Strength training increases walking tolerance in intermittent claudication patients: Randomized trial

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Objective: To analyze the effects of strength training (ST) in walking capacity in patients with intermittent claudication (IC) compared with walking training (WT) effects.

Methods: Thirty patients with IC were randomized into ST and WT. Both groups trained twice a week for 12 weeks at the same rate of perceived exertion. ST consisted of three sets of 10 repetitions of whole body exercises. WT consisted of 15 bouts of 2-minute walking. Before and after the training program walking capacity, peak VO₂, VO₂ at the first stage of treadmill test, ankle brachial index, ischemic window, and knee extension strength were measured.

Results: ST improved initial claudication distance (358 ± 224 vs 504 ± 276 meters; P < .01), total walking distance (618 ± 282 to 775 ± 334 meters; P < .01), VO₂ at the first stage of treadmill test (9.7 ± 2.6 vs 8.1 ± 1.7 mL · kg⁻¹ · minute; P < .01), ischemic window (0.81 ± 1.16 vs 0.43 ± 0.47 mm Hg minute meters⁻¹; P = .04), and knee extension strength (19 ± 9 vs 21 ± 8 kg and 21 ± 9 vs 23 ± 9; P < .01). Strength increases correlated with the increase in initial claudication distance (r = 0.64; P = .01) and with the decrease in VO₂ measured at the first stage of the treadmill test (r = −0.52; P = .04 and r = −0.55; P = .03). Adaptations following ST were similar to the ones observed after WT; however, patients reported lower pain during ST than WT (P < .01).

Conclusion: ST improves functional limitation similarly to WT but it produces lower pain, suggesting that this type of exercise could be useful and should be considered in patients with IC. (J Vasc Surg 2010;51:89-95.)

Intermittent claudication (IC) is the most prevalent symptom of peripheral arterial disease. It is caused by a reduction of arterial oxygen delivery to the lower leg during exercise, resulting in functional limitations and reduced quality of life. Supervised exercise of walking training (WT) is currently recommended as the first-line therapy for patients with IC. To promote greater improvements, WT should be performed at an intensity that elicits claudication pain. However, pain during exercise sessions may reduce treatment adherence. Thus, another form of exercise that elicits the same benefits with lower or no pain is desirable for these patients.

Positive correlation between knee extension strength and walking tolerance has been found in patients with IC, suggesting that interventions that improve leg strength and walking tolerance have not been studied. Therefore, the main objective of this study was to analyze the effects of 12 weeks of ST on exercise tolerance in patients with IC, comparing its effects with those observed with WT. Moreover, we compared the intensity of pain during ST and WT sessions. We hypothesized that ST would improve exercise tolerance similarly to WT; however, it would cause less pain during exercise sessions.

METHODS

Patient recruitment and screening. This study was approved by the Joint Committee on Ethics of Human Research of the Public Health of the University of São Paulo (process 1370/05). Each patient was informed of...
the risks and benefits involved in the study, and signed a written informed consent before participation. This study was registered in the www.clinicaltrials.gov and the registration number is NCT00879697.

From July 2005 to December 2006, 300 patients with IC who were enrolled in a tertiary center specialized in vascular disease and were able to walk for at least 2 minutes at 2 miles per hour (mph), were invited to a meeting at which explanations about this study were given. Eighty patients attended the meeting, 60 of them decided to take part in the study, and 52 attended for the screening tests.

Patients were included in the study if they met the following criteria: Fontaine stage II peripheral arterial disease,14 symptoms of IC for at least 6 months, ankle brachial index (ABI) at rest ≤0.90 in 1 or 2 legs, reduction of ABI after treadmill test, and exercise tolerance limited by IC. Patients were excluded under the following conditions: presence of chronic lung disease, inability to obtain ABI measurement due to noncompressible vessels, exercise tolerance limited by factors other than claudication (eg, dyspnea or orthopedic problems), poorly controlled blood pressure, presence of electrocardiogram response suggestive of myocardial ischemia during the exercise test, and history of revascularization in the previous year. Seven patients did not present symptoms of claudication during the treadmill test, 5 presented electrocardiogram response suggestive of myocardial ischemia, 4 presented exercise tolerance limited by other factors than claudication, and 2 presented poorly controlled blood pressure. None of these patients were included in the study. A total of 34 patients were considered eligible for the study.

