Original Paper

The Influence of Physical Exercise on Smoking Patients with Peripheral Arterial Disease

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ABSTRACT: Smoking should be identified as a major risk factor for Peripheral arterial disease. The purpose of this prospective, randomized, controlled clinical study was to determine whether a rehabilitation program is more efficient than the usual healthcare assistance (medication, hygiene and diet) for improving walking function on the smoking and nonsmoking patients with PAD. For smokers, there were no significant differences after 12 weeks and also 24 weeks, although the 4MWS mean values increased compared to the control. At 24 weeks study time point nonsmokers in the group performed special massage techniques along with the supervised kinesiotherapy had significantly greater improvement in their 4MWS, compared to the group with physical exercises or control. A well-structured rehabilitation program, in terms of intensity, duration and frequency may be of great help for improving the functional status of these patients with peripheral ischemia syndrome.

KEYWORDS: peripheral arterial disease, exercises, physical therapy, smoking

Introduction

Peripheral Arterial Disease (PAD) is an atherosclerotic syndrome and therefore its incidence depends on the classical risk factors predicting problems related to decreased coronary and cerebral arterial blood flow. Smoking and Diabetes Mellitus (DM) are risk factors with the highest predictive value, followed by high blood pressure (HBP), dyslipidemia (especially a low level of HDL-C) and alterations of homocysteine metabolism.

Smoking also plays a major part in the pathogenesis of Thromboangiitis Obliterans (TAO), but its mechanisms of action have not been clarified yet. Most of the TAO patients are smokers, even though there have been several cases of non-smokers [1,2,3] and former smokers [4]. The severity of its evolution is closely related to the persistence of tobacco poisoning [5], while the tobacco type and manner of intake (cigarettes, herbal cigarettes, inhaling, smoking without inhalation) were less studied. Still, the prevalence of the disease is quite important in India where Bidi smoking is very high [6].

There were no randomized prospective clinical trials studying the effects of smoking cessation upon the risk of adverse cardiovascular events in PAD patients. Observational studies found that the risk for death, myocardial infarction and amputation was significantly increased for the patients who continue to smoke compared to those that quit smoking. The ratio of smoking cessation per year is 5% in those who received specialized aid from a doctor, in comparison to only 0.1% in those who tried to quit smoking without the intervention of a specialist. Pharmacological interventions, such as nicotine-replacement therapy and the Bupropion treatment have a success ratio per year of 16% and 30%, respectively [7]. Interventions regarding smoking cessation are essential especially in those with TAO, as it is believed that certain tobacco components are responsible for this syndrome. Smoking should be identified as a major risk factor for PAD, while smokers should follow cognitive behavioral therapy that will help them quit this habit.

In the past few years, various experimental studies on both humans and animals have shown that atheroma plaque regression is possible through the alteration of major atherogenic risk factors (hypercholesterolemia, high blood pressure, obesity and smoking) [8].

The purpose of this prospective, randomized, controlled clinical study was to determine whether a rehabilitation program is more efficient than the usual healthcare assistance (medication, hygiene and diet) for improving the walking function in the patients with PAD and intermittent claudication.

Material and Method

We have included in the study the inferior limbs PAD patients from the Rehabilitation Department within the Emergency County Clinical Hospital of Craiova and the study was performed between October 2015 and May 2017.

The patients included in the study had to comply with the following inclusion criteria: (1) to be diagnosed with PAD in the lower limbs,

Fontaine stage 2; (2) to comply with the Edinburgh Claudication Questionnaire criteria, and (3) to have an Ankle-Arm Index (AAI) lower or equal to 0.90.

The following categories of patients were not included in the studied group: (1) those with inability of performing the exercise program or walking on the rolling carpet; (2) with locomotion disorders caused by other diseases than PAD; (3) with New York Heart Association (NYHA) class 2 heart failure and minimum effort angina pectoris at rest; (4) patients with silent ischemia, (5) patients with revascularization at lower limbs level, major orthopedic or surgical interventions three months before study inclusion or planned for the next 12 months, (6) those with other major diseases that may impede the patient to end the study, (7) with difficult to control values of blood pressure (BP), (8) with PAD secondary to Buerger disease, autoimmune arthritis, fibromuscular dysplasia, chronic traumas, venous stasis and hyper-coagulation or arterial embolism, (9) with unbalanced DM (serum glucose values fasting >110mg/dl), and (10) those with Raynaud Syndrome.

