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Original Article

Effects of elastic-band power training interspersed with aerobic exercise on hemodynamic parameters and lower-limb function in older adults

Efectos del entrenamiento de fuerza con bandas elásticas intercalado con ejercicio aeróbico sobre los parámetros hemodinámicos y el funcionamiento de las extremidades inferiores en adultos mayores

Efeitos do treinamento de força com bandas elásticas, intercalado com exercício aeróbico, sobre os parâmetros hemodinâmicos e o funcionamento dos membros inferiores em pessoas idosas

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Author Contributions

LTG, LFCC, TMSS, SSS, CSR, ARMS, LPCC, PAS, and BBG contributed to the conceptualization and methodology. PAS, and BBG contributed to the formal analysis. LTG, LFCC, TMSS, SSS, CSR, ARMS, LPCC, and BBG performed the investigation. BBG performed supervision and project administration. LTG, LFCC, TMSS, SSS, CSR, ARMS, LPCC, PAS, and BBG contributed to original draft. BBG performed writing - review & amp; editing.

ABSTRACT

Introduction. In 2022, ischemic heart disease, stroke, and chronic obstructive pulmonary disease were the primary causes of death globally. Although there is evidence of exercise in reducing blood pressure in older adults, there is still no consensus on the benefits of concurrent training on hemodynamic parameters in this population. This study aimed to investigate the effects of elastic-band power training interspersed with aerobic exercise on hemodynamic parameters (HP) and the lower-limb function in older adults. **Methodology.** Twenty-four participants were randomly assigned to the control group (CG; n=12) and the intervention group (IG; n=12). IG participants performed power exercises with elastic bands interspersed with aerobic exercise twice a week for 8 weeks. HP were measured with an automatic, noninvasive, calibrated, and validated arterial blood pressure monitor. Lower limb functional capacity was assessed through the test of lifting and sitting down 5 times or as quickly as possible. Statistical analysis was performed using Prism software. **Results.** No changes in HP ($P>0.05$) were observed after the 8 weeks, whereas the lower limb functional capacity improved after the intervention ($P<0.05$). **Discussion.** One hypothesis to explain our findings is the baseline blood pressure levels. The participants in this research do not present high baseline values. On the other hand, studies have shown the benefits of exercise in PH of older adults with high blood pressure. **Conclusions.** These findings indicate that power exercises interspersed with aerobic exercise improve only the lower limb functional capacity of older adults' lower limbs. Although no significant differences were found in PH, it is important to highlight the important clinical reduction in systolic blood pressure ($\Delta = -6.0$ mmHg), with the consequent reduction in the risk of cardiovascular mortality in the sample investigated.

Keywords:

Aged; Resistance Training; Exercise Therapy; Hemodynamics; Motor Activity; Exercise; Blood Pressure; Physical Function.

RESUMEN

Introducción. En 2022, la cardiopatía isquémica, los accidentes cerebrovasculares y la enfermedad pulmonar obstructiva crónica constituyeron las principales causas de muerte a nivel mundial. Aunque hay evidencia de que el ejercicio reduce la presión arterial en los adultos mayores, todavía no hay consenso sobre los beneficios del entrenamiento simultáneo en los parámetros hemodinámicos de esta población. El objetivo de este estudio fue investigar los efectos del entrenamiento de fuerza con bandas elásticas intercalado con ejercicio aeróbico sobre los parámetros hemodinámicos (HP) y el funcionamiento de las extremidades inferiores en adultos mayores. **Metodología.** Se asignó aleatoriamente a veinticuatro participantes al grupo de control (CG; n = 12) y al grupo de intervención (IG; n = 12). Los participantes del IG realizaron ejercicios de fuerza con bandas elásticas intercalados con ejercicios aeróbicos dos veces por semana durante 8 semanas. Los HP se midieron con un monitor de presión arterial automático, no invasivo, calibrado y validado. La capacidad funcional de las extremidades inferiores se evaluó mediante una prueba que consistía en levantarse y sentarse 5 veces o tan rápido como fuera posible. El análisis estadístico se realizó con el software Prism. **Resultados.** No se observaron cambios en los HP ($P>0.05$) luego de 8 semanas, mientras que la capacidad funcional de las extremidades inferiores mejoró tras la intervención ($P<0.05$). **Discusión.** Una hipótesis para explicar nuestros hallazgos son los valores de referencia de la presión arterial. Los participantes en esta investigación no presentan valores de referencia elevados. Por otro lado, los estudios han demostrado los beneficios del ejercicio en los HP de los adultos mayores con hipertensión arterial. **Conclusiones.** Estos hallazgos indican que los ejercicios de fuerza intercalados con ejercicios aeróbicos solo mejoran la capacidad funcional de las extremidades inferiores de los adultos mayores. Aunque no se encontraron diferencias significativas en los HP, es importante destacar la importante reducción clínica de la presión arterial sistólica ($\Delta = -6.0$ mmHg), con la consiguiente reducción del riesgo de mortalidad cardiovascular en la muestra investigada.

