Efficacy of a short-course intensive rehabilitation program in patients with moderate-to-severe intermittent claudication

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Exercise; Peripheral vessels; Rehabilitation.

Background. **Many rehabilitation programs for intermittent claudication include physical training for several months, since the outcome of short-course protocols is still unclear. The aim of this study was to evaluate the efficacy of a short course of exercise therapy in patients with moderate-to-severe intermittent claudication in terms of walking distance variations.**

Methods. **Twenty-six patients (males 88%, mean age 59 ± 8 years, ankle-brachial index ≤ 0.8 and ≤ 0.5 before and after exercise respectively) were evaluated. Moderate-to-severe stenoses or occlusions were localized at color Doppler scanning of the abdominal aorta/iliac arteries and femoral/popliteal/tibial arteries in 15 and 31% of patients respectively, while in 54% of cases both the proximal and distal sites were involved. The initial and absolute claudication distances were recorded by means of the constant treadmill test (3 km/hour speed, 0% grade) at the time of presentation and after a short-course comprehensive rehabilitation program (4 week duration) including physical training, educational intervention, psychological support, and cardiovascular risk management.**

Results. **At the end of the program, 1 patient (4%) became asymptomatic (walked > 1000 m without pain). In 25 patients who still developed pain, the average increase in the initial claudication distance was 132% (from 75 to 174 m). Among these, 20 patients (77%) were still unable to complete the treadmill test due to maximal claudication pain, but the absolute claudication distance increased by 87% from 204 to 381 m ($p < 0.05$). No cardiovascular complication occurred during the study period. Major clinical variables failed to predict an unsatisfactory increase in walking capacity.**

Conclusions. **Short-course training programs enhance the walking ability even in patients with moderate-to-severe intermittent claudication and seem to be well tolerated, supporting their widespread use in rehabilitation centers.**

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Introduction

Treatment strategies for symptomatic peripheral arterial obstructive disease (PAOD) range from non-pharmacological and pharmacological interventions to revascularization procedures performed with the aim of ameliorating symptoms, slowing progression of the disease or reducing local obstructions.

Physical training is claimed to be the most effective conservative therapy for intermittent claudication[1]. According to studies evaluating changes in walking ability with a constant-load treadmill protocol, the improvement in the pain-free walking distance ranged from 44 to 290%, with an average increase of 134%[2].

A meta-analysis of exercise rehabilitation programs performed by Gardner and Poehlman[3] in the mid '90s established the optimal characteristics of exercise treadmill sessions: at least 30 min per session, 3 times per week, for more than 6 months.

Nevertheless, for patients without critical ischemia[4], the role of invasive procedures is often overemphasized. This may partly be attributed to the scarcity of vascular rehabilitation facilities and to the program length. Consequently, physical training is not usually regarded as the first step of PAOD treatment especially in patients with moderate-to-severe claudication.

As for the recommended program length (≥ 6 months), it was previously shown that a short course of intensive physical training can produce a significant improvement in the walking distance covered by patients with PAOD[5]. However, to date information regarding its effectiveness in patients with severe symptoms is scarce.

The aim of this study was to evaluate the efficacy, in terms of the walking distance covered, of a short rehabilitation program (4 weeks) including intensive physical training in patients with moderate-to-severe intermittent claudication.

Methods

Patient selection. All patients with PAOD and intermittent claudication admitted to our Institute for physical training were considered. Intermittent claudication was defined as pain of the extremities, discomfort or weakness that is constantly produced by the same amount of walking or equivalent muscular activity in a given patient and that is promptly relieved by cessation of that activity. Among these, those who were capable of a pain-free walking distance < 100 m at a constant treadmill test were included in the study. Patients with advanced PAOD (ischemic rest pain or tissue loss, i.e. stage III and IV according to Fontaine's classification), as well as those in whom an endovascular procedure was the treatment of choice (type A according to the TASC statement[6], i.e. single stenosis of the common iliac artery or external iliac artery < 3 cm) were excluded.

Other requirements were as follows: 1) stable claudication symptoms over a 6 month period before enrolment, 2) PAOD confirmed at ultrasonographic examination or conventional angiography, and 3) the absence of any exclusion criteria for physical training (severe coronary artery disease, severe renal failure, hemodynamically unstable valvular disease, long-term oxygen therapy for chronic respiratory failure, orthopedic problems affecting the patient's walking ability, recent myocardial infarction, hemiplegia, poorly controlled hypertension).

