

## Please cite the Published Version

Azevêdo, LM, Brito, LCD, Peçanha, T, Fecchio, RY, Rezende, RA, da Silva, GV, Pio-Abreu, A, Mion Junior, D, Halliwill, JR and Forjaz, CLDM (2023) Can blood pressure decrease after maximal exercise test predict the blood pressure lowering effect of aerobic training in treated hypertensive men? Journal of Human Hypertension. ISSN 0950-9240

DOI: https://doi.org/10.1038/s41371-023-00853-7

Publisher: Springer Nature

Version: Accepted Version

Downloaded from: https://e-space.mmu.ac.uk/632968/

Usage rights: C In Copyright

**Additional Information:** This version of the article has been accepted for publication, after peer review and is subject to Springer Nature's AM terms of use, but is not the Version of Record and does not reflect post-acceptance improvements, or any corrections. The Version of Record is available online at: <a href="http://dx.doi.org/10.1038/s41371-023-00853-7">http://dx.doi.org/10.1038/s41371-023-00853-7</a>.

## Enquiries:

If you have questions about this document, contact openresearch@mmu.ac.uk. Please include the URL of the record in e-space. If you believe that your, or a third party's rights have been compromised through this document please see our Take Down policy (available from https://www.mmu.ac.uk/library/using-the-library/policies-and-guidelines)

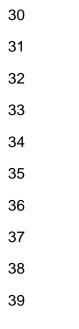
1	Can blood pressure decrease after maximal exercise test predict the blood pressure lowering effect of
2	aerobic training in treated hypertensive men?
3	
4	Luan Morais Azevêdo <sup>1*</sup> ; Leandro Campos de Brito <sup>1*</sup> ; Tiago Peçanha de Oliveira <sup>1</sup> ; Rafael Yokoyama
5	Fecchio <sup>1</sup> ; Rafael Andrade Rezende <sup>1</sup> ; Giovânio Vieira da Silva <sup>2</sup> ; Andrea Pio de Abreu <sup>2</sup> ; Décio Mion
6	Junior <sup>2</sup> ; John Robert Halliwill <sup>3</sup> ; Cláudia Lúcia de Moraes Forjaz <sup>1†</sup>
7	
8	<sup>1</sup> Exercise Hemodynamic Laboratory, School of Physical Education and Sport, University of São Paulo,
9	São Paulo, Brazil;
10	<sup>2</sup> Hypertension Unit, Hospital das Clínicas, Medical School, University of São Paulo, Brazil;
11	<sup>3</sup> Department of Human Physiology, University of Oregon, Eugene, Oregon, USA.
12	
13	
14	<sup>†</sup> Correspondence author: Cláudia Lúcia de Moraes Forjaz
15	School of Physical Education and Sport, University of São Paulo, São Paulo, Brazil.
16	Av. Professor Mello Moraes, 65 - Cidade Universitária, São Paulo, SP
17	Zipcode 05508-030, Brazil. E-mail: <u>cforjaz@usp.br</u>
18	
19	* These authors contributed equally to this manuscript
20	
21	
22	
23	
24	
25	
26	
27	

#### What is known about this topic

- Significant correlations have been reported between the reductions in blood pressure observed after a maximal exercise test and after a period of aerobic training in healthy individuals.
- Blood pressure decrease observed after a maximal exercise test may be used to predict the blood pressure lowering effect of aerobic training in hypertensives.

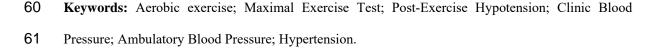
### What this study adds

- The decrease in blood pressure observed 30 min after a maximal exercise test was not associated with the blood pressure reduction induced by aerobic training in treated hypertensive men.
- The blood pressure reduction observed 30 min after a maximal exercise test cannot be used to predict hypertensives responders or non-responders to the blood pressure lowering effect of aerobic training.



41

42 The acute decrease in blood pressure (BP) observed after a session of exercise (called post-exercise 43 hypotension) has been proposed as a tool to predict the chronic reduction in BP induced by aerobic 44 training. Therefore, this study investigated whether post-exercise hypotension observed after a maximal 45 exercise test is associated to the BP-lowering effect of aerobic training in treated hypertensives. Thirty 46 hypertensive men (50 $\pm$ 8 years) who were under consistent anti-hypertensive treatment underwent a 47 maximal exercise test (15 watts/min until exhaustion), and post-exercise hypotension was determined 48 by the difference between BP measured before and at 30 min after the test. Subsequently, the patients 49 underwent 10 weeks of aerobic training (3 times/week, 45 min/session at moderate intensity), and the 50 BP-lowering effect of training was assessed by the difference in BP measured before and after the 51 training period. Pearson correlations were employed to evaluate the associations. Post-maximal exercise 52 test hypotension was observed for systolic and mean BPs ( $-8 \pm 6$  and  $-2 \pm 4$  mmHg, all P<0.05). Aerobic 53 training reduced clinic systolic/diastolic BPs ( $-5 \pm 6/-2 \pm 3$  mmHg, both P<0.05) as well as awake and 54 24h mean BPs ( $-2 \pm 6$  and  $-2 \pm 5$  mmHg, all P<0.05). No significant correlation was detected between 55 post-exercise hypotension and the BP-lowering effect of training either for clinic or ambulatory BPs (r 56 values ranging from 0.00 to 0.32, all p > 0.05). Post-exercise hypotension assessed 30 min after a 57 maximal exercise test cannot be used to predict the BP-lowering effect of aerobic training in treated 58 hypertensive men.



