Blood Pressure Monitoring

Comparison of morning versus evening aerobic-exercise training on heart rate recovery in treated hypertensive men: A randomized controlled trial

--Manuscript Draft--

Manuscript Number:	BPMJ-21-7R1
Full Title:	Comparison of morning versus evening aerobic-exercise training on heart rate recovery in treated hypertensive men: A randomized controlled trial
Article Type:	Brief Report
Keywords:	autonomic nervous system; circadian rhythm; Hypertension; Exercise
Corresponding Author:	LEANDRO Campos BRITO, Ph.D University of Sao Paulo: Universidade de Sao Paulo SAO PAULO, SP BRAZIL
Corresponding Author Secondary Information:	
Corresponding Author's Institution:	University of Sao Paulo: Universidade de Sao Paulo
Corresponding Author's Secondary Institution:	
First Author:	LEANDRO Campos BRITO, Ph.D
First Author Secondary Information:	
Order of Authors:	LEANDRO Campos BRITO, Ph.D
	Tiago Peçanha, PhD
	Rafael Y. Fecchio, M.S
	Andrea Pio-Abreu, PhD
	Giovânio Silva, PhD
	Décio Mion-Junior, PhD
	John R. Halliwill, PhD
	Cláudia L. M. Forjaz, PhD
Order of Authors Secondary Information:	
Manuscript Region of Origin:	BRAZIL
Abstract:	Heart rate recovery (HRR) is a marker of cardiac autonomic regulation and an independent predictor of mortality. Aerobic-exercise training conducted in the evening (ET) produces greater improvement in resting cardiac autonomic control in hypertensives than morning training (MT), suggesting it may also result in a faster autonomic restoration post-exercise. OBJECTIVE : This study compared the effects of MT and ET on HRR in treated hypertensive men. METHODS: Forty-nine treated hypertensive men were randomly allocated into three groups: MT, ET, and control (C). Training was conducted 3 times/week for 10 weeks. Training groups cycled (45min, moderate intensity), while C group stretched (30 min). In the initial and final assessments of the study, HRR60s and HRR300s were evaluated during the active recovery (30W) from cardiopulmonary exercise tests (CPET) conducted in the morning and evening. Between–within ANOVAs were applied (P≤ 0.05). RESULTS: Only ET increased HRR60s and HRR300 differently from C at morning CPET (+4±5 and +7±8 bpm, respectively, P<0.05) and only ET increased HRR300s differently from MT and C at after evening CPET (+8±6 bpm, P<0.05). CONCLUSIONS: ET improves HRR in treated hypertensive men, suggesting that this time of day is better for eliciting cardiac autonomic improvements via aerobic training in hypertensives.

Comparison of morning versus evening aerobic-exercise training on heart rate recovery in treated hypertensive men: A randomized controlled trial

Exercise, Circadian Rhythm, and Hypertension

Leandro C. Brito[1]; Tiago Peçanha[1]; Rafael Y. Fecchio[1]; Andrea Pio-Abreu[2]; Giovânio Silva[2]; Décio Mion-Junior, PhD[2]; John R. Halliwill, PhD[3]; Cláudia L. M. Forjaz[1]

1 – Exercise Hemodynamic Laboratory, School of Physical Education and Sport, University of São Paulo, São Paulo, São Paulo, Brazil;

2 – Hypertension Unit, General Hospital, University of São Paulo, São Paulo, São Paulo, Brazil.

3 - Department of Human Physiology, University of Oregon, Eugene, OR, USA.

The authors declared no conflict of interest

Fundings: Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP 2014/21676-6), Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq 304436/2018-6), and Coordenação de Aperfeiçoamento Pessoal de Nível Superior–Brasil (CAPES, financial code 001)

Correspondece: Leandro Campos de Brito

School of Physical Education and Sport, University of São Paulo, São Paulo, Brazil.

