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Citation: Cucato, Gabriel Grizzo, Chehuen, Marcel Da Rocha, Costa, Luis Augusto Riani, Ritti-Dias, Raphael Mendes, Wolosker, Nelson, Saxton, John and Forjaz, Cláudia Lúcia de Moraes (2013) Exercise prescription using the heart of claudication pain onset in patients with intermittent claudication. Clinics (São Paulo, Brazil), 68 (7). pp. 974-978. ISSN 1980-5322

Published by: UNSPECIFIED

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NEWCASTLE

Exercise prescription using the heart of claudication pain onset in patients with intermittent claudication

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OBJECTIVE: To assess the acute metabolic and cardiovascular responses to walking exercise at an intensity corresponding to the heart rate of claudication pain onset and to investigate the effects of a 12-week walking training program at this intensity on walking capacity.

METHODS: Twenty-nine patients with intermittent claudication were randomly allocated to the walking training (n = 17) or control (CO, n = 12) group. The walking training group performed an acute exercise session comprising 15 × 2-min bouts of walking at the heart rate of claudication pain onset, with 2-min interpolated rest intervals. The claudication symptoms and cardiovascular and metabolic responses were evaluated. Walking training was then performed at the same intensity twice each week for 12 weeks, while the control group engaged in twice weekly stretching classes. The claudication onset distance and total walking distance were evaluated before and after the interventions. Brazilian Registry Clinical Trials: RBR-7M3D8W.

RESULTS: During the acute exercise session, the heart rate was maintained within tight limits. The exercise intensity was above the anaerobic threshold and >80% of the heart rate peak and VO_{2peak} . After the exercise training period, the walking exercise group (n = 13) showed increased claudication onset distance (309 ± 153 vs. 413 ± 201 m) and total walking distance (784 ± 182 vs. $1,100 \pm 236$ m) compared to the control group (n = 12) ($p < 0.05$).

CONCLUSION: Walking exercise prescribed at the heart rate of claudication pain onset enables patients with intermittent claudication to exercise with tolerable levels of pain and improves walking performance.

KEYWORDS: Peripheral Artery Disease; Functional Capacity; Exercise Intensity; Cardiovascular System; Metabolism.

Cucato GG, Chehuen MR, Costa LA, Ritti-Dias RM, Wolosker N, Saxton JM, et al. Exercise prescription using the heart of claudication pain onset in patients with intermittent claudication. *Clinics*. 2013;68(7):974-978.

Received for publication on February 4, 2013; First review completed on February 22, 2013; Accepted for publication on March 20, 2013

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INTRODUCTION

Walking exercise is recommended for patients with intermittent claudication (1,2) because it improves the claudication onset distance and total walking distance. However, the degree of improvement varies according to different studies (3); this discrepancy might be explained by different exercise prescriptions that vary in intensity, duration and total amount of exercise prescribed (3–5).

Guidelines recommend that walking exercise should be performed at an intensity that elicits claudication symptoms within 3 to 5 min (1,2). However, the intensity of exercise needed to elicit claudication symptoms in 3 min is greater than that needed to elicit symptoms in 5 min. Hence, because of the variability in exercise training prescriptions, it is difficult to understand the impact of exercise training intensity on the changes in walking performance in this patient group and the discrepant results among different trials (6,7). Furthermore, the guidelines recommend that patients walk until they achieve claudication of moderate severity before resting briefly and repeating the exercise (2). However, this approach could prevent patients from engaging in exercise rehabilitation because of the level of pain experienced.

We have previously demonstrated in patients with intermittent claudication that claudication pain onset assessed during a graded treadmill test occurred at an intensity that was higher than the individual's anaerobic

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No potential conflict of interest was reported.

DOI: 10.6061/clinics/2013(07)14



threshold (8). Exercise above the anaerobic threshold is known to be an effective stimulus for inducing metabolic and cardiovascular adaptations (9); therefore, exercise at this intensity could effectively improve the walking capacities of patients with intermittent claudication.

Walking exercise above the anaerobic threshold has previously been prescribed for patients with cardiovascular disease, and heart rate was used to prescribe and monitor the exercise intensity (10). However, using heart rate to control exercise intensity in patients with intermittent claudication, whose capacity to exercise is limited by ischemic leg pain, has not been previously investigated.

The present study, which was designed to test the feasibility and efficacy of using the heart rate of claudication pain onset to prescribe walking exercise for patients with intermittent claudication, was the first step in analyzing the utility of this type of exercise prescription. Thus, the purpose of this study was to analyze the pain, cardiovascular and metabolic responses experienced by patients during walking exercise performed at the heart rate corresponding to the claudication pain onset, and to investigate the effects of a 12-week walking training program at this intensity on walking capacity in patients with intermittent claudication. We hypothesized that an exercise prescription at this intensity would elicit tolerable claudication symptoms, while inducing an exercise training stimulus above the individual's anaerobic threshold. Second, we hypothesized that a low-volume walking exercise training program at this intensity would induce walking performance improvements in this patient group.