- 62
- 63

### 64 INTRODUCTION

65 Hypertension is an idiopathic chronic disease, affecting 31% of adults worldwide, and indirectly 66 responsible for about 14% of the all-cause deaths [1]. Although pharmacological treatment decreases 67 blood pressure (BP), rates of BP control are still low (approximately 30%) [2], and a better control may 68 be obtained by its association with aerobic training (AT) [3–5]. Strong evidence shows that AT reduces 69 clinic and ambulatory BPs in hypertensives [6] with the magnitude of reduction being similar to the 70 pharmacological treatment [7]. Therefore, AT is recommended for hypertension treatment [3–5], but 71 approximately 25% of the hypertensives may not respond to AT with BP decrease [8], being important 72 to find tools to detect these non-responder patients.

A single session of aerobic exercise induces an acute and long lasting decrease in BP during the post-exercise period that has been called post-exercise hypotension (PEH) [9–11]. It has been proposed that PEH may be used to predict the chronic BP-lowering effect of AT [10, 11]. Therefore, for clinical application, it would be useful if PEH after a maximal exercise test, a procedure already used in the pretraining screening of hypertensives [3, 12], could predict the BP-lowering effect of AT.

78 Some studies reported strong correlations between the BP decrease observed after a maximal 79 exercise test and the BP reduction obtained after a period of AT in healthy individuals [13, 14]. However, 80 this association was not found in patients with chronic kidney disease who were receiving 81 antihypertensive drugs [15], suggesting that it might not happen in treated hypertensives, which needs 82 to be checked. Additionally, the studies reporting significant associations have employed the same initial 83 BP to calculate both, PEH and the BP-lowering effect of AT [13, 14]. This procedure might result in a 84 mathematical coupling known as regression to the mean that is a well-known experimental pitfall, and 85 can lead to spurious significant correlations [16, 17]. Thus, a more robust experimental design is still 86 needed to confirm the association.

87 Therefore, the present study investigated the association between PEH after a maximal exercise
88 test and the BP-lowering effect of AT in hypertensive men receiving antihypertensive medication and
89 used different initial BPs to calculate PEH and the BP-lowering effect of AT.

## 91 METHODS

92 This study employed secondary data from a randomized controlled trial designed to compare
93 the BP-lowering effects of morning and evening AT in treated hypertensive men. The main results were
94 published elsewhere [18]. The study was approved by the Research Ethical Committee of the School of
95 Physical Education and Sport (no. 966.072) and registered in the Brazilian Clinical Trials platform

96 (RBR-7q7pz7). All patients signed a written consent form before enrollment.

97

```
98 Subjects
```

99 The patients were recruited through printed and digital media. As study's criteria, patients 100 should: i) be male; ii) age between 30 and 65 years old; iii) present hypertension and be taking 101 antihypertensive medications with classes and doses constant for at least the last 4 months; iv) have 102 resting systolic/diastolic BP  $\leq$  160/105 mmHg; v) present neither chronotype (i.e. scores between 41 103 and 59 in the Horne and Ostberg morningness-eveningness questionnaire); vi) not be taking  $\beta$ -blockers 104 or dihydropyridine calcium channel blockers; (vii) be nonactive (practicing < 150 min/week of physical 105 activity according to the International Physical Activity Questionnaire); and viii) not have physical 106 limitations to perform aerobic exercise. The patients were excluded if they presented: i) obesity at stage 107 2 or higher (i.e. body mass index  $\geq$  35 kg/m<sup>2</sup>); ii) diabetes with complications or in use of insulin; iii) 108 hypertensive target-organ damage; iv) other cardiovascular diseases besides hypertension; and v) 109 electrocardiogram abnormality at rest or during an exercise test.