Av. Professor Mello Moraes, 65 - Cidade Universitária, São Paulo, SP

Zipcode 05508-030, Brazil. E-mail: leandrobrito@usp.br

ABSTRACT

Heart rate recovery (HRR) is a marker of cardiac autonomic regulation and an independent predictor of mortality. Aerobic-exercise training conducted in the evening (ET) produces greater improvement in resting cardiac autonomic control in hypertensives than morning training (MT), suggesting it may also result in a faster autonomic restoration post-exercise. OBJECTIVE*:* This study compared the effects of MT and ET on HRR in treated hypertensive men. METHODS: Forty-nine treated hypertensive men were randomly allocated into three groups: MT, ET, and control (C). Training was conducted 3 times/week for 10 weeks. Training groups cycled (45min, moderate intensity), while C group stretched (30 min). In the initial and final assessments of the study, HRR60s and HRR300s were evaluated during the active recovery (30W) from cardiopulmonary exercise tests (*CPET)* conducted in the morning and evening. Between–within ANOVAs were applied ($P \leq 0.05$). RESULTS: Only ET increased HRR60s and HRR300 differently from C at morning *CPET* (+4±5 and +7±8 bpm, respectively, $P<0.05$) and only ET increased HRR300s differently from MT and C at after evening *CPET* (+8±6 bpm, $P<0.05$). CONCLUSIONS: ET improves HRR in treated hypertensive men, suggesting that this time of day is better for eliciting cardiac autonomic improvements via aerobic training in hypertensives.

Key words: autonomic nervous system; circadian rhythm; hypertension; exercise

INTRODUCTION

Autonomic dysfunction is one of the main pathophysiological mechanisms involved in hypertension. Heart rate recovery (HRR) after maximal exercise testing is a low-cost, non-invasive, and useful tool to assess cardiac autonomic function[1]. It has also been shown to be an independent predictor of all-causes and cardiovascular mortalities[2,3].

Aerobic-exercise training is recommended for treatment of hypertension. In addition to decrease blood pressure, aerobic training improves resting cardiovascular autonomic modulation in hypertensives and accelerates HRR after exercise[4]. However, the effects of aerobic training on autonomic control may vary depending on the time of day in which training sessions are performed. Along these lines, recent studies have reported different HRR and sympathovagal balance after a single session of aerobic exercise performed in the morning versus in the evening[6,7].

Furthermore, the chronic effects of aerobic training have been shown to vary depending on the time of day of the training, with late afternoon training promoting greater improvement in HRR than morning training in healthy subjects[5]. In hypertensives, we have demonstrated greater blood pressure reductions and improvement in resting cardiac baroreflex sensitivity after evening than morning training[12]. Hence, training at this time of day may also produce greater improvements in cardiac autonomic regulation after exercise, resulting in a greater HRR. To the best of our knowledge, this has not been investigated in this population.

Therefore, the present study tested this hypothesis, comparing the effects of morning versus evening aerobic-exercise training on HRR during the active recovery from a maximal exercise test in treated hypertensive men.

METHODS

The study used secondary data from a randomized controlled trial approved by the Research Ethical Committee of the School of Physical Education and Sport of the University of São Paulo (nº 966.072) and registered at the Brazilian Clinical Trials (www.ensaiosclinicos.gov.br - RBR-7q7pz7). The main results of the original trial have been published elsewhere[12].

Study design and experimental protocol

The current study is a randomized controlled trial in which hypertensive men receiving consistent antihypertensive treatment for at least 4 months and attending to all study criteria (Appendix 1) underwent two maximal cycle ergometer cardiopulmonary exercise tests (CPET) conducted with a ramp protocol of 15 watts increment every minute, preceded by a 3-min warm-up at 30 watts and followed by 5 min of active recovery at 30W (detailed in Appendix 2). The tests were conducted in a random order (simple raffle) with an interval of at least 72 h between them. One test was conducted in the morning (7-9a.m.) and the other in the evening (8-10p.m.). After this initial evaluation, the subjects were randomly allocated as previously described [12] in one of three groups: morning training (MT, 7-9a.m); evening training (ET, 6-8p.m.); and control (C - stretching training – half of the subjects in the morning and half in the evening). Interventions were conducted 3 times per week for 10 weeks with aerobic training performed on a cycle ergometer (CEFISE, Biotec 2100, Campinas, Brazil) at moderate intensity and lasting from 30 to 45 min (detailed at Appendix 3). At least 48 hours after the last intervention session, a final evaluation was conducted in which morning and evening CPETs were repeated at the same order as in the initial evaluation.

