



Effects of a single bout of power exercise training on ambulatory blood pressure in older adults with hypertension: A randomized controlled crossover study

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ABSTRACT

Objective: To evaluate the effect of a single bout of power exercise training (PT) on office and ambulatory blood pressure (BP).

Methods: Twenty-four older adults with essential hypertension participated in two experimental sessions in a randomized order: the PT composed of 3 sets of 8–10 repetitions in 5 power training exercises and the non-exercise control at seated rest (Con). Both experimental sessions lasted 40 min. Office BP was measured continuously for 1 h in the laboratory and 24 h BP through ambulatory blood pressure monitoring.

Results: Compared with Con, office systolic/diastolic BP decreased after PT (Systolic BP: 10 mmHg, $p < 0.001$; Diastolic BP: 4 mmHg, $p = 0.015$). A trend toward decrease ($p = 0.06$) was found in diastolic ambulatory BP during daytime (2 mmHg; $p = 0.062$) and nighttime (3 mmHg; $p = 0.063$) after PT. No differences were found between PT and Con sessions for systolic and mean ambulatory BP.

Conclusion: A single bout of PT decreases office BP but this hypotensive effect is not sustained under ambulatory conditions in older patients with essential hypertension.

1. Introduction

Skeletal muscle mass, muscle strength and power, and physical independence decrease with advancing age.^{1,2} These declines are associated with development of cardiovascular diseases and mortality.^{3,4} Hypertension is one of the most important modifiable risk factors for developing cardiovascular disease and increases its prevalence and severity throughout lifespan.^{5–7} Regular physical exercise is a cornerstone intervention to attenuate and prevent the age-related increases in hypertension⁸ and increase functional independence.⁹ In particular, resistance training has emerged as one of the best strategies to improve neuromuscular function and the capacity to perform daily living activities in the older populations.¹⁰ Moreover, results of a meta-analysis suggest resistance training as viable stand-alone antihypertensive lifestyle therapy.¹¹

After a single bout of exercise, BP decreases when compared with the baseline values of the same session or if compared to a usual day without

exercise, a phenomenon termed post-exercise hypotension (PEH).¹² This acute post-exercise reduction of BP may predict the extent of BP lowering after chronic training interventions, since important correlations between the acute and chronic BP reduction after exercise were found.^{15,16} To improve its clinical relevance, PEH should be followed and assessed throughout long periods (24 h) and under usual or ambulatory conditions.¹⁷ However, few studies have assessed the effects of resistance exercise on ambulatory BP and none of them used older participants with hypertension.¹⁸ It remains uncertain how long a single session of resistance exercise exerts PEH effects among older individuals with hypertension under ambulatory conditions including daily activities and sleeping.

The available literature suggests that exercise prescription should include power exercises based on greater enhancements in functional outcomes after power exercise training when compared with traditional resistance training in older adults.^{9,19} Power exercise training is performed at lower intensities (30–50 % of one repetition maximum or

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1-RM), lower volumes per set (up to ten repetitions) and are not set to failure or volitional exhaustion. These exercise characteristics are attractive to higher risk populations such as older patients with hypertension who demonstrate compromised cardiovascular and musculoskeletal functions. The number of repetitions per set greatly and adversely affects BP response during exercise when resistance training is performed to volitional exhaustion.^{20–22}

To the best of our knowledge, studies investigating an effect of a single bout of power exercise training (PT) on BP are scarce, and the available studies only assessed BP under office conditions,^{23,24} and no data are available on the effects of power exercise training on ambulatory BP. Accordingly, the aim of the present study was to evaluate the effect of PT on office and 24 h blood pressure in older adults with hypertension. The working hypothesis was that a single bout of power exercise would decrease both office and 24 h BP in comparison to a non-exercising control session.