110

### 111 Preliminary Exams

To check accomplishment to the study's criteria, the patients underwent preliminary evaluations. They were interviewed regarding their health history, medication use and physical activity practice, and answered the Horne and Ostberg's morningness-eveningness [19] and the International Physical Activity [20] questionnaires. They underwent a clinical exam performed by a physician, and their body mass and height were measured. Their BP was measured three times after 5 min of seated rest on two different occasions. Finally, blood and urine samples were collected to evaluate the presence of secondary hypertension and target-organ damage according to the Brazilian Guideline forHypertension [3].

- 120
- 121 Procedures

Before and after 10 weeks of AT, the patients who fulfilled the study's criteria attended to the laboratory for two different visits conducted with an interval of at least 48h. One visit was dedicated to evaluate PEH by measuring BP before and at 30 minutes after a maximal exercise test. The other visit was used to evaluate the chronic BP-lowering effect of AT by measuring clinic and ambulatory BP. After the training period, the visits were conducted at least 48 hours after the last training session.

127

## 128 Assessment of PEH after the maximal exercise test

129 Maximal exercise test was conducted in a temperature controlled (20-22°C) laboratory between 130 7 and 9 a.m. The patients were instructed to have a light meal two hours before, to avoid caffeinated 131 beverages and smoking in the testing day, and to avoid alcoholic drinks and vigorous physical efforts in 132 the previous 24 hours. The test was carried out on a cycle ergometer (Lode Medical Technology, 133 Corival, Groningen, Netherland) with a ramp protocol of 15 watts increment each minute until the 134 patients were unable to keep pedaling frequency at 60 rpm. The test was preceded by a 3-min warm-up 135 at 30 watts and followed by a 5-min cool-down period pedaling at 30 watts. During the test, auscultatory 136 BP (Unitec, São Paulo, Brazil) was measured every two minutes, electrocardiogram (EMG System, 137 030110/00B, São Paulo, Brazil) was continuously recorded, and breath-by-breath oxygen consumption 138 (VO<sub>2</sub>) was continuously analyzed by a metabolic card (CPX Ultima, Medical Graphics Corporation, St. 139 Paul, MN). VO<sub>2</sub>peak was considered as the highest value achieved during exercise in means of 30s. For 140 10 min before and 30 min after the test, the patients rested seated on a comfortable chair. At the end of 141 each of these moments, BP was measured three times with an interval of 1 min, and the mean value was 142 calculated. The measures were taken by an experienced evaluator, using the auscultatory method and a 143 mercury column sphygmomanometer (Unitec, São Paulo, Brazil). PEH was calculated by the difference

between the BP measured after (at 30 min) and before the maximal exercise test conducted before the

training period.

146

## 147 Assessment of the effect of AT on clinic and ambulatory BPs

148 Before and after the training period, in a visit different from the maximal test, clinic BP was 149 measured using the auscultatory method and a mercury column sphygmomanometer (Unitec, São Paulo, 150 Brazil). The measurements were performed 3 times after 5 min of seated rest and with an interval of 1 151 min between the measures. The mean of the three measures was considered as the clinic BP. In the same 152 day, an oscillometric ambulatory BP monitor (Spacelabs Healthcare, 90207, USA) was positioned on 153 the non-dominant arm of the patients, and they left the laboratory being instructed to perform their 154 normal daily activities and to come back to the laboratory after 24h. The monitor was programmed to 155 take measures every 15 min for 24 hours, and the patients were instructed to avoid physical efforts 156 during the monitoring. Additionally, they should record their daily activities and take notes regarding 157 the time of sleeping and awaking. In the monitoring conducted after the training period, the patients 158 were asked to keep the same daily activities as in the pre-training monitoring. For analyses, only records 159 that presented at least 85% of the measures valid were considered. Twenty-four hour, asleep and awake 160 BP were calculated, respectively, by the average of all measures taken during whole monitoring period, 161 the period that the patient reported to be sleeping and the period that he reported to be awake. The clinic 162 BP-lowering effect of AT ( $\Delta$ clinic BP) was determined by the difference in clinic BP measured after 163 and before the training period, while the ambulatory BP-lowering effect of AT ( $\Delta$ ambulatory BP) was 164 determined by the difference in 24-h, awake and asleep BP assessed after and before the training period.

165

166 *AT protocol* 

AT was performed on cycle ergometer (CEFISE, Biotec 2100, Campinas, Brazil), 3 times per week for 10 weeks. Training duration and intensity progressed along the training period. Exercise duration increased from 30 to 45 min in the first two weeks of training and this duration was maintained until the end of the training period. Exercise intensity was set at the heart rate of the anaerobic threshold during weeks 1 to 4 and increased progressively to achieve 10% below the heart rate of the respiratory
compensation point at weeks 9 and 10. The maximal exercise test conducted before the training period
was used to establish the anaerobic threshold and the respiratory compensation point according to
literature criteria [21]. During the training sessions, heart rate was monitored (POLAR 800cx, Kempele,
Finland) to keep intensity within the desirable range.

