# **REVIEW ARTICLE**

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# The effects of various forms of rehabilitation on patients with lower limb ischemia

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Introduction. Intermittent claudication is one of the most distinctive symptoms in Peripheral Arterial Disease (PAD), which causes gradually increasing muscle pain in the lower limbs during physical activity. Guided kinesiotherapy of patients suffering from intermittent claudication is an integral part of the treatment. Aim of the Study. The paper discusses various forms of exercises used in the treatment of intermittent claudication. Conclusions. The most common form of rehabilitation of patients with PAD is unassisted treadmill training in a home environment or assisted treadmill training. Alternative options include strength exercises of the lower limbs, osteopathic techniques, stationary bike exercises or the combination of the mentioned methods. The alternative methods of rehabilitation have a positive effect on PAD patients; however, their efficacy has been studied only recently. Due to the lack of reliable data in peer-reviewed journals it is difficult to establish which of the alternative methods is the most effective. The effects of treadmill training have been studied for many years and have been widely reported in science journals. Currently, treadmill training is considered to be the most effective, evidence-based, form of rehabilitation of patients with intermittent claudication.

KEYWORDS: intermittent claudication, lower limb ischemia, rehabilitation.

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# What is already known on this topic?

Physical exercises in the form of assisted rehabilitation are recommended as an initial conduct in the treatment of patients suffering from intermittent claudication. Treadmill training, with fixed slope and speed, is considered to be the most common and the most effective form of rehabilitation. Less common methods of rehabilitation are strength exercises of the lower limbs, bicycle ergometer exercises, and interval treadmill training with regulated speed and slope.

# Introduction

Peripheral artery disease (PAD) is most commonly defined as a gradual obstruction of arteries leading to impaired blood flow. A distinctive symptom of chronic lower limb ischemia is intermittent claudication. The term "claudication" comes from Latin, where *claudicatio* means "limping". Intermittent claudication is the pain in the lower limbs during walking, which forces the person to stop walking. The discomfort is located below the arterial stenosis and reappears after every continuous and considerable physical activity [1, 2].

#### The aim of the Study

The aim of the paper is to discuss, on the basis of recently published studies, various forms of rehabilitation used in PAD patients.

# **Epidemiology**

According to epidemiological studies, the prevalence of lower extremity ischemia in the general population is 3-10%. In people over the age of 70 the prevalence increases to 12-24%. In Poland there is no reliable epidemiological data which would allow assessment of the number of people suffering from peripheral artery disease. It is estimated that each year around 30.000 Poles visit their physician due to lower-extremity ischemia [3, 4, 5].

# **Etiology**

According to the TransAtlantic Inter-Society Consensus (TASC II) the most common cause of chronic lower-extremity ischemia is atherosclerosis, and, less often, arterial inflammation, dyslipidemia, hypertension and hyperhomocysteinemia. Chronic ischemia can also be caused by the coexistence of atherosclerosis and diabetes [1]. Chain smokers are four times more likely to develop the disease than non-smokers [6].

# Histological, metabolic and electrophysiological changes in lower-extremity muscles

The narrowing of large blood vessels reduces the flow of oxygenated blood to skeletal muscles. However, claudication and reduced physical activity are not caused merely by the impaired blood flow in large blood vessels. Other important factors include changes in microcirculation, structure of skeletal muscles and their metabolism [7].

Increased fatigability of lower-extremities and low tolerance of physical activity in PAD sufferers can also be caused by microstructure disorders connected with the quality and the type of muscle fibers. It is likely that the progression of the disease is associated with a reduction in the number of type I and type IIA fibers, and an increase in the number of IIB fibers [8].

Changes in the bioelectric activity of muscles in the lower extremities of PAD sufferers cause impaired gait patterns [11]. The swing phase is reduced by 5% and the stance phase increases by 3%. During the stance phase, the single-stance is reduced by 5% and the double-stance increases by 16%. PAD sufferers are slower and they have a tendency to have shorter stride length, which results in greater energy expenditure and worsened walk economy [9].

# **Diagnostics**

There are several classifications describing the progression of peripheral artery disease, including Fontaine's and Rutherford's (Table 1) [10, 11].