■ MATERIAL AND METHODS

This study was approved by the Ethics Committee of the School of Physical Education and Sport of University of São Paulo (process 2008/55) and was registered in the Brazilian Registry of Clinical Trials (RBR-7M3D8W). Patients with stable symptoms of intermittent claudication were recruited from a tertiary center specializing in vascular disease. Male patients with Fontaine stage II symptoms of intermittent claudication for more than 6 months, an ankle-brachial index ≤ 0.90 at rest in 1 or 2 legs and who were able to walk for at least 2 min at 3.2 km/h on a treadmill were invited to participate. The following exclusion criteria were applied: obesity (body mass index ≥ 30 kg/m²), use of β -blockers, non-dihydropyridine calcium channel blockers, or peripheral vasodilators, inability to obtain the ankle-brachial index, exercise tolerance limited by factors other than claudication (i.e., arrhythmias, cardiac symptoms or exaggerated blood pressure rise), electrocardiogram response suggestive of myocardial ischemia and history of revascularization in the previous year.

Twenty-nine patients participated in the study and were randomized into 2 groups: the walking training group ($n = 17$) and the control group ($n = 12$). The study comprised 2 phases. In phase 1, during an acute walking exercise session conducted at intensity of heart rate of claudication pain onset, the cardiopulmonary responses and claudication symptoms were assessed in the patients who were randomized to walking training. In phase 2, the patients in the walking training group engaged in twice-weekly walking exercise training for 12 weeks, while patients in the control group engaged in stretching exercise classes for the

same amount of time. Both groups were evaluated at the beginning and end of the 12-week period.

Maximal graded treadmill test

All patients performed a progressive graded treadmill exercise test to maximum claudication pain at baseline and after 12 weeks. Speed was maintained at 3.2 km/h, and the grade was increased by 2% every 2 min (11). A 12-lead electrocardiogram was continuously monitored, and the heart rate was measured at the end of each stage. Oxygen uptake (VO₂) was continuously measured using a metabolic cart (Medical Graphics Corp CPX/D, St Paul, Minnesota, USA), and the data were averaged over 30-s intervals for use in the analysis. The anaerobic threshold was independently detected by 2 evaluators; the threshold was defined by a nonlinear increase in the respiratory exchange ratio, carbon dioxide production and ventilation, and an increase in the end-tidal oxygen partial pressure and a decrease in the ventilatory equivalent for oxygen (12). During the test, patients reported the onset of claudication symptoms, and the heart rate at this point was used for the walking exercise training prescription. Claudication onset distance and total walking distance were defined as the distance walked when the patient first reported leg pain and the distance at which the patient was unable to continue exercising because of leg pain, respectively (13,14).

Phase 1: Acute exercise responses

Patients in the walking training group performed a session of walking exercise that comprised 15×2-min walking bouts, with 2-min intermittent rest periods. During each of the 2-min walking bouts, exercise intensity was adjusted to maintain heart rate within 4 beats per minute (bpm) above or below the heart rate of claudication pain onset (e.g., if the patient reported the claudication pain onset in the maximal treadmill test at 100 bpm, the heart rate exercise zone was set at 96 to 104 bpm). The treadmill speed was set at 3.2 km/h, while the grade was adjusted to achieve the target heart rate, which was continuously monitored (Polar A3, Helsinki, Uusimaa, Finland). In addition, the pain levels were monitored throughout the session, and VO₂ was measured during the 1st, 5th and 12th walking exercise bouts.

Phase 2: Exercise training intervention

Patients in the walking training group engaged in a twice-weekly 12-week walking exercise training program that consisted of the same protocol used in phase 1 of the study. Each session comprised 15×2-min walking exercise bouts at the heart rate of claudication pain onset ± 4 bpm, with 2-min interpolated rest periods. In all exercise training sessions, the heart rate was continuously monitored. The walking speed was set at 3.2 km/h, and the grade was adjusted to maintain the heart rate within the target range. If the patient failed to reach the target heart rate during a particular walking exercise session, the treadmill grade was increased for the next session. Patients in the control group performed stretching exercises using the upper and lower limbs twice a week for 30 min per session.

Statistical analysis

Chi-squared tests and t-tests were used to compare the baseline characteristics of the groups. In phase 1, the



Table 1 - Clinical characteristics of the study patients.