176

## 177 Statistical Analysis

178 Since this study used a database from a bigger study [18], sample size was originally calculated 179 for the main variable of the bigger study and accepted by convenience for this investigation. Normality 180 of data was evaluated by Shapiro-Wilk test. Paired t-test were used to confirm the occurrence of PEH 181 (pre-vs. post-maximal exercise test) and the effect of AT (before vs. after training). Pearson correlations 182 and linear regressions were used to analyze the association between PEH and the clinic and ambulatory 183 BP-lowering effect of AT. The analyses were performed in SPSS software (SPSS for windows; IBM, 184 Chicago, IL). Data were expressed in mean  $\pm$  standard deviation, and the level of significance adopted 185 was  $p \le 0.05$ .

186

#### 187 RESULTS

188

A total of 68 patients signed the informed consent form to participate. After checking for the study criteria, 32 were excluded. Therefore, 36 patients were enrolled in the experimental protocol, but during the training phase, 6 patients dropped out. Thus, 30 patients finished the study's protocol and had their data analyzed (Figure 1).

193

194

#### [FIGURE 1 ABOUT HERE]

196	The sample was composed by middle-aged hypertensive men, taking different types of
197	antihypertensive drugs, mostly as monotherapy (Table 1). Maximal exercise tests were interrupted by
198	fatigue in all patients.
199	
200	[TABLE 1 ABOUT HERE]
201	
202	Adherence to training sessions was 96 $\pm$ 4%. VO <sub>2</sub> peak increased significantly after AT
203	$(VO_2peak = 21.4 \pm 3.3 \text{ vs. } 23.1 \pm 4.2 \text{ mL.kg}^{-1}.min^{-1}, p = 0.04)$ , while weight did not change (88.6 ± 13.3 mL.kg^{-1}.min^{-1}, p = 0.04).
204	vs $88.3 \pm 13.0$ kg, p = 0.21).
205	Maximal exercise test promoted PEH, significantly reducing systolic and mean BPs, but not
206	diastolic BP (Table 2). AT decreased clinic systolic, diastolic, and mean BPs (Table 3). Considering
207	ambulatory BP, AT significantly reduced 24h and awake mean BPs; tended to reduce 24h and awake
208	diastolic BPs; and did not significantly change 24h, awake and asleep systolic BPs nor asleep diastolic
209	and mean BPs (Table 3).
210	
211	[TABLE 2 AND 3 ABOUT HERE]
212	
213	Considering the main objective of the study, no significant association was observed between
214	the systolic or diastolic BP changes observed after the maximal exercise test (PEH) and the changes in
215	clinic or ambulatory BPs observed after AT (Table 4, Figure 2).
216	
217	[TABLE 4 AND FIGURE 2 ABOUT HERE]
218	
219	DISCUSSION
220	This study investigated the association between PEH assessed 30 min after a maximal exercise
221	test and the chronic BP reduction induced by AT in treated hypertensive men using an experimental
222	design that overcame previous limitations. The existence of such association would have supported the

use of BP reduction observed after a maximal exercise test as a clinical tool to identify those hypertensives who would mostly respond to AT with BP reduction. However, contrary to this expectation, the main finding of the present study was that there was no association between PEH assessed 30 min after a maximal exercise test and either the clinic or the ambulatory BP reduction induced by 10 weeks of AT.

228 In the present study, maximal exercise test induced PEH, decreasing systolic BP by  $-7.6 \pm 5.7$ 229 mmHg, which is in accordance with the previous studies that also reported PEH after maximal exercise 230 tests in health individuals [13, 14]. Additionally, as expected, AT increased VO<sub>2</sub>peak as previously 231 reported [18], and promoted significant reductions in clinic systolic/diastolic BPs ( $-4.6 \pm 6.4 / -1.8 \pm 3.2$ 232 mmHg) as well as in some parameters of ambulatory BP (24h and awake mean BPs,  $-2.1 \pm 4.9$  and -2.3233  $\pm$  6.0 mmHg, respectively). These BP reductions were lower than those reported in a recent meta-234 analysis [6], but may have clinical importance since a -5 mmHg decrease in clinic systolic BP may be 235 associated with a reduction of 14% in the risk of death from stroke and 9% from coronary heart disease 236 [22].