Physical examination looks for pale and dry skin, loss of hair, low skin warmth, loss of subcutaneous fat tissue, muscle dystrophy and thickening of nails [1, 2]. Non-invasive examination methods in the diagnostics of PAD patients include the Ankle Brachial Index (ABI), segmental blood pressure measurement, Doppler strength test, measuring the strength of the pulse and 2D ultrasound [1, 2, 10, 11].

# Methods of functional evaluation

In order to evaluate the patient's functional capabilities and to choose proper training parameters, Maximal Claudication Distance (MCD) and Pain-Free Walking Distance (PFWD) should be established. Usually these measurements are carried out with the use of treadmill. When a treadmill is not available, the Six-Minute Walk Test (6MWT) is an equally important diagnostic tool evaluating the capacity of peripheral arteries in the lower extremities [13].

#### Rehabilitation

Scientific literature describes several different rehabilitation treatment algorithms used in PAD patients. Depending on the desired therapeutic outcome chosen by researchers, the recommendations for patients are following: treadmill march/bicycle ergometer training, strength exercises of the lower and upper extremities, osteopathic techniques, general physical exercises, treadmill training in a home environment, and other exercises (Table 2). The main goal of rehabilitation is to reduce the strength symptoms, increase the claudication

**Table 1.** Fontaine's and Rutherford's chronic lower limb ischemia classification

Fontaine's classification		Rutherford's classification	
Stage	Clinical symptoms	Stage	Clinical symptoms
I	Asymptomatic	0	Asymptomatic
II a	Intermittent claudication > 200 m	I	Mild claudication
II b	Intermittent claudication < 200 m	II	Moderate claudication
III	Rest pain	III	Severe claudication
IV	Necrosis or gangrene of the limb	IV	Ischemic Rest pain
		V	Minor necrosis
		VI	Major necrosis

distance, and improve the patient's physical fitness and quality of life. Training regime has to be matched to each patient individually, taking into account other existing conditions [14].

Most training is performed 3 times a week, in sessions lasting from 6 weeks to 6 months [15, 16, 17]. The duration of an individual session spans from 30 to 45 minutes. 60-minute trainings are less common. Common inclusion criteria for participation in PAD rehabilitation research are stage II of chronic limb ischemia (Fontaine's classification) and the value of Ankle Brachial Index below 0.9 [18, 19, 20]. The most common exclusion criteria are disabling pathologies, not related to claudication, cardiovascular diseases, chronic obstructive pulmonary disease (COPD), critical peripheral artery disease of the lower extremities, resistant hypertension and history of revascularization in the last six months [21, 22, 23, 24].

# Treadmill training

Treadmill training is the most popular form of rehabilitation for PAD patients. Performed under the supervision of a physiotherapist it leads to increased claudication distance, and improved maximal oxygen consumption and quality of life. Regular exercises and quitting smoking can cause a 4-8 fold increase in Pain-Free Walking Distance and may help patients avoid the surgery [6, 13].

According to the TransAtlantic Inter-Society Consensus (TASC) rehabilitation of intermittent claudication patients should take the form of assisted treadmill march and last for 12 weeks at the minimum. It is recommended that the marching cause moderate ischemic pain (below 4 on a 5-point scale). When the pain appears, the patient stops the exercise and rests before repeating it. As the claudication distance gradually increases, the assisting person can increase the speed or the slope of the treadmill during next sessions [25, 26, 27].

According to pain-free rehabilitation model, walking should stop with the first symptoms of intermittent claudication. It is thought that training causing moderate pain is a sign of inflammatory response. Recurring episodes of ischemia and reperfusion, occurring during intermittent exercise, lead to the increase in oxidation processes and the production of free radicals. As a result, the endothelium is damaged, mediators of inflammation are released, and platelets and neutrophils are aggregated and activated. This process can cause systemic inflammatory response [28].

Researchers describe various forms of treadmill training differing in duration, speed and slope. Gardener et al. compared the effects of a 12-week supervised treadmill training of low intensity with home-based walking, where patients were given a step activity monitor and were instructed to wear it on their ankles. The parameters of both training forms were similar. The walking time started with 15 minutes in the first two weeks of the program. After two weeks, it increased by 5 minutes biweekly. In the last two weeks of the study, the walking time was 40-45 minutes. Both forms of rehabilitation increased the claudication onset time (COT) and peak walking time (PWT). Homebased walking with a step activity monitor resulted in a greater increase in daily ambulatory activity than supervised exercise [15].

