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Effects of aerobic versus combined training on WELCH questionnaire score and resting heart rate in patients with peripheral artery disease: randomized clinical trial

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ABSTRACT
Background: Peripheral arterial disease (PAD) reduces walking performance (WELCH questionnaire). In addition, patients with PAD may have higher resting heart rate (RHR) values. Exercise may be an alternative to improve the WELCH and RHR score. Aerobic training (AT) is indicated by the guidelines. Strength training (ST) may also be an alternative for improving the WELCH and RHR score. However, the combination of AT and ST (combined training - CT) is rarely used in PAD, raising questions about its effects on the WELCH and RHR score. *Objective:* To evaluate the effect of AT versus CT on the WELCH and RHR score in patients with PAD. *Methods:* Randomized clinical trial that enrolled 17 patients with PAD. All had classification of Fontaine 2b. They were divided into 2 groups: aerobic training group (ATG, n = 9) and combined training group (CTG, n = 8). Outcomes were assessed before and after 12 weeks of intervention. *Results:* ATG increased the WELCH score from 23 ± 9 to 48 ± 8 and CTG increased from 16 ± 3 to 45 ± 8 (P <0.001). ATG reduced RHR from 87 ± 3 to 84 ± 2 beats per minute (bpm) and CTG reduced from 89 ± 3 to 85 ± 4 bpm (P = 0.006). *Conclusion:* Both models significantly improved the WELCH and RHR score and can be applied to patients with PAD. Peripheral vascular rehabilitation is an attractive strategy for these patients.

Keywords – Aerobic Exercise, Intermittent Claudication, Peripheral Artery Disease, Strength Training.

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I. INTRODUCTION

Intermittent claudication (IC) of the lower limbs is the most common clinical manifestation of peripheral obstructive arterial disease (PAD) [1]. About 200 million people are estimated to have some degree of PAD worldwide. In Brazil, the prevalence is around 10.5%, and after age 70, the prevalence increases to 20% [2]. This limitation in ambulation can also alter other physiological parameters such as resting heart rate (RHR) and after exercise [3].

Patients with PAD may have autonomic dysfunction followed by changes in the speed of ankle pressure recovery, which represents a worse arterial blood flow response to exercise as well as less venous return [4]. The WELCH questionnaire, which consists of four questions related to walking speed (slow, normal, fast, the fourth question being a summary of the previous domains) compared to peers can assess gait impairment [5].

One of the non-pharmacological treatments for improving the WELCH score is aerobic exercise [1, 6, 7]. In addition, strength exercise can improve walking ability due to increased lower limb muscle strength [8]. However, there is a gap in the literature about the impact of different physical training models on the WELCH score and RHR in patients with PAD. The aim of the present study was to evaluate the effects of two different 12-week training models (aerobic and combined) on the WELCH questionnaire and RHR in patients with PAD.

II. METHODS

2.1. Study Design

Randomized clinical trial in which participants were divided into two groups: aerobic training group (ATG) and combined training group (CTG). All participants read and signed the informed consent form. The instrument available at

http://www.randomization.org was used for the 1: 1 ratio randomization process.

This research was conducted at the *Hospital de Clinicas de Porto Alegre* (HCPA) linked to the Department of Physiatrics and Vascular Surgery Outpatient. The institution's ethics committee (140381) previously approved the project. The present study used blind evaluator. We conduct our research in accordance with the ethical standards in the Helsinki statement.

2.2. Subjects

The patients were recruited from the HCPA Vascular Surgery Outpatiet. The diagnosis of PAD was made by an experienced vascular physician through clinical examination and confirmed by measurement of the Ankle Brachial Index (ABI) [9]. The participants' eligibility criteria included: 1) presenting ABI <0.9; 2) symptoms of IC between 100-200 meters, Rutherford class 2 and Fontaine 2b; 3) optimized clinical treatment with the use of standard medicines for PAD (Cilastozol, Simvastatin and ASA); 4) cognitive ability to follow the instructions of the present study; 5) do not have severe heart disease or any other disease that prevents physical exercise; 6) Not participating in regular physical training programs for at least the last 6 months.