237 Regarding the use of PEH after a maximal test to predict the BP-lowering effect of AT, the 238 present findings do not support this application in treated hypertensive men as no significant association 239 was observed between the acute and chronic responses of BP to aerobic exercise. This absence of 240 association was also reported in patients with chronic kidney disease [15], but differs from prior findings 241 of strong associations reported in healthy individuals [13, 14]. Some factors may be raised to explain 242 the discrepancy among the studies. First, the time after the maximal exercise test when PEH was 243 assessed may influence the association. The previous studies that have reported significant associations 244 assessed PEH at 7 [14] and 60 min [13] after the maximal exercise test, while the present study assessed 245 PEH at 30 min, a midpoint between these periods, which suggests that the time of measurement may 246 not have been the reason for the absence of association. However, a recent review conducted by our 247 group [23] reported that in many studies the greatest PEH happened after 30 min of recovery, being 248 possible that the use of other specific times points or the greatest reduction in BP after the exercise test 249 could reveal a different result from using the assessment at 30 min of recovery. Nevertheless, this time

250 point was employed in the present study based on the previous studies that have employed maximal 251 exercise tests and on the feasibility in clinical routine, where a long-term assessment after a maximal 252 exercise test is difficult. Another possible reason for the difference in the results of the present study in 253 comparison with those that found significant correlations is the use of antihypertensive medication that 254 may affect the relationship between the acute and the chronic responses of BP to exercise. Along this 255 line, a recent meta-analysis concluded that PEH is less evident in patients receiving anti-hypertensive 256 drugs [9], while the BP-lowering effect of AT is greater in patients receiving medication [24, 25]. 257 Finally, an important explanation, as cited before, may be the mathematical approach adopted in the 258 previous studies [13, 14] that considered the same initial BP for calculating both PEH and the BP-259 lowering effect of AT, which may have caused spurious significant correlations [16, 17].

260 The absence of association (i.e. a null result) between PEH assessed 30 min after a maximal 261 exercise test and the BP-lowering effect of AT might seem an inconsequential finding. However, it may 262 have important clinical impact considering the readiness to generalize the positive previous results 263 obtained in healthy individuals [13, 14] to other populations. Therefore, despite the importance of 264 maximal exercise test to guide AT for hypertensives, the findings of the present study do not support 265 the use of the BP response measured after this test to identify responder and non-responders to AT 266 among treated hypertensives. Therefore, other tools should be identified for this specific purpose. Along 267 this line, in pre-hypertensives, PEH after a submaximal session of aerobic exercise (30 min at 65% of 268  $VO_2$  peak) has been reported to be associated with the BP-lowering effect of AT [26], however, this 269 relationship needs to be tested in treated hypertensives by future research.

Finally, we would like to highlight some of the strengths and limitations of the present study. The assessment of PEH and the BP-lowering effect of AT using different initial BP values reduces the chances for mathematical bias. Additionally, as all patients were under consistent anti-hypertensive treatment for 4 months or more, their clinical condition was stable, reducing any possible influence of medication changes. On the other hand, the results are limited to the study cohort's characteristics. Inactive middle-aged men under antihypertensive treatment were investigated. So, results cannot be generalized to women, physically active patients, other age groups, and untreated patients. These 277 specific populations need to be studied in the future. Additionally, maximal tests were conducted in the 278 morning. As BP presents daily variations, results could be different if tests were conducted at other times 279 of day, which also should be tested in the future. As discussed before, PEH was assessed at 30 min after 280 the maximal exercise test, and future research should test other times points and the association with the 281 greatest PEH. Finally, a lack of statistical power due to a small sample may be a concern. However, the 282 previous studies [13, 14] that revealed strong correlations used samples smaller than the present study 283 (i.e. 12 and 23 subjects) for these calculations. In addition, if the sample size for this study had been 284 calculated a priori based on the data of these studies and considering an alpha error of 5% and a power 285 of 90%, the smaller number needed would be 20 subjects. 286 In conclusion, although a maximal exercise test generates PEH and AT decreases clinic and 287 ambulatory BPs in medicated hypertensive men, these acute and chronic BP changes were not 288 correlated. Thus, in this population, BP response assessed 30 min after a maximal exercise test cannot 289 be used to predict the chronic BP-lowering effect of AT. 290 291 **Data Availability Statement** 292 Additional data will be provided by the corresponding author on reasonable request. 293 294 References 295 296 1. Mills KT, Stefanescu A, He J. The global epidemiology of hypertension. Nat Rev Nephrol. 2020; 297 16:223-237. https://doi.org/10.1038/s41581-019-0244-2 298 2. Thoenes M, Neuberger H-R, Volpe M, et al. Antihypertensive drug therapy and blood pressure 299 control in men and women: an international perspective. J Hum Hypertens. 2010; 24:336-344. 300 https://doi.org/10.1038/jhh.2009.76 301 3. Barroso WKS, Rodrigues CIS, Bortolotto LA, et al. Diretrizes Brasileiras de Hipertensão Arterial 302 - 2020. Arq Bras Cardiol. 2021; 116:516–658. https://doi.org/10.36660/abc.20201238 303 4. Chobanian A V, Bakris GL, Black HR, et al. Seventh Report of the Joint National Committee on