Palabras clave:

Anciano; Entrenamiento de Resistencia; Terapia por Ejercicio; Hemodinámica; Actividad Motora; Ejercicio; Presión Arterial; Función Física.

RESUMO

Introdução. Em 2022, a cardiopatia isquêmica, os acidentes vasculares cerebrais (AVC) e a doença pulmonar obstrutiva crônica foram as principais causas de morte em todo o mundo. Embora existam evidências de que o exercício reduz a pressão arterial em idosos, ainda não há consenso sobre os benefícios do treinamento simultâneo nos parâmetros hemodinâmicos dessa população. O objetivo deste estudo foi investigar os efeitos do treinamento de força com bandas elásticas, intercalado com exercício aeróbico, sobre os parâmetros hemodinâmicos (HP) e o funcionamento dos membros inferiores em pessoas idosas. **Metodologia.** Vinte e quatro participantes foram aleatoriamente distribuídos para o grupo controle (GC; n = 12) e o grupo intervenção (GI; n = 12). Os participantes do GI realizaram exercícios de força com bandas elásticas, intercalados com exercícios aeróbicos, duas vezes por semana durante 8 semanas. Os parâmetros hemodinâmicos (PH) foram medidos com um monitor automático de pressão arterial, não invasivo, calibrado e validado. A capacidade funcional dos membros inferiores foi avaliada por um teste que consistia em levantar-se e sentar-se cinco vezes o mais rápido possível. A análise estatística foi realizada utilizando o software Prism. **Resultados.** Não foram observadas alterações nos parâmetros hemodinâmicos ($P > 0.05$) após 8 semanas, enquanto a capacidade funcional dos membros inferiores melhorou após a intervenção ($P < 0.05$). **Discussão.** Uma hipótese para explicar nossos achados são os valores de referência da pressão arterial. Os participantes desta pesquisa não apresentaram valores de referência elevados. Além disso, estudos têm demonstrado os benefícios do exercício sobre os parâmetros hemodinâmicos em pessoas idosas com hipertensão arterial. **Conclusões.** Esses achados indicam que os exercícios de força combinados com exercícios aeróbicos melhoram apenas a capacidade funcional dos membros inferiores de pessoas idosas. Embora não tenham sido encontradas diferenças significativas nos parâmetros hemodinâmicos, é importante destacar a redução clinicamente significativa da pressão arterial sistólica ($\Delta = -6.0$ mmHg), com consequente diminuição do risco de mortalidade cardiovascular na amostra estudada

Palavras-chave:

Idoso; Treinamento Resistido; Terapia por Exercício; Hemodinâmica; Atividade Motora; Exercício; Pressão Arterial; Função Física.

Introduction

Aging is a natural process, with structural losses (reduction in the size and number of type II fibers, increase in body fat, loss of elasticity, and increase in arterial stiffness) followed by functional impairments (loss of muscle strength, decreased ability to carry out daily activities, increased blood pressure), consequently increasing the risk of cardiovascular death (1-5). It is estimated that the number of older adults (60–79 years) with hypertension will increase from roughly 494 million in 2015 to 1.07 billion in 2050 (6). Additionally, in the state of Maranhão, Brazil, a worrying prevalence of individuals with high blood pressure was found, with an expressive number of females (7). The percentage of hospitalizations in the state of Maranhão (Brazil) due to hypertension between 2014 and 2024 was 14.1% for individuals aged 80 or over, 20.2% for individuals aged between 70 and 79 years, and 21.8% for older adults aged between 60 and 69 years (7).