The sample consisted of 20 volunteers (Figure 1) aged over 50 years, 60% men and 40% women, with clinical diagnosis of PAD and class 2 of Rutherford and 2b of Fontaine. All participants met eligibility criteria, including PAD-optimized clinical treatment, ability to understand verbal instructions for all stages of the clinical trial, and none of the participants participated in the last 6 months of other studies with regular physical training.

2.3. Randomization Procedures

Each participant received a code based on interview order and anamnesis. The codes were then passed on to a researcher not involved at any stage of the assessment or intervention. This researcher was responsible for blind and random allocation of participants (via online via https://www.randomization.org) into two groups, ATG and CTG. After the randomization process, the researcher shared the results with the project coordinator only. Volunteers were not allowed to modify the intervention group once assigned. The experimental procedures were started following.

2.4. Training Program

2.4.1. Aerobic Training

To perform the training protocol, a treadmill (Inbramed®, model KT 10200 (Porto Alegre, Brazil) was used. The patients trained twice a week for 12 weeks. The sessions lasted around 45 minutes, with five minutes of stretching and warming up, 30 minutes of main part and 10 minutes back to calm and final stretches.

Intensity was adjusted to around 40-60% of the heart rate reserve (HRR), which was calculated using the Karvonen equation to predict training zones [10]. To predict the maximum heart rate (HRmax), we used the Tanaka equation [11]. For patients using some type of beta blocker, we used the equation of Brawner et al., 2002 [10]. We also used the BORG perceived exertion scale for intensity control and the visual analog scale (VAS) for lower limb pain control [12, 13].

2.4.2. Combined Training

The combined protocol consisted of the initial 30 minutes of aerobic exercise (same ATG protocol) and 15 minutes of strength exercises. The strength training load was prescribed between 4 and 7 of the OMNI perceived exertion scale for resistance exercises [14]. Due to the logistical difficulty in performing a maximum repetition test (1 RM) for this group of patients, we used an alternative method, but validated by the scientific literature and used for prescription. We based the repetitions between 15 in the initial phase of the training, with reduction to 10 repetitions according to the progression of the training. We applied five strength exercises: bench press, horizontal elbow flexion (row), elbow flexion (biceps), knee extension and plantar flexion.

2.5. Data Collection

2.5.1. WELCH Questionnaire

The WELCH (Walking Estimated-Limitation Calculated by History) questionnaire, validated for Portuguese, was used to assess gait impairment in patients with IC, and consists of four questions related to walking speed (slow, normal, and fast). The fourth question covers the summary of the previous areas. The four questions on the questionnaire are always compared to peers, and the higher the score, the greater the ability to withstand higher walking intensities. The present questionnaire was validated for Portuguese version by comparison with the gold standard (Gardner Protocol), which showed positive and significant correlations in relation to the WELCH score and the distance to the onset of pain ($r = 0.64$, $P = 0.01$), besides the total walking distance ($r = 0.61$, $P = 0.01$).

2.5.2. Resting Heart Rate

For RHR evaluation, a model FT1 cardiac monitor (Polar Electro Oy, Kempele, Finland) was used. The patient was instructed to sit quietly in a room alone for two minutes. After two minutes, the researcher in charge would collect the heart rate

measured by the heart monitor every 10 seconds for one minute. For the values corresponding to the RHR variable, we performed an average of the 10 HR measurements during this minute after the initial rest. Measurements were always taken before the training session [15].

2.6. Statistical Analysis

Continuous variables were described as mean and confidence interval (95% CI) for symmetrical distribution and as median and interquartile range for asymmetric distribution. Categorical variables were described as numbers and percentages. To analyze differences between the groups in the sample characterization data we used a t-test or Mann-Whitney when continuous variable and chi-square test for categorical variables. The differences between the groups in the WELCH questionnaire and RHR values were determined by the Generalized Estimating Equations (GEE), which tests the main effects of the group and time, as well as their respective interactions. A post hoc comparison of Bonferroni was performed. All data were analyzed using the Statistical Package for Social Sciences software - SPSS version 20.0. (IMB Corporation Armonk, NY). We adopted a P value <0.05 for statistical significance.