Evaluation of peripheral arterial obstructive disease. All patients completed the following standard protocol for the functional evaluation of PAOD:

• recording of individual walking speed and claudication distance by inviting patients to walk until the occurrence of pain;

• constant treadmill test (after treadmill familiarization) at a workload of 3 km/hour, 0% grade for 20 min[7]. During the test, heart rate (at 3-lead electrocardiogram) was continually monitored, while brachial blood pressure was recorded before and after exercise. Patients were also asked to grade the severity of the claudication pain using a scale of 1 to 4, with 1 = onset of pain, 2 = mild pain, 3 = moderate pain, and 4 = severe pain (i.e. degree of pain incompatible with the completion of the test)[8]. The onset of pain (grade 1) and severe pain (grade 4) identified the initial and absolute claudication distances respectively. The pain recovery time was also measured;

• evaluation of the ankle and brachial pressures by means of continuous wave Doppler at rest and after repeated dorsiflexion of the foot with the leg elevated 30°. The arterial pulse was detected in both the dorsalis pedis and posterior tibial arteries and the highest pressure was used to assess the ankle-brachial index (ABI). In patients with diabetes mellitus, if the ankle pressures were difficult to measure due to calcification of the media, the toe systolic pressures were assessed;

• detection of arterial stenosis at ultrasonic duplex scanning coupled with color flow imaging (color Doppler scanning). The lesion site was classified according to the arterial segment (proximal = aorta/iliac arteries; distal = common femoral/superficial femoral/profunda/popliteal/tibial arteries) and the degree of arterial narrowing was also assessed [mild, corresponding to a stenosis < 49% (increase in peak systolic velocity > 30% but < 100% compared to the preceding segment); moderate to severe, corresponding to a 50 to 99% stenosis (increase in peak systolic velocity > 100% from one segment to the next); total occlusion (no flow)][2].

Training program. All patients were trained according to a 4 week supervised intensive day-hospital program focused on exercise therapy.

The program consisted of twice daily training sessions from Monday to Saturday: after a 5 min warm-up period, patients completed a 30 min treadmill walking exercise and then 5 min of cool-down activity. During the treadmill exercise (3 km/hour speed, 0% grade), patients were educated to stop when moderate pain developed and to rest until the pain disappeared. Patients were also given written instructions to continue the walking exercise at home.

Training sessions included resistive isotonic exercises based on bilateral contractions of specific muscle groups (anterior tibialis, gastrocnemius-soleus, hamstrings, quadriceps femoris, gluteus medius and gluteus maximus).

Complementary interventions. As shown in table I, a comprehensive risk reduction intervention was also performed. Patients were informed about PAOD and its treatment during interactive educational sessions conducted by a specially trained health operator. Sessions were scheduled on a 30 min weekly basis and were reinforced by individual counseling at the beginning and the end of the program. The key components of basic education were as follows: information about the risk factors and natural history of the disease, how to promote a better lifestyle, training in the use of medications and in the performance of physical exercise at home and how to recognize worsening of symptoms. Individual counseling by a trained dietitian was implemented in order to obtain weight and lipid control. Food intake was strictly controlled during hospitalization, while written information concerning the nutritional behavior to be adopted at home were given at discharge. Risk factor assessment included lifestyle, family history, smoking, hypercholesterolemia, diabetes, hypertension, obesity, alcohol abuse, and salt intake. Risk stratification for coronary artery disease was performed on the basis of the patient's history, physical examination, electrocardiography, echocardiography, and maximal exercise stress test. The presence of carotid plaques was assessed at ultrasonography.

Table I. Risk reduction interventions included in the program.

Intervention	Health care operator	Tools
Health education	Physician	Educational sessions
Smoking cessation	Nurse	Individual counseling
	Psychologist	
Correction of hypercholesterolemia	Angiologist	Clinical evaluation
Correction of hypertension	Vascular surgeon	Non-pharmacologic interventions
Correction of hyperglycemia	Cardiologist	Pharmacologic interventions
Detection of thrombophilic conditions	Internist	Individual counseling
		Educational sessions
Weight reduction	Dietitian	Individual counseling
Dietary modification		Balanced diet during in-hospital stay
		Diet prescription at home

Psychological support, provided by a trained pool of psychologists during twice weekly sessions of intensive counseling, was organized so as to optimize patient compliance and promote smoking cessation.

Statistical analysis. The Student's t test was used to compare the walking distance covered at the time of enrolment to that at the time of discharge. Values were reported as mean ± SD and a two-tailed p value < 0.05 was considered statistically significant. Univariate and stepwise logistic regression analyses were used to determine the relation between medical comorbidities and an unsatisfactory improvement in the walking performance after the training program. An unsatisfactory improvement in the walking performance was defined as a change lower than the average increase (119%) in the pain-free walking distance in stage IIb PAOD reported by the only available trial evaluating a short-course exercise program[9].