The effects of low-intensity treadmill exercise were also studied by Barak. The first 2-3 minutes of walking were performed at the speed of 2.4 km/h or slower. If the exercise was tolerated by the patients well, the speed was increased every 1-2 minutes. The study used a six-stage scale of claudication. A patient could receive 0-1 points during walking. Whenever claudication symptoms appeared, the speed was reduced to 0.8 km/h or less, until the symptoms faded away. The training resulted in a walking distance (WDI) increase by 104% and a walking duration (WDU) increase by 55% [24].

Treadmill interval training is an alternative to commonly used fixed speed and slope treadmill training. Villemur et al. divided thirty-minute training sessions into 5 six-minute cycles. Each cycle consisted of three minutes of active workout followed by three minutes of active recovery. The study lasted for two weeks. In the first week speed was increased by 0.1 km/h with each training. In the second week, the slope was increased by 0.5% while running but the speed was constant. At the beginning of rehabilitation the mean walking distance was 610 m and by the end of the program it increased to 1,252 m [23].

# Resistance training

Previous reports on the methodology and the effects of resistance training in intermittent claudication patients are scarce. Patients with lower extremity peripheral arterial disease (PAD) have greater functional impairment and lower calf muscle mass than persons without PAD [29, 30].

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Table 2. The effects of various forms of rehabilitation on the functional abilities of PAD patients

Study	Duration of study and type of training	Frequency/duration of the training	Changes in claudication distance
Gardner AW, et al. (Circulation 2011)	12 weeks HBWT, STWT	HBWT: 3 x week (20-45 min) STWT: 3 x week (15-40 min)	HBWT:  ↑ 65% PFWT  ↑ 31% MWT  STWT:  ↑ 84% PFWT  ↑ 66% MWT
Murphy TP, et al. (J Vasc Surg 2009)	24 weeks HBWT, STWT, ER	STWT: 3 x week (1h)	HBWT: ↑ MWT 1.2 ± 2.6 STWT: ↑ MWT 5.8 ± 4.6 ER: ↑ MWT 3.7 ± 4.9
Lombardini R, et al. (Manual Therapy 2009)	24 weeks OMT	1-12 weeks: 1 x 2 week (30 min) 13-24 weeks: 1 x 3 week (30 min)	↑ PFWT $(2.8 \pm 0.3 \text{ v. } 3.7 \pm 0.4)$ ↑ MWT $(4.5 \pm 0.8 \text{ v. } 4.7 \pm 0.4)$
Manfredini F, et al. (Circulation 2008)	24 weeks STWT with V not causing claudication symptoms HBWT with self-selected V	STWT with fixed V: 2 x day, 6 x week (10 min) HBWT with self-selected V: 6 x week (20-30 min)	STWT with fixed V:  ↑ PFWD (86 ± 41 v. 137 ± 46)  ↑ MCD (133 ± 64 v. 216 ± 74)  HBWT with self-selected V:  ↑ PFWD (89 ± 47 v. 119 ± 47)  ↑ MCD (139 ± 75 v. 183 ± 76)
Dermott MM, et al. (JAMA 2009)	24 weeks STWT, ST	STWT: 3 x week (15-40 min) ST: 3 x week	STWT:  ↑ 6MWT (327 v. 348)  ↑ MWT (409 v. 622)  ↑ PFWD (135 v. 295)  ST:  ↑ MWT (360 v. 501)  ↑ PFWD (159 v. 259)  ↑ lower extremity strength
Parr BM, et al. (SAMJ 2009)	6 weeks ST DT (walking, cycling, circuit)	ST and HBWT: 3 x week (45 min)	DT:  ↑ PFWD (121 ± 108 v. 152 ± 109)  ↑ MCD (368 ± 124 v. 421 ± 128)  ST:  PFWD: no changes  ↑ MCD (441 ± 128 v. 484 ± 122)
Villemur B, et al. (Ann Phys Re- habil Med 2011)	2 weeks STWT (interval training)	5 x week 2 x day (30 min)	↑ PFWD (610 v. 1252)
Barak S, et al. (Angiology 2009)	6 weeks STWT (low-intensity pain-free treadmill exercise)	2 x week (45 min)	↑ 104% PFWD ↑ 55% PFWT ↑ 41% average walking speed
Kowalski R, (Kardiologia Polska 2009)	12 weeks STWT CT	3 x week (30 min)	STWT  ↑ PFWT (1.2 v. 3.27)  CT:  ↑ PFWT (1.12 v. 2.56)