A body of evidence demonstrated the benefits of exercise training on cardiovascular and functional parameters in older adults (8-15). Studies have found positive effects of resistance training and endurance training on older adults' blood pressure (BP), maximal cycling power output, and peak oxygen uptake, physical function biomarkers, functioning, physical fitness, muscle morphology and metabolic parameters (8-15).

Hence, such findings recommend concurrent training (resistance training associated with endurance training to improve older people's health parameters (16). In addition to CT, Izquierdo et al. (16) also recommends power training for optimal aging and maintenance of functional capacities. Other studies likewise demonstrate the benefits of concurrent training involving power training with endurance training on older people's cardiovascular and functional variables (8-11,13-15,17). Additionally, improvements in hemodynamic parameters in older adults were demonstrated after short periods of concurrent training (8,9).

Nevertheless the benefits demonstrated and there are recommendations for RT (frequency ≥ 2 to 3 days/week, low-moderate intensity, 2 to 4 sets of 8 to 12 repetitions) and endurance training (frequency ≥ 5 days/week, moderate intensity, ≥ 30 minutes/day of continuous or cumulative physical exercise) for older adults with hypertension (18), little is known about elastic-band power training interspersed with aerobic exercise on hemodynamic parameters in this population.

Thus, this research aimed to investigate the effects of elastic-band power training interspersed with aerobic exercise on hemodynamic parameters and lower-limb function in older adults.

Methodology

Experimental design

This interventional controlled randomized trial was conducted upon approval by the Ethics Committee at CEUMA University (Sao Luis, MA, Brazil). All participants signed an informed consent form after learning about the study approach and procedures they would undergo and the potential risks and benefits. The study was conducted following the Helsinki Declaration of 1975.

Participants

Sample size calculation was performed using G*Power software (Heinrich-Heine-Universität Düsseldorf, Düsseldorf, Germany, release 3.1.9.4, 2019) before conducting further statistical analyses. Based on input parameters of effect size (large) (8), $\alpha = 0.05$, power = 0.95, and recommendations by Beck (19), a total of 12 participants per group were calculated to assess the effects of elastic-band PT interspersed with aerobic exercise on hemodynamic parameters and lower-limb function in older adults. To account for possible dropouts, 13 participants per group were selected.

Inclusion criteria consisted of being 60 years old or above, able to walk with or without assistance, performing basic daily activities, and not having engaged in regular exercise training for the past 6 months. Exclusion criteria included experiencing disabling pain during exercise, inability to perform exercise sessions, and inability to participate in evaluations.

Twenty-six older adults were recruited by publicizing the project through digital media (e.g., Instagram). The inclusion criteria will be applied after recruitment. The 26 selected older adults were randomized with a computer-generated list of random numbers, and allocation concealment was ensured using opaque and sequentially numbered sealed envelopes. They were randomly assigned to the control group (CG) (n = 13) and the intervention group (IG) (n = 13).

Procedures

All assessments (hemodynamic parameters, and function of the lower limbs) were performed before and after 8 weeks of training by the same experienced exercise physiologists using identical procedures. Experiments were performed in a quiet air-conditioned room (22 to 24°C) always in the mornings (08:00 to 10:00 AM) in the Laboratory of Assessment and Physiology of Ceuma University, in four distinct phases.

During the initial phase (familiarization, 2 weeks), participants underwent an orientation period to familiarize

themselves with the assessments and proper exercise techniques. In the second phase (2 weeks), experienced exercise physiologists administered the initial assessments. In the third phase (8 weeks), experienced exercise physiologists assisted with the protocol. Finally, in phase four (2 weeks), experienced exercise physiologists administered the final assessments.

Assessments

Anthropometric

The participants' total body mass in kilograms (kg) and height in centimeters (cm) were measured with a properly calibrated (NBR ISO/IEC 17025:2005) anthropometric scale (PL-200, Filizola S.A. Pesagem e Automação Sao Paulo, SP, Brazil), with an accuracy of 50 grams and 0.1 cm. BMI was determined by body mass (kg) divided by the square of height (m²).

Hemodynamic measures

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were measured according to the procedures detailed in the 2023 Brazilian guidelines for in-office and out-of-office blood pressure measurement (20). Pulse pressure (PP) was calculated as the difference between SBP and DBP (20,21). The automated monitor can be used as an alternative for the evaluation of BP in the office. According to research conducted by Eguchi, (22) the ICC were 0.953 for SBP and 0.906 for DBP.

