# openheart Evaluation of vascular responses to moderate-intensity continuous and high-intensity interval physical exercise in subjects with elevated blood pressure: a randomised, cross-over clinical trial

Sara Rodrigues , <sup>1</sup> Renata Gomes Sanches Verardino, <sup>1</sup> Valéria Costa - Hong, <sup>1</sup> Camila Paixao Jordao, <sup>2</sup> Marcel Jose Andrade da Costa, <sup>3</sup> Luiz Bortolotto <sup>1</sup>

To cite: Rodrigues S, Verardino RGS, Costa - Hong V. et al. Evaluation of vascular responses to moderate-intensity continuous and high-intensity interval physical exercise in subjects with elevated blood pressure: a randomised, crossover clinical trial. Open Heart 2025;12:e003121. doi:10.1136/ openhrt-2024-003121

Received 10 December 2024 Accepted 7 March 2025



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<sup>1</sup>Unidade de Hipertensão, Instituto do Coração (InCor), Hospital das Clinicas HCFMUSP, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, Brazil

<sup>2</sup>Universidade de São Paulo Instituto do Coração, Sao Paulo, Brazil

<sup>3</sup>Unidade de Exercício Físico e Reabilitação, Instituto do Coração (InCor), Hospital das Clinicas, HCFMUSP, Faculdade de Medicina FMUSP. Universidade de Sao Paulo, Sao Paulo, Brazil

#### **Correspondence to**

Luiz Bortolotto; hipluiz@incor. usp.br

#### **ABSTRACT**

**Objective** In this randomised two-period crossover trial, the objective was to compare acute changes in arterial distensibility between high-intensity interval physical exercise (HIIPE) and moderate-intensity continuous physical exercise (MICPE) sessions in subjects with elevated blood pressure (BP).

Methods and analysis Participants underwent either MICPE-HIIPE or HIIPE-MICPE sequences with intensity based on cardiopulmonary exercise testing. The main outcome measures included arterial stiffness (by pulse wave velocity (PWV)) at baseline, until 30 min and 24 hours after each physical exercise session. Other measures include office BP, 24-hour ambulatory blood pressure monitoring (ABPM) and applanation tonometry. Results The study involved 29 subjects with elevated BP

(76% female, 48±7 years, body mass index=28.3±4.3 kg/ m<sup>2</sup>, systolic BP=126±9 mm Hg and diastolic BP=84±4 mm Hg). They presented lower PWV 24 hours after MICPE compared with baseline and to 24-hour HIIPE ((-0.83 (-1.29; -0.37) p=0.001) and (-0.98 (-1.84; -0.12),p=0.021), respectively). Despite no differences in office BP, aortic systolic BP was lower after HIIPE compared with baseline and to 24-hour MICPE (113±19; 118±10 and 117±10 mm Hg; p=0.013).

Conclusion In subjects with elevated BP, arterial distensibility is greater 24 hours after MICPE, while aortic systolic BP is lower after HIIPE. The particularities of each method and each exercise intensity can provide specific mechanisms of vascular response to exercise and detect vascular damage early in these subjects.

Trial registration number NCT04200716.

#### INTRODUCTION

Arterial stiffness is a potential predictor of stroke, coronary heart disease and mortality, in addition to being highly associated with cardiovascular disease.1 It may result from vascular dysfunction due to arterial wall

# WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The acute effects of physical exercise (PE) on skeletal muscle vasculature (vasodilation) are widely known; however, large artery responses to PE are controversial, in part, due to differences between measurement methods, exercise intensity and groups studied.

#### WHAT THIS STUDY ADDS

⇒ Changes in office blood pressure (BP) levels may represent different vascular behaviour in response to PE. Pulse wave velocity is lower than baseline values in subjects with elevated BP 24 hours after a moderate-intensity continuous physical exercise (MIIPE) session. Similarly, aortic systolic blood pressure decreases after high-intensity interval physical exercise (HIIPE).

# HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The vascular response from MIIPE seems to last longer: however, that from HIIPE can be significant. We need studies to better understand the mechanisms and responses of long-term physical training.

thickening, impaired endothelial function and/or autonomic imbalance; additionally, it may be involved in the onset and progression of hypertension.<sup>3</sup> Blood pressure (BP) changes, particularly sustained high levels, can increase pulse wave velocity (PWV), a marker of arterial stiffness. Hypertension is classified as BP levels ≥140 mm Hg for systolic and/or ≥90 mm Hg for diastolic BP; despite disagreement in classification below these levels, the American and European guidelines agree that systolic BP above 120 may increase cardiovascular risk, 4-6 identifying a 'BP risk zone' that can be targeted



for prevention. This reinforces the notion that cardiovascular risk from BP is more the result of cumulative exposure to elevated BP levels rather than a specific threshold value that defines risk.<sup>6</sup>

Physical exercise (PE) is recommended for preventing and treating hypertension due to its hypotensive effects. PE can improve arterial distensibility, endothelial function and autonomic balance, with benefits on BP depending on exercise type, duration and intensity.<sup>7</sup> Acute PE responses can predict long-term adaptations. 89 While vasodilation in skeletal muscle vasculature is wellstudied, the response of large arteries remains controversial, partly due to the diversity of measurement methods. Some studies showed increased aortic compliance while others report a decrease<sup>11</sup> after submaximal PE in sedentary males. Although many studies evaluate PWV changes in acute PE, <sup>2 9 12-14</sup> randomised controlled trials are scarce, <sup>12</sup> <sup>15</sup> and conclusive studies with subjects in the 'BP risk zone' are lacking. While arterial stiffness significantly changes within months of BP treatment, <sup>16</sup> understanding acute variations in arterial stiffness and BP can shed light on physiological processes, as PE acts as a stressor

Given that subtle baseline BP changes may affect vascular and sympathetic responses and that PE intensities offer different stimuli, we hypothesised that the high-intensity interval physical exercise session (HIIPE) will trigger stronger acute vascular responses than moderate-intensity continuous physical exercise (MICPE) session in subjects with elevated BP. Therefore, our primary objective is to compare acute changes in arterial function between HIIPE and MICPE in subjects with Elevated BP.

# **METHODS**

# Study design and participants

This is a randomised, two-period crossover trial, conducted from July 2018 to October 2021. Community advertisements, including targeted and passive outreach (eg, web and mass emails), were used to recruit study participants from Hospital das Clínicas da Universidade de São Paulo. The study was approved by the Scientific Commission of the Heart Institute (InCor) and by the Ethics in Research Commission of the Clinical Hospital, University of São Paulo (#0565/11) in August 2017. All participants provided written informed consent prior to any study procedures in accordance with the Declaration of Helsinki.

# Equity, diversity and inclusion statement

Our study included all cases of elevated BP among personal work and partners, covering various occupations, genders, races and socioeconomic levels. The author team comprised four women and two men from diverse disciplines (medicine, sports training, nursing and biology), including one graduate and five postdoctoral researchers. Possible sex inequities in PWV outcomes are presented in the discussion session.

#### INCLUSION CRITERIA

Age ≥30 and ≤60 years old, sedentary or recreationally active, both sexes, elevated BP levels (systolic blood pressure (SBP) 120 to 139 and/or diastolic blood pressure (DBP) 70 to 89 mm Hg) [6].

#### **EXCLUSION CRITERIA**

Engaged in other studies or PE training programmes, on drug treatment (for hypertension), smokers, unable to perform exercise on ergometer bike, presence of cardiovascular or metabolic disease (eg, diabetes, dyslipidaemia), pregnancy, body mass index (BMI) ≥40 kg/m².

The visits were performed individually in the early morning at InCor - Faculdade de Medicina da Universidade de São Paulo.

Figure 1 details all research phases, from participant screening to completion of interventions, as described above.

Screening and Recruitment: assessment of eligibility.

Randomisation: eligible participants were randomly allocated in a crossover design, ensuring participation in both interventions. Randomisation was performed using the RAND function in Microsoft Excel 2010,(1:1 ratio). Sessions occurred within 7 days. All steps were carried out by the same researcher.