III. RESULTS

Three participants did not complete the 12 weeks of training due to unspecified personal reasons (ATG = 1 and CTG = 2), representing a 15% drop-out rate. Therefore, 17 participants completed the 24 training sessions and performed all final evaluations after the intervention period (Figure 1). All participants get 100% attendance at the sessions, demonstrating optimal adherence to the proposed training program. Sample characterization data are presented in Table 1.

The WELCH questionnaire score did not show differences between the groups at both times evaluated. However, both groups showed significant improvements after 12 weeks of training (P <0.001) without significant interactions (P = 0.437). ATG increased the WELCH questionnaire score from 23 ± 9 to 48 ± 8 and CTG increased from 16 ± 3 to 45 ± 8 (Figure 2).

RHR values decreased significantly after 12 weeks of training for both groups (P = 0.006). ATG reduced RHR from 87 ± 3 to 84 ± 2 beats per minute (bpm) and CTG reduced from 89 ± 3 to 85 ± 4 bpm (Figure 3). However, no significant interactions were observed.

Concomitantly with the outcome variables mentioned above, we controlled the progression of training by means of the BORG and VAS scale for lower limb pain. Both groups showed significant progression to both the subjective sensation on exertion and lower limb pain (P <0.001 and P = 0.017 respectively). The ATG presented a mean BORG value for the first month of training of 5.3 ± 0.5 and progressed to a value of 6.1 ± 0.4 for the third month of training. The CTG presented a BORG value for the first month of training of 5 ± 0.4 and for the third month of training of 5.9 ± 0.5. Regarding VAS, ATG presented a value of 5.2 ± 0.5 for the first month and progressed to 5.8 ± 0.4 in the third month, while CTG presented a value of 4 ± 0.4 for the first month. the first month and increased the value to 4.7 ± 0.5 for the third month.

IV. DISCUSSION

The present study evaluated the effects of 12 weeks of combined and aerobic training on the WELCH questionnaire and RHR score in patients with PAD and IC. The aerobic part of the training programs had intensity individualized by HRR and controlled by BORG. The strength part of the combined training was conducted with simple and easily applied exercises for these patients. The main finding of the present study was that both groups improved the WELCH questionnaire and RHR values after 12 weeks of intervention, demonstrating positive effects for both CTG and ATG.

There was a significant effect after the intervention period for the WELCH questionnaire score in both groups (Figure 2). We hoped that combined training could provide greater benefits compared to aerobic training due to the sum of the effects of aerobic and strength exercises in a single session [16, 17]. We know that aerobic training improves peripheral vasodilation due to increased bioavailability of nitric oxide [18]. Regarding the benefits of strength training, we can mention the improvement of lower limb musculature strength, which promotes greater dynamic stability for walking, thus, this mechanism could help in improving the values for the WELCH score, which is directly related to walking speed [19]. However, our hypothesis has not been confirmed. Probably aerobic exercise may negatively interfere with expected results of strength training, causing CTG to have no additional benefits compared to ATG [20].

The WELCH questionnaire directly assesses walking speed compared to peers, and was validated using the gold standard method called the Gardner protocol [5]. Physically active and stronger lower limb patients may have higher WELCH scores compared to sedentary individuals [21]. Therefore, a protocol that includes aerobic and strength training in the same session would be highly recommended for this group of patients [22].

Aerobic training may interfere adaptations of strength training when developed in the same session due to a possible inhibition of muscle hypertrophy and a possible reduction in testosterone

levels [23]. It is unclear whether aerobic training can interfere negatively on strength training for patients with IC, making combined training a background recommendation for rehabilitation guidelines in PAD [9]. However, some evidence suggests that combined training can improve up to 18% functional capacity and up to 38% lower limb muscle strength without demonstrating aerobic component interference in strength training [24]. Therefore, the question remains for future studies on a possible interference of the aerobic component in strength training for patients with PAD.

