Effects of treadmill training on walking distance and lower limb blood flow in patients with intermittent claudication

Zmiany dystansu marszu i przepływu tętniczego w kończynach dolnych podczas treningu marszowego u pacjentów z chromaniem przestankowym

Piotr Mika#, Krzysztof Spodaryk#, Andrzej Cencora*

Key words
claudication, blood flow, arteriosclerosis, exercise

Summary
Background: In patients with intermittent claudication treadmill training improves their walking ability. While the benefits of an exercise rehabilitation programme are recognized, the mechanisms involved are not completely appreciated. The improvement in lower limb blood flow may by one of the mechanisms leading to the increase in walking distance. In the present study arterial blood flow in lower limb as well as walking distance were assessed before and after supervised pain-free treadmill training.
Methods: Eighty patients with peripheral arterial occlusive disease (stage II according to Fontaine) were randomised into the treadmill program or to the control group. Patients in the exercising group participated for 3 months 3 times a week in supervised treadmill trainings. Each session consisted of 3 cycles, each amounting to 85% of the pain-free walking distance. Changes in arterial blood flow and the onset of claudication pain were assessed in both groups.
Results: After 12 weeks of the treadmill training lower limb blood flow in exercising group significantly improved ($p<0.05$). Pain-free walking distance was prolonged by 119,6% in the exercising group and only 16.9% in the control group. Those changes were statistically significant in both groups ($p<0.05$).
Conclusion: The results indicate that exercise training program using intermittent walking to 85% of the onset of claudication pain leads to a significant improvement in lower limb blood velocity and increase in pain-free walking distance.

Słowa kluczowe
chromanie przestankowe, przepływ tętniczy, miażdżyca, trening

Streszczenie
Cel: U pacjentów z chromaniem przestankowym regularnie prowadzony trening marszowy na bieżni prowadzi do wzrostu dystansu marszu. Mechanizm tej poprawy jest wieloczynnikowy a jedną z prawdopodobnych przyczyn może być wzrost przepływu tętniczego w kończynach dolnych. Przedmiotem badań była ocena zmian dystansu marszu oraz przepływu tętniczego w kończynach dolnych podczas treningu marszowego na bieżni u pacjentów z chromaniem przestankowym.
Metoda: 80 pacjentów z miażdżycą zarostową kończyn dolnych (II stopień według Fontaine) było randomizowanych do programu treningowego lub do grupy kontrolnej. Pacjenci z grupy badawczej przez okres 3 miesięcy uczestniczyli 3 razy tygodniowo w treningu marszowym. Sesje składały się z wysiłków marszowych powtarzanych 3-krotnie, każdy o dystansie marszu wynoszącym 85% indywidualnie określonego dystansu chromania. Przed rozpoczęciem programu i po jego zakończeniu w obu grupach oceniano dystans pojawienia się chromania oraz zmiany w prędkości przepływu tętniczego w kończynach dolnych (pomiar indeksu pulsacji metodą dopplerowską).
Wyniki: Po 12 tygodniach programu w grupie badawczej zaobserwowano wzrost indeksu pulsacji mierzony na tętnicy podkolanowej (43%), piszczelowej tylnej (59%) i grzbietowej stopy (78,8%). W grupie kontrolnej niewielki wzrost (11,4%) odnotowano na tętnicy podkolanowej. Towarzyszyła temu poprawa dystansu pojawienia się chromania – 119,6% w grupie badawczej i 16,9% w grupie kontrolnej. Zmiany były istotne statystycznie ($p< 0,05$).
Wnioski: Wyniki badań wskazują, że trening marszowy prowadzony u pacjentów z chromaniem przestankowym prowadzi do korzystnych zmian przepływu tętniczego w kończynach dolnych w zakresie poprawy jego prędkości oraz znacznej poprawy dystansu marszu pokonywanego bez bólu.

