2014; Peters et al., 2006; Taylor et al., 2003). However, the mechanisms involved in this decrease are not fully elucidated. In this study it was verified that the IHG training in moderate intensity was able to increase antioxidant defense in older prehypertensive and hypertensive patients. Therefore, these results indicate that the BP reduction after eight weeks IHG was partly mediated by the improvement of redox balance, resulting in the increase of the NO- bioavailability, possibly decreasing the total peripheral resistance. Some limitations of study need to be mentioned: i) The heart rate variability has not been evaluated, and it was not possible to use ambulatory BP measurements; however, BP was measured three time a week on nonconsecutive days (the weekly average was used)

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during IHG training, keeping the same time and place of the long-term care institution for elderly people; ii) This study was not a randomized controlled trial. Therefore, its external validity is limited to this population "prehypertensive and hypertensive elderly people institutionalized". Furthermore, it was not possible to constitute non-exercise prehypertensive control group (a considerable number of volunteers was excluded at the beginning of the project because they were not able to perform the handgrip test due to osteomyoarticular problems in the hands); iii) The sample size limited the analysis of gender influence, of medications use and race in the magnitude of BP reduction. Finally, considering that hypertension is a chronic disease and needs continuous lifelong treatment, it is important to ratify that the long-term effects (> 10 weeks) as well as the adjustment of the volume vs. intensity during IHG training about BP control in hypertensive elderly people are still unknown.

This study provided important insights of the possible molecular variables that could be associated to BP control. Furthermore, demonstrating IHG training as relevant clinical application due to its potential benefits in BP control, NO- metabolism and redox balance. In this sense, hospitals or clinics would not need to bought strength training machines or weights that could be expensive and take up a lot of place, just with one handgrip dynamometer, prehypertensive and hypertensive patients would be beneficiated by a simple training protocol, which could be applied in any place and any time.

In summary, we conclude that IHG training may be practical in improving clinical status of prehypertensive and hypertensive patients, by improving BP control, NO-bioavailability and redox balance. Further studies are required to elucidate the pathways of lactate concentration in blood-flow during exercise.

In suggestion for future researchs we believe that other type of exercise or training models can also be another prospect for new studies. We must emphasize that both dynamic strength, aerobic and combined training have already found quite positive effects in relation to hemodynamic aspects in hypertensive patients (Schroeder et al., 2019; Sabbahi et al.,2016; Ferrari et al.,2017). Based on this assumption, the use of different types of exercises can be somewhat effective in the metabolic parameters such as the lactate level. Another question is also the intensity of the exercise for hypertensive people, which is also already described in the literature as an extremely important factor in the responses of the physical exercise (Boutcher & Boutcher, 2017). Other hemodynamic assessments such as heart rate variability, the use of echocardiography may be relevant aspects for new studies on the influence of the protocol used in our study its perpetuations. However, further studies are needed to assess the effects of physical exercise on hemodynamic and metabolic aspect and pre-hypertensive and hypertensive individuals, especially in terms of blood lactate values.

Conflicts of interest

No potential conflict of interest relevant to this article was reported.

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References

Baradaran, A., Nasri, H., & Rafieian-Kopaei, M. (2014). Oxidative stress and hypertension: Possibility of hypertension therapy with antioxidants. *Journal of research in medical sciences: the official journal of Isfahan University of Medical Sciences, 19*(4), 358.

Boutcher, Y. N., & Boutcher, S. H. (2017). Exercise intensity and hypertension: what's new?. *Journal of human hypertension, 31*(3), 157-164.

Chalmers, J., MacMahon, S., Mancia, G., Whitworth, J., Beilin, L., Hansson, L., . . . Clark, T. (1999). 1999 World Health Organization-International Society of Hypertension Guidelines for the management of hypertension. Guidelines sub-committee of the World Health Organization. *Clinical and experimental hypertension (New York, NY: 1993), 21*(5-6), 1009-1060.