Regarding attenuation of sympathetic nervous system response and improvement of parasympathetic activation, we found a significant reduction in RHR in both groups after 12 weeks of training. This attenuation of RHR is directly related to an improvement in autonomic balance [25]. Patients with PAD may have some degree of ischemic heart disease, which directly interferes with autonomic balance [26]. The results indicate substantial clinical effects of both training protocols for PAD patients on the RHR outcome [27, 28]. Aerobic training may promote greater left ventricular (LV) contraction, increasing cardiac output [29]. In addition, aerobic training promotes greater bioavailability of nitric oxide and increase in both size and number of mitochondria, resulting in greater use of ejected blood, thus reducing myocardial oxygen consumption, with repercussions in the reduction of RHR [18]. Strength training, on the other hand, has a greater effect on total peripheral resistance, significantly reducing such resistance to LV-ejected blood, enabling shorter diastole times, and causing a reduction in RHR [30].

We also observed that there was a significant progression of training intensity as well as an increase in pain sensation for the lower limbs at the end of the third month. From the results presented above, we can determine that the training dose response was sufficient to promote such changes in the main outcomes [31, 32].

The greatest merit of this study may relate to patient selection since, unlike literature studies, we included only patients of the same degree of ischemia (Rutherford 2 and Fontaine 2b) who had not responded to optimal clinical treatment.

On the other hand, the study has some limitations. One is the short intervention time, which can determine a greater magnitude of effect as a function of the exposure time to the intervention. Interestingly, future studies will evaluate longer intervention times, such as six months or even one year of training. In addition, performing strength exercise without a gold standard (1 RM) based prescription may not be sufficient to generate the expected adaptations.

V. CONCLUSION

Our results indicate that both aerobic and combined training is safe and effective to improve the WELCH questionnaire score and RHR value. However, future studies should consider protocols that may promote specific adaptations for the lower limbs as well as order of execution of aerobic and strength exercise. Finally, we conclude that both training protocols promote similar adaptations in the WELCH questionnaire score and RHR value in patients with PAD and IC.