2. Materials and methods

2.1. Study design and participants

A randomized controlled clinical trial with crossover design was performed in order to evaluate the effect of PT on office and 24 h BP of hypertensive patients. The protocol followed the CONSORT guidelines for non-pharmacological treatment.²⁵ Participants performed two experimental sessions in a random order: a power exercise training session (PT) and a non-exercising control session (Con). The randomization list composed of random block sizes of four participants was generated by an epidemiologist using a computer software. This epidemiologist did not participate in the recruitment or assignment to the experimental sessions. Participants and the research team were blinded to the randomization list until the moment of assignment.

Men and women aged 60–75 years with previously diagnosed hypertension by a physician were recruited if they had not engaged in structured exercise programs in the last 3 months prior to the start of the trial. Exclusion criteria included previous diagnosis of ischemic heart disease, heart failure, current smokers or ex-smokers for less than 6 months, body mass index over 39.9 kg/m², musculoskeletal problems that prohibit them from exercising, and diabetes with retinopathy.

The study was conducted from 12 June 2018 to 20 July 2019 at a tertiary referral hospital in southern Brazil. All participants read and signed an informed consent form before beginning the study. Participation was voluntary and all ethical principles of confidentiality and data protection were followed. The study protocol was conducted according to the principles of the Declaration of Helsinki and in compliance with the Brazilian legal and regulatory framework for research involving human beings (NR 466/12). The study protocol was approved by the Institutional Review Board of Hospital de Clínicas de Porto Alegre, Brazil, and registered on clinicaltrials.gov under identifier number NCT03615625.

2.2. Preliminary sessions

Each participant completed a clinical screening, resting electrocardiogram, manual BP and anthropometric measurements in the research laboratory. Participants were then instructed to attend three preliminary sessions on 3 different days separated by 48–96 hours. On the first and second sessions, the research team performed office BP assessments in duplicate using an automated BP device (Dinamap, Critikon, EUA). The stability of BP was confirmed in this run-in period. The participants were also familiarized with power exercises involved in PT and maximal strength testing during the first two sessions. Since most participants included in the study had no previous experience with power exercise training, we implemented two familiarization sessions in order to ensure that the participants' properly perform the prescribed exercises. During the third preliminary session, participant's maximal strength was

assessed using one repetition maximal strength (1-RM) test. Before the test, resting BP was assessed after 20 min of rest in supine position and these values were used to describe the baseline characteristics of participants.

Height and body mass were assessed by a stadiometer and a balance scale (FILIZOLA, Brasil) and used to calculate body mass index (BMI). Waist circumference was assessed using an inelastic standardized measure-tape (Cescorf, Brazil) at the middle point between upper iliac crest and the lower costal rib in the horizontal plane. To determine the proper cuff size used in the BP monitoring, arm circumference was assessed at middle point between acromion and the cubital fossa on the non-dominant arm.

Maximal dynamic strength was evaluated using the one repetition maximum test (1-RM) in 5 resistance exercises: leg press, bench press, knee extension, upright row, and knee flexion. A specific warm-up composed of 2 sets of 10 and 5 repetitions, using 50 % and 75 % of estimated 1-RM load was performed prior to the test. After the first attempt, the load was adjusted through Lombardi coefficients, if necessary. Each participant's 1RM was determined with no more than three attempts with a five-minute recovery between attempts and a two-minute recovery between exercises. These results were used to determine the intensity or load of the experimental sessions. The tests were conducted by the same trained investigator with previous experience in this method.

2.3. Experimental sessions

Participants performed two experimental sessions: power exercise training (PT) and non-exercising control at seated rest (Con). Participants were instructed to avoid physical exercise for 24 h before the experimental sessions, keep the usual dietary intake, avoid alcohol, coffee, and other stimulant substances before the experimental sessions and have the same meal 4 h before each session. Participants maintained their current antihypertensive medications throughout the trial.

Both experimental sessions started between 2–3 PM (at the same time of day to account for potential diurnal variation in BP and residual effects of antihypertensive medications) and lasted approximately 2 h. Each session was composed of 20 min of rest in the supine position, 40 min of PT or Con protocols, and 60 min of rest in supine position after protocols. Standardized office BP and heart rate assessments were performed before, immediately after each exercise during PT session or in intervals of 8 min during Con, and during the first hour (in intervals of 15 min) after the experimental sessions using an automatic oscillometric device (Dinamap 1846 SX/P; Critikon, FL, USA). Afterwards, participants underwent 24-h ambulatory blood pressure monitoring (90702, Spacelabs Medical, EUA).