	Control (n = 12)	Walking training (n = 13)	p-value
Age (years)	61 ± 8	64 ± 6	0.39
Weight (kg)	74.1 ± 13.6	70.7 ± 8.2	0.54
Body mass index (kg/m ²)	25.9 ± 3.8	25.4 ± 2.3	0.73
ABI at rest	0.60 ± 0.03	0.61 ± 0.03	0.40
Iliofemoral (%)	50	38	0.69
Femoropopliteal (%)	33	46	0.68
Tibiofibular (%)	17	15	0.99
Claudication onset distance (m)	328 ± 161	309 ± 153	0.77
Total walking distance (m)	828 ± 286	784 ± 182	0.64
Cardiovascular Risk Factors and Comorbidities			
Current smoking (%)	33	15	0.34
Hypertension (%)	83	84	0.93
Diabetes mellitus (%)	25	15	0.64
Dyslipidemia (%)	100	85	0.15
Medication			
Antihypertensive agent (%)	83	84	0.93
Lipid-lowering agent (%)	50	77	0.12
Anticoagulants/antiplatelet agent (%)	92	100	0.28

Continuous variables are presented as the mean ± SD.
ABI = ankle brachial index.

acute responses to walking training were analyzed using a one-way analysis of variance (ANOVA). In phase 2, the claudication onset and total walking distances were compared between the groups using a two-way ANOVA; Newman-Keuls post-hoc tests were used to identify differences. Significance was set at $p < 0.05$. The data are presented as the mean ± standard deviation (SD).

RESULTS

The clinical characteristics of the patients with intermittent claudication are shown in Table 1. Baseline anthropometric and disease characteristics were similar between the walking training and control groups. Most patients were elderly, non-obese, hypertensive and were receiving anti-hypertensive, lipid-lowering and antiplatelet drug therapy.

The acute responses assessed during the walking exercise are presented in Table 2. Heart rate was maintained at the target intensity throughout the acute exercise session (approximately 100% of the heart rate of claudication pain onset). In comparison with the resting values, both the VO_2 and heart rate increased during the 1st, 5th and 12th exercise bouts. After the 5th bout, the VO_2 and heart rate were >80% of the peak values recorded in the maximal graded treadmill test. After the 5th bout most patients reported experiencing tolerable claudication symptoms during walking.

Twenty-five patients completed phase 2 of the study. Four patients in the walking training group did not complete the training program for personal reasons. During the training program, heart rate was kept at the target intensity by increasing the treadmill grade as patients adapted to the exercise program. After 12 weeks, the claudication onset distance and total walking distance increased significantly ($p < 0.05$) in the walking training group, while no change was observed in the control group (Table 3).

DISCUSSION

Although regular walking exercise is recommended as an initial treatment for many patients with intermittent claudication, the exercise prescription intensity is poorly defined in peripheral arterial disease guidelines (1,2). The results of the present study indicate that walking exercise prescribed at the heart rate corresponding to claudication pain onset induces tolerable levels of ischemic leg pain and a cardiopulmonary exercise stimulus that is above the anaerobic threshold. Previous studies have suggested that exercise intensities that evoke claudication symptoms are important for improving walking capacity (3,7), and an exercise stimulus which is above the anaerobic threshold is particularly effective for promoting cardiovascular and metabolic adaptations (9,15). Hence, our results show that a walking exercise prescription at the heart rate of

Table 2 - Cardiopulmonary responses and prevalence of claudication symptoms evaluated during a walking training session performed with the intensity prescribed at the heart rate of claudication pain onset (n = 17).

	Rest	1 st bout	5 th bout	12 th bout
VO_2 (ml.kg ⁻¹ .min ⁻¹)	4.0 ± 0.8	12.0 ± 3.3 ^a	14.9 ± 2.2 ^{ab}	14.7 ± 2.7 ^{ab}
VO_2 peak (%)	22 ± 7	65 ± 20 ^a	81 ± 16 ^{ab}	80 ± 16 ^{ab}
VO_2 anaerobic threshold (%)	32 ± 9	94 ± 33 ^a	117 ± 27 ^{ab}	114 ± 27 ^{ab}
Heart rate (bpm)	73 ± 10	94 ± 13 ^a	99 ± 16 ^a	101 ± 16 ^a
Heart rate peak (%)	60 ± 13	76 ± 6 ^a	81 ± 8 ^a	82 ± 7 ^{ab}
Heart rate of claudication pain onset (%)	—	95 ± 7	100 ± 3 ^b	102 ± 5 ^b
Pain (% patients)	—	47	94	100

Continuous variables are presented as the mean ± SD.

^aSignificant difference from rest ($p < 0.05$).