**Procedures.** Patients were randomly divided into 2 groups: strength (ST, n = 17) and walking (WT, n = 17) training. Randomization was performed by computer random number generation (www.randomizer.org). They were evaluated at baseline (pre-training) and after 12 weeks of exercise training (post-training) by a physician who was blinded to the exercise program performed by patients. Exercise tolerance and strength were assessed during evaluations.

**Exercise test.** Patients performed a progressive-graded cardiopulmonary treadmill test until maximal claudication pain, as previously described for these patients.15 All patients were already familiarized with the test protocol before the experiments. During the test, the electrocardiogram was continuously monitored and registered at the end of each stage. Oxygen uptake (VO2) was continuously measured by a metabolic cart (Medical Graphics Corp CPX/D, St Paul, Minn), and VO2 was averaged every minute for analysis. Peak VO2 was defined as the highest VO2 achieved during the treadmill test.

ICD and TWD were defined, respectively, as the distance walked when the patient first reported pain in the leg, and the distance at which the patient was unable to continue to exercise due to leg pain. These procedures resulted in reliability coefficient (r) of 0.89 for ICD,15 0.93 for TWD,15 and 0.88 for peak VO2.16

Walking economy was analyzed based on the VO2 measured during the last minute of the first stage of the treadmill test (2 mph without inclination).17

**Ankle brachial index and ischemic window.** Systolic brachial blood pressure was obtained by auscultation using a mercury sphygmomanometer. Systolic ankle blood pressure was measured by Doppler ultrasound (Martec DV 6000, Ribeirão Preto, Brazil). These procedures were employed based on a previous study that observed similar results between auscultatory and Doppler scan methods in the assessment of brachial blood pressure.18 Ankle blood pressure was measured in the dorsalis pedis artery and posterior tibial artery, and the higher of these two pressures in each leg was recorded as the resting ankle systolic pressure. Blood pressure measurements were obtained after patients rested in the supine position for at least 20 minutes before and at 1, 3, 5, and 7 minutes after the progressive-graded treadmill test used to assess claudication distances and peak VO2.

The ABI was calculated for each leg as the quotient between systolic ankle and brachial blood pressures, and the value of the worst leg was used in the sample description. The ischemic window was calculated using rest and recovery ankle blood pressure as previously described.19 Briefly, the reduction in ankle systolic blood pressure after the treadmill test from the resting value was quantified by calculating the area under the curve. Since the ischemic window is affected by the total amount of exercise performed, its value was divided by TWD to normalize it for meters walked in the treadmill test.

**Maximal leg strength.** Maximal concentric strength was evaluated by the 1 repetition maximal (1RM) test using unilateral knee extension exercise.20 Briefly, after 10 submaximal repetitions for warming-up, the workload was gradually increased subjectively until the patient could not lift the load more than once. Three to 5 trials were performed with 1 to 2 minutes of recovery between them. Before the 1RM test, patients performed four familiarization sessions, conducted with the same protocol as the maximal strength test.

**Exercise training programs.** Both training programs (ST and WT) consisted of two sessions per week during 12 weeks. ST and WT were conducted by two exercise physiologists, who supervised 4 patients in each training session. In both programs, rate of perceived exertion during exercise was kept between 11 to 13 on the 15-grade Borg scale.21 Furthermore, ST and WT training sessions lasted approximately 60 minutes, consisting of 30 minutes of exercise and 30 minutes of passive recovery.

