TITLE PAGE

Effects of cycling bouts performed with different intensities and amounts of energy expended on central pressure and pulse wave reflection in normotensive and hypertensive men

Running head: Aerobic exercise and central hemodynamic responses

Tainah de Paula[1,2], Felipe A. Cunha[2,3], Walace Monteiro[2,3,4], Paulo Farinatti[2,3,4], Wille Oigman[1,5], Adrian Midgley[6] and Mario Fritsch Neves[1,5]

1) Postgraduate Program in Medical Sciences, Faculty of Medical Sciences, State University of Rio de Janeiro, Rio de Janeiro, Brazil

2) Laboratory of Physical Activity and Health Promotion, State University of Rio de Janeiro, Rio de Janeiro, Brazil.

3) Postgraduate Program in Exercise Science and Sports, State University of Rio de Janeiro, Rio de Janeiro, Brazil

4) Postgraduate Program in Physical Activity Sciences, Salgado de Oliveira University, Niterói, Rio de Janeiro, Brazil

5) Department of Clinical Medicine, State University of Rio de Janeiro, Rio de Janeiro, Brazil.

6) Department of Sport and Physical Activity, Edge Hill University, Ormskirk, Lancashire, England

Address for correspondence: Mario Fritsch Neves, PhD. Department of Clinical Medicine, University of Rio de Janeiro State. Av. 28 de Setembro, 77/329, Vila Isabel, Rio de Janeiro, Brazil. CEP: 20551-030; Phone: (21) 2868-8484. E-mail: mariofneves@gmail.com

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Abstract

Objective: This study investigated pulse wave analysis in normotensive and hypertensive men after cycling bouts with different intensities and amounts of energy expended. **Methods:** Twenty-four men were assigned into normotensive [n=14; age:40.7±2.8yr; 24-h ambulatory systolic/diastolic BP (SBP/DBP):121±2/74±1mmHg] and hypertensive [n=10; age:39.2±2.3yr; 24-h ambulatory SBP/DBP:139±3/86±2mmHg] groups. Participants undertook a maximal cardiopulmonary exercise test, a non-exercise control session (CTL), and three cycling bouts [two prolonged bouts expending 300 kcal at 50% (i.e. P-MOD) and 70% (i.e. P-VIG) oxygen uptake reserve (VO_2R) and one short bout expending 150 kcal at 50% VO_2R (i.e. S-MOD)] performed in a randomized order. Central systolic blood pressure (cSBP), pulse pressure (cPP), augmentation pressure (AP), augmentation index (AIx), heart rate (HR), and AIx adjusted for HR (AIx@75) were determined 10 min before, and 30- and 70-min post-intervention. **Results:** Compared to CTL, only the P-VIG changed the cSBP [*70-min* (Δ -11.7mmHg)], cPP [*70-min* (Δ:-7.4mmHg)], AP [*30-min* (Δ:-5.7mmHg); *70-min* (Δ:-7.3mmHg)], AIx [*30-min* (Δ:-15.3 %); *70-min* (Δ:-16.4 %)], AIx@75 [30-min (Δ:-12.8 %); *70-min* (Δ:-13.9 %)], and HR [70-*min* (Δ:9.9bpm)] in hypertensive group. However, all exercise bouts mitigated the increased cSBP responses post-CTL in the hypertensive group. **Conclusion:** The present study provides evidence that vigorous-intensity aerobic exercise reduces acute central pressure and pulse wave reflection in hypertensive men.

Keywords: Blood pressure; Energy metabolism; Exercise; Hypertension; Post-exercise hypotension; Pulse wave analysis.

INTRODUCTION

Lifestyle changes such as regular exercise, especially aerobic exercise, have been recommended as non-pharmacological interventions for the initial management of hypertension and for reducing cardiovascular events [1]. According to the American College of Sports Medicine guidelines, hypertensive adults should engage in 30-60 min of moderate-intensity aerobic exercise on most days of the week to elicit chronic reductions in blood pressure of approximately 5 to 7 mmHg [2]. Emerging literature, however, suggests that the acute and chronic reductions in blood pressure observed after exercise have a dose-response relationship with exercise intensity [3]. Consequently, exercise programs that incorporate vigorous-intensity aerobic exercise also have been recommended for hypertensive individuals [4]. Evidence supports the hypothesis that the chronic reductions in blood pressure from engaging in long-term aerobic exercise programs are largely due to the summative effects of the reductions in blood pressure observed after each bout of aerobic exercise [see 5 for a review].

Early research investigating the blood pressure lowering effects of exercise used peripheral brachial artery pressures [see 6 for a review]. Current evidence, however, supports the notion that central pressure, influenced by pulse wave reflection and arterial stiffness, is a stronger predictor of adverse cardiovascular events. This is because the heart, kidneys, and major arteries supplying the brain are exposed to central pressures, highlighting the importance of blood pressure evaluation in other segments of the arterial tree beyond brachial blood pressure [7]. Indeed, the importance of central pressure and pulse wave reflection for predicting the risk of cardiovascular events appears clearly established and highlights the need for research investigating the direct impact of aerobic exercise on central hemodynamic markers [8]. Systematic reviews and meta-analyses have observed that chronic aerobic exercise appears to improve arterial stiffness and pulse wave reflection in adults [9,10]. It remains unclear, however, to what extent aerobic exercise affects the acute central responses of systolic/diastolic blood pressure (cSBP/cDBP), augmentation pressure [AP (i.e. augmentation of cSBP induced by return of the reflected wave)], central pulse pressure [cPP (i.e. cSBP *minus* cDBP)], and the augmentation index [AIx (ratio between AP and cPP)]. Some studies observed a decrease in pulse wave reflection during the postexercise period [11,12], while others did not observe such acute changes [12,13], or noted increased responses after exercise [14]. A question arises as to what could explain these contrasting research findings. Acute reductions in

peripheral blood pressure have been observed after aerobic exercise bouts requiring only 40% of maximal aerobic capacity [15]. Accordingly, another unanswered question is whether exercise bouts performed with different intensities and amounts of energy expended influence the postexercise central pressure and pulse wave reflection. Finally, there is a lack of research investigating these acute responses in hypertensive adults.

Given these limitations, the purpose of this study was to investigate the acute central pressure and pulse wave reflection responses in normotensive and hypertensive men following submaximal cycling bouts with different intensities and amounts of energy expended. We hypothesized that aerobic exercise performed with greater intensity and volume would result in greater acute changes in central pressure and pulse wave reflection, particularly in individuals with high blood pressure levels.

METHODS

Participants

Potentially eligible participants were recruited from our outpatient clinics. Considering the lack of knowledge of cutoff values for central pressure and pulse wave reflection at rest and during postexercise recovery, data from a control group with normal blood pressure were also analyzed to provide reference values for comparison with the individuals with hypertension.

A randomized controlled clinical trial was performed to evaluate apparently healthy men, aged between 25-55 years, with body mass indexes of 18.5-34.9 kg/m^2, and resting systolic (SBP) and diastolic (DBP) blood pressures lower than 160 and 100 mmHg, respectively. The following exclusion criteria were applied: a) evidence of secondary hypertension; b) diabetes mellitus; c) renal disease with glomerular filtration rates < 60ml/min/1.73m^2; d) coronary artery disease, clinically evidenced by a previous myocardial infarction and/or coronary revascularization; e) clinical signs of heart failure or history of stroke; f) any condition, disease or therapy that might compromise the safety of physical exercise; and g) use of antihypertensive or any other medication that could influence cardiovascular and respiratory responses to exercise.

Thirty candidates initially volunteered to participate in the study, with 27 considered eligible after the initial health screening. Three participants dropped out of the experimental sessions and were not considered for

analysis. The remaining 24 participants were assigned into normotensive (*n*=14) and hypertensive (*n*=10) groups, through ambulatory blood pressure monitoring (ABPM) results after a non-exercise control session (CTL). The study gained approval from the institutional ethics committee (CAAE: 30358614.9.0000.5259) and participants were informed of the benefits and risks of the study prior to signing an institutionally approved informed consent document to participate in the study.

Procedures

Each participant visited the laboratory five times. During the first visit, a pre-participation questionnaire for assessment of cardiovascular risk was applied, the blood pressure at-office and anthropometric profile were evaluated, blood samples were taken, resting oxygen uptake (VO_2) was determined, and then a maximal cardiopulmonary exercise test (CPET) was performed on a cycle ergometer (Cateye EC-1600, Cateye^{TM}, Tokio, Japan). The seat height of the ergometer was adjusted for each participant and standardized across all exercise bouts for a given participant. Following the outcome of blood sample analysis, participants who remained eligible underwent either a CTL session, or three cycling bouts separated by a minimum interval of 48 h, which possessed the following combination of short *vs*. prolonged and moderate *vs*. vigorous exercise: 1) energy expenditure of 150 kcal performed at 50% oxygen uptake reserve (VO_2R) (S-MOD); 2) energy expenditure of 300 kcal performed at 50% VO_2R (P-MOD); and 3) energy expenditure of 300 kcal performed at 70% VO_2R (P-VIG). The order of CTL and the cycling bouts was established according to a randomized, counterbalanced crossover design. Before the exercise and CTL conditions, baseline assessments consisting of measurement of central and peripheral blood pressures, were performed after 10 min of bed rest in a quiet environment. The CTL mimicked the exercise bouts in that participants remained seated at rest for 20 min. Within 5 sec of exercise (or CTL) termination, participants were placed in the supine position, and acquisition markers for central wave reflection were collected after 30 and 70 min of recovery in a quiet room, kept at a relatively constant temperature and relative humidity ranging from 21 to 23°C and 50 to 70%, respectively. After 30 min of recovery from CTL, 24-h ambulatory blood pressure monitoring (ABPM) was performed to confirm or not the diagnosis of hypertension. All visits were conducted at approximately the same time of day, between 07:00 and 11:00 a.m.

Blood samples analysis

Biochemical analysis was performed from venous blood samples taken after 8 to 12 h of fasting. Hemoglobin, total-cholesterol, high-density lipoprotein [HDL]-cholesterol, triglycerides, glucose, and creatinine were analyzed using enzymatic methods, while the low-density lipoprotein [LDL]-cholesterol fraction was estimated using the Friedewald equation when the triglyceride concentration did not exceed 400 mg/dL. The glomerular filtration rate was estimated by the CKD-EPI creatinine equation [16].

Blood pressure assessment

Blood pressure was measured using an automated Omron 705IT device (Omron™ Healthcare Co., Kyoto, Japan). Participants laid in a quiet and comfortable environment to stabilize blood pressure. Three measurements were performed at 10-min intervals during 30 min of rest, with resting blood pressure calculated as the mean of the three readings. Participants were classified as normotensive or hypertensive from 24-h ABPM using an automatic noninvasive ambulatory monitor (Spacelabs™ Medical, Redmond, WA, USA) according to the British Hypertension Society guidelines [17]. Measurements were taken every 20 min during the daytime or awake period (between approximately 7 a.m. to 10 p.m.) and every 30 min during the night or sleep time (between approximately 10 p.m. and 7 a.m.). Recordings were averaged over 24 h through the ABP Report Management System Software (v.2.00.09) (Spacelabs™ Medical, Redmond, WA, USA). Normotensives were defined as those with 24-h SBP < 130 mmHg and 24-h DBP < 80 mmHg, and hypertensives as those with 24-h SBP ≥ 130 mmHg or 24-h DBP ≥ 80 mmHg.

Pulse wave reflection assessment

Central hemodynamic markers were evaluated using a SphygmoCor™ system (AtCor Medical Pty Ltd, Sydney, Australia), which employs the principle of applanation tonometry, as previously described [18]. In brief, from radial artery recordings, central pressure was derived with the use of a generalized transfer function, which is an accurate estimate of the central pressure waveform. Waveforms of radial pressure were calibrated according to mean arterial pressure and diastolic blood pressure measured in the brachial artery. The AP is the pressure added to the incident wave by the returning reflected wave and represents the aortic blood pressure that the left ventricle must overcome during systole. AIx was calculated as the AP divided by the cPP and was expressed as a percentage.

Maximal and submaximal exercise tests

The ramp-incremented maximal CPET was performed as described elsewhere [19]. The incremental test was considered maximal if the participant satisfied at least three of the four following criteria: a) maximum voluntary exhaustion as reflected by a score of 10 on the Borg CR-10 scale; b) 90% of the predicted maximal heart rate [HR_{max} = 220 – age], or presence of a heart rate plateau (ΔHR between two consecutive work rates ≤ 4 bpm); c) presence of a VO_2 plateau (ΔVO_2 between two consecutive work rates < 2.1 $mL \cdot kg^{-1} \cdot min^{-1}$); and d) a maximal respiratory exchange ratio (RER_{max}) > 1.10. All participants were verbally encouraged to provide a maximal effort.

Based on the VO_{2max} obtained in the CPET, and on the resting VO_2, the values corresponding to 50% and 70% VO_2R were calculated to determine the intensity of the cycling bouts. The absolute VO_2 value corresponding to a given $\%VO_2R$ was used to calculate the associated cycling power by applying the equation: VO_2 cycling = 3.5 + 12.24 x power x BW^{-1}, where VO_2 is in $mL \cdot kg^{-1} \cdot min^{-1}$, power is in watts, and body weight is in kilograms [20]. Cycling cadence was maintained at 70 (±5) $revs \cdot min^{-1}$ throughout the bouts and, when necessary, power output was adjusted to maintain the target metabolic intensity. The energy expenditure was calculated individually from the VO_2 and VCO_2 in L/min, using the Weir equation: Energy expenditure in kcal = [(3.941 × average VO_2) + (1.106 × average VCO_2)] × exercise time in minutes [21]. The first 5-min interval of each exercise bout was omitted from all analyses, to negate the confounding effects of the anaerobic energy component of total energy expenditure associated with the initial (fast) VO_2 on-kinetics.

Pulmonary gas exchange was determined during rest, the CPET, and the submaximal cycling bout using a VO2000 analyzer (Medical GraphicsTM, Saint Louis, MO, USA) and a silicone face mask (Hans Rudolph™, Kansas, MO, USA). The gas exchange variables were 30-s stationary time-averaged, which provided a good compromise between removing noise in the data while maintaining the underlying trend. Prior to testing, the gas analyzers were calibrated according to the manufacturer's instructions using a certified standard mixture of oxygen (17.01%) and carbon dioxide (5.00%), balanced with nitrogen (AGA®, Rio de Janeiro, RJ, Brazil). The flows and amounts of energy expended of the pneumotacograph were calibrated with a syringe graduated for a 3 L capacity (Hans RudolphTM, Kansas, MO, USA). Heart

rate was measured continuously using a cardiotachometer (V800, Polar™, Kempele, Finland) and beat-by-beat data were 30-s stationary time-averaged.

Statistical Analyses

Data normality was tested using the Shapiro-Wilk test and data are presented as the mean and standard error of the mean. Baseline differences between groups were checked using independent-samples t-test. Changes in central pressure and pulse wave reflection were calculated as Δ values [i.e. difference between post- and pre-intervention values]. Possible differences in regard to central pressure and pulse wave reflection between groups (i.e. normotensive vs. hypertensive), experimental sessions [i.e. intensity and (CTL *vs.* S-MOD *vs.* P-MOD) volume (CTL *vs.* P-MOD *vs.* P-VIG) main effects], and time (i.e. 30- and 70-min post-intervention) were tested by factorial ANOVA followed by Sidak post hoc tests in the event of significant *F* ratios. All statistical analyses were performed using IBM Statistical Package for the Social Sciences (SPSS®) version 22 (SPSS™ Inc., Chicago, IL, USA) and statistical significance was accepted as $P \leq 0.05$.

RESULTS

Table 1 shows the mean ± SEM values for age, anthropometric profile, biochemical markers, peripheral and central pressures, pulse wave reflection, maximal physiological responses from the CPET, and times to achieve 150 kcal at 50% VO_2R and 300 kcal at 50% and 70% VO_2R during the continuous cycling bouts, respectively. Participants assigned to the hypertensive group had significantly higher body mass indexes ($P = 0.015$) and resting peripheral and central pressures ($P < 0.001$) than those in the normotensive group.

INSERT TABLE 1

Figure 1 shows the mean ± SEM values for central pressure and pulse wave reflection in the normotensive and hypertensive groups following 30 and 70 min of recovery from CTL and each cycling bout. Significant main effects were found for exercise intensity and intensity *vs.* group interaction for cSBP ($F = 3.1$; $P = 0.011$), cPP ($F = 3.4$; $P = 0.007$), AP ($F = 2.9$; $P = 0.016$), AIx@75 ($F = 2.4$; $P = 0.039$), and HR ($F = 2.4$; $P = 0.039$), which revealed that the differences between CTL and exercise conditions increased in the hypertensive group, especially after P-VIG. Compared to CTL, cSBP [*70-min* (mean diff: -11.7 mmHg, *P*

= 0.009)], cPP ([*70-min* (mean diff: -7.4 mmHg, *P* = 0.044)], AP [*30-min* (mean diff: -5.7 mmHg, *P* = 0.018), *70-min* (mean diff: -7.3 mmHg, *P* = 0.001)], AIx [*30-min* (mean diff: -15.3 %, *P* = 0.045), *70-min* (mean diff: -16.4 %, *P* = 0.030)], and AIx@75 [*30-min* (mean diff: -12.8 %, *P* = 0.048), *70-min* (mean diff: -13.9 %, *P* = 0.028)] where significantly reduced after P-VIG. All these reductions occurred concomitantly with the increase in HR [*70-min* (mean diff: 9.9 bpm, *P* = 0.007)] (see Figure 1). There was no significant main effect for group (*P* > 0.05), neither for volume *vs.* group interaction (*P* > 0.05). Furthermore, post hoc pairwise comparisons revealed significant increases over time post-CTL for cSBP (mean diff: 9.2 mmHg, *P* = 0.05) in the hypertensive group, which in turn were mitigated in all exercise conditions. In the normotensive group, HR was significantly decreased between 30- and 70-min after the P-VIG (mean diff: -6.5 bpm; *P* = 0.002).

INSERT FIGURE 1

DISCUSSION

The present study adds to current knowledge by investigating whether aerobic exercise bouts of different intensities and amounts of energy expended would influence the acute central pressure and pulse wave reflection responses in normotensive and hypertensive men. The major findings were: 1) exercise intensity is of primary importance for exercise prescription in hypertensive men, since only the vigorous-intensity exercise (i.e. 300 kcal at 70% VO_2R) was able to induce a significant reduction in central pressure and pulse wave reflection; 2) regardless of volume, moderate-intensity aerobic exercise bouts (i.e. 150 or 300 kcal at 50% VO_2R) may mitigate the increased cSBP response observed post-CTL in hypertensive men, but without affecting the acute pulse wave responses; and 3) the recovery pattern of central pressure and pulse wave reflection responses seems to be affected by clinical blood pressure status. The hypertensive group, for example, exhibited a delayed hypotensive response (i.e. ↓ cSBP and cPP only detected at 70 min of recovery) following the P-VIG, which occurred via reduction of pulse wave reflection. On the other hand, there was an absence of central pressure reduction in the normotensive group, since the pulse wave reflection markers remained unchanged throughout the recovery period.

To date, most of the available studies have investigated the acute central pressure and pulse wave reflection responses to aerobic exercise in healthy subjects [11,12,22], or using mixed samples, such as

prehypertensive and hypertensive individuals [23,24], metabolic syndrome and hypertension [25], and patients with peripheral and hypertensive arterial disease [26], and have reported contradictory findings. A possible explanation for these inconsistent findings may be due to methodological issues, such as no control group (i.e. a normotensive group), adopting a pre-post intervention design without a control condition on a separate day, and lack of clear adoption of components for aerobic exercise prescription (e.g. intensity, time, type, volume) to facilitate the practical application of the findings for the initial management of hypertension.

In this context, the absence of an acute central pressure reduction (i.e. ↔ cSBP) in 25 untreated hypertensive patients aged 18 to 65 yr, throughout 60-min of recovery from a maximal treadmill CPET, has been reported by Gkaliagkousi, Gavriilaki [24]. Boutcher, Hopp [13] also observed no reduction in pulse wave reflection (i.e. ↔ AIx) after 30-min of recovery from a single bout of cycling at 60% VO_{2max}, in 40 normotensive men aged between 18 and 27 yr who had either a family history or no family history of hypertension. In contrast, Millen, Woodiwiss [23] observed that a 50-min vigorous exercise bout promoted acute changes in central pressure and pulse wave reflection markers (e.g. baseline *vs.* 15-min postexercise: ↓cSBP: -10 mmHg; ↓AP: -7.1 mmHg; ↓AIx: -18.5%; ↓AIx@75: -6.1%; ↑HR: 25 bpm), in 20 pre-hypertensive and hypertensive men and women aged between 30 and 57 yr (VO_{2max}: 26.5 ± 4.6 $mL \cdot kg^{-1} \cdot min^{-1}$). However, the authors prescribed different exercise intensities (e.g. 60 to 75% VO_{2max}) and modalities (e.g. stationary bike and/or a treadmill). The interaction between exercise intensity, duration and mode determines the energy expenditure, which reflects the volume of the exercise bout ($kcal \cdot bout^{-1}$). It is therefore unclear whether the findings of Millen, Woodiwiss [23] were due to differences in exercise intensity, the isolated effect of exercise mode, or exercise volume. Our findings support the notion that reductions in acute central pressure and pulse wave reflection after aerobic exercise primarily depend on exercise-intensity.

The systematic review and meta-analysis of Ashor, Lara [9] investigated the chronic effects of aerobic, resistance, and concurrent training on pulse wave velocity and AIx, which are commonly used as markers of arterial stiffness. After reviewing forty-two randomized controlled studies, the authors concluded that only aerobic exercise was able to significantly improve pulse wave velocity and AIx, while exercise intensity rather than exercise volume (e.g. frequency and duration of bouts) was positively associated with improvement in AIx. Nevertheless, such changes after short-term aerobic exercise (i.e. ≥ 4 weeks) appear

to depend on the level of baseline arterial stiffness and exercise intensity. Greater baseline arterial stiffness (e.g. hypertensive patients) and vigorous compared to moderate intensity exercise appear to elicit greater chronic changes in arterial stiffness and pulse wave reflection following aerobic exercise, which is in agreement with the acute changes observed in the present study.

Additionally, the evaluation of postexercise pulse wave reflection has usually been performed only once, and the assessment time has not exceeded 30-min after the end of the exercise [23,25]. In the present study, assessment time influenced the observation of main outcomes, especially in hypertensive men. Although vigorous-intensity exercise has been able to reduce the pulse wave reflection markers (i.e. AP, AIx, and AIx@75) throughout the recovery period, reductions in cSBP and cPP were observed only after 70-min from exercise termination. In the normotensive group, regardless of the exercise condition and the time of evaluation, it was not possible to observe significant changes in the reflection markers or central pressure. These results seem to agree with other studies that also did not observe acute benefits of aerobic exercise in the reflection markers when performed with healthy individuals [27-29], although other studies have observed a reduction, especially for AIx, after aerobic exercise [30,31].

Moreover, postexercise responses may also differ depending on the reflection indicators of the pulse wave used. Radhakrishnan, Swaminathan [25] have emphasized the importance of using AIx@75 due to the influence of heart rate on AIx. Increased heart rate reduces the absolute duration of the cardiac cycle, which in turn causes the reflex wave to occur during diastole, with a consequent reduction of AIx and increased coronary perfusion. On the other hand, when it occurs during systole it is related to myocardial overload and, consequently, to increased oxygen uptake. This behavior suggests that reductions in AIx could occur only as a result of the increase in HR that occurs soon after exercise, regardless of changes in pulse wave reflection. Thus, normalization of AIx by a HR of 75 bpm would abolish the influence of a shorter cardiac cycle, thus favoring beneficial AIx results, without necessarily modifying vascular properties. On the other hand, there is evidence that the statistical model used in the HR correction factor is inappropriate [32], since the method assumes that the relationship between HR and arterial stiffness is the same for all populations.

Although the use of AIx normalization is still controversial in the assessment of vascular function, the largest study (n=253) conducted to assess the relationship between HR and arterial stiffness reported a

strong association between elevated HR and reduced blood pressure, carotid artery distension and increased pulse wave velocity [33]. This result suggests that the relationship between HR and arterial stiffness may change if HR remains chronically elevated. Thus, current recommendations suggest the use of AIx@75 only in cases of acute evaluations, as there may be compensations in wave morphology with increased HR. In longitudinal studies, this indicator should be used with caution in the interpretation of results, since HR behaviour may help explain changes in arterial stiffness [32]. In this sense, the present study opted to use both pulse wave reflection indexes (AIx and AIx@75). As observed in hypertensive men, only P-VIG was able to reduce these rates, even with the concomitant increase in HR throughout the recovery period (see Figure 1A-F). In addition, significant differences were observed between groups for AIx@75 at 70 min recovery. This result confirms that the intensity of the exercise added to the initial pressure levels is decisive in producing acute effects on the pulse wave reflection.

Among the studies that observed acute reductions in central pressure and pulse wave reflection over a 30-min recovery period [11,12,22,34], only the study by Nieman, Dew [34] applied an experimental control. Physiological responses were investigated over a 5-h period following a 2-h treadmill run at 75% VO_{2max} in trained men (n=8, age 39.3 ± 2.3 yr, VO_{2max}: 54.8 ± 1.7 $mL \cdot kg^{-1} \cdot min^{-1}$) and women (n=8, age 35.8 ± 2.8 yr, VO_{2max}: 49.6 ± 1.8 $mL \cdot kg^{-1} \cdot min^{-1}$), with significant reductions in AIx@75 restricted to the female runners. Regardless of the findings, the lack of ecological validity of the exercise protocol adopted in this study is evident, especially within the context of training programs for the initial management of hypertension. However, in the present study, the mean cSBP data between 30 and 70-min of recovery post-CTL revealed an increased response of these markers only in the hypertensive group, which in turn was mitigated after all exercise bouts (see Figure 1A). In practical terms, it is feasible that the adoption of a pre-post intervention design without an experimental control may lead to a misinterpretation of the data due to the interaction between the normally higher pre-exercise (or baseline) values versus the low values postexercise.

Some limitations of the present study must be recognized. Firstly, only middle-aged individuals with mild arterial hypertension were included, which may have reduced the difference between the groups. It is known that hypertension is closely linked to increased arterial stiffness, and both of these factors are associated with advancing age. Although this was not the objective of the present study, mainly due to the risk of

immediate complications resulting from the practice of vigorous exercises in this population, further studies should be carried out with older hypertensive patients to investigate if they present similar responses with matched middle-aged men. Secondly, a short-duration vigorous intensity exercise bout was not included, therefore, it is not possible to say whether this would elicit the same responses observed in the prolonged vigorous intensity exercise bout. Additional research is therefore needed to verify these responses for different levels of blood pressure and exercise protocol.

In conclusion, a single bout of vigorous-intensity cycling can lower central pressure and reduce pulse wave reflection only in hypertensive men. Regardless of exercise-related energy expenditure, aerobic bouts performed at moderate-intensity did not affect the acute pulse wave reflection among hypertensive and normotensive men, but in the former this may be a strategy to mitigate the increased central pressure responses observed after non-exercise days. Taken together, these findings may have important implications within the context of aerobic exercise prescription for the initial management of hypertension.

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REFERENCES

1. Williams B, Mancia G, Spiering W, Agabiti Rosei E, Azizi M, Burnier M, et al. 2018 ESC/ESH Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension: The Task Force for the management of arterial hypertension of the European Society of Cardiology and the European Society of Hypertension. J Hypertens 2018; 36 (10):1953-2041.

2. Riebe DE, J. K.; Liguori, G.; Magal, M.; American College of Sports Medicine,. ACSM's guidelines for exercise testing and prescription. Philadelphia: Wolters Kluwer; 2018.

3. Pescatello LS, MacDonald HV, Lamberti L, Johnson BT. Exercise for hypertension: A prescription update integrating existing recommendations with emerging research. Curr Hypertens Rep 2015; 17 (11):87.

4. Eckel RH, Jakicic JM, Ard JD, De Jesus JM, Houston Miller N, Hubbard VS, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: A report of the American college of cardiology/American heart association task force on practice guidelines. Journal of the American College of Cardiology 2014; 63 (25 PART B):2960-2984.

5. Pescatello LS. Effects of exercise on hypertension: from cells to physiological systems. Springer International Publishing; 2015.

6. Cornelissen VA, Smart NA. Exercise training for blood pressure: a systematic review and meta-analysis. J Am Heart Assoc 2013; 2 (1):e004473.

7. Bortolotto LA, Safar ME. Blood pressure profile along the arterial tree and genetics of hypertension. Arquivos brasileiros de cardiologia 2006; 86 (3):166-169.

8. Sabovic M, Safar ME, Blacher J. Is there any additional prognostic value of central blood pressure wave forms beyond peripheral blood pressure? Curr Pharm Des 2009; 15 (3):254-266.

9. Ashor AW, Lara J, Siervo M, Celis-Morales C, Mathers JC. Effects of exercise modalities on arterial stiffness and wave reflection: a systematic review and meta-analysis of randomized controlled trials. PLoS One 2014; 9 (10):e110034-e110034.

10. Zhang Y, Qi L, Xu L, Sun X, Liu W, Zhou S, et al. Effects of exercise modalities on central hemodynamics, arterial stiffness and cardiac function in cardiovascular disease: Systematic review and meta-analysis of randomized controlled trials. PLoS One 2018; 13 (7):e0200829.

11. Milatz F, Ketelhut S, Ketelhut RG. Acute effects of moderate continuous training on stress test-related pulse pressure and wave reflection in healthy men. High Blood Pressure and Cardiovascular Prevention 2017; 24 (1):61-67.

12. Hanssen H, Nussbaumer M, Moor C, Cordes M, Schindler C, Schmidt-Trucksäss A. Acute effects of interval versus continuous endurance training on pulse wave reflection in healthy young men. Atherosclerosis 2015; 238 (2):399-406.

13. Boutcher YN, Hopp JP, Boutcher SH. Acute effect of a single bout of aerobic exercise on vascular and baroreflex function of young males with a family history of hypertension. Journal of Human Hypertension 2011; 25 (5):311-319.

14. Chandrakumar D, Boutcher SH, Boutcher YN. Acute exercise effects on vascular and autonomic function in overweight men. The Journal of sports medicine and physical fitness 2015; 55 (1-2):91-102.

15. Thompson PD, Crouse SF, Goodpaster B, Kelley D, Moyna N, Pescatello L. The acute versus the chronic response to exercise. Med Sci Sports Exerc 2001; 33 (6 Suppl):S438-445; discussion S452-433.

16. Levey AS, Stevens LA, Schmid CH, Zhang YL, Castro AF, Feldman HI, et al. A new equation to estimate glomerular filtration rate. Annals of internal medicine 2009; 150 (9):604-612.

17. McGrath BP, National Blood Pressure Advisory Committee of the National Heart Foundation of A. Ambulatory blood pressure monitoring. The Medical journal of Australia 2002; 176 (12):588-592.

18. Agabiti-Rosei E, Mancia G, O'Rourke MF, Roman MJ, Safar ME, Smulyan H, et al. Central blood pressure measurements and antihypertensive therapy: a consensus document. Hypertension (Dallas, Tex : 1979) 2007; 50 (1):154-160.

19. Cunha FA, Midgley A, Montenegro R, Vasconcellos F, Farinatti P. Utility of a non-exercise VO_{2max} prediction model for designing ramp test protocols. International journal of sports medicine 2015; 36 (10):796-802.

20. Acsm. ACSM's guidelines for exercise testing and prescription. Philadelphia: Kluwer, Wolters; 2018.

21. Weir JB. New methods for calculating metabolic rate with special reference to protein metabolism. J Physiol 1949; 109 (1-2):1-9.

22. Sugawara J, Komine H, Miyazawa T, Imai T, Ogoh S. Influence of single bout of aerobic exercise on aortic pulse pressure. European journal of applied physiology 2015; 115 (4):739-746.

23. Millen AME, Woodiwiss AJ, Norton GR. Post-exercise effects on aortic wave reflection derived from wave separation analysis in young- to middle-aged pre-hypertensives and hypertensives. European journal of applied physiology 2016; 116 (7):1321-1329.

24. Gkaliagkousi E, Gavriilaki E, Nikolaidou B, Triantafyllou G, Douma S. Exercise-induced pulse wave velocity changes in untreated patients with essential hypertension: the effect of an angiotensin receptor antagonist. J Clin Hypertens (Greenwich) 2014; 16 (7):482-487.

25. Radhakrishnan J, Swaminathan N, Pereira NM, Henderson K, Brodie DA. Acute changes in arterial stiffness following exercise in people with metabolic syndrome. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 2016.

26. Sacre JW, Holland DJ, Jenkins C, Sharman JE. Augmentation index immediately after maximal exercise in patients with type 2 diabetes mellitus. Medicine & Science in Sports & Exercise 2012; 44 (1):75-83.

27. Burr JF, Boulter M, Beck K. Arterial stiffness results from eccentrically biased downhill running exercise. Journal of Science and Medicine in Sport 2015; 18 (2):230-235.

401 28. Kingsley JD, Tai YL, Vaughan JA, Mayo X. High-Intensity Interval Cycling Exercise on Wave
402 Reflection and Pulse Wave Velocity. J Strength Cond Res 2017; 31 (5):1313-1320.

403 29. Staniszewska M, Pudło A, Ryterska K, Stachowska E. Influence of physical effort on aortic stiffness
404 in young male athletes. 2016:3440-3446.

405 30. Lane AD, Ranadive SM, Yan H, Kappus RM, Cook MD, Sun P, et al. Effect of Sex on Wasted Left
406 Ventricular E ff ort Following Maximal Exercise. 2013:770-776.

407 31. Siasos G, Athanasiou D, Terzis G, Stasinaki A, Oikonomou E, Tsitkanou S, et al. The acute impact of
408 different types of aerobic exercise on arterial wave reflections and inflammation. Cardiology 2016; 135
409 (2):81-86.

410 32. Stoner L, Faulkner J, Lowe A, D ML, J MY, Love R, et al. Should the augmentation index be
411 normalized to heart rate? Journal of atherosclerosis and thrombosis 2014; 21 (1):11-16.

412 33. Sa Cunha R, Pannier B, Benetos A, Siche JP, London GM, Mallion JM, et al. Association between
413 high heart rate and high arterial rigidity in normotensive and hypertensive subjects. J Hypertens 1997; 15
414 (12 Pt 1):1423-1430.

415 34. Nieman D, Dew D, Krasen P. Gender difference in the acute influence of a 2-hour run on arterial
416 stiffness in trained runners. Research in Sports Medicine 2013; 21 (1):66-77.

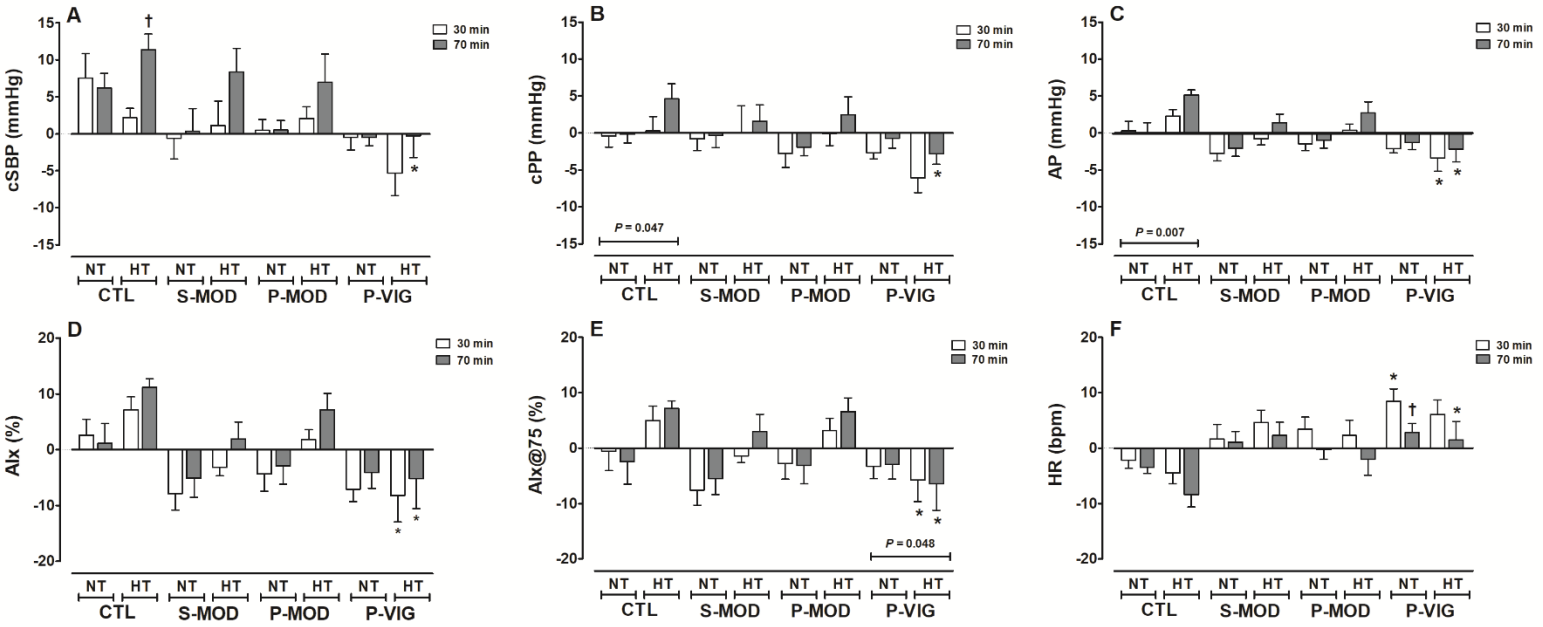
417 35. Costa EC, Kent DE, Boreskie KF, Hay JL, Kehler DS, Edye-Mazowita A, et al. Acute Effect of High-
418 Intensity Interval Versus Moderate-Intensity Continuous Exercise on Blood Pressure and Arterial
419 Compliance in Middle-Aged and Older Hypertensive Women With Increased Arterial Stiffness. J
420 Strength Cond Res 2020; 34 (5):1307-1316.

421 36. Aizawa K, Petrella RJ. Acute and chronic impact of dynamic exercise on arterial stiffness in older
422 hypertensives. The open cardiovascular medicine journal 2008; 2:3-8.

423 **Table 1.** Baseline participant characteristics.

Assessments	Variable	Normotensive group (n =14)	Hypertensive group (n =10)	*P-value*
		Mean ± SEM	Mean ± SEM	
Anthropometric	Age (yr)	40.7 ± 2.8	39.2 ± 2.3	0.823
	Height (cm)	177.6 ± 3.5	177.3 ± 2.8	0.901
	Body mass (kg)	81.6 ± 1.3	92.1 ± 2.2	0.042
	Body mass index (kg/m^2)	25.7 ± 0.9	29.3 ± 1.0	0.015
Biochemical	Hemoglobin (g/dl)	15.1 ± 0.3	15.0 ± 0.4	0.848
	Glucose (mg /dl)	88 ± 3	90 ± 3	0.742
	Creatinine (mg/dl)	1.0 ± 0.1	1.0 ± 0.0	0.482
	Glomerular filtration rate (mg/min)	96 ± 6	88 ± 4	0.992
	Total cholesterol (mg/dl)	207 ± 9	218 ± 13	0.467
	HDL-cholesterol (mg/dl)	56 ± 4	48 ± 3	0.197
	LDL-cholesterol (mg/dl)	126 ± 8	145 ± 11	0.155
	Triglycerides (mg/dl)	126 ± 22	127 ± 20	0.989
Blood pressure and pulse wave reflection markers	Office systolic blood pressure (mmHg)	113 ± 2	133 ± 4	< 0.001
	Office diastolic blood pressure (mmHg)	71 ± 1	84 ± 4	< 0.001
	24h-ambulatory systolic blood pressure (mmHg)	121 ± 2	139 ± 3	< 0.001
	24h-ambulatory diastolic blood pressure (mmHg)	74 ± 1	86 ± 2	< 0.001
	Aortic systolic blood pressure (mmHg)	101 ± 1	116 ± 4	< 0.001
	Aortic diastolic blood pressure (mmHg)	71 ± 1	84 ± 3	< 0.001
	Aortic pulse pressure (mmHg)	30 ± 1	32 ± 2	0.386
	Augmentation pressure (mmHg)	5 ± 1	4 ± 2	0.628
	Augmentation index (%)	14 ± 3	12 ± 4	0.681
Incremental exercise test	Maximal oxygen uptake (mL·kg^{-1}·min^{-1})	31.3 ± 1.8	26.7 ± 0.8	0.056
	Maximal heart rate (beats·min^{-1})	179.8 ± 1.8	176.3 ± 3.1	0.313
	Maximal power output (W)	223.2 ± 7.6	207.8 ± 15.0	0.328
Cycling bouts	Time to achieve 150 kcal at 50% VO_2R (min)	23.0 ± 0.8	22.1 ± 1.1	0.482
	Time to achieve 300 kcal at 50% VO_2R (min)	43.5 ± 1.7	44.3 ± 1.9	0.762
	Time to achieve 300 kcal at 70% VO_2R (min)	34.6 ± 1.4	33.6 ± 1.1	0.584

424 SEM = standard error of the mean.



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426 **Fig. 1** Mean ± SEM changes in cSBP (A), cPP (B), AP (C), AIx (D), AIx@75 (E), and HR (F) at 30 and 70 min of recovery in each condition (Δ = post- minus pre-
427 intervention assessment). NT = normotensive group; HT = hypertensive group; CTL = control session (non-exercise day); %VO_2R = percentage of oxygen uptake
428 reserve; cSBP = central systolic blood pressure; cPP = central pulse pressure, AP = augmentation pressure; AIx = aumengtation index; AIx@75 = heart rate-corrected
429 augmentation index; HR = heart rate; S-MOD = energy expenditure of 150 kcal performed at 50% VO_2R; P-MOD = energy expenditure of 300 kcal performed at 50%
430 VO_2R; P-VIG = energy expenditure of 300 kcal performed at 70% VO_2R. *P* values indicate significant differences between normotensive and hypertensive groups.
431 *: Significant difference compared to CTL ($P < 0.05$). †: Significant between 30- and 70-min post-intervention ($P < 0.05$).