The PT was composed of 3 sets of 8–10 repetitions of 5 exercises performed in the following order: leg press, bench press, knee extension, upright row, and knee flexion, using an intensity corresponding to 50 % of 1-RM and two-minute intervals between sets and exercises. The concentric phase of exercises during each repetition was performed "as fast as possible" while the eccentric phase lasted 1–2 seconds. During the Con, the participants remained seated rest on the same exercise machines, but without any exercise.

Office BP was assessed under laboratory conditions according to the VII Brazilian National Guidelines in Cardiology.²⁶ Participants were instructed to remain in silence without using any electronic device (i.e., smartphones, notebooks). A proper-sized cuff was placed in the arm about 2 cm from the antecubital fossa. Measurements of BP were performed on both arms with a time difference of 1 min between procedures. Measurements were performed twice in the arm with the highest BP values. The mean of these BP values was used to represent office BP. The arm with the highest BP values was used for the subsequent assessments.

The primary outcome of the present study was the difference in 24 h ambulatory BP assessed after each experiment session. Measurements of

BP were taken every 15 min at daytime and every 20 min at nighttime. The first daytime period started between 4–5 PM (immediately after laboratory session), nighttime between 11 PM and 7 AM, and the second daytime finished at 5 PM on the day after the experimental session. Participants filled a diary about activities, symptoms, sleep and wake-up time. Each exam was considered valid when at least 70 % of the expected readings were available and recorded.²⁷

2.4. Statistical analyses

Sample size was estimated according to the results of a previous study using a similar study design.²⁸ An initial sample size of 24 individuals with hypertension, allowing a dropout rate of 10 %, would be able to detect a difference of 5 mmHg in systolic BP between the protocols with 80 % of statistical power and a type I error rate of 5%. WinPepi software calculator was used to estimate the sample size.

Data were entered in duplicate by three different researchers and expressed as means and standard deviation for variables with normal distribution or medians and interquartile range for non-normal distributions and 95 % confidence intervals (CI95 %). Generalized Estimating Equations (GEE) analysis was used to compare main effects between experimental sessions using absolute BP values, assessing the condition (2 session: PT and Con) by time (3 factors: day-time 1, night-time, and day-time 2). Post-hoc comparisons were performed with Bonferroni test. Statistical significance was set at $P < 0.05$, and a borderline significance was detected for P-values ranging from 0.05 to 0.10. All statistical analyses were performed using SPSS Statistics for Windows, version 22.0 (IBM, Armonk, NY).

3. Results

A flowchart of the experiments is presented in Fig. 1. Participants' characteristics at baseline assessed during the preliminary sessions are shown in Table 1. Overall, participants were overweight and had been

Table 1
Selected participant characteristics.

Age, years (SD)	66.7 (4.3)
Sex, n (%)	
Men	12 (50)
Women	12 (50)
Race/Ethnicity, n (%)	
White	20 (83.3)
Black	3 (12.5)
Asian	1 (4.2)
Anti-hypertensive medications, median (range)	2 (1–4)
Diuretics, n (%)	19 (79.2)
β blockers, n (%)	17 (70.8)
Angiotensin converting enzyme inhibitors, n (%)	8 (33.3)
Angiotensin receptor antagonists, n (%)	14 (58.3)
Calcium channel blockers, n (%)	19 (79.2)
α -2 agonists, n (%)	1 (4.2)
Combined Therapy, n (%)	23 (95.8)
Anthropometric measures	
Body weight, kg (range)	76 (69–87)
Height, cm (range)	162 (156–169)
BMI, kg/m ² (SD)	29.7 (3.7)
Waist circumference, cm (range)	96.5 (87.5–106.8)
Waist-height ratio (range)	0.6 (0.55–0.66)
Hemodynamic measures	
Systolic BP, mmHg (SD)	132 (12)
Diastolic BP, mmHg (SD)	76 (8)
Mean BP, mmHg (SD)	96 (8)
Heart rate, bpm (SD)	66 (11)
RPP, mmHg/bpm (SD)	8824 (1728)
Muscle strength tests	
1-RM Leg Press, kg (SD)	137.6 (57.0)
1-RM Knee Extension, kg (SD)	86.5 (28.2)
1-RM Knee Flexion, kg (SD)	53.5 (18.6)
1-RM Bench Press, kg (SD)	37.9 (14.9)
1-RM Upright row, kg (SD)	29.8 (11.6)