### **Visits and interventions**

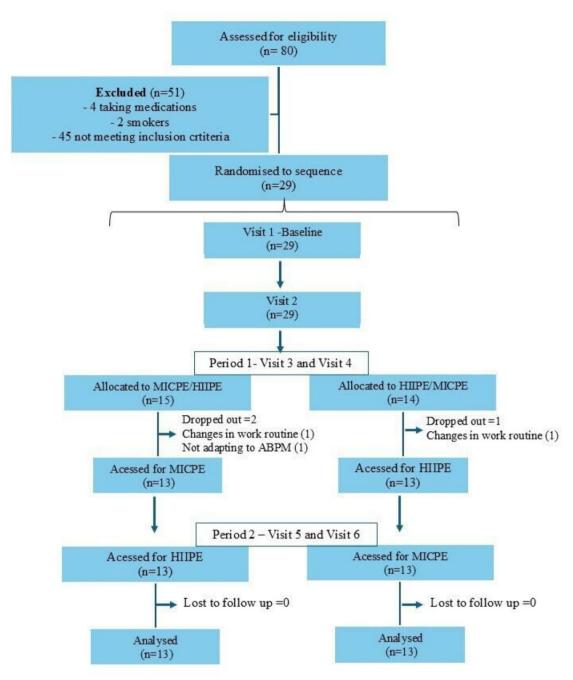
- ▶ Visit 1 (baseline): measurement of brachial and central BP, PWV and placement of the ambulatory blood pressure monitoring (ABPM) device.
- ▶ Visit 2 (24hours after visit 1): ABPM removal and execution of the cardiopulmonary exercise test (CPET) on a cycle ergometer to determine exercise intensity and equalise energy expenditure.
- ▶ Visits 3 and 5 (post-MICPE or post-HIIPE, it is the first visit in each period): PE session execution, PWV and aortic BP were measured during the first 30 min after PE and then placed ABPM.
- ▶ Visits 4 and 6 (MICPE24h or HIIPE24h, it is the second visit in each period): 24 hours after visits 3 and 5, ABPM removal, PWV and aortic BP measurement.

For a better understanding of the analysis, we name sessions 3 and 4 as period 1 of the crossover and sessions 5 and 6 as period 2.

# Patient and public involvement

No participants were directly involved in the design, conducting or research question, or analysis of results. They were asked about any discomfort experienced and encouraged to invite colleagues and partners to participate in the study, were informed about the personal and study results, and invited to the doctoral thesis defence.

The study is registered as a clinical trial via clinical-trials.gov (identifier number: Unique Protocol ID: 72503117.0.0000.0068; NCT04200716). We used the Consolidated Standards of Reporting Trials reporting guidelines. <sup>17</sup>



**Figure 1** Flow diagram. ABPM, Ambulatory blood pressure monitoring; HIIPE, high-intensity interval physical exercise; MICPE, moderate-intensity continuous physical exercise.

# **Procedures**

#### Blood pressure measurement

It was performed with a validated manual sphygmomanometer and a cuff suitable for arm circumference placed on the right arm. For resting BP, the average of at least two measurements was taken, with a 1-min interval between them.<sup>4</sup>

#### Maximal cardiopulmonary exercise test

To determine peak oxygen consumption (VO2peak), use a SensorMedics computerised ergospirometer: model Vmax 229 Pulmonary Function/Cardiopulmonary Exercise Testing Instrument, Yorba Linda, CA, USA. CPET was performed on a cycle ergometer (Ergoline ViaSprint 150P, Bitz, Germany). Heart rate (HR) was assessed by an ECG with 12 standard leads and BP by auscultatory method, monitored and evaluated by an experienced doctor. The test followed a protocol with constant increase in load (increments from 10 to 20 W/min), with 60 to 70 rotations per minute (RPM) until exhaustion. <sup>18</sup>

#### Physical exercise protocol

Both sessions were supervised by a sports instructor and were performed on a cycle ergometer (Ergoline ViaSprint 150P, Bitz, Germany), consisted of 5 min of warm-up and 5 min of cool-down, both at 50 RPM, without



| Table 1 Baseline characteris | etics                 |
|------------------------------|-----------------------|
|                              | Elevated BP<br>(n=29) |
| Sex (M/F)                    | 7/22                  |
| Race (B/W)                   | 7/22                  |
| Age (years)                  | 48±7                  |
| Weight (kg)                  | 75.7±15.8             |
| BMI                          | 28.34±4.31            |
| VO <sub>2max</sub>           | 23.89±4.35            |
| HRrest (BPM)                 | 78±11                 |
| HRmax (BPM)                  | 168±13                |
| OfficeBP (mm Hg)             |                       |
| SBP                          | 126±9                 |
| DBP                          | 84±4                  |
| Vascular measurements        |                       |
| PWV (m/s)                    | 7.85±0.78             |

Values are presented as mean  $\pm$  SD BMI, body mass index; DBP, diastolic blood pressure; HIIPE, high-intensity interval physical exercise; HR, heart rate; MICPE, moderate-intensity continuous physical exercise; PWV, pulse wave velocity; SBP, systolic blood pressure.

load, and main part. Total workload was calculated based on individual energy expenditure in CPET. <sup>19</sup> <sup>20</sup> HR was monitored with the Polar throughout the exercise and maintained at target levels. The main-part prescription was as follows:

#### ▶ MICPE

Thirty minutes of exercise at  $60\%\text{VO}_{2\text{peak}}$ , determined by CPET.