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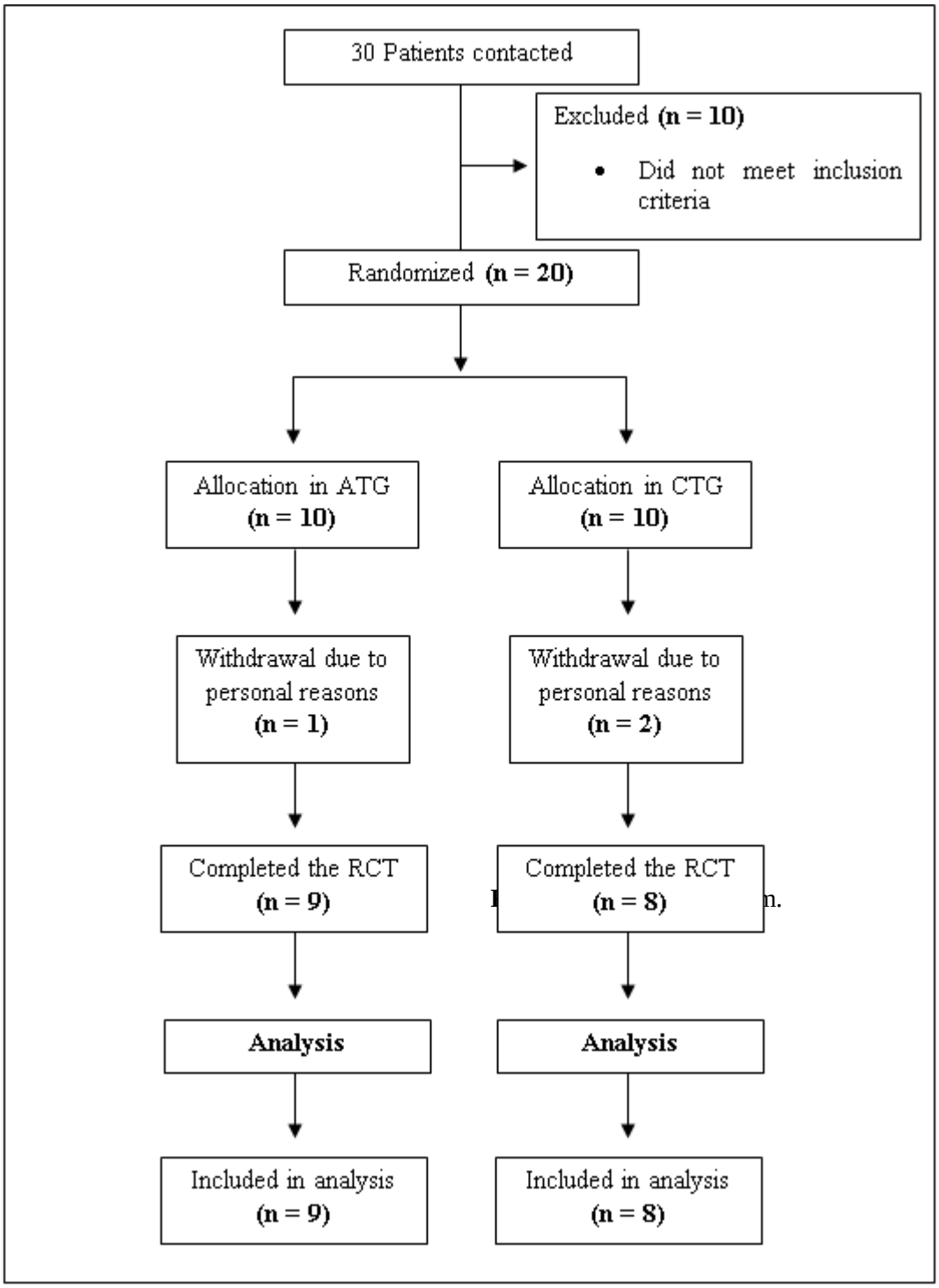
30 Patients contacted
Excluded (n = 10)
Did not meet inclusion criteria
Randomized (n = 20)
Allocation in ATG (n = 10)
Allocation in CTG (n = 10)
Withdrawal due to personal reasons (n = 1)
Withdrawal due to personal reasons (n = 2)
Completed the RCT (n = 9)
Completed the RCT (n = 8)
Analysis
Analysis
Included in analysis (n = 9)
Included in analysis (n = 8)

Table 1. Sample characterization of both training groups.

Characteristics	**ATG (N=9)**	**CTG (N=8)**	***P* value**
Age (years)	65 ± 3	61 ± 3	0.376
Body mass (kg)	82 ± 4	73 ± 4	0.141
Height (cm)	172 ± 2	165 ± 2	0.006*
BMI	28 ± 2	27 ± 2	0.755
ABI	0.78 (0.73; 0.87)	0.74 (0.70; 0.83)	0.326
Fontaine 2b Class n (%)	9 (100%)	8 (100%)	--------
Risk Factors			
Hypertension n (%)	9 (100%)	6 (75%)	0.206
Diabetes Mellitus n (%)	5 (56%)	5 (62%)	1.000
Dyslipidemia n (%)	9 (100%)	8 (100%)	--------
Smokers n (%)	3 (33%)	3 (37%)	1.000
Ex-smokers n (%)	1 (11%)	3 (37%)	0.294
Never smoke n (%)	5 (56%)	2 (25%)	0.335
Alcoholism n (%)	2 (22%)	5 (62%)	0.153
Drug Therapy			
Anti-hypertensive n (%)	9 (100%)	6 (75%)	0.206
Glycemic control n (%)	5 (56%)	5 (62%)	1,000
Beta-Blocker n (%)	6 (67%)	3 (37%)	0.347

BMI: body mass index; **ABI:** ankle-brachial index; ***** indicate difference statically significant.