Means \pm SD for parametric data and medians \pm interquartile interval for non-parametric data; BMI = body mass index; BP: blood pressure; RPP = rate-pressure product; 1-RM = one repetition maximal strength.

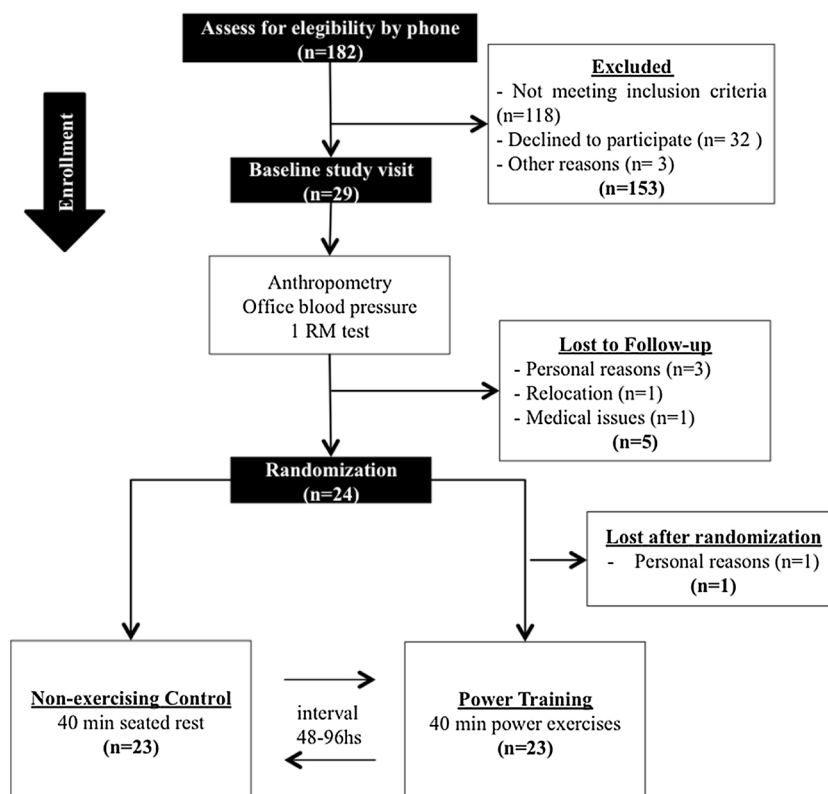


Fig. 1. Participant flow chart of the present study. 1-RM = one-repetition maximal strength.

taking two anti-hypertensive drugs. There were no reported adverse events during the PT session. The quality of the ambulatory BP recorded was considered satisfactory in all patients. Analyses on the activity diary filled out by the participants showed a similar pattern in both experimental sessions days, with similar domestic activities performed, a similar pattern in meal times and medications. Additionally, no adverse symptoms or difficulties to sleep were reported by the participants.

Time vs. session interaction was found for systolic ($p < 0.001$), mean ($p < 0.001$), and diastolic ($p < 0.001$) office BP. Baseline BP values were similar for systolic BP (132 vs. 131 mmHg; $p = 0.616$), mean BP (91 vs. 95 mmHg; $p = 0.509$), and diastolic BP (76 vs. 75 mmHg; $p = 0.576$) between PT and Con. During the first hour in the research laboratory, office systolic (-10 mmHg, CI95 %: -15 to -5; $p < 0.001$), mean (-6 mmHg, CI95 %: -9 to -3; $p = 0.001$), and diastolic BP (-4 mmHg, CI95 %: -7 to -1; $p = 0.015$) decreased significantly after PT when compared with Con.