HBWT – home-based walking training, STWT – supervised treadmill walking training, PFWT – pain-free walking time (measured in minutes), MWT – maximal walking time (measured in minutes), ER – endoluminal revascularization, OMT – osteopathic manipulative treatment, DT – dynamic training, PFWD – pain-free walking distance (measured in meters), MCD – maximal claudication distance (measured in meters), ST – strengthening training, 6MWT – 6 minutes walking time (measured in meters), CT – cycle training

In a study by Dermott resistance training led to increased lower-extremity maximal treadmill walking time and legs' muscle mass, as well as improved patients' quality of life. The study compared supervised treadmill exercise with lower extremity resistance training. Both forms of rehabilitation were used for 6 months, 3 times a week. The training consisted of 3 sets of 8 repetitions of knee extension, leg press, and leg curl exercises using standard equipment. Patients practicing treadmill exercises were encouraged to continue training even when lower extremity pain was present (to a level of 12 to 14 on the Borg rating of perceived exertion scale). Both forms of rehabilitation significantly increased patients' maximal treadmill walking time and treadmill time to onset of ischemic leg symptoms; however, the increase was greater in the treadmill group. Lower extremity resistance training improved muscle strength performance, quality of life, and stair climbing ability [21].

Parr et al. found upper body strength training to be a valid form of PAD treatment. The study compared two forms of rehabilitation: upper body strength training program and dynamic training consisting of walking, cycling and circuit training. Dumbbells and plateloaded machines were used in the strength training. The initial weight allowed the patient to comfortably complete 15 repetitions. The weights were then increased between 1.8 and 7.3 kg per week. Dynamic training consisted of 20 minutes of walking (with changing walking speed or the gradient), 5 minutes of cycling and 15 minutes of circuit training on the upper and lower body weight plated machine. The dynamic training resulted in a greater improvement of maximal walking distance and peak oxygen uptake than the strength training [22].

Upper body strength training and cycling can be an alternative for patients who are not able to undergo rehabilitation of the lower extremities due to degenerative changes, amputation, rest pain and a very short claudication distance [28].

#### **Home-based training**

In order to ensure the safety of patients and the validity of exercises, training should be supervised by a physiotherapist [2]. The easiest, but also the least effective, form of intermittent claudication treatment is unassisted walking in a home environment. Manfredini et al. carried out a large-group study comparing the effects of assisted and unassisted walking training.

Patients from the supervised group were given a specific walking speed; patients from the other group were told to walk 20-30 minutes a day at self-selected speeds up to pain tolerance. The assisted training program had more positive effects on the claudication distance, the speed of walking and hemodynamic parameters than did the unassisted program [20].

# Osteopathic Manipulative Treatment

A study by Lombardini et al. used osteopathic techniques in the treatment of claudication symptoms. Manual techniques were performed once every 2 weeks for the first 2 months of the study. The third month was a resting interval followed by manual therapy session every 3 weeks for 2 months. Therapists used the following techniques: myofascial release, strain/counterstrain, muscle energy, high-velocity low-amplitude thrust, lymphatic drainage and craniosacral manipulation. After 6 months, the claudication distance increased, IL-6 and adhesive molecules levels went down and the quality of life was improved [19].

#### **Conclusions**

- 1. The most effective form of rehabilitation for people with intermittent claudication is treadmill training, which is confirmed in scientific literature.
- 2. Strength and endurance programs should be individualized and carried out under supervision.

# What this study adds?

This paper provides up-to-date knowledge on rehabilitation in peripheral arterial disease of the lower limbs. Resistance training, bicycle ergometer training, osteopathic techniques, treadmill training with changing speed and slope improve the functional abilities of patients with intermittent claudication, and can be an alternative to the standard treadmill training.

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