Crosby, C. A., & Wehbé, M. A. (1994). Hand strength: normative values. *The Journal of hand surgery, 19*(4), 665-670.

de Sousa, C. V., Sales, M. M., Rosa, T. S., Lewis, J. E., de Andrade, R. V., & Simoes, H. G. (2017). The antioxidant effect of exercise: a systematic review and meta-analysis. *Sports Medicine, 47*(2), 277-293.

Devereux, G. R., Coleman, D., Wiles, J. D., & Swaine, I. (2012). Lactate accumulation following isometric exercise training and its relationship with reduced resting blood pressure. *Journal of sports sciences, 30*(11), 1141-1148.

Durnin, J. V., & Womersley, J. (1974). Body fat assessed from total body density and its estimation from skinfold thickness: measurements on 481 men and women aged from 16 to 72 years. *British journal of nutrition*, *32*(1), 77-97.

Farah, B. Q., Germano-Soares, A. H., Rodrigues, S. L. C., Santos, C. X., Barbosa, S. S., Vianna, L. C., . . . Ritti-Dias, R. M. (2017). Acute and chronic effects of isometric handgrip exercise on cardiovascular variables in hypertensive patients: a systematic review. *Sports, 5*(3), 55.

Fess, E. (1981). Clinical assessment recommendations. *American society of hand therapists*, 6-8.

Ferrari, R., Umpierre, D., Vogel, G., Vieira, P. J., Santos, L. P., de Mello, R. B., ... & Fuchs, S. C. (2017). Effects of concurrent and aerobic exercises on postexercise hypotension in elderly hypertensive men. *Experimental gerontology, 98*, 1-7.

Frederiksen, H., Hjelmborg, J., Mortensen, J., Mcgue, M., Vaupel, J. W., & Christensen, K. (2006). Age trajectories of grip strength: cross-sectional and longitudinal data among 8,342 Danes aged 46 to 102. *Annals of epidemiology, 16*(7), 554-562.

Gaffney, F., Sjøgaard, G., & Saltin, B. (1990). Cardiovascular and metabolic responses to static contraction in man. *Acta physiologica Scandinavica*, *138*(3), 249-258.

Griess, P. (1879). Bemerkungen zu der Abhandlung der HH. Weselsky und Benedikt „Ueber einige Azoverbindungen" . *Berichte der deutschen chemischen Gesellschaft, 12*(1), 426-428.

Hein, T. W., Xu, W., & Kuo, L. (2006). Dilation of retinal arterioles in response to lactate: role of nitric oxide, guanylyl cyclase, and ATP-sensitive potassium channels. *Investigative ophthalmology & visual science*, *47*(2), 693-699.

Lott, M. E., Hogeman, C. S., Vickery, L., Kunselman, A. R., Sinoway, L. I., & MacLean, D. A. (2001). Effects of dynamic exercise on mean blood velocity and muscle interstitial metabolite responses in humans. *American Journal of Physiology-Heart and Circulatory Physiology*, *281*(4), H1734-H1741.

Malachias, M. V. B. (2016). 7th Brazilian guideline of arterial hypertension: presentation. *Arquivos brasileiros de cardiologia*, *107*(3), XV-XIX.

Millar, P. J., Bray, S. R., MacDonald, M. J., & McCartney, N. (2008). The hypotensive effects of isometric handgrip training using an inexpensive spring handgrip training device. *Journal of Cardiopulmonary Rehabilitation and Prevention*, *28*(3), 203-207.

Millar, P. J., McGowan, C. L., Cornelissen, V. A., Araujo, C. G., & Swaine, I. L. (2014). Evidence for the role of isometric exercise training in reducing blood pressure: potential mechanisms and future directions. *Sports Medicine*, *44*(3), 345-356.

Moraes, M. R. d., Bacurau, R. F. P., Simões, H. G., Campbell, C. S. G., Pudo, M. A., Wasinski, F., . . . Araujo, R. C. (2012). Effect of 12 weeks of resistance exercise on post-exercise hypotension in stage 1 hypertensive individuals. *Journal of human hypertension*, *26*(9), 533-539.

Mortensen, S. P., & Saltin, B. (2014). Regulation of the skeletal muscle blood flow in humans. *Experimental physiology*, *99*(12), 1552-1558.

Nawab, Z., Daugirdas, J., Ing, T., Leehey, D., Reid, R., & Klok, M. (1984). Calcium-complexing versus vasorelaxant effect of acetate, lactate, and other bases. *Transactions-American Society for Artificial Internal Organs*, *30*, 184-188.

Pereira A.S. et al. (2018). *Metodologia da pesquisa científica*. [*e-book*]. Santa Maria. Ed. UAB/NTE/UFSM. Disponível em: https://repositorio.ufsm.br/bitstream/handle/1/15824/Lic_Computacao_Metodologia-Pesquisa-Cientifica.pdf?sequence=1.

Pescatello, L. S., Franklin, B. A., Fagard, R., Farquhar, W. B., Kelley, G. A., & Ray, C. A. (2004). Exercise and hypertension. *Medicine & science in sports & exercise*, *36*(3), 533-553.

Peters, P. G., Alessio, H. M., Hagerman, A. E., Ashton, T., Nagy, S., & Wiley, R. L. (2006). Short-term isometric exercise reduces systolic blood pressure in hypertensive adults: possible role of reactive oxygen species. *International journal of cardiology*, *110*(2), 199-205.

Pickering, T. G., Hall, J. E., Appel, L. J., Falkner, B. E., Graves, J., Hill, M. N., . . . Roccella, E. J. (2005). Recommendations for blood pressure measurement in humans and experimental animals: part 1: blood pressure measurement in humans: a statement for professionals from the Subcommittee of Professional and Public Education of the American Heart Association Council on High Blood Pressure Research. *Hypertension*, *45*(1), 142-161.

Proia, P., Di Liegro, C. M., Schiera, G., Fricano, A., & Di Liegro, I. (2016). Lactate as a Metabolite and a Regulator in the Central Nervous System. *International journal of molecular sciences*, *17*(9), 1450.

Sabbahi, A., Arena, R., Elokda, A., & Phillips, S. A. (2016). Exercise and hypertension: uncovering the mechanisms of vascular control. *Progress in Cardiovascular Diseases*, *59*(3), 226-234.

Saltin, B., Rådegran, G., Koskolou, M., & Roach, R. (1998). Skeletal muscle blood flow in humans and its regulation during exercise. *Acta physiologica Scandinavica*, *162*(3), 421-436.

Sarelius, I., & Pohl, U. (2010). Control of muscle blood flow during exercise: local factors and integrative mechanisms. *Acta Physiologica*, *199*(4), 349-365.

Siri, W. E. (1961). Body composition from fluid spaces and density: analysis of methods. *Techniques for measuring body composition*, *61*, 223-244.

Souza, L. R., Vicente, J. B., Melo, G. R., Moraes, V. C., Olher, R. R., Sousa, I. C., . . . Ferreira, A. P. (2018). Acute hypotension after moderate-intensity handgrip exercise in hypertensive elderly people. *The Journal of Strength & Conditioning Research*, *32*(10), 2971-2977.

Schroeder, E. C., Franke, W. D., Sharp, R. L., & Lee, D. C. (2019). Comparative effectiveness of aerobic, resistance, and combined training on cardiovascular disease risk factors: a randomized controlled trial. *PloS one*, *14*(1), e0210292.

Taylor, A. C., McCartney, N., Kamath, M. V., & Wiley, R. L. (2003). Isometric training lowers resting blood pressure and modulates autonomic control. *Medicine & science in sports & exercise*, *35*(2), 251-256.

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