Lower limb functional capacity

5-Repetition Sit-To-Stand (5XSTS) test: 5XSTS was performed according to Guralnik (23) e Bohannon (24). For this test, the mean adjusted intraclass correlation coefficient (ICC) reported for this test was 0.81 (24).

Intervention Group

Considering frequency, intensity, type and time (duration) of exercise (FITT), the protocol was performed twice a week with rest intervals of 48 hours between sessions in the same week, with moderate intensity, concurrent training practice (practicing power exercises with elastic bands interspersed with aerobic exercise), lasting approximately 30 to 40 minutes (from the first to the eighth week).

The protocol was described following the recommendations of the Basic Guidelines for the Application of the Main Variables of RT in the Elderly (25). Protocol consisted of multiarticular and monoarticular exercises (vertical chest press, plantar flexion, seated row, hip abduction, trunk flexion, and squat on the chair) performed with elastic bands

(strong) (LIVEUP® SPORTS, Araucária, PR, Brazil), with intensity moderate, controlled using the rating of perceived effort (RPE) (26). At the end of each exercise set participants were asked to provide their RPE (easy, low, moderate, hard, maximal) for the last repetition of the set. For example, whenever the intensity was reported as easy or low in the previous set of exercise, the participant's elastic band tension was adjusted (increased) in the upcoming training session to provide a moderate intensity (26).

During the protocol familiarization period (2 weeks, 6 sessions), elastic bands offering moderate intensity were used to familiarize the participants with the initial and final positions of the exercises (e.g., reduce and increase elastic band tension; concentric and eccentric movement speed). The exercise professionals controlled the concentric and eccentric movement speed through verbal/tactile cues.

Except for the squat on the chair exercise, all exercises were performed with a full range of motion, with concentric contractions performed as fast as possible, while the eccentric contractions were performed slowly within 3 seconds. The protocol consisted of a sequence of five combinations of muscle power exercises interspersed with aerobic exercise without intervals of absolute rest throughout the session. The protocol consisted of, that is, two sets

1. vertical chest press interspersed with aerobic exercise (Walking with the same duration as the power exercise set);

Vertical Chest Press interspersed with aerobic exercise (Walking with the same duration as the power exercise set).

2. plantar flexion interspersed with aerobic exercise (Walking with the same duration as the power exercise set);

plantar flexion interspersed with aerobic exercise (Walking with the same duration as the power exercise set).

3. seated row interspersed with aerobic exercise (Walking with the same duration as the power exercise set);

seated row interspersed with aerobic exercise (Walking with the same duration as the power exercise set).

4. hip abduction interspersed with aerobic exercise (Walking with the same duration as the power exercise set);

hip abduction interspersed with aerobic exercise (Walking with the same duration as the power exercise set).

5. trunk flexion interspersed with aerobic exercise (Walking with the same duration as the power exercise set);

trunk flexion interspersed with aerobic exercise (Walking with the same duration as the power exercise set).

The target perceived exertion level during walking was set at 3 (intensity moderate) on an adapted Borg Scale, which ranges from 1 to 10 (27).

Protocol was performed two times per week over 8 weeks, with a minimum 48-hour rest interval provided between each exercise session in the same week. The exercise training volume was increased over the 8 weeks as shown below:

4 weeks: 3 sets x 12 reps;

4 weeks: 4 sets x 12 reps.

Control Group

Participants were instructed not to participate in any systematic exercise program for 8 weeks.

Statistical analysis

Statistical analysis was performed using Prism software (GraphPad Inc., San Diego, CA, USA, version 8.4.3, 2020). The normality of the distribution and the homogeneity of the outcome measures were tested using the Shapiro-Wilk and Levene tests, respectively. Means and standard deviations were calculated for each dependent variable. A two-way ("group" x "time") analysis of variance (ANOVA) with repeated measures was used to evaluate training-related effects over time or between groups. The Greenhouse-Geisser was used to assess changes in the outcomes; when a significant interaction effect was found, a Bonferroni post hoc test was applied to check for intragroup differences over time. All measurements were two-tailed, and p-values calculated with significance levels set at 5%. The effect size (ES) was determined using partial eta-squared (η^2p) values (28). According to Espírito Santo and Daniel (29), values of $\eta^2p \geq 0.01$ were considered small ES, $\eta^2p \geq 0.06$ was considered medium ES, and $\eta^2p \geq 0.14$ was considered large ES.