# ► HIIPE

Four to six bouts (according to the calculation to equalise energy expenditure with MICPE)  $30\,\mathrm{s}$  with resistance based on CPET at the maximum tolerated speed, aiming to reach at least  $90\%\mathrm{VO}_{\mathrm{2peak}}$ , interspersed for  $4\,\mathrm{min}$  at a low cadence ( $50\,\mathrm{RPM}$ ) and resistance ( $30\mathrm{W}$ ).

# Post-exercise hypotension (PEH) measurement

Post-exercise hypotension (PEH) is the name given to post-exercise BP, even though it does not reach hypotensive levels. To evaluate PEH, the ABPM device (Spacelabs) was placed after the end of each session. ABPM measured BP every 10 min while awake and every 20 min during sleep, accomplishing 24-hour monitoring.

# Pulse wave velocity (PWV)

Carotid-femoral PWV was evaluated using the automatic device Complior (Colson, France), which allows an online pulse wave recording and automatic calculation of PWV,<sup>21</sup> by a trained and experienced sports coach. The technique TY-306 Fukuda pressure-sensitive transducer (Fukuda, Tokyo, Japan) was put in carotid and femoral arteries, calculating time delay between the two transducers. The distance travelled by the pulse wave was

**Table 2** Mixed model results for PWV in post-PE at visits 3 and 5

|                      | Coefficient (I.C. 95%)                                      | P value |
|----------------------|---|---------|
| Intercept            | 7.82 (7.42; 8.22)   | 0.001   |
| Period (second)      | -0.12 (-0.40; 0.15)   | 0.364   |
| PE intensity (HIIPE) | -0.05 (-0.33; 0.22)   | 0.690   |
| •                    | as coefficient (IC 95%).<br>nterval; PE, physical exercise. |         |

measured over the body surface as the distance between the two recording sites (D), while pulse transit time (t), measured between the feet of the pressure waveforms recorded at these different points (foot-to-foot method), was automatically determined by the device: PWV=D/t.

# Aortic blood Pressure

Central BP assessment and pressure wave characteristics were non-invasively assessed by applanation tonometry using SphygmoCor (AtCor Medical) by a trained nurse. The pressure wave was obtained by a tonometer in the radial artery of the left arm using a high-sensitivity sensor (Millar Instruments, Houston, Texas), and by a transfer function, the central parameters were determined.

# Statistical analysis

The sample size was calculated using the OPEN EPI website  $^{22}$  and based on previous studies.  $^{10}$  With 80% power and two-sided type I error of 0.05, 11 subjects per group were needed to detect a 15% difference in PWV between exercise types, assuming a control (HIIPE) value of 6.2±0.4 (mean±SD) and assuming a loss of 15% of participants per group; we add at least three more in each group. Parametric data are presented as mean±SD, non-parametric as median (IQR).  $\chi 2$  tested categorical variables, and Kolmogorov–Smirnov and Levene tests assessed the normality and homogeneity. Repeated measures analysis of variance analysed variables across the sessions for BP. Analyses were performed using SPSS (IBM) V.20.

PWV variation ( $\Delta$  MICPE or  $\Delta$  HIIPE) was calculated by subtracting post-PE session and 24h PE values from baseline. A mixed model was applied to PWV for post-PE (periods 1 and 2), while a linear regression was used for period 1 (due to the carryover effect), using R software V.4.0.5 (R Core Team, 2021). All analysis considered p<0.05 as significant.

**Table 3** Linear regression model results for PWV in PE24h at visit 4

|                      | Coefficient (I.C. 95%) | P value |
|----------------------|------------------------|---------|
| Intercept            | 6.93 (6.44; 7.42)      | 0.001   |
| PE intensity (HIIPE) | 1.04 (0.35; 1.72)      | 0.005   |

Values are presented as coefficient (I.C. 95%). HIIPE, high-intensity interval; PE, physical exercise; PWV, pulse wave velocity.