Results

Clinical characteristics of the study population. Twenty-six patients were included in the study (Table II). Four of them (15%) had a history of peripheral vascular surgery or angioplasty. The prevalence of risk factors was as follows: current cigarette smoking 54%, hypertension 46%, diabetes mellitus 23%, and hypercholesterolemia 65%. One patient (4%) also had cerebrovascular disease and 6 (23%) had documented coronary heart disease. Proximal or distal arterial lesions were confirmed at the time of entry by means of color Doppler scanning in 4 (15%) and 8 (31%) patients respectively, while in 14 (54%) cases lesions were present in both arterial territories. In all patients an ABI ≤ 0.8 and ≤ 0.5 before and after exercise was measured by means of continuous wave Doppler and all were prescribed lifelong aspirin therapy to prevent progressive arterial occlusion. At admission, 8 (31%) patients were treated with pentoxifylline, which was continued during the program. In addition to antiplatelet agents and pentoxifylline, the basic treatment of patients included antidiabetic, antihypertensive and lipid control drugs. Among diabetic patients, 2 (8%) were on insulin therapy necessary in order to maintain a fasting blood glucose range between 80 and 120 mg/dl, while 4 (15%) were on oral hypoglycemic drugs. All 17 (65%) patients with hypercholesterolemia were *de novo* placed on or continued statins (in addition to dietary restrictions) in order to achieve an LDL cholesterol serum level < 100 mg/dl. Again, all 12 (46%) patients with hypertension were administered specific treatment at the beginning of the program, mainly consisting of calcium channel blockers (67%), ACE-inhibitors (33%), and diuretics (17%). In any case, beta-blockers were also prescribed. When satisfactory blood pressure control was achieved in all patients, unnecessary modifications in antihypertensive drug treatment were avoided.

Table II. Clinical characteristics of the study population.

No. patients	26
Males	23 (88%)
Age (years)	59 ± 8
Ankle-brachial index at rest	0.53 ± 0.15
Ankle-brachial index after exercise	0.34 ± 0.12
Mild stenoses*	0
Moderate-to-severe stenoses*	3 (12%)
Occlusions*	23 (88%)
Initial claudication distance (m)	76 ± 20
Absolute claudication distance (m)	217 ± 99
Recovery time (s)	208 ± 74
Biochemistry	
Total cholesterol (mg/dl)	215 ± 49
HDL cholesterol (mg/dl)	60 ± 11
LDL cholesterol (mg/dl)	125 ± 35
Triglycerides (mg/dl)	156 ± 45
Glucose (g/dl)	111 ± 36
Hemoglobin (g/dl)	126 ± 36
Platelets (/mm^3)	320 000 ± 83 000
Fibrinogen (g/dl)	0.33 ± 0.08

* = in case of bilateral peripheral arterial obstructive disease, the lowest leg value identified the individual ankle-brachial index. In case of multiple lesions, the highest degree of narrowing identified the individual patient's profile.

Treatment outcome. All patients showed differences < 0.5 km/hour between their personal walking speed and the treadmill test speed (3 km/hour). This allowed us to utilize the treadmill test for the evaluation of the patient's walking performance before and after the training period.

Changes in walking ability are presented in figures 1 and 2. At the end of the program, 1 patient (4%) became asymptomatic (he could walk a distance > 1000 m without pain). With regard to the 25 patients who still developed pain, the average initial claudication distance increased by 132% (from 75 to 174 m, $p < 0.05$). In 5 (19%) of them, maximal pain was not perceived. Twenty patients (77%) were still unable to complete the treadmill test due to claudication pain, but the absolute claudication distance increased by 87% from 204 to 381 m ($p < 0.05$).

Among symptomatic patients, no significant increase in the ABI was appreciated at the end of the program.

Overall, 14 (54%) out of 26 enrolled patients showed a > 119% increase in the initial claudication distance at the end of the program, while 12 (46%) did not manage to achieve such an improvement. The clinical characteristics of both groups are reported in table III. With regard to those patients who did not show a > 119% initial claudication distance increase, the clinical variables included in the logistic regression model failed to predict this unsatisfactory outcome.

With regard to the patients with hypercholesterolemia, the mean total and LDL cholesterol serum levels decreased by 33% (from 238 to 184 mg/dl) and 29% (from 147 to 105 mg/dl) respectively following dietary restriction, physical activity and statin therapy.