^bSignificant difference from the 1st bout ($p < 0.05$). VO_2 : oxygen uptake.

**Table 3 - Walking performance in the exercise and control groups. Walking training was prescribed at the heart rate of claudication pain onset.**

	Pre	Post	Group effect	Time effect	Interaction effect
Claudication onset distance (m)					
Control group (n = 12)	328 ± 161	253 ± 118	0.24	0.56	<0.01
Exercise training (n = 13)	309 ± 153	413 ± 201*			
Total walking distance (m)					
Control group (n = 12)	828 ± 286	771 ± 262	0.14	<0.01	<0.01
Exercise training (n = 13)	784 ± 182	1100 ± 236*			

Continuous variables are presented as the mean ± SD.

*Significant difference from baseline ($p < 0.05$).

claudication pain onset is consistent with the physiological evidence for optimal exercise training intensity to improve walking performance and aerobic exercise tolerance in this patient group. Furthermore, patients can exercise at this intensity without experiencing intolerable levels of ischemic leg pain.

This conclusion is supported by the patient responses to the exercise training program. Twelve hours of walking exercise at the heart rate of claudication pain onset spread over 12 weeks induced improvements (in the claudication onset distance and total walking distance) that were similar in magnitude to the improvements previously observed after higher volume walking exercise training programs in patients with intermittent claudication (16–18). Claudication onset distance and total walking distance were increased by 104 ± 141 m and 316 ± 141 m, respectively, which represent clinically meaningful changes, particularly because our patient cohort had a higher walking capacity at baseline than that reported in previous studies (3,5,7). Evidence from a previous meta-analysis suggests that for optimal improvements in walking capacity, exercise sessions should be >30 min in duration and should be performed at least 3 times per week for a minimum of 6 months (3). Our evidence suggests that walking exercise prescribed at the heart rate corresponding to the claudication pain onset in the form of short bouts is an effective exercise training regimen that can induce walking performance improvements comparable to those of higher volume walking exercise programs in patients with intermittent claudication. Furthermore, exercise training at the heart rate of claudication pain onset is well tolerated by patients and can be easily controlled in the clinic or community setting using a heart rate monitor.

The present study had limitations. The proposed walking training protocol focused only on the exercise intensity; exercise duration and frequency may also influence responses to walking training. However, these parameters can be objectively stated and did not vary greatly between the studies. The present investigation did not include women and did not include patients who were using beta-blockers or non-dihydropyridine calcium channel blockers; thus, the results cannot be extrapolated to patients with intermittent claudication with those characteristics. In addition, we did not include patients using vasodilators, such as cilostazol, which are used by some patients and might improve walking distance. Thus, the results might change with vasodilator treatment, which should be tested in the future. Finally, in this study, our control group followed another type of training and did not employ the traditional walking prescription for intermittent claudication patients. Therefore, it was not possible to determine

whether this study's exercise protocol was better than, equal to or worse than others. This study was intended to be the first step in verifying whether the protocol as feasible and resulted in walking improvements. Future research should compare this protocol with other classical training protocols.

In conclusion, walking exercise prescribed at an intensity corresponding to the heart rate of claudication pain onset induces tolerable levels of ischemic leg pain and a cardiopulmonary exercise training stimulus that is above the anaerobic threshold ($>80\%$ of peak aerobic capacity). A short-term, low-volume exercise training program at this intensity is effective in evoking clinically meaningful improvements in walking performance in this patient group. Hence, the heart rate of claudication pain onset may be useful for optimizing exercise prescriptions in patients with intermittent claudication.

■ ACKNOWLEDGMENTS

This research was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (2009–17371-6), Conselho Nacional de Desenvolvimento Científico e Tecnológico (141057/2011-4) and Coordenação de Aperfeiçoamento de Pessoal de Nível Superior (0851/12-4). In addition, the authors would like to thank the study volunteers for their participation.

■ AUTHOR CONTRIBUTIONS

Cucato GG held overall responsibility for the study and was responsible for the following items: study conception and design, statistical analysis, data collection and interpretation, manuscript writing and approval of the final version of the manuscript. Chehuen MR was responsible for the following items: study conception and design, statistical analysis, data interpretation and collection, manuscript writing and approval of the final version of the manuscript. Costa LA was responsible for data collection and approval of the final version of the manuscript. Dias RM and Wolosker N were responsible for writing the manuscript and approval of the final version of the manuscript. Saxton JM was responsible for manuscript writing, critical revision of the manuscript, and approval of the final version of the manuscript. Moraes CL held overall responsibility for the study and was responsible for the study conception and design, obtaining funding, statistical analysis and data interpretation, writing and critical revision of the manuscript and approval of the final version of the manuscript.

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