Once the diagnosis of PAD was confirmed, the patients were included in the study after obtaining the written informed consent and after analyzing the inclusion and exclusion criteria. The randomization was performed in three groups according to the inclusion order.

Patients in Control Group (62 included, 51 completed) followed the usual healthcare procedures, consisting in: hygiene and diet treatment, and drug treatment according to the cardiologist or nutritionist, previous study inclusion, both in the first stage (the first 12 weeks), as well as in the final stage (the following 12 weeks).

The patients in Physical Training Group, with physical exercises (39 included, 24 completed) followed a special supervised kinesiotherapy program in the first 12 weeks, easy to understand, easy to learn and especially easy to repeat at home, without requiring any special equipment. These patients continued this program at home for the following 12 weeks, with no supervision. The training starts with a 10 minutes warm-up, consisting of exercises for mobility and respiration, followed by exercises of analytical gymnastics, Buerger gymnastics, exercises for increasing the cardiac flow and codified walking (15-60 minutes daily), ending with relaxation exercises (5-10 minutes). Exercises were chosen according to the

localization of the obliterations. The number of exercise repetitions was established individually, according to the physical state of every patient, these being practiced up to the onset of moderate claudication, a moment followed by a short moment of rest until the symptoms diminished. Initially, the sessions lasted for approx. 30 minutes, whilst the training time gradually increased with every session up to approx. 60 minutes. The kinesiotherapy sessions took place 3 times a week.

Patients in Training and Massage Group (45 included, 36 completed) performed special massage techniques along with the supervised kinesiotherapy program that have effects mainly upon the blood and lymphatic flows. The techniques used were made up of three components: drainage of lymphatic ganglions, drainage of collectors and reabsorption drainage [9]. The manual lymphatic drainage was used for psychic relaxation of the patients. This relaxation is due to the slow rhythmic motions in association with the gentleness of the execution. We also used the Knap method which is a massage procedure with combined effects in order to stimulate blood flow [10].

The patients were included in a data-base where we recorded the following initial characteristics: name, surname, gender, age, education level, Body Mass Index (BMI) expressed as a weight(kg)/height^2/(m^2) ratio, AAI, systolic and diastolic blood pressure, comorbidities history, claudication start, smoking, concomitant medication.

We assessed the walking speed in the studied group with a parameter frequently used in the PAD research studies, namely 4MWS. The patients were instructed to walk at their usual rhythm, "as if going shopping", on a 4-meter distance, between two reference points, by exemplifying the walking type. The participants received the command "On your marks, get set" and when uttering the command "Go!" the chronometer was started. Every test was performed twice and for the analyses we chose the fastest speed for every pair.

The assessment was performed at baseline, 12 weeks after interventions and at the end of the study.

Statistical analysis

Data were recorded and plotted using Microsoft Excel, and statistical analysis was performed utilizing the Microsoft Analysis Tool pack. Differences between the averages of two categories were assessed utilizing the Student

t test, while for three groups of data we have performed a one-way analysis of variance (ANOVA) with post hoc comparisons using Tukey's honestly significant difference (HSD) test. In all cases, p <0.05 was used to indicate statistical significance.

Results

A total of 113 patients were included in the study, 68 smoking patients (93% were men) and 43 non-smoking patients (58% were men). The mean age of smokers was over 2 years younger than the mean age of non-smokers, although this did not reach statistical significance (67.9 vs. 70.4, p=0.37). The situation differs between the smokers and non-smokers patients regarding the association of the most important risk factors for PAD. Most frequently, smokers were also diagnosed with HBP (74%), followed by dyslipidemia in 54%, chronic obstructive

pulmonary disease (COPD) (38%) and diabetes mellitus (26%). In non-smokers, HBP and dyslipidemia (59%), followed by DM and COPD (39%) were the most frequently associated comorbidities.

Regarding the influence smoking may have on the walking speed and its improvement under treatment, we established that the mean values of 4MWS were lower than in non-smokers, at all levels, both at the beginning of the study, as well as after 12 or 24 weeks. Anova single factor analysis was performed to determine whether there is a perceived significant difference between the three groups.