- 304 Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. Hypertension. 2003;
  305 42:1206–1252. https://doi.org/10.1161/01.HYP.0000107251.49515.c2
- Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH Guidelines for the management of
  arterial hypertension. Eur Heart J. 2018; 39:3021–3104.
  https://doi.org/10.1093/eurheartj/ehy339
- 309 6. Cao L, Li X, Yan P, et al. The effectiveness of aerobic exercise for hypertensive population: A
  310 systematic review and meta-analysis. J Clin Hypertens. 2019; 21:868–876.
  311 https://doi.org/10.1111/jch.13583
- 312 7. Naci H, Salcher-Konrad M, Dias S, et al. How does exercise treatment compare with
  antihypertensive medications? A network meta-analysis of 391 randomised controlled trials
  assessing exercise and medication effects on systolic blood pressure. Br J Sports Med. 2019;
  53:859–869. https://doi.org/10.1136/bjsports-2018-099921
- 8. Hagberg JM, Park J-J, Brown MD. The Role of Exercise Training in the Treatment of
  Hypertension. Sport Med. 2000; 30:193–206. https://doi.org/10.2165/00007256-20003003000004
- 319 9. Carpio-Rivera E, Moncada-Jiménez J, Salazar-Rojas W, Solera-Herrera A. Acute effects of
  acute effects of exercise on blood pressure: A meta-analytic investigation. Arq Bras Cardiol. 2016; 106:422–
  433. https://doi.org/10.5935/abc.20160064
- 322 10. Brito LC, Fecchio RY, Peçanha T, et al. Postexercise hypotension as a clinical tool: a "single 323 brick" wall. 2018; in the J Am Soc Hypertens. 12:e59–e64. 324 https://doi.org/10.1016/j.jash.2018.10.006
- Luttrell MJ, Halliwill JR. Recovery from exercise: vulnerable state, window of opportunity, or
   crystal ball? Front Physiol. 2015; 6:204. https://doi.org/10.3389/fphys.2015.00204
- 327 12. ACSM. ACSM's Guidelines for Exercise Testing and Prescription, 10th ed. 2017; Wolters
  328 Kluwer Health, Philadelphia
- 329 13. Hecksteden A, Grütters T, Meyer T. Association Between Postexercise Hypotension and Long330 term Training-Induced Blood Pressure Reduction. Clin J Sport Med. 2013; 23:58–63.

- 331 https://doi.org/10.1097/JSM.0b013e31825b6974
- 332 14. Wegmann M, Hecksteden A, Poppendieck W, et al. Postexercise Hypotension as a Predictor for
- 333
   Long-Term Training-Induced Blood Pressure Reduction: A Large-Scale Randomized Controlled
- 334 Trial. Clin J Sport Med. 2018; 28:509–515. https://doi.org/10.1097/JSM.00000000000475
- Headley S, Germain M, Wood R, et al. Blood pressure response to acute and chronic exercise in
  chronic kidney disease. Nephrology. 2017; 22:72–78. https://doi.org/10.1111/nep.12730
- 337 16. Barnett AG. Regression to the mean: what it is and how to deal with it. Int J Epidemiol. 2004;
  338 34:215–220. https://doi.org/10.1093/ije/dyh299
- 339 17. Pearson K. Mathematical contributions to the theory of evolution.—On a form of spurious
  340 correlation which may arise when indices are used in the measurement of organs. Proc R Soc
  341 London. 1897; 60:489–498. https://doi.org/10.1098/rspl.1896.0076
- Brito LC, Peçanha T, Fecchio RY, et al. Morning versus Evening Aerobic Training Effects on
  Blood Pressure in Treated Hypertension. Med Sci Sport Exerc. 2019; 51:653–662.
  https://doi.org/10.1249/MSS.00000000001852
- 345 19. Horne JA, Ostberg O. A self-assessment questionnaire to determine morningness-eveningness
  346 in human circadian rhythms. Int J Chronobiol. 1976; 4:97–110
- 347 20. Benedetti TRB, Antunes P de C, Rodriguez-Añez CR, et al. Reprodutibilidade e validade do
- Questionário Internacional de Atividade Física (IPAQ) em homens idosos. Rev Bras Med do
  Esporte. 2007; 13:11–16. https://doi.org/10.1590/S1517-86922007000100004
- 350 21. Skinner JS, McLellan TH. The Transition from Aerobic to Anaerobic Metabolism. Res Q Exerc
  351 Sport. 1980; 51:234–248. https://doi.org/10.1080/02701367.1980.10609285
- 352 22. Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular
  353 disease and death: A systematic review and meta-analysis. Lancet. 2016; 387:957–967.
  354 https://doi.org/10.1016/S0140-6736(15)01225-8
- 355 23. de Brito LC, Fecchio RY, Peçanha T, et al. Recommendations in Post-exercise Hypotension:
  356 Concerns, Best Practices and Interpretation. Int J Sports Med. 2019; 40:487–497.
  357 https://doi.org/10.1055/a-0938-4415