The WT program was performed using a treadmill. In each session, patients performed fifteen 2-minute bouts of exercise followed by a 2-minute rest interval between them. Walking speed was set in order to induce perceived exertion of 11 to 13, and claudication pain in the last 30 seconds of each exercise bout.

The ST program consisted of eight exercises performed on specific ST machines (Biodelta, São Paulo, Brazil) in the following order: leg press, crunches, unilateral knee exten-
tion, seated row, unilateral knee flexion, seated bench press, calf raises on leg press, and seated back extension. ST was performed in a set sequence, employing three sets of 10 repetitions with a 2-minute interval between sets and between exercises.

Speed (for WT) or weights (for ST) were adjusted in the next set or bout every time perceived exertion was, respectively, lower or higher than 11 and 13 on the 15-grade Borg scale.21

Physical activity performed between exercise sessions was not controlled. However, patients were instructed to maintain their previous physical activity levels throughout the study.

Assessment of pain during training. In training session number 22 (ie, week 11), the level of the patient’s perceived pain during exercise was assessed using a validated self-rated visual analog scale.22 This session was chosen because patients were already adapted to training. The visual analog scale included a 10-cm long ungraded line representing the severity of pain marked at its ends with 0 and 10 (0 = no pain and 10 = unbearable pain). Patients were instructed to indicate in the scale how much pain they were experiencing during each set in ST, and in each bout of walking in WT group. The mean pain during the walking session and the mean pain during upper arm and lower leg strength exercises were calculated.

Statistical analysis. The sample size was statistically calculated based on data from a previous study13 to produce a power of 80% and an α error of 5%. A total number of 16 (8 in each group) and 26 subjects (13 in each group) were needed to detect differences between groups in ICD (75% ± 65%) and TWD (38% ± 45%), respectively.

Normality and homogeneity of variance of data were confirmed by Shapiro-Wilks and Levene tests, respectively. The χ² test was used to compare gender, risk factors, and medication prevalence between groups. The independent t test was used to compare groups for the following: continuous variables at baseline, duration of exercise training sessions, and intensity of pain during the training session. The effect of training in both groups were assessed by two-way analysis of variance (ANOVA) (time × group) for repeated measures. When significance was obtained, Newman-Keuls post hoc test was used to identify the differences. Pearson correlation was used to evaluate the relationship between knee extension strength changes and other parameter changes and Spearman correlation was used to evaluate the relationship between pain levels and the rate of perceived exertion. The significance level was set at P < .05. Data are presented as mean ± standard deviation.

RESULTS

Seventeen subjects were randomized to each training group. However, 4 patients (2 in ST and 2 in WT) did not complete the training programs for the following reasons: inguinal hernia (n = 1), gastrointestinal infection (n = 1), ongoing treatment for lung cancer (n = 1), and diagnosis of abdominal aneurysm (n = 1). Therefore, 30 patients completed the study (ST = 15 and WT = 15).

Pre-training clinical characteristics were similar in ST and WT groups, and are presented in Table I. In both groups, patients were mostly elderly, male, overweight nonsmokers or ex-smokers, and were receiving antihypertensive and antiplatelet medications.

Adherence to exercise training was similar between ST and WT groups (95% ± 5% and 94% ± 5%, respectively; P = .98). Furthermore, the duration of exercise sessions was also similar between ST and WT (67.4 ± 4.5 and 68.6 ± 3.6 minutes, respectively; P = .91).

In the pre-training test, exercise performance variables were similar between ST and WT groups (Table II). The ICD and TWD increased significantly (P < .05) and similarly during the study in both groups (P < .01). The distance walked while in pain (TWD – ICD) did not change significantly in either group (ST = 259 ± 192 vs 271 ± 205 meters, and WT = 230 ± 135 vs 252 ± 116 meters, P = .82). The VO₂ at the first stage of the treadmill test and ischemic window improved significantly and similarly during the study in both groups (P < .05). Neither group had significant change in peak VO₂ after the exercise programs (P > .05). Only the ST group increased knee extension strength in both legs (P < .01).