For smokers, there were no significant improvements in their 4MWS after 12 weeks for both physical training group and training and massage group compared to the beginning of the study (Fig.1).
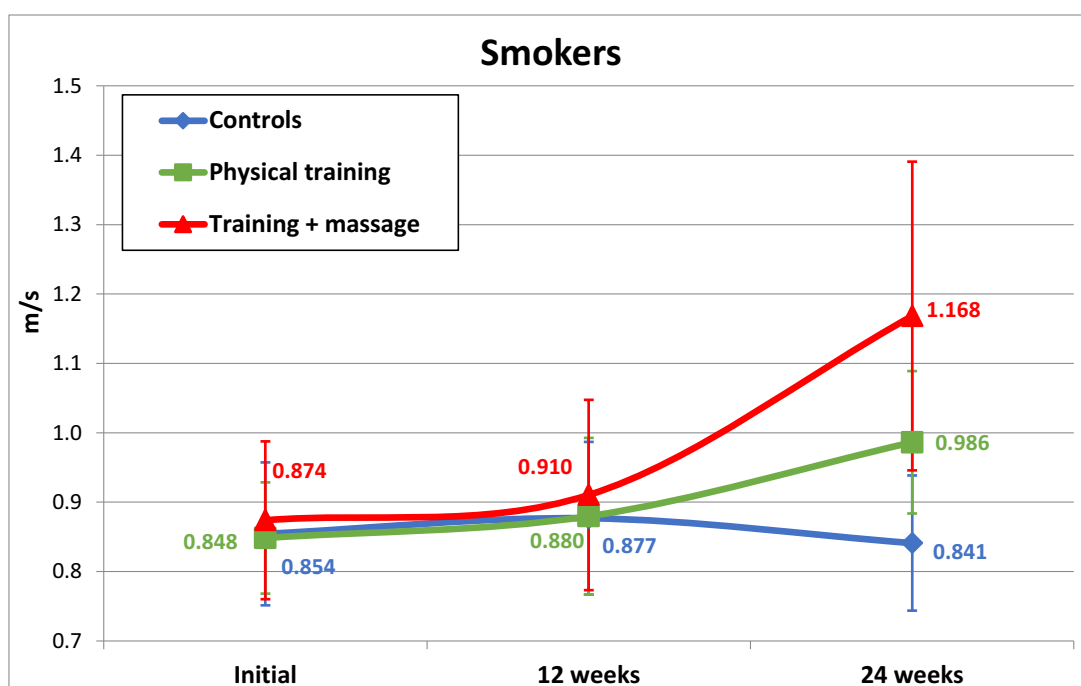

Fig.1. 4MWS recordings on smokers

At 24 weeks study time point, the 4MWS mean values increased for both physical training group and training and massage group compared to control, but the improvement was statistically significant over the control group only for the

patients training and benefiting from the massage (p<0.5) (Fig.1).

For non-smokers from the Physical Training Group there were no significant 4MWS improvements both at 12 and 24 weeks, or over the control trend lines (Fig.2).
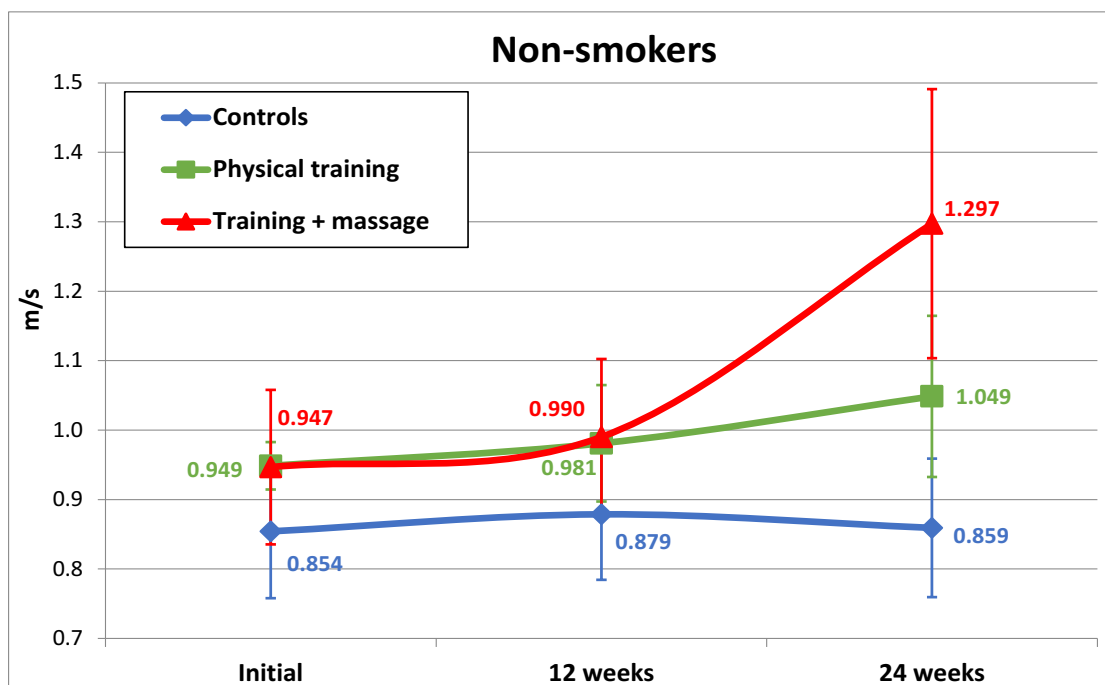
Fig.2. 4MWS recordings on non-smokers