Ambulatory BP data are presented in Table 2. No differences were found between PT and Con sessions for day-time, night-time and total 24 h systolic and mean BP. A borderline significance reduction in the first day-time ($p = 0.063$) and night-time ($p = 0.062$) diastolic BP was found after the PT session when compared with Con. There were no differences in 24 h diastolic BP between PT and Con sessions.

Table 3 describes the hemodynamic response data during the experimental protocols. A significant increase in mean BP was seen after upright row exercise when compared to the corresponding baseline value. Rate-pressure product was consistently elevated during PT when compared with Con.

4. Discussion

Office BP has often been used to diagnose hypertension. However, due to a number of methodological issues including white coat hypertension, ambulatory BP has become the gold-standard measurement for

Table 2

Ambulatory (24 h) blood pressure in the power exercise training and non-exercising control sessions.

	Control	Power Training	Delta	p-value PT vs. Con
Systolic BP				
24 -h	131.5 ± 2.7 (126–137)	131.4 ± 2.3 (127–136)	0.1 ± 1.6 (-2.9 to 3.1)	0.931
Day-time 1	138.9 ± 2.7 (134–144)	137.4 ± 3.0 (132–144)	1.4 ± 1.9 (-5.2–2.3)	0.448
Night-time	126.4 ± 3.2 (120–133)	123.8 ± 2.9 (118–130)	2.6 ± 2.1 (-6.9 to 1.6)	0.375
Day-time 2	131.4 ± 2.8 (126–137)	131.0 ± 2.5 (126–136)	0.3 ± 1.9 (-3.4 to 4.0)	0.870
Mean BP				
24 -h	96.0 ± 2.0 (92–100)	95.1 ± 1.8 (91–99)	0.9 ± 1.2 (-3.3 to 1.4)	0.432
Day-time 1	102.2 ± 2.1 (98–106)	100.3 ± 2.2 (96–105)	1.8 ± 1.3 (-4.4 to 0.6)	0.149
Night-time	91.1 ± 2.3 (87–96)	88.9 ± 1.9 (85–93)	2.2 ± 1.7 (-5.6 to 1.1)	0.201
Day-time 2	96.3 ± 2.2 (92–101)	95.5 ± 1.9 (92–99)	0.7 ± 1.4 (-3.4 to 2.0)	0.599
Diastolic BP				
24 -h	77.2 ± 1.9 (73–81)	76.1 ± 1.9 (72–80)	1.0 ± 0.9 (-2.9 to 0.8)	0.279
Day-time 1	82.7 ± 2.1 (79–87)	80.6 ± 2.3 (76–85)	2.0 ± 1.1 (-4.2 to 0.1)	0.063
Night-time	73.2 ± 1.9 (69–77)	69.7 ± 2.1 (66–74)	3.4 ± 1.8 (-7.1 to 0.1)	0.062
Day-time 2	79.0 ± 2.1 (75–83)	77.3 ± 2.0 (73–81)	1.6 ± 1.1 (-3.8 to 0.5)	0.135

Values are means ± SEM (95 % confidence interval); BP = blood pressure. PT: power exercise training session; Con: control session.

Table 3

Hemodynamic responses during the power exercise training and the non-exercising control sessions.

	Control	Power Training	p value PT vs. Con
Mean blood pressure			
Pre	91.0 (81–101)	94.7 (91–99)	0.509
Leg press	102.5 (97–108)	99.3 (93–105)	0.171
Bench press	103.6 (99–109)	99.7 (94–105)	0.114
Knee extension	105.2 (100–111)	100.3 (96–105)	0.014
Upright row	103.4 (98–109)	105.8 (100–112)*	0.353
Knee flexion	104.7 (99–110)	98.1 (95–102)	0.001
Rate-pressure product			
Pre	8502 (7887 to 9118)	8504 (7914 to 9093)	0.996
Leg press	8831 (8083 to 9579)	11,657 (10,831 to 12,483)*	<0.001
Bench press	8960 (8211 to 9709)	10,780 (9913 to 11,646)*	<0.001
Knee extension	8986 (8224 to 9748)	12,015 (11,118 to 12,912)*	<0.001
Upright row	8862 (8184 to 9541)	12,062 (11,244 to 12,881)*	<0.001
Knee flexion	8959 (8316 to 9602)	11,212 (10,388 to 12,036)*	<0.001