Correlation matrix between knee extension strength change and changes in exercise-related variables observed in the patients undergoing ST are presented in Table III. Strength increase obtained in the leg with higher ABI, presented a significant and positive correlation with the increase in ICD (r = 0.64; P = .01). Strength increases observed in the leg with lower ABI and in both legs presented significant and negative correlations with VO₂ measured at the first stage of the treadmill test (r = −0.52;
In neither leg did strength improvement correlate with the change in TWD and VO2 peak. Self-rated pain reported during ST and WT are presented in the Fig. Patients in the ST group reported higher pain levels during lower-body than during upper-body exercises (1.5 ± 1.2 vs 1.0 ± 0.9; P < .02). Nevertheless, in comparison with pain reported during WT (2.9 ± 1.2), lower and upper body strength exercises elicited significantly lower pain levels (P < .01).

**DISCUSSION**

The major findings of this investigation were: (1) ST improved walking tolerance in patients with IC, (2) gains in strength after ST are correlated with improvements in ICD and walking economy, (3) adaptations after ST were similar to those observed with WT with similar frequency, duration, and rate of perceived exertion, and (4) during ST, patients reported less pain than during WT.

Although ST might be a useful therapy in patients with IC, who present muscle dysfunction and reduction in lower leg strength that compromise walking capacity,1,2 few previous studies12,13 have investigated ST efficacy in these patients. The present study showed that 12 weeks of ST for the whole body, performed twice a week at a submaximal intensity based on perceived exertion, increases both ICD and TWD in patients with IC. A similar ST program in patients with IC (exercise for the whole body, two sets of 8 to 15 repetitions maximum, three times/week) produced significant increases in ICD and TWD.12 On the other hand, a different training program (six lower leg exercises, sets of six maximal repetitions using cuff weights, three times/week) produced an increase only in TWD.13 Some methodologic characteristics of the present study might explain the greater improvements observed: (1) more subjects, (2) the involvement of whole body (not just lower leg exercises), (3) more exercises, and (4) the use of machines instead of cuff weights. These differences suggest that a general protocol including more exercises for the whole body might promote greater adaptation. Nevertheless, comparisons between different ST protocols were out of the scope of the present study and have not been studied yet.

The possible mechanisms underlying the increase in exercise tolerance after ST in patients with IC remain poorly understood. In the present study, there was a signif-

### Table II. Performance variables in patients with intermittent claudication submitted to strength (n = 15) or walking training (n = 15)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pre-training</th>
<th>Post-training</th>
<th>Group effect</th>
<th>Time effect</th>
<th>Interaction effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial claudication distance (meters)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength training</td>
<td>358 (224)</td>
<td>504 (276) a</td>
<td>0.75</td>
<td>&lt;0.01</td>
<td>0.72</td>
</tr>
<tr>
<td>Walking training</td>
<td>342 (182)</td>
<td>469 (237) a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total walking distance (meters)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength training</td>
<td>618 (282)</td>
<td>775 (334) a</td>
<td>0.63</td>
<td>&lt;0.01</td>
<td>0.85</td>
</tr>
<tr>
<td>Walking training</td>
<td>572 (231)</td>
<td>721 (289) a</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Peak VO2 (mL · kg−1 · min−1)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength training</td>
<td>16.1 (4.3)</td>
<td>15.8 (3.6)</td>
<td>0.57</td>
<td>0.31</td>
<td>0.88</td>
</tr>
<tr>
<td>Walking training</td>
<td>14.3 (2.9)</td>
<td>14.1 (2.8)</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>VO2 at the first stage of treadmill test (mL · kg−1 · min−1)</td>
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<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength training</td>
<td>9.7 (2.6)</td>
<td>8.1 (1.7) a</td>
<td>0.24</td>
<td>&lt;0.01</td>
<td>0.81</td>
</tr>
<tr>
<td>Walking training</td>
<td>9.8 (1.6)</td>
<td>8.4 (0.7) a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic window (mm Hg · min · m−1)</td>
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<tr>
<td>Strength training</td>
<td>0.81 (1.16)</td>
<td>0.43 (0.47) a</td>
<td>0.12</td>
<td>0.04</td>
<td>0.20</td>
</tr>
<tr>
<td>Walking training</td>
<td>0.31 (0.52)</td>
<td>0.20 (0.22) a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength in leg with lower ABI (kg)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength training</td>
<td>19 (9)</td>
<td>21 (8) a</td>
<td>0.49</td>
<td>0.82</td>
<td>0.01 a</td>
</tr>
<tr>
<td>Walking training</td>
<td>18 (8)</td>
<td>16 (8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Strength in leg with higher ABI (kg)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Strength training</td>
<td>21 (9)</td>
<td>23 (9) a</td>
<td>0.46</td>
<td>0.07</td>
<td>0.01 a</td>
</tr>
<tr>
<td>Walking training</td>
<td>21 (9)</td>
<td>20 (9)</td>
<td></td>
<td></td>
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</tbody>
</table>