Outcomes

During CPET and active recovery, heart rate (HR) was continuously assessed by a HR monitor (POLAR 800cx, Kempele, Finland). After data transmission to the Polar Pro Trainer Software®, HR signal underwent a moving average filter before analyses (v. 5.0, Polar Inc., Kempele, Finland). Peak HR was considered as the highest value achieved at the end of the exercise phase of the test. HRR was analyzed by HRR60s and HRR300s calculated by the absolute differences between peak HR and HR obtained at 60s and 300s of recovery, respectively. The first index represents cardiac parasympathetic reactivation, while the second index represents cardiac parasympathetic reactivation plus sympathetic withdraw[1,13].

Statistical Analysis

As this study used secondary data from another trial[12], a priori sample size was not calculated for HRR. Nevertheless, posteriori power analyses revealed $\beta \geq 0.80$ for all variables, showing an adequate statistical power for all of the study outcomes.

Comparisons among the interventions were applied separately for CPETs conducted in the morning and the evening using two-way mixed ANOVAs that considered group (MT, ET, and C) as the between main factor and time (Initial vs. Final) as the within main factor. Newman-Keuls tests were applied as post-hoc when necessary.

Analyses used a specific statistical software package (Statsoft v.5, Statistic for windows, USA). Data are shown as mean±SD, and $P \leq 0.05$ was considered significant.

RESULTS

The study flowchart is presented in accordance with the CONSORT in Appendix 4. After randomization, 3 subjects from each training groups dropped out for personal reasons (i.e. total of 6). Forty-nine subjects (MT = 15, ET = 15, and C = 19) underwent all the study phases and composed the final sample. Physical and clinical characteristics were similar among the groups at the beginning of the study (Table 1). Adherence to interventions, workload, and HR achieved during the aerobic training as well as improvements obtained in peak VO_2 and workload were similar between MT and ET as previously shown [12] and described in Appendix 5.

CPETs conducted between 7-9 a.m.- Peak HR achieved during morning CPET did not change from the initial to the final evaluation in either group (MT - 156±14 vs. 153±20; ET - 163±15 vs. 164±14; and C - 157±16 vs. 151±18 bpm, P=0.17). HRR60s and HRR300s increased significantly from the initial to the final evaluation only in ET, and these indexes measured at the final evaluation were significantly higher in both MT and ET than in C (Figure 1, panels A and B).

CPETs conducted between 8-10 p.m.- Peak HR achieved in evening CPET did not change from the initial to the final evaluation in either group (MT - 160±17 vs. 157±17; ET - 163±13 vs. 166±12; and C - 158±15 vs. 153±15 bpm, P=0.08). HRR60s increased significantly and similarly from the initial to the final evaluation in all groups ($P<0.01$ for time factor), while HRR300s increased significantly only in ET, and HRR300s in the final evaluation was significantly greater in ET than MT and C (Figure 1, panels C and D).

DISCUSSION

The main finding of this study was that only aerobic-exercise training conducted in the evening improved HRR as observed after CPET in treated hypertensive men, indicating, as hypothesized, that training at this time of day produces greater improvements in cardiac autonomic restoration after exercise.

ET consistently increased the fast (HRR60s) and the slow (HRR300s) phases of HRR, indicating that training at this time of day improved both branches of the cardiac autonomic system (parasympathetic and sympathetic)[1,13]. Additionally, this benefit after ET was observed in CPETs conducted at both times of day (7-9 a.m. and 8-10 p.m), showing that the effect is not limited to the time when subjects have exercised. It is also interesting to note that HRR indexes were greater in MT than C at the final evaluation although there was no significant change from the initial to the final evaluation in MT. Such results suggest a slight but not significant effect of training conducted in the morning on HRR which is consistent with a previous study[14]. It is possible that MT needs a longer period of training or a higher intensity to promote significant autonomic adaptations. This could be a focus of future studies.