Values are means (95 % confidence interval); Mean blood pressure (mmHg); Rate-pressure product (mmHg·bpm); PT: power exercise training session; Con: control session; * $p < 0.05$ vs. Pre.

BP behavior and a methodology of choice to understand the time course of post-exercise hypotension in a usual living condition.²⁹ To the best of our knowledge, this is the first trial investigating the acute effects of power training on 24 h BP. We found significant reductions in office BP at 1 h following 40 min of power exercises. However, under ambulatory conditions, only a borderline significance reduction in daytime and nighttime diastolic BP was found after the PT session. No differences between the sessions were found for 24 h, daytime and nighttime systolic and mean BP. These findings partially confirm the results of two recent studies that found office BP reduction during 1 h after the power training session^{23,24} and add new information related to the effects of power training on 24 h BP in older men and women with essential hypertension.

In contrast to our working hypothesis, a single bout of power training did not reduce systolic or diastolic 24 -h ambulatory blood pressure. The absence of studies assessing the power exercise effects on 24 h BP limits the ability to compare our present findings with others using a similar exercise protocol. However, in studies using traditional resistance exercise protocols, PEH is frequently reported in the laboratory conditions (i.e., 30–90 min after exercise) but the results are controversial when PEH was assessed under ambulatory conditions over 24 h.¹⁸ Two previous studies failed to report a decrease in ambulatory BP after a single session of traditional resistance exercise in middle-aged hypertensive men^{30,31} while significant decreases in nighttime and 24 h systolic/diastolic BP (~4 mmHg) was found following a resistance exercise session in middle-aged overweight/obese women.³² Data in older adults that evaluated resistance exercise alone on PEH assessed via ambulatory BP are rare, but a combined exercise (resistance + aerobic) protocol failed to demonstrate PEH when BP was assessed under ambulatory conditions.²⁸ A variety of factors, including an initial BP level, intensity and duration of the exercise, and exercise mode, are involved in determining both the PEH magnitude and duration in participants with essential hypertension.³³ Similarly, the duration of disease and the co-existence of pharmacological treatments may also influence these outcomes.^{18,34} A lack of differences in ambulatory BP after the PT protocol could be due to the lower baseline BP values observed in the present study. Our sample consisted of older individuals with well-controlled hypertension who used antihypertensive medications,

which could partially explain the smaller magnitude and duration in ambulatory BP found in our study.

The results of a meta-analysis suggested that one bout of resistance exercise can reduce ambulatory BP in hypertensive individuals, especially when large muscle groups are used during the exercise.¹⁸ However, our power training session composed of 5 exercises using large muscle groups did not reduce total 24 h ambulatory BP. We speculate that the total resistance/load performed during the exercise session (sets x repetitions/time under tension x load x exercises) may be a key component in predicting the magnitude and duration of PEH. A significant reduction in nighttime and 24 h systolic/diastolic BP following a resistance exercise protocol is not commonly observed but could result from a higher total overload (i.e., 19 sets of 10 repetitions at 60 % 1RM³² than that used in the present study (i.e., 15 sets of 8–10 repetitions at 50 % 1RM). Our exercise protocol provided a sufficient stress to reduce systolic/diastolic BP for 1 h after exercise in a controlled laboratory condition, but this reduction was not sustained under ambulatory conditions. Interestingly, the first daytime (2 mmHg; $p = 0.063$) and nighttime (3 mmHg; $p = 0.062$) diastolic BP had a tendency to decrease after the power training session. These results have important clinical relevance, providing a potential to reduce the cardiovascular stress during daily activities and sleeping in older individuals with hypertension.