Table 4 Comparisons of PWV post-PE and PE24h based on a mixed model

|                                   | post-PE (visit 3)   |         | PE24h (visit 4)      |         |
|-----------------------------------|---------------------|---------|----------------------|---------|
|                                   | I.C. 95%            | P value | I.C. 95%             | P value |
| HIIPE and HIIPE baseline          | 0.11 (-0.44; 0.66)  | 0.945   | 0.12 (-0.33; 0.56)   | 0.879   |
| MICPE and MICPE baseline          | -0.17 (-0.70; 0.36) | 0.804   | -0.83 (-1.29; -0.37) | 0.001   |
| MICPE baseline and HIIPE baseline | -0.09 (-0.95; 0.77) | 0.991   | -0.03 (-0.84; 0.79)  | 1.000   |
| MICPE and HIIPE                   | -0.38 (-1.26; 0.51) | 0.651   | -0.98 (-1.84; -0.12) | 0.021   |
| $\Delta$ MICPE and $\Delta$ HIIPE | -0.28 (-0.85; 0.29) | 0.316   | -0.95 (-1.43; -0.47) | 0.001   |

Values are presented as coefficient (I.C. 95%).

HIIPE, high-intensity physical exercise; MICPE, moderate intensity physical exercise; PE24h, 24h post physical exercise; postPE, post physical exercise; PWV, pulse wave velocity; Δ HIIPE, pulse wave velocity variation subtracting postHIIPE from baseline and HIIPE24h from baseline; Δ MICPE, pulse wave velocity variation subtracting postMICPE from baseline and MICPE24h from baseline.

#### **RESULTS**

We initially recruited eighty (80) subjects to be included in this study. Four<sup>4</sup> are taking drugs for hypertension, two (2) were smokers, and 45 did not meet the inclusion criteria. Therefore, 29 subjects remained (figure 1) with elevated BP (126±9 mm Hg SBP, 84±4 mm Hg DBP, 48±7 years, 76% female, BMI=28.3±4.3 kg/m²) (table 1). Fifteen subjects were allocated to the MICPE-HIIPE sequence and 14 to the HIIPE-MICPE sequence.

Comparison among PE intensities: there was no carryover effect in the post-PE session (p=0.389), and individuals with high BP did not present different PWV values in visits 3 and 5 (post-PE) (table 2). However, there was a carryover effect in the PE24h session (p=0.031); therefore, linear regression analysis, comparing the groups according to the PE sequence in visit 4, was performed to analyse the PE24h sessions. In the MICPE24h, PWV was 1.04 m/s (95% CI of 0.35 m/s to 1.72 m/s) lower than the HIIPE24h (table 3). Reinforcing the difference found in the MICPE24h, comparing PWV in a mixed model considering the baseline, third and fourth visits (ie, excluding the crossover period 2- table 4), there was no difference between the PE intensities in visit 3 (post-PE). However, for visit 4 (24hPE), there is a difference between 24hMICPE and baseline, between 24hMICPE and 24hHIIPE, and between variations from baseline and visit 4 ( $\Delta$ PWV) (table 4).

Exploratory analyses: despite no differences in auscultatory BP among sessions, aortic systolic BP was lower immediately after HIIPE compared with baseline and to 24hours after MICPE (table 5).

Measurements of ABPM allowed us to identify the presence of masked hypertension (24-hour BP  $\geq$ 130/80 mm Hg) which was found in 16 (55.2%) subjects.

### DISCUSSION

The main finding of the present study is that even small increases in office BP levels may represent different vascular behaviours in response to stressor stimuli, such as PE.

PWV presented a lower value 24 hours after a MIIPE session than 24 hHIIPE session in subjects with elevated

BP. Reinforcing these findings, PWV 24hMIIPE was lower than baseline, and the  $\Delta$ 24hMICPE was greater than  $\Delta$ 24hHIIPE.

Our results are conflicting with others that used the same method for PWV (Complior). PWV was lower at the 30-min measurement but returned to baseline values after 1-hour cycling at moderate intensity in young sedentary healthy men. 10 Conversely, PWV increased 2 min after one bout (30s) sprint cycling high-intensity PE.<sup>23</sup> However, similarly to our results, PWV decreases 24 hours after 30 min of moderate-to-vigorous intensity treadmill running in young healthy individuals.<sup>13</sup> These discrepancies are intriguing, but we can assume three possible reasons: unlike these studies in healthy people, our participants presented elevated BP, and most were women who show smaller changes in PWV 24hours after exercise than men. Finally, there are possible differences in realtime post-exercise measurement, affecting the PWV acute behaviour post-exercise, which is time-dependent. 924

Other studies have measured PWV by applanation tonometry. Paradoxically, some authors did not find changes in PWV in healthy men after high-intensity compared with moderate-intensity or baseline values. However, PWV increased after PE, returning to baseline after 20 min<sup>26</sup> or even earlier. PWV decreases in healthy subjects after an exhaustive PE session. In hypertensive patients PWV returned to baseline levels in the first hour after aerobic PE and remained stable in the next 24 hours. Thee aortic backward waves decreased after aerobic PE; notably, these changes were not detected by aortic augmentation indexes. See high authors augmentation indexes.