At 24 weeks, non-smokers from the training and massage group had significantly greater improvement in their 4MWS, compared to their initial evaluation, and the evaluation at 12 weeks ($p<0.05$). Also, at 24 weeks the improvement of this group was significantly superior to the evolution of controls and physically trained-only groups at this time point ($p<0.05$).

Discussions

The risk factors associated to an AAI below 1.0 were investigated and statistically assessed in order to determine the relative risk. Newman and colleagues [11] considered that the most important four risk factors correlated with age, involved in the assessment of the risk for developing peripheral arterial disease, are the following:

- DM-with a relative risk of 4.05
- Smoking-with a relative risk of 2.55
- HBP-with a relative risk of 1.51
- total cholesterol (10mg/dl)-with a relative risk of 1.10

Another analysis performed on 295 subjects previously developing obstructive peripheral arterial disease, within the Framingham study, showed that smoking, HBP and lactose intolerance were the highest risk factors for PAD and intermittent claudication, while the level of blood cholesterol was considered to be a poor risk factor. Generally speaking, HBP alone increases the risk for claudication by 2.5 times in men and four times in women, while in normotensive patients, with normal serum cholesterol and lactose tolerance, smoking increases the relative risk for claudication up to 3.5. The effects of smoking are even greater in patients with HBP and dyslipidemia, in whom the relative risk for claudication increases up to 10, in comparison to 3.1 in non-smokers. The risk factors have a great synergic effect: in the patients in whom all these risk factors were present the relative risk for developing claudication was 43, unlike 18 in those with very high values of BP, serum cholesterol and serum glucose, but non-smokers [12].

The arterial damage is proportional with the importance of intoxication: after smoking cessation, the risk does not immediately disappear, the published literature indicating a relative risk for PAD of 3.7 in the case of active intoxication, the same as after three or five years after smoking cessation [13].

The main therapeutic objectives in the peripheral ischemia syndrome are: slowing or cessation of the pathological processes that affect the arteries and solving the complications aroused from these processes; these objectives may be performed through hygiene measurements, drug, kinetic physical treatment or interventional therapy. One of the important issues in treating the peripheral ischemia syndrome is the alteration of risk factors, namely giving up smoking, drug balancing of DM, HBP and hyperlipidemia, factors that are considered

major risk in the evolution of peripheral ischemia.

The clinical characteristics and those of walking at study inclusion were comparable in all three groups. Some studies showed that a rehabilitation program is more efficient in improving the functional status of the PAD patients, after 24 weeks rather than after 12 weeks. In our study, we showed that the benefits of the physical therapy are minimal after 12 weeks and statistically significant only for non-smokers at 24 weeks.

The rehabilitation program represents another major reference point in the medical treatment of intermittent claudication, this treatment following the regularity and not the intensity of exercises, a better use of the energetic resources at the level of lower limb muscles, thus representing a factor that contributes to the slowing of claudication evolution, manifested through the increase of walking distance.

There were no complications during the physical training or massage.

Our study had some limitations. There was an inequality in the study groups after randomization. 4MWS is a parameter whose measurement mainly quantifies the way in which PAD affects the physical function, without information regarding the level of arterial obstruction or individual reaction concerning the intervention of vegetative nervous system in the altered peripheral perfusion of PAD patients.

Conclusions

In conclusion intermittent claudication has a negative impact on walking, which may limit the ability of PAD patients to perform their social and professional daily activities. Nevertheless, a well-structured exercise program, in terms of intensity, duration and frequency, may be of great help for improving the functional status of these patients.

A prolonged rehabilitation program is more effective on walking improvement even on non-smokers patients. Smoking undermines the effectiveness of physical training and massage on peripheral arterial disease patients. We obtained better results with a complex rehabilitation program including exercises and a

special massage technique with effects upon the blood and lymphatic flows.

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