This project was approved by the Ethics and Research Committee of Ceuma University (CAAE: 12699519.7.0000.5084). All participants provided written informed consent after being fully briefed on the study's objectives, procedures, and potential risks and benefits. The study adhered to the principles of the Declaration of Helsinki (1975).

Results

Participants

Two participants withdrew before the assessments due to unavailability to train during the research program.

Twenty-four older adults completed the pre-8 and post-8-week measurements and had their data included in the statistical analysis (CG: n = 12; IG: n = 12). Twenty-four participants attended 80% of the training sessions. Their clinical characteristics are shown in Table 1.

Table 1. Baseline clinical characteristics of the participants (n = 24)

Variables	CG (n = 12)	IG (n = 12)	P-value
Age, years*	66.7 ± 5.3	66.0 ± 7.8	0.83
Body mass index, kg/m ² *	27.3 ± 5.3	25.5 ± 2.9	0.32
Women, n (%)	10 (83.3)	10 (83.3)	1.00
Associated Comorbidities (%)			
Hypertension	50.0	66.7	0.41
Diabetes mellitus type II	33.3	25.0	0.65
Medications (%)			
Angiotensin receptor blockers	25.0	33.3	0.65
Calcium channel blocker	16.7	25.0	0.62
Beta-blockers	16.7	16.7	1.00
Diuretics	8.3	25.0	0.27
Not medicated	8.3	---	0.31
Hypoglycemic agents	33.3	25.0	0.65

*Values are expressed as mean ± standard deviation; CG: control group; IG: intervention group.

Source: prepared by authors.

Pulse pressure, systolic and diastolic blood pressures

The results of the ANOVA indicated no significant differences statistically for PP ($p > 0.05$) (Table 2). In addition, SBP and DBP remain unchanged ($p > 0.05$) post the experimental period (Table 2).

Functional capacity

The results of the ANOVA indicated statistically significant time vs. group interaction ($P < 0.05$) for the five-repetition sit-to-stand test (Table 2). Post hoc analyses further confirmed significant improvements in functional parameters. In addition, an important clinical was found in for the five-repetition sit-to-stand test. (time × group interaction: $\eta^2p = 0.63$) (Table 2).

Discussion

Although the benefits of concurrent training on hemodynamic parameters in older adults have been demonstrated in some studies, there is still no consensus on the subject. Additionally, little is known about the effects of

practicing power exercises with elastic bands interspersed with aerobic exercise on hemodynamic parameters in older adults. This research aimed to investigate the effects of elastic-band power training interspersed with aerobic exercise on hemodynamic parameters and lower-limb function in older adults. The main finding of this research was the absence of improvement in hemodynamic parameters after 8 weeks of intervention.

Despite not finding significant differences in hemodynamic parameters, an important clinical reduction in systolic blood pressure ($\Delta = -6.0$ mmHg) was observed in the sample. These findings have significant clinical implications, since a reduction of 5 mmHg in SPB has led to a 14% decrease in stroke-related mortality, a 9% decrease in mortality due to coronary heart disease, and a 7% decrease in all-cause mortality (30).

Although studies have demonstrated the benefits of concurrent training on older people's health parameters (31), there is no consensus on the effects of concurrent training on blood pressure in this population (8,9,11,17,32-37). This may be due to the different characteristics of the sample (i.e., normotensive, hypertensive, sedentary, and previously trained older adults) and different exercise

interventions (i.e., concurrent training with different resistance training protocols).

One hypothesis to explain our findings is the baseline blood pressure levels. The participants in this research did not present high blood pressure levels, as observed in Table 2. In line with these findings, in another study conducted by our group, no improvement in hemodynamic parameters

was demonstrated in older adults with controlled blood pressure levels after the practice of concurrent training (11). On the other hand, contrary to our findings, an improvement in hemodynamic parameters was observed in older adults with high blood pressure (8,32,33). Additionally, studies have demonstrated improvements in hemodynamic parameters in hypertensive older adults after practicing concurrent training (34,35).