358 24. Sosner P, Guiraud T, Gremeaux V, et al. The ambulatory hypotensive effect of aerobic training:
a reappraisal through a meta-analysis of selected moderators. Scand J Med Sci Sports. 2017;
27:327–341. https://doi.org/10.1111/sms.12661

- 361 25. Saco-Ledo G, Valenzuela PL, Ruiz-Hurtado G, et al. Exercise Reduces Ambulatory Blood 362 Pressure in Patients With Hypertension: A Systematic Review and Meta-Analysis of 363 Randomized Controlled Trials. J Am 2020; 9:18487. Heart Assoc. 364 https://doi.org/10.1161/JAHA.120.018487
- 26. Liu S, Goodman J, Nolan R, et al. Blood Pressure Responses to Acute and Chronic Exercise Are
  Related in Prehypertension. Med Sci Sport Exerc. 2012; 44:1644–1652.
  https://doi.org/10.1249/MSS.0b013e31825408fb
- 368

### 369 Acknowledgements

- 370 The authors thank the volunteers for participating.
- 371

#### **372** Author Contributions

LA and LCB collaborate to the study design, collected data, carried out the statistical analysis, contributed to the interpretation of results, and drafted the initial manuscript; TP, RF, RR collected data, and revised the manuscript; GS, AA, DMJ were responsible for patients clinical evaluation and followup, and revised the manuscript; JH contributed to the interpretation of results and revised the manuscript; CF designed the study, get grants for the study, supervised data collection, contributed to the interpretation of results and revised the manuscript version submitted for publication.

380

#### **381** Funding information

382 This study was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP
383 2014/216676-6), Programa de Excelência Acadêmica (PROEX 88882.327719/2019-01), Conselho

384 Nacional de Desenvolvimento Científico e Tecnológico (CNPq 304436/2018-6), and Coorder	ıação	de
--	-------	----

385 Aperfeiçoamento Pessoal de Nível Superior-Brasil (CAPES, financial code 001).

## 387 Ethical Approval

388 All patients signed a written consent form. The study from which data of the present389 investigation was derived was approved by the Research Ethical Committee of the School of Physical

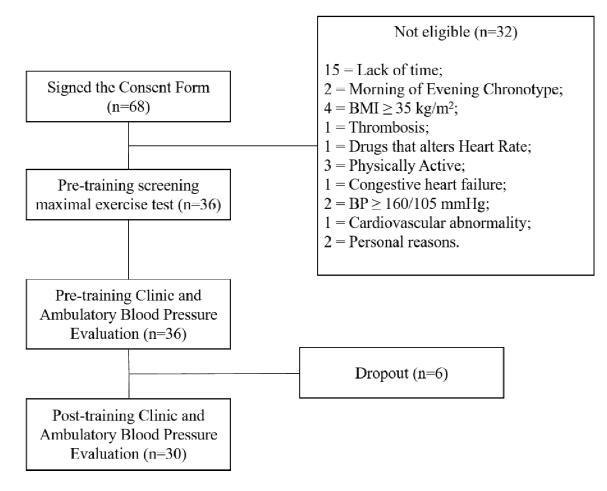
- 390 Education and Sport (no. 966.072) and registered in the Brazilian Clinical Trials platform (RBR-
- 391 7q7pz7), and its procedures followed the standards proposed by the Helsinki Declaration.

The authors declare no competing interests.

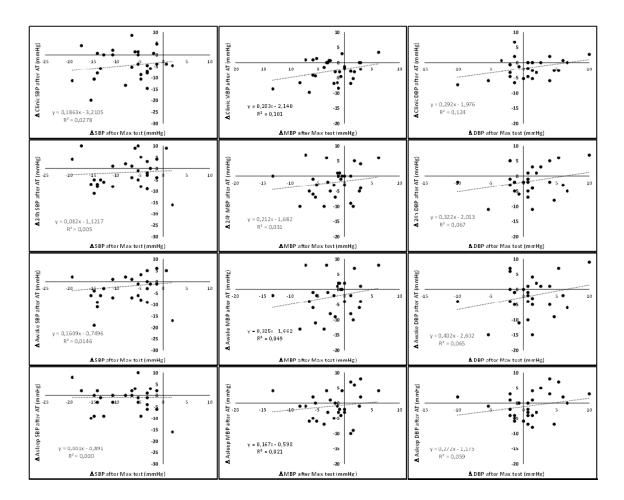
## Competing Interest

# **Figure 1** – Study Flowchart.

- 412 Figure 2 Associations between the changes clinic and ambulatorial systolic (SBP), mean
- 413 (MBP) and diastolic (DBP) blood pressures assessed after a maximal exercise test ( $\Delta$  after Max
- 414 test) and after a period of aerobic training ( $\Delta$  after AT).