The improvement in HRR observed after ET may have clinical impact. Although this study did not include a healthy group for comparison, the mean HRR300s assessed in the initial evaluation in the three groups were lower than 55 bpm (i.e. the cutoff point for increased risk for mortality), indicating an impaired cardiovascular autonomic control[2]. After ET, HRR300s increased in all but one subject, with mean values increasing by +7±8 and +8±6 bpm for CEPTs conducted at 7-9a.m. and 8-10p.m, respectively. This result demonstrates a faster restoration of cardiac autonomic control induced by training at this time. These increases may represent an important clinical improvement since a 10 bpm decrease in this variable is associated with an increase of 1.1 of the hazard ratio of death[3]. Noteworthy, in addition to the benefits revealed in the present study, our previously published data showed greater effects of ET than MT in reducing clinic and ambulatory blood pressure and improving cardiac baroreflex sensitivity[12]. These observations strengthens the case that there is a clinical impact of training at this time of day in these patients.

The current study's results are limited to treated hypertensive men who were middle-aged, not physically trained, and not extreme chronotypes. Although an important aspect of this research is the clear benefit of aerobic-exercise training in the evening for hypertensive men, it will be important to extend these results by performing studies in hypertensive women, trained subjects, and older patients. It would also be interesting to know if individuals with extreme chronotypes show a similar response to training at different times of day.

In conclusion, aerobic-exercise training conducted in the evening improves HRR in treated hypertensive men, suggesting that training at this time of day is better for inducing cardiac autonomic adaptations in hypertension.

Acknowledgements

The authors also thank all volunteers for participating.

References

1. Peçanha T, Bartels R, Brito LC, Paula-Ribeiro M, Oliveira RS, Goldberger JJ. Methods of assessment of the post-exercise cardiac autonomic recovery: A methodological review. *Int J Cardiol* 2017; 227:795-802.

2. Cheng YJ, Lauer MS, Earnest CP, Church TS, Kampert JB, Gibbons LW, et al. Heart rate recovery following maximal exercise testing as a predictor of cardiovascular disease and all-cause mortality in men with diabetes. *Diabetes Care* 2003; 26 (7):2052-2057.

3. Qiu S, Cai X, Sun Z, Li L, Zuegel M, Steinacker JM, et al. Heart Rate Recovery and Risk of Cardiovascular Events and All-Cause Mortality: A Meta-Analysis of Prospective Cohort Studies. *J Am Heart Assoc* 2017; 6 (5).

4. Amaro-Vicente G, Laterza MC, Martinez DG, Alves MJ, Trombetta IC, Braga AM, et al. Exercise Training Improves Heart Rate Recovery after Exercise in Hypertension. *Motriz* 2019; 25 (1):e101902.

5. Torii J, Shinkai S, Hino S, Kurokawa Y, Tomita N, Hirose M, et al. Effect of time of day on adaptive response to a 4-week aerobic exercise program. *J Sports Med Phys Fitness* 1992; 32 (4):348-352.

6. Brito L, Pecanha T, Tinucci T, Silva-Junior N, Costa L, Forjaz C. Time of day affects heart rate recovery and variability after maximal exercise in pre-hypertensive men. *Chronobiol Int* 2015; 32 (10):1385-1390.

7. de Brito LC, Rezende RA, da Silva Junior ND, Tinucci T, Casarini DE, Cipolla-Neto J, et al. Post-Exercise Hypotension and Its Mechanisms Differ after Morning and Evening Exercise: A Randomized Crossover Study. *PLoS One* 2015; 10 (7):e0132458.

8. Brito LC, Azevedo L, Pecanha T, Fecchio RY, Rezende RA, da Silva GV, et al. Effects of ACEi and ARB on post-exercise hypotension induced by exercises conducted at different times of day in hypertensive men. *Clin Exp Hypertens* 2020; 42 (8):722-727.

9. Brito LC, Rezende RA, Mendes C, Silva-Junior ND, Tinucci T, Cipolla-Neto J, et al. Separate aftereffects of morning and evening exercise on ambulatory blood pressure in prehypertensive men. *J Sports Med Phys Fitness* 2018; 58 (1-2):157-163.