Ambulatory BP can be affected by the time of day at which exercise is performed. Our present study is unique as exercise was performed at the same time of the day in the afternoon. Afternoon or evening exercise can increase melatonin releases during nighttime periods,³⁵ which might lead to a decrease in nighttime BP. It is plausible to speculate that the borderline significance decrease in nighttime diastolic BP (CI 95 %: -7.1 to 0.1 mmHg) and the non-significance decrease in nighttime systolic BP (CI 95 %: -6.9 to 1.6 mmHg) observed in the present study could be partially explained by melatonin since it is known to modulate cardiac autonomic function³⁶ influencing BP subsequently. These acute effects on BP have a substantial clinical implication as these acute changes are linked to chronic reductions in BP brought on by regular exercise.³⁷ Additionally, nighttime BP is a stronger predictor of all-cause mortality and cardiovascular events than daytime blood pressure in patients with hypertension.^{38,39} Future studies using different combinations of exercise are necessary to confirm PEH during nighttime periods.

Office BP was lower after PT session than that obtained in Con, confirming the post-exercise hypotensive effect after PT session and the effectiveness of this alternative form of resistance exercise to acutely reduce BP.²⁴ However, exercise professionals should prescribe effective and proper resistance exercises not only to achieve maximal benefits but also to avoid exacerbated hemodynamic responses during exercise⁴⁰ that increases the risk of acute adverse events especially in patients at higher cardiovascular risks.²⁰ Slight increases in cardiac load as assessed by rate pressure products that occurred during the PT session were expected, and no adverse events occurred during the exercise session. Collectively these results suggest that resistance exercises using low intensity and repetitions not to failure such as power exercises can reduce cardiac demand during the resistance exercise session.

Poor health and disability are not the inevitable consequences of aging.⁹ Older individuals who adopt a healthy lifestyle is more likely to exercise, have lower health-related medical costs and a better quality of life.⁴¹ Although various modes, formats, and doses of physical activity protocols are available to reduce BP, optimal exercise prescriptions for individuals with hypertension remain controversial.⁴² Power exercise training involving large muscle groups used in the present study was feasible, and no adverse effects were reported during the study. The results of this trial provide evidences of acute effects of power exercises on BP management, supporting recommendations for exercise prescription in older patients with hypertension. Because power training may also promote benefits in musculoskeletal functionality,^{10,19} this mode of exercise may be ideal for older individuals who tend to suffer from hypertension as well as sarcopenia. Chronic studies using this

exercise modality are warranted.

Some limitations should be addressed in the present study. Our present sample consisted of individuals between 60–75 years, therefore limiting the generalization of our findings to younger or older populations with hypertension. Additionally, only two familiarization sessions were performed before the strength tests. The prescribed exercise intensity may have been underestimated reducing total overload, and as consequence, influenced the PEH magnitude and duration. Strengths of the present study include the use of ambulatory BP monitoring, the gold-standard method to assess PEH, statistical analyses using a robust method that encompasses proper adjustments that control the type I error rate using Bonferroni tests, and independent evaluators, avoiding possible analysis bias to interpret the results.

5. Conclusion

In summary, a single bout of PT decreases office BP but this hypotensive effect is not sustained under ambulatory conditions in older patients with essential hypertension. Future studies need to investigate the long-term effects of a power training program on 24 h ambulatory blood pressure and its associated mechanisms in this population.

CRedit authorship contribution statement

Renato P Schmitt: Conceptualization, Investigation, Writing - original draft. **Leandro O Carpes:** Investigation, Formal analysis, Writing - review & editing. **Lucas B Domingues:** Investigation, Formal analysis, Writing - review & editing. **Hirofumi Tanaka:** Formal analysis, Writing - review & editing. **Sandra C Fuchs:** Formal analysis, Writing - review & editing. **Rodrigo Ferrari:** Conceptualization, Investigation, Formal analysis, Funding acquisition, Writing - original draft, Writing - review & editing.

Declaration of Competing Interest

The authors report no declarations of interest.

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