**Figure 1 –** Study Flowchart.



**Figure 2** – Correlations between changes ( $\Delta$ ) in systolic (SBP), diastolic (DBP) and mean (MBP) blood pressures assessed after a maximal exercise test (Max test) and after a period of aerobic training (AT).

Characteristic	Mean ± SD
General	
Age (years)	$50 \pm 8$
Body mass index (kg/m <sup>2</sup> )	$29.9 \pm 4.3$
Systolic blood pressure (mmHg)	$133 \pm 7$
Diastolic blood pressure (mmHg)	$90 \pm 6$
Antihypertensive Drugs	n (%)
Angiotensin II receptor blockers	15 (50)
Angiotensin converting enzyme inhibitors	11 (37)
Dihydropyridine calcium channel blockers	7 (23)
Diuretics	9 (30)
Antihypertensive Strategy	n (%)
Monotherapy	21 (70)
Polytherapy	9 (30)

**Table 1 –** Sample characteristics (n = 30).

	Pre-test	Post-test	Р
Systolic BP (mmHg)	$131 \pm 14$	123 ± 15 *	< 0.01
Mean BP (mmHg)	$104 \pm 9$	102 ± 10 *	0.01
Diastolic BP (mmHg)	$90 \pm 8$	91 ± 8	0.29

**Table 2.** Post-exercise hypotension evaluated by systolic, mean, and diastolic blood pressures

 (BP) measured before and at 30 min after the maximal exercise test.

\* Significantly lower than pre-test

	Before	After	Р
	training	training	1
Clinic BP			
Clinic systolic BP (mmHg)	$131 \pm 12$	126 ± 11 †	< 0.01
Clinic mean BP (mmHg)	$104 \pm 8$	102 ± 8 †	< 0.01
Clinic diastolic BP(mmHg)	91 ± 6	89 ± 6 †	0.01
Ambulatory BP			
24h systolic BP (mmHg)	$129 \pm 9$	127 ± 8	0.17
24h mean BP (mmHg)	$100 \pm 8$	97 ± 6 †	0.03
24h diastolic BP(mmHg)	85 ± 7	$83 \pm 6$	0.06
Awake systolic BP (mmHg)	$134 \pm 10$	$132 \pm 7$	0.17
Awake mean BP (mmHg)	$104 \pm 8$	102 ± 6 †	0.05
Awake diastolic BP(mmHg)	$90 \pm 8$	$87 \pm 6$	0.06
Asleep systolic BP (mmHg)	$119 \pm 10$	$118 \pm 9$	0.45
Asleep mean BP (mmHg)	88 ± 7	$88 \pm 7$	0.29
Asleep diastolic BP (mmHg)	73 ± 7	$72 \pm 7$	0.25

**Table 3.** Aerobic training blood pressure lowering effect assessed by clinic and ambulatory BPs

 measured before and after 10 weeks of aerobic training.

† Significantly different from before training.

**Table 4.** Correlations between blood pressure change after the maximal exercise test ( $\Delta$  BP after Max test) and clinic and ambulatory blood pressure changes observed after the aerobic training ( $\Delta$  BP after AT).

-	$\Delta$ <b>BP</b> after		$\Delta$ <b>BP</b> after			
	Max test		AT	n	r	р
Systolic BP (mmHg)	$-7.6 \pm 5.7$	Clinic	$-4.6\pm6.4$	30	0.17	0.38
		24 hour	$-1.8 \pm 6.7$	29	0.07	0.72
	$-7.8 \pm 5.7$	Awake	$-2.0\pm7.6$	29	0.12	0.53
		Asleep	$\textbf{-0.9}\pm6.4$	29	0.00	1.00
Diastolic BP (mmHg)	$+0.8 \pm 3.8$	Clinic	$-1.8 \pm 3.2$	30	0.35	0.06
		24 hour	-1.7 ± 4.8	29	0.26	0.18
	$+0.9\pm3.8$	Awake	$\textbf{-2.2}\pm6.0$	29	0.25	0.18
		Asleep	$\textbf{-0.9}\pm4.3$	29	0.24	0.20
Mean BP (mmHg)	$-2.0 \pm 4.0$	Clinic	$-2.7\pm3.6$	30	0.32	0.09
		24 hour	$-2.1 \pm 4.9$	29	0.18	0.36
	$-2.0 \pm 4.1$	Awake	$-2.3 \pm 6.0$	29	0.22	0.25
		Asleep	$\textbf{-0.9}\pm4.6$	29	0.15	0.45

Data: Mean  $\pm$  standard deviation.