*ABI, Ankle brachial index.

aSignificant difference from pre-training.

### Table III. Linear relationship between improvement in strength and changes in exercise responses in patients with intermittent claudication submitted to strength training (n = 15)

<table>
<thead>
<tr>
<th></th>
<th>Δ Strength leg with lower ABI</th>
<th>Δ Strength leg with higher ABI</th>
<th>Δ Sum strength of both legs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Δ Initial claudication distance</td>
<td>0.28</td>
<td>0.64 a</td>
<td>0.48</td>
</tr>
<tr>
<td>Δ Total walking distance</td>
<td>0.02</td>
<td>0.07</td>
<td>-0.01</td>
</tr>
<tr>
<td>Δ VO2 at the first stage of treadmill test</td>
<td>-0.52 a</td>
<td>-0.43</td>
<td>-0.55 a</td>
</tr>
<tr>
<td>Δ Peak VO2</td>
<td>0.01</td>
<td>0.07</td>
<td>-0.01</td>
</tr>
</tbody>
</table>

*ABI, Ankle brachial index.

aSignificant correlation (P < .05).

P = .04 and r = −0.55; P = .03, which represent positive correlation with walking economy. In neither leg did strength improvement correlate with the change in TWD and VO2 peak.

Self-rated pain reported during ST and WT are presented in the Fig. Patients in the ST group reported higher pain levels during lower-body than during upper-body exercises (1.5 ± 1.2 vs 1.0 ± 0.9; P < .02). Nevertheless, in comparison with pain reported during WT (2.9 ± 1.2), lower and upper body strength exercises elicited significantly lower pain levels (P < .01).
Significant and positive correlation between the increase in muscle strength and the improvement in ICD. Pain during walking in patients with IC has been attributed to the ischemic process caused by arterial obstruction, which blocks the oxygen supply required by muscle demand during exercise. Thus, an increase in pain-free distance after ST might be a result of an increase in oxygen supply to the muscle, and/or of a decrease in walking oxygen cost, delaying the occurrence of ischemia. Since changes in lower leg strength are also correlated with walking economy, our results suggest that, at least partly, the decrease in oxygen cost for walking is a mechanism responsible for the increase in ICD after ST training. The improvement in walking economy and its relationship with walking tolerance has already been reported after WT in patients with IC and after ST in older subjects, but our study is the first to demonstrate it in patients with IC after ST. This improvement might be a result of several factors, such as an increase in capillarity, changes in muscle fibers properties, and an increase in mitochondrial content. However, the exploration of these mechanisms was out of the scope of this study and should be the target of future investigations.

Interestingly, strength improvement did not correlate with an increase in TWD or distance walked while in pain. Since the onset of ischemia reflects the metabolic acidosis in skeletal muscle and an increase in the predominance of anaerobic metabolism, these results suggest that training did not improve muscle tolerance to acidosis and walking capacity under anaerobic metabolism.

After the ST program, there was a decrease in the ischemic window, showing that ST resulted in decreased magnitude and/or duration of ischemia after a single bout of walking exercise. The decrease in the ischemic window has been systematically described after WT, but this is the first study to show this effect after ST. The decrease in ischemic window suggests an improvement in muscle reperfusion of lower extremities after exercise, which may be caused by an improvement in endothelial function. Nevertheless, McDermott et al did not find any effect of ST on reactive hyperemia in patients with peripheral arterial disease. However, these authors investigated patients with and without IC together, and endothelial dysfunction might be greater in patients with IC, favoring a greater training effect in these patients. Moreover, these authors employed only lower leg ST and did not report any changes in time to claudication with ST. In other populations with chronic disease, such as patients with heart failure, 3 months of ST have been reported to improve reactive hyperemia.

There is a considerable body of evidence confirming the efficacy of WT in improving exercise performance and quality of life of patients with IC. The percentage of increases in walking distances in the present study were lower than previously reported. Several factors might explain this controversy. First, the patients enrolled in the present study had a higher walking capacity at baseline. Therefore, the analysis of improvements in relative changes might have masked the results. In fact, when analyzing the absolute changes, the improvements in walking capacity after WT were similar to the ones reported in literature. Second, the exercise protocol used in this study was based on perceived exertion, instead of on claudication symptoms. As the achievement of maximal pain has been considered important for greater training adaptation, the low pain levels observed in this study might also explain the lower relative improvements observed in relation to the literature. However, the prescription based on perceived exertion allowed the comparison between ST and WT keeping similar training overload (frequency, duration, and intensity). Thus, the present results indicated that ST might be as
Statistical analysis: CC
Obtained funding: RR, MM
Overall responsibility: RR, MM

REFERENCES


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INVITED COMMENTARY

Thomas G. Lynch, MD, and Jason M. Johanning, MD, Omaha, Neb

The authors report a randomized trial comparing the benefits of strength training (ST) and walking training (WT) in patients with intermittent claudication. The study uses standard outcome measures to objectively quantify improvements in ambulation and physiological function, including walking distance, oxygen consumption, walking economy, ischemic window, and leg strength. It also raises questions about the underlying cause of exercise-induced discomfort and the value of potential new therapeutic alternatives.

The authors modified previously reported exercise therapy protocols, proposing another possible option for the treatment of claudication. It is becoming clear from basic science studies and clinical trials that significant abnormalities are present in the lower extremity musculature, leading to altered gait. The authors succinctly point to these abnormalities as a justification for the use of ST to improve ambulatory function. The exact nature of the abnormalities, and their effect on gait, is becoming more evident as analogical scales as ratio scale measures for chronic and experimental pain. Pain 1983;17:49-56.

In contrast to previous studies that have relied on a predetermined level of ambulatory effort, and to compare ST and WT, the current protocol uses perceived exertion measured by the validated Borg scale to determine therapeutic effort. This approach is new within the supervised exercise literature; however, perceived exertion in exercise provides a relatively stable measure of work unrelated to objective measurements, especially in elite athletes. Interestingly, patients in the current study had a perceived exertion that resulted in significantly less claudication pain than in other studies, suggesting a potential need to standardize patient effort in future trials.

Although the current results demonstrate significant improvement in ambulation with both protocols, to conclude that ST is comparable to WT from these results and those of related studies would be inappropriate. Despite previously well-designed and executed trials comparing supervised WT with ST, very little can be concluded based on the significant variations in conduct and outcome measures. The current study, in the context of recent literature, clearly illustrates the need for standardization. For the field of PAD treatment to progress, common outcome measures need to be agreed upon and reported to allow for accurate comparisons among the myriad of medical, exercise, and operative treatments available.

REFERENCES