10. Jones H, Pritchard C, George K, Edwards B, Atkinson G. The acute post-exercise response of blood pressure varies with time of day. *Eur J Appl Physiol* 2008; 104 (3):481-489.

11. Jones HG, K; Edwards, B; Atkinson, G. Effects of time of day on post-exercise blood pressure: circadian or sleep-related influences? *Chronobiol Int* 2008; 25 (6):987-998.

12. Brito LC, Pecanha T, Fecchio RY, Rezende RA, Sousa P, N DAS-J, et al. Morning versus Evening Aerobic Training Effects on Blood Pressure in Treated Hypertension. *Med Sci Sports Exerc* 2019; 51 (4):653-662.

13. Kannankeril PJ, Le FK, Kadish AH, Goldberger JJ. Parasympathetic effects on heart rate recovery after exercise. *J Investig Med* 2004; 52 (6):394-401.

14. MartinezAguirre-Betolaza A, Mujika I, Fryer SM, Corres P, Gorostegi-Anduaga I, Arratibel-Imaz I, et al. Effects of different aerobic exercise programs on cardiac autonomic modulation and hemodynamics in hypertension: data from EXERDIET-HTA randomized trial. *J Hum Hypertens* 2020.

Figure Legends:

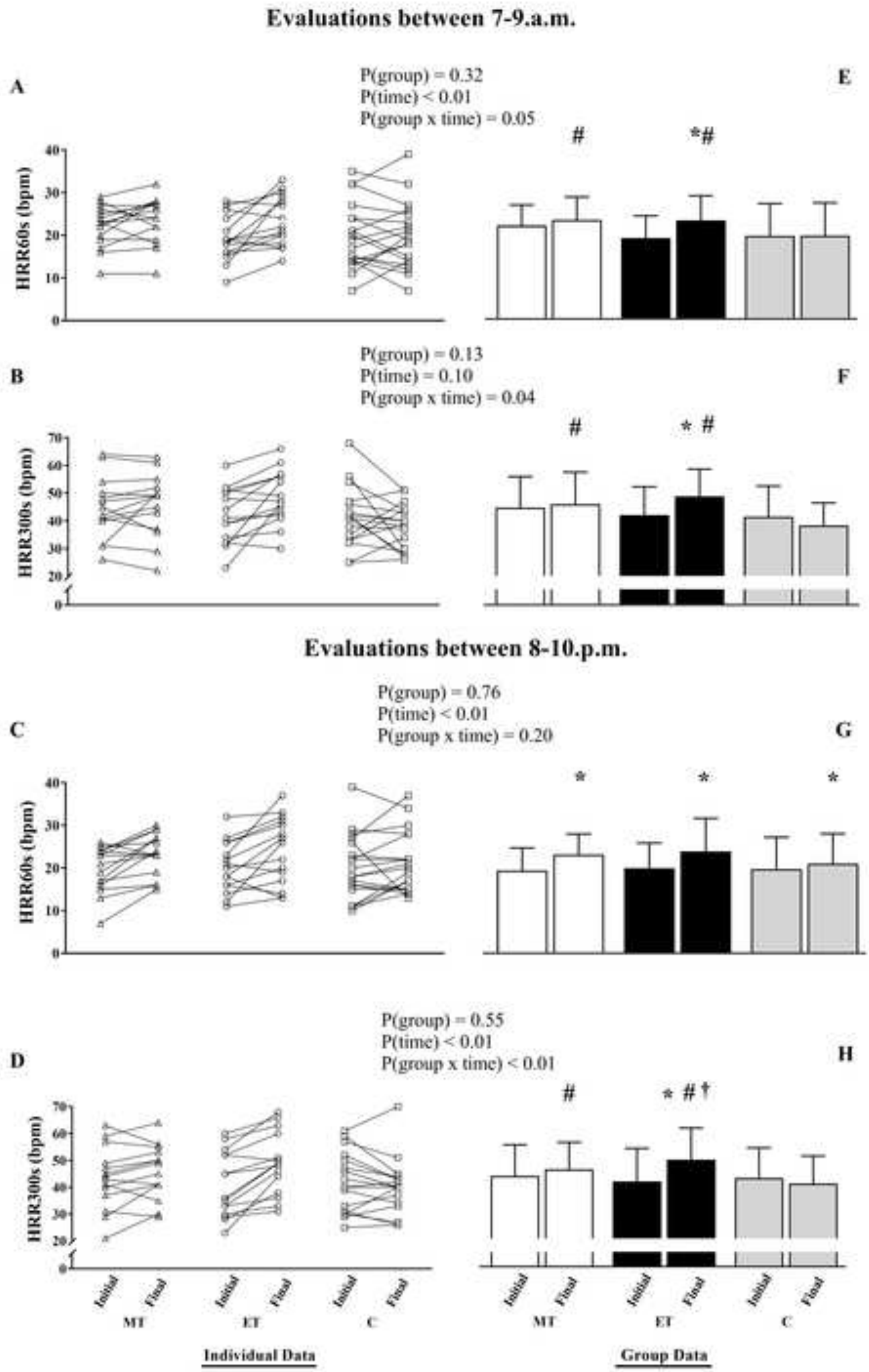
Figure 1. Heart rate recovery indexes measured in the morning (7-9a.m. – Individual data: panels A and B; Group data: panels E and F) and evening (8-10p.m. – Individual data: panels C and D; Group data: panels G and H) evaluations conducted at the initial and the final assessments of the study in three groups: Aerobic training in the morning (MT, white bars; triangles), aerobic training in the evening (ET, black bars; circles), and control (C, gray bars; squares). HRR60s – heart rate recovery at 60 s of recovery; HRR300s - heart rate recovery at 300 s of recovery. * Significantly different from the initial evaluation in the same group ($P \leq 0.05$). # Significantly different from the C group at the same evaluation ($P \leq 0.05$). † Significantly different from the MT group at the same evaluation ($P \leq 0.05$).