Article from the Department of Rehabilitation, Academy of Physical Education in Cracow# and Department of Vascular Surgery and Angiology, Jagiellonian University*, Cracow, Poland
Received 15.03.2005; accepted 10.05.2005

Introduction

Intermittent claudication is a common manifestation of Fontaine stage II of peripheral arterial occlusive disease (PAOD) [1,2]. It is caused by ischemic muscular pain due to an imbalance of oxygen supply and demand, which in turn is usually due to an arteriosclerosis obstruction[3]. Arterial occlusions and stenosis in PAOD lead to limited blood flow, both during the physical effort and at the rest[4]. Patients with claudication have sufficient skeletal muscle blood flow at the rest and insufficient during walking effort. The rest value of femoral arterial blood flow velocity may be no more than 20 cm/s. Under these conditions arterial stenosis to 90% may be not hemodynamically significant, but in stenosis of more than 90% the blood flow and pressure rapidly decrease. During physical effort the femoral arterial blood flow velocity may increase to 150 cm/s. It causes that 50% of arterial stenosis is a serious hemodynamic problem[5]. This inability to increase lower limb blood flow during effort results in muscle cramps, pain and leads to limited capability to walk[6,7]. The muscle pain occurs usually peripherally to the arterial stenosis. Femoral and popliteal arteries are most often affected by arteriosclerotic process and therefore the pain usually appears in the calf muscles. The development of arteriosclerotic process causes decrease of systolic arterial blood pressure and maximal arterial blood velocity distally to the point of stenosis[4].

Walking exercise and cessation of smoking are most important in conservative treatment of patients with claudication[8]. It has been suggested that the optimal program to increase claudication distance should consist of supervised treadmill walking exercises[9]. The improvement in walking distance usually reaches more than 100%[10], but the mechanism of this improvement has not been fully elucidated. Increases in claudication distance after physical training may result from changes in oxidative capacity of the skeletal muscle, greater utilization of oxygen, improvement in the biomechanics of walking and better redistribution or adaptation of blood flow[2,4,10,11]. Some study suggests that there is relationship between physical training and elastic vessels properties[12]. Also, the decrease in arteriosclerotic process after physical training has been observed in patients with PAOD[13]. But there is no agreement between studies as to the influence of physical training on changes in leg blood flow and its relationship to improvement in walking ability[10,14–16]. Therefore the aim of this study was to assess the potential changes in lower limb blood flow in response to a treadmill training in patients with claudication.

Material and Methods

Subjects' characteristics

Subjects 50–70 years old (127 male; 18 female), with a history of peripheral arterial occlusive disease (PAOD) and intermittent claudication (Fontaine stage II) volunteered to participate in the study. The subjects attended an outpatient Vascular Clinic. The diagnosis of PAOD was confirmed by Doppler ultrasound and an ankle/brachial index of less then 0.9 at rest with decrease to less then 0.75 after exercise[17,18]. Patients were recruited for this study if the walking distance to the onset of claudication pain, measured on the treadmill (speed 3.2 km/h, inclination 12°), was between 50–200 m, and claudication was stable over a 3-month period prior to enrolment[4]. Written informed consent was obtained from each patient before testing.

Out of 145 patients who volunteered for the study, after initial screening 98 were qualified for further testing but 47 were excluded based on one or more of the following criteria: angina pectoris, recent myocardial infraction, vascular surgery within the previous year, impaired cardiac or lung function, diabetes mellitus, cancer, kidney and liver disease, arthritis that limited walking or other conditions presenting contraindications to the proposed exercise regimen[17].

Pharmacological treatment of the patients was continued with no change during the study. Patients taking β-adrenergic-blocking drugs or pentoxifylline and other hemorheologicaly active drugs, were excluded because of the possible effects of these medicines on exercise training[15,17].

Patients were informed about influence of smoking on progression of arteriosclerosis of lower limbs and asked for smoking cessation.

Local ethics committee approval was obtained for the study.

Experimental procedure

All 98 patients were initially familiarized with the treadmill walking exercises[17]. After baseline testing all patients were randomly divided in two groups. Experimental subjects (n = 49) were enrolled in 12-week exercise program. Comparison subjects (n = 49) were instructed to maintain their usual level of activity. The testing was performed in the morning hours between 8–9 am. Subjects were asked to refrain from smoking 12 hours prior to the tests. The examination was performed 2 times for both groups: on entry into the study and on exit (12th week) from the program. Each time claudication distance, lower limb blood flow and amount of