Tolerability of the program. No cardiovascular complication (i.e., stroke, myocardial infarction, critical leg ischemia, major cardiac arrhythmias, symptomatic hypo/hypertension) or accidents during the treadmill exercise occurred during exercise sessions.

Discussion

The aim of this study was to evaluate the efficacy, in terms of walking ability, of a 4 week rehabilitation pro-

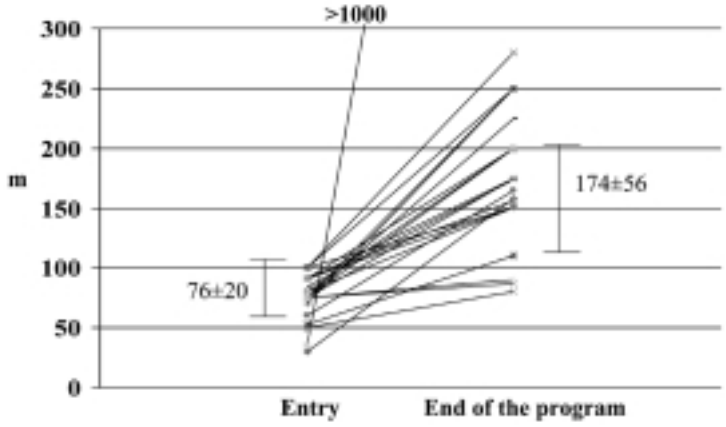

Figure 1. *Initial claudication distance at the time of entry and after a short-course intensive rehabilitation program in patients with peripheral arterial obstructive disease.*

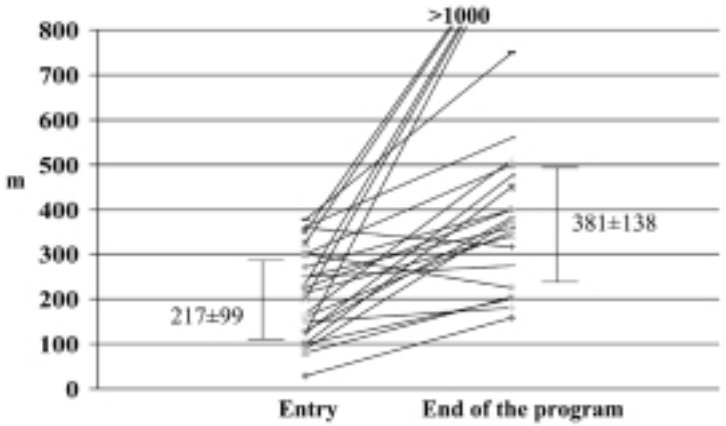

Figure 2. *Absolute claudication distance at the time of entry and after a short-course intensive rehabilitation program in patients with peripheral arterial obstructive disease.*

Table III. Relationship between clinical conditions and a satisfactory/unsatisfactory change in walking ability after the program in patients with severe peripheral arterial obstructive disease (PAOD).

Clinical condition	ICD increase		p
	> 119%	≤ 119%	
Male	12 (52%)	11 (48%)	0.352
Age > 65 years	5 (42%)	7 (58%)	0.436
Diabetic	4 (67%)	2 (33%)	0.960
Current smoker	10 (71%)	4 (29%)	0.251
Hypertension	7 (58%)	5 (42%)	0.729
Dyslipidemia	8 (47%)	9 (53%)	0.269
Coronary artery disease	4 (67%)	2 (33%)	0.960
Previous CABG	1 (33%)	2 (67%)	0.788
Exercise-induced cardiac ischemia	2 (67%)	1 (33%)	0.770
Extended PAOD	6 (75%)	8 (25%)	0.212

CABG = coronary artery bypass graft; Extended PAOD = extension of lesions to both proximal and distal sites; ICD = initial claudication distance.

gram based on intensive physical training in patients with moderate-to-severe intermittent claudication. We found that this short intensive program may increase the pain-free walking distance covered in the absence of major cardiovascular complications and that the patient's clinical conditions are weak predictors of an unsatisfactory improvement in walking capacity.

Exercise therapy including risk factor modification is the cornerstone of conservative management of PAOD and efficacious exercise programs have been validated. Since claudication symptoms are not only related to the contribution of large artery blood flow, they can be significantly improved by exercise without revascularization. In this perspective, as suggested by some authors[4], one should query why revascularization procedures are universally available, widely promulgated and reimbursed, whereas exercise rehabilitation is not.