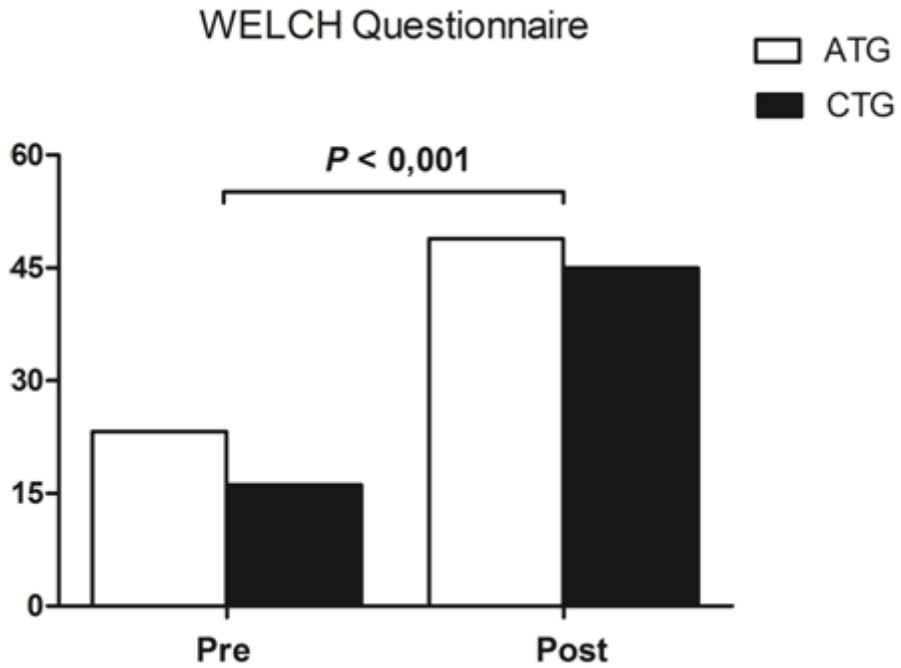

Figure 2. WELCH Questionnaire scores for both groups before and after 12 weeks of training. ATG: Aerobic Training Group; CTG: Combined Training Group; Pre: period before training; Post: period after training.

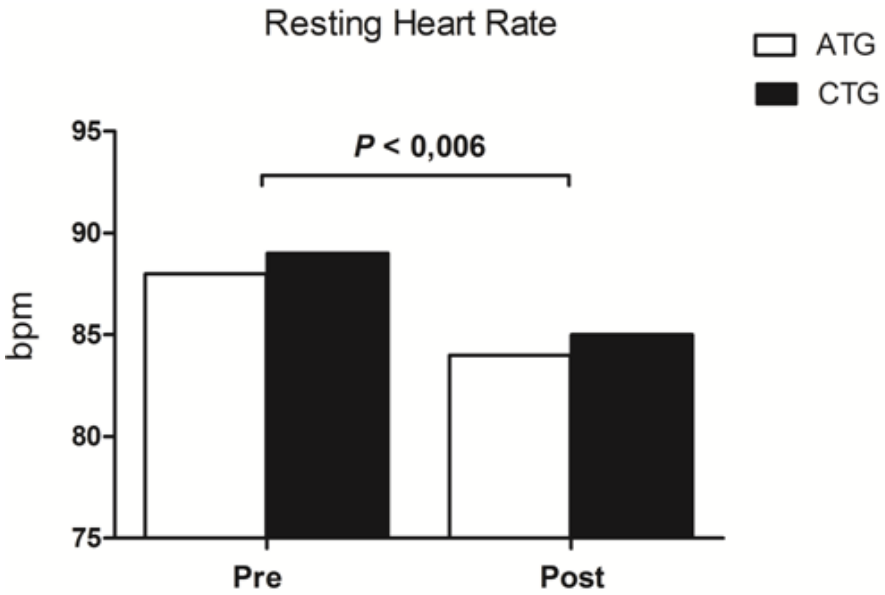

Figure 3. RHR values of both groups before and after 12 weeks of training. ATG: Aerobic Training Group; CTG: Combined Training Group; Pre: period before training; Post: period after training; bpm: beats per minute

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