Due to the functional decrease of sympathetic activity, <sup>29</sup> <sup>30</sup> we expected vascular response in greater magnitude to HIIPE than MICPE. This expectation was not matched by PWV, but rather by Aortic SBP. Interestingly, we noted lower values of aortic SBP after HIIPE compared with baseline and MICPE24h in our sample. These results suggest that HIIPE may induce a vascular response more dependent on the reflection wave, since aortic SBP is determined by aortic forward and reflected (backward) wave pressures, and alterations in Aortic BP are more dependent on medium-sized artery function.<sup>3</sup>

| OfficeBP         SBP         125±10         Nost-MICPE         MICPE24h         Nost-HIIPE         HIIPE24h         P.3           OfficeBP         SBP         125±10         124±15         124±16         124±10         122±10         125±10         124±1 | Table 5 Bloc     | od pressure in eleva   | Blood pressure in elevated BP subjects among sessions | ions       |          |           |          |       |
|---|------------------|------------------------|---|------------|----------|-----------|----------|-------|
| SBP         125±10         124±15         124±15         124±16         124±16         124±17         122±11           DBP         83±5         81±7         82±6         82±7         81±7           DBP         84±6         84±6         84±6         117±10         117±10         117±11           Nean BP         99±7         99±9         98±7         84±7         82±7           shanbulatory blood pressure monitoring         72±10*         66±9         90±3         17±11           sp         SBP         125±10         -         126±9         -         125±0           sp         SBP         125±10         -         126±9         -         125±0         92±0           sp         SBP         128±11         -         126±9         -         125±0         92±0           sp         SBP         111±9         -         128±9         -         13±1         92±0         92±0           sp         SBP         111±10         -         114±10         -         92±0         92±0         92±0         92±0         92±0         92±0         92±0         92±0         92±0         92±0         92±0         92±0         92±0  |                  |                        | Baseline  | Post-MICPE | MICPE24h | PostHIIPE | HIIPE24h | Ь     |
| SBP         83±5         81±7         82±6         82±7         81±8         81±8  | OfficeBP         | SBP                    | 125±10  | 124±15     | 124±11   | 122±9     | 122±11   | 0.387 |
| SBP         118±10         117±14         117±14         117±14         117±11           DBP         84±5         84±6         84±7         84±7         82±7           Mean BP         99±7         99±9         98±7         97±7         97±7           International plant of pressure monitoring         72±10*         66±9         80±13***         62±10\$           SBP         125±10         -         126±9         -         79±8           SBP         128±11         -         128±9         -         79±8           SBP         128±11         -         114±10         -         81±9           SBP         111±9         -         83±9         -         81±9           SBP         67±7         -         69±9         -         69±8           SBP         131±9         -         69±9         -         69±8           SBP         8±8         -         127±9*   |                  | DBP                    | 83±5  | 81±7       | 82±6     | 82±7      | 81±7     | 0.464 |
| DBP Mean BP By 4±5         84±6         84±6         84±7         84±7         84±7         82±7           Mean BP 99±7         99±9         98±7         98±7         97±7         97±7         97±7           In the stand of pressure monitoring ambulatory blood pressure monitoring SBP         125±10*         -         126±9         -         125±9           SBP         125±10         -         80±8         -         79±8           SBP         128±11         -         128±9         -         81±9           SBP         111±9         -         83±9         -         81±9           SBP         67±7         -         69±9         -         68±8           SBP         131±9         -         69±9         -         68±8           SBP         44±9         -         63±9         -         68±8 <td>AorticBP</td> <td>SBP</td> <td>118±10</td> <td>117±14</td> <td>117±10</td> <td>113±19*‡</td> <td>117±11</td> <td>0.013</td>   | AorticBP         | SBP                    | 118±10  | 117±14     | 117±10   | 113±19*‡  | 117±11   | 0.013 |
| Mean BP         99±7         99±9         98±7         97±7         97±7           ambulatory blood pressure monitoring         125±10         -         126±9         -         125±9           sP         125±10         -         126±9         -         79±8           sP         80±8         -         79±8           sP         128±11         -         128±9         -         81±9           sP         83±9         -         83±9         -         81±9           DBP         67±7         -         69±9         -         68±8           SBP         131±9         -         69±9         -         68±8           DBP         86±8         -         127±9*         -         68±8           SBP         131±9         -         69±9         -         68±8         -           DBP         86±8         84±9         -         127±9*         -         -  |                  | DBP                    | 84±5  | 84±6       | 84±7     | 84±7      | 82±7     | 0.651 |