Table

Table 1. Physical and clinical characteristics of the morning training, evening training and control groups assessed at the beginning of the study.

Variables	MT	ET	C
N	15	15	19
Age (years)	51±8	49±8	50±10
Height (m)	1.72±0.06	1.70±0.10	1.71±0.07
Weight (kg)	87.4±12.1	89.5±14.9	87.3±15.8
Body mass index (kg/m^2)	29.6±3.1	30.7±3.3	29.6±4.3
Chronotype (score)	52±6	56±3	53±4
Hemodynamics			
Resting systolic BP (mmHg)	135±9	132±6	134±13
Resting diastolic BP (mmHg)	92±7	89±5	89±8
Heart rate (bpm)	74±9	77±10	76±11
Type of anti-hypertensive therapy			
One – no. (%)	11(73)	10(67)	14(74)
Two or more – no. (%)	4(27)	5(33)	5(26)
Anti-hypertensive drugs			
Angiotensin II receptor blockers – no. (%)	8(53)	7(47)	9(47)
Angiotensin-converting enzyme inhibitors – no. (%)	6(40)	7(47)	7(37)
Dihydropyridine calcium channel blockers – no. (%)	4(27)	3(20)	4(21)
Diuretics – no. (%)	4(27)	5(33)	4(21)

Data: mean±standard deviation. BP, blood pressure; MT, morning training; ET, evening training; C, control. Comparison with one-way ANOVA or chi-square test. No significant differences.



Evaluations between 7-9.a.m.
A
P(group) = 0.32
P(time) < 0.01
P(group x time) = 0.05
E
HRR60s (bpm)
B
P(group) = 0.13
P(time) = 0.10
P(group x time) = 0.04
F
HRR300s (bpm)
Evaluations between 8-10.p.m.
C
P(group) = 0.76
P(time) < 0.01
P(group x time) = 0.20
G
HRR60s (bpm)
D
P(group) = 0.55
P(time) < 0.01
P(group x time) < 0.01
H
HRR300s (bpm)
Initial
Final
MT
ET
C
Individual Data
Group Data

Click here to access/download

Supplemental Data File (.doc, .tif, pdf, etc.)

Appendix 3 - Interventions.docx