According to Gardner and Poehlman[3], the length of optimal exercise programs necessary for the improvement of claudication pain distances is > 6 months. In our experience, long home-based programs are often difficult to implement because of poor patient compliance. If physical training may be considered as a "drug" *per se*, an appropriate short-course treatment could represent a possible means of rapidly evaluating the real efficacy of this therapy, minimizing side effects and, theoretically, decreasing the need and costs of subsequent revascularization procedures and their complications.

In our knowledge, few data are available regarding short-course exercise programs in patients with PAOD (< 1 month duration). The recent review by Girolami et al.[1] considered six level-two trials (level-one studies were not available) and evaluated the efficacy of physical training: analysis of the pooled results revealed a significant increase in the initial and absolute claudication distances induced by physical training programs, all of them with a duration ≥ 3 months. In their review of the English language literature from 1966 to 1993, Gardner and Poehlman[3] found only one exercise program including patients with mild claudication and lasting 4 weeks. The only study that evaluated the efficacy of a 4 week exercise program on severe claudicants was performed by Scheffler et al.[9]. The authors randomized patients in two treatment groups (exercise therapy vs exercise plus prostaglandin E_1) and reported a 119% increase in the symptom-free walking distance covered by the patients who were prescribed exercise only. The benefit was greater when prostaglandin therapy and training procedures were combined, but unfortunately side effects occurred.

A previous controlled study tested a 4 week supervised training program including patients with stage II PAOD and showed a significant and lasting improvement in the walking distance compared with antiplatelet therapy alone[5]. Regression analyses revealed a trend towards a possible negative result of exercise therapy in patients with a low initial claudication distance at baseline. Thus, it was not clear whether severe claudicants should be enrolled in such an intensive training program.

In order to address this issue, in our study we only enrolled subjects who were not able to cover a 100 m pain-free walking distance.

Comparing our results with those available in the literature, we found that the outcome of this short-course training program was similar to the average 179% increase in the initial claudication distance and to the 122% increase in the absolute claudication distance observed in controlled trials including unselected claudicants treated for 6 months[3]. The globally successful outcome of our program also reflects the facts that we selected claudicants on the basis of a constant low-speed and non-graded test (showing a greater walking impairment in comparison to graded tests with the higher speed adopted by several studies) and that following completion of the training program, some patients were able to complete the treadmill test. Consequently, the absolute claudication distance increase re-

ported in this study was calculated only for patients who were still symptomatic at the end of the program.

This study did not include a control group; therefore the additional benefit of exercise therapy reported for these patients could be an overestimate.

The mechanism involved in the enhancement of the patient's walking ability following exercise training is not completely clear: since the ABI and other hemodynamic parameters were not substantially increased, a possible explanation might be the improved metabolic capacity in the muscles and their altered gait consequent to the use of the more proximal non-ischemic muscles[10]. The impression that this metabolic effect could also explain the walking improvements observed after short-course training needs to be confirmed by *ad hoc* pathophysiologic studies.

The aim of our study was to determine the initial and absolute claudication distances at the end of a short-term training and rehabilitation program, in order to evaluate changes in objective outcome measures. It is reasonable that a 2-fold or 3-fold increase in walking performance, as we observed in many patients, could result in a great benefit in terms of quality of life; nevertheless the success of this intervention and the efficacy of reinforced education should be tested at different times during long-term follow-up.

The prevalence of comorbidities at the time of admission did not significantly differ from those of other studies reported in the literature[11] and we tried to understand whether these conditions could affect the outcome of our intervention. The > 119% or ≤ 119% initial claudication distance increases, based on a previous experience[11], were arbitrarily chosen to distinguish between a satisfactory and an unsatisfactory outcome. No clinical condition was found to be related to the walking performance at the end of the exercise program and consequently, in our opinion, comorbidities were not suitable predictors of a potentially unsatisfactory outcome when prescribing exercise therapy. Diabetics and current smokers were not excluded from this study, as our proposal was to verify the immediate outcome of the program. The data obtained at univariate and logistic regression analyses did not show an unsatisfactory increase in the initial claudication distance among these patients, suggesting that these conditions should not be considered as absolute exclusion criteria for entry into an exercise rehabilitation program.

In conclusion, exercise therapy enhances the walking ability even of patients with moderate-to-severe intermittent claudication. A short-course intensive program (< 1 month duration) seems to be well tolerated and to ensure a substantial increase in the pain-free walking distance, supporting the wider use of comprehensive rehabilitation programs providing multidisciplinary interventions with medical supervision.

The precise additional benefits of short rehabilitation programs need to be assessed by randomized, placebo-controlled studies including larger populations.

A holistic approach to PAOD patients, based on their assessment and on the use of preventive treatment and rehabilitation programs, may probably ensure the best management and minimize the risk of disease progression.

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