| ambulatory blood pressure monitoring         72±10*         66±9         80±13**         62±10§           ambulatory blood pressure monitoring         SBP         125±10         -         126±9         -         125±9           SP         80±8         -         80±8         -         79±8           SP         128±11         -         83±9         -         81±9           BP         67±7         -         69±9         -         68±8           SBP         131±9         -         69±9         -         68±8           BP         86±8         128±9*         -         83±9         -         68±8  |                  | Mean BP                | 264−7   | 6766       | 28±7     | 97±7      | 97±7     | 0.180 |
| ambulatory blood pressure monitoring           SBP         125±10         -         126±9         -         79±8           BP         80±8         -         80±8         -         79±8           BP         128±11         -         128±9         -         81±9           BP         83±9         -         81±9         113±11           BP         67±7         -         69±9         -         68±8           SBP         131±9         128±9*         -         127±9*         -           BP         86±8         84±9         -         83±9         -   | HR (bpm)         |                        | 64±9  | 72±10*     | 6∓99     | 80±13*#   | 62±10§   | 0.001 |
| SBP         125±10         -         126±9         -         125±9           BBP         80±8         -         80±8         -         79±8           BBP         128±11         -         128±9         -         126±9           BBP         83±9         -         111±10         -         81±9           BBP         67±7         -         69±9         -         68±8           SBP         131±9         128±9*         -         127±9*         -           BBP         86±8         84±9         -         83±9         -   | 24 hours ambulat | ory blood pressure mor | nitoring  |            |          |           |          |       |
| ABP         80±8         -         80±8         -         70±8           SBP         128±11         -         128±9         -         126±9           DBP         83±9         -         81±9         -         81±9           DBP         67±7         -         69±9         -         68±8           SBP         131±9         128±9*         -         127±9*         -           DBP         86±8         84±9         -         83±9         -  | 24H              | SBP                    | 125±10  | I          | 126±9    | I         | 125±9    | 0.433 |
| SBP         128±11         -         128±9         -         126±9           DBP         83±9         -         81±9         -         81±9           DBP         111±9         -         69±9         -         68±8           SBP         131±9         128±9*         -         127±9*         -           DBP         86±8         84±9         -         83±9         -  |                  | DBP                    | 80±8  | I          | 80±8     | I         | 79±8     | 0.776 |
| DBP         83±9         -         83±9         -         81±9           SBP         111±9         -         114±10         -         113±11           DBP         67±7         -         69±9         -         68±8           SBP         131±9         128±9*         -         127±9*         -           DBP         86±8         84±9         -         83±9         -  | DaytimeBP        | SBP                    | 128±11  | I          | 128±9    | I         | 126±9    | 0.343 |
| SBP         111±9         -         114±10         -         113±11           DBP         67±7         -         69±9         -         68±8           SBP         131±9         128±9*         -         127±9*         -           DBP         86±8         84±9         -         83±9         -   |                  | DBP                    | 83±9  | I          | 83±9     | I         | 81±9     | 0.354 |
| DBP         67±7         -         69±9         -         68±8           SBP         131±9         128±9*         -         127±9*         -           DBP         86±8         84±9         -         83±9         -   | SleepBP          | SBP                    | 111±9   | I          | 114±10   | I         | 113±11   | 0.250 |
| SBP 131±9 128±9* – 127±9* – 127±9* – DBP 86±8 84±9 – 83±9 –   |                  | DBP                    | <i>L</i> ∓ <i>L</i> 9                                 | I          | 6∓69     | I         | 8=89     | 0.328 |
| 86±8 84±9 - 83±9 -  | 2H               | SBP                    | 131±9   | 128±9*     | I        | 127±9*    | I        | 0.027 |
|   |                  | DBP                    | 86±8  | 84±9       | I        | 83±9      | I        | 0.057 |

Values are presented as mean±SD.

\*p<0.05 versus baseline,

†p<0.05 versus MICPE. ‡p<0.05 versus MICPE24h.

DBP, diastolic blood pressure; HIIPE, high-intensity interval physical exercise; HR, heart rate; MICPE, moderate-intensity continuous physical exercise; PWV, pulse wave velocity; SBP systolic blood SBP, systolic blood pressure. §p<0.05 versus HIIPE.