Table 2. Changes in pulse pressure, systolic blood pressure, diastolic blood pressure, and in the functional parameter at baseline and after 8 weeks of intervention (n = 24)

Variables*	CG (n = 12)	IG (n = 12)	CG vs. IG	Group	p (η ² p) values	
			MD (95% CI)		Time	Interaction
Blood pressure, mmHg						
Pulse pressure				0.8779 (0.01)	0.2273 (0.07)	0.1491 (0.09)
Pre	55.3 ± 14.8	57.0 ± 10.6	- 1.7 (-13.8 – 10.4)			
Post	55.8 ± 15.3	52.5 ± 9.5	3.2 (-8.9 – 15.4)			
Systolic blood pressure				0.6137 (0.10)	0.3372 (0.04)	0.1054 (0.11)
Pre	131.5 ± 17.4	131.8 ± 13.4	- 0.3 (-16.9 – 16.3)			
Post	133.1 ± 25.1	125.8 ± 10.8	7.3 (-9.3 – 23.9)			
Diastolic blood pressure				0.4332 (0.13)	0.9222 (0.00)	0.3955 (0.03)
Pre	76.2 ± 11.2	74.8 ± 5.9	1.4 (-7.2 – 10.0)			
Post	77.3 ± 12.4	73.3 ± 4.5	4.0 (-4.6 – 12.7)			
Functional parameter						
5XSTS, (seconds)				0.0001 (0.68)	0.2183 (0.07)	0.0006 (0.42)
Pre	9.3 ± 0.9	8.6 ± 0.3	0.7 (- 0.3 – 1.7)			
Post	10.6 ± 1.7	7.9 ± 0.8*	2.7 (1.7 – 3.7)			

*Values are expressed as mean ± standard deviation; CG: control group; IG: intervention group; 5XSTS: five-repetition sit-to-stand; MD: mean difference; CI: confidence interval; η²p: partial eta squared; *: within-group change over time.co

Source: prepared by authors.

In addition to having observed a significant clinical reduction in SBP, in the present research, found an improvement in lower limb functional capacity – which agrees with several studies on concurrent training and older people’s functional parameters (12-14). This finding also corroborates a study conducted by our group, which found an improvement in older people’s functional capacity in two tests, namely: rising from the prone position and the timed up-and-go (TUG) dynamic balance test (11). The improvement in lower limb function observed in this study also has important clinical implications, since increased muscle strength reduces the risk of mortality (38). Additionally, in agreement with a systematic review and meta-analysis by Shailendra et al. (39), the practice of RT is associated with decreased cardiovascular mortality risk.

The characteristic of muscle power training is particularly interesting to improve older adults’ functional capacity because the type of muscle action performed mainly stimulates type IIX fibers. Literature traditionally describes this muscle fiber subtype as the most impacted by the aging

process, and its reduction is associated with a higher risk of falls and mortality from all causes in older people (40).

The present study has limitations, such as its short duration (8 weeks) and heterogeneous sample (normotensive and hypertensive older adults). Nonetheless, this study has strengths, including the use of elastic bands, a low-cost and easy-to-handle option to improve functional parameters in older adults. Finally, considering that the proposed protocol is easy to access, low-cost, and widely applicable, further studies about the topic covered are needed with longer duration and more homogeneous samples. Probably, with longer duration (e.g., 12, 16 weeks) could allow greater physiological adaptations, possibly influencing hemodynamic parameter responses.

In addition, the protocol approach used in the present study has other advantages, which makes it a promising alternative for this population. These include greater dynamism in training since the combination of exercises with different characteristics, performed sequentially and without breaks, can help their adherence to practicing exercises. In this

sense, studies comparing this protocol of this research with other exercise programs are needed to confirm the potential for adherence when alternating power exercises with aerobic exercise.

Conclusions

Our findings show that the combination of elastic-band power training interspersed with aerobic exercise effectively improves the lower limb functional capacity of older adults' lower limbs. Although no significant differences were found in hemodynamic parameters, it is important to highlight the important clinical reduction in systolic blood pressure ($\Delta = -6.0$ mmHg), with the consequent reduction in the risk of cardiovascular mortality in the sample investigated. Importantly, no adverse effects were observed, considering that the sample consisted of normotensive older adults and those with hypertension, a condition of cardiovascular risk. In this sense, the results of this study apply to normotensive older adults or those with controlled blood pressure, and that effectiveness may vary in populations with different risk profiles.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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