Additionally, other studies demonstrated a decrease in aortic SBP after moderate-intensity PE in healthy individuals <sup>10</sup> and in level 1 or prehypertension, <sup>31</sup> with a decrease in the backward wave pressures, despite no changes in PWV

While the reduction in aortic SBP after HIIPE appears to be due to the decrease in reflected wave magnitude, which in turn is influenced by peripheral vasodilation, <sup>23 32 33</sup> the mechanisms involved in the lower values of PWV 24 hours after MICPE may be more related to large proximal vessel vasodilation and the vasa vasorum. <sup>10</sup>

Peripheral vasodilation by PE occurs due to shear stress, but the response of central arteries to PE is contradictory; peripheral vasodilation after PE is not clearly intensity-dependent.<sup>34</sup> Nevertheless, it seems that there is a post-exercise biphasic response, that is, vasodilation reduces immediately after high-intensity PE, increasing or normalising later, and increases or does not change immediately after moderate-intensity PE, but increasing or normalising later.<sup>35</sup>

Unexpectedly, BP measurements during the first 2 hours in baseline were approximately 4 mm Hg higher than daytime values. We speculated that it is due to the white coat effect, which is more prevalent in females (the majority in our sample).<sup>36</sup> Participants may have been more anxious during the first visit<sup>36</sup> when placing the ABPM. This makes it difficult to determine whether the numerical drop in BP after the exercise sessions was due to desensitisation from the first measurement, or a reduction, without statistical significance, in SBP and DBP values.

According to Perissiou *et al,*<sup>2</sup> in healthy older adults, the arterial stiffness response to PE is dependent on exercise intensity and cardiorespiratory fitness level. Our participants presented a similar cardiorespiratory fitness level (VO2máx=23.9±4.3 mL/Kg<sup>-1</sup>/min<sup>-1</sup>, therefore, enabling us to evaluate the PE intensity properly. In the same positive manner, the equivalence in the caloric expenditure eliminates other factors (such as PE volume) that could influence the arterial response.

#### Limitations

A greater BP reduction is expected in males than in females in response to PE, <sup>3</sup> as our participants are mostly female, and due to the small number of men, a sex comparison analysis was not possible. Another limitation is that only one basal PWV measurement was performed, preventing comparison with immediate pre-exercise PWV. However, the vascular measurements used in the study have acceptable short-term variation, <sup>37 38</sup> and the intervals between sessions were sufficient to avoid any carryover effects. All measurements strictly followed the guidelines and were performed in a temperature-controlled environment, at the same time, by the same observer.

#### **Conclusion and clinical implications**

In subjects with elevated BP, arterial distensibility is greater 24 hours after MICPE, while aortic SBP is lower

after HIIPE, that is, the vascular response from MIIPE seems to last longer; however, that from HIIPE can be significant. The particularities of each method and exercise intensity can provide specific mechanisms of vascular response to exercise and detect vascular damage early in these subjects.

X Sara Rodrigues @saradapersonal

Acknowledgements We thank all volunteers for participating in the study.

Contributors SR performed BP and PWV measurements, followed the PE sessions, designed and supervised the study, carried out the statistics/analysis, data interpretation, wrote the original draft and finalised the manuscript. RGSV collaborated with PWV technical execution and reviewed the final manuscript. VCH collaborated with PWV technical planning and reviewing final manuscript. CPJ collaborated with reviewing final manuscript. tMJAC collaborated with CPET technical execution and reviewing final manuscript. LAB is the guarantor, designed and supervised the study, and collaborated with the writing and reviewing of the manuscript.

**Funding** Sara Rodrigues was supported by Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq# 165778/2017-2) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (CAPES-PRINT# 88887.470405/2019-0). Renata Gomes Sanches Verardino, CAPES# 88887.185675/2018-00.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval All participants gave written informed consent in accordance with the Declaration of Helsinki, before taking part. The protocol was approved by Scientific Commission of the Heart Institute (InCor), and the Ethics in Research Commission of the Clinical Hospital, University of São Paulo (# 0565/11) approved this study in August 2017. The study is registered as a clinical trial via clinicaltrials. gov (identifier number: Unique Protocol ID: 72503117.0.0000.0068; NCT04200716. Brief Title: Arterial Function After Two Different Physical Exercise Intensities in Prehypertension (PREHTEXVAS)).

Provenance and peer review Not commissioned; externally peer-reviewed.

Data availability statement Data are available upon reasonable request. For data availability, please request.

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#### ORCID if

Sara Rodrigues http://orcid.org/0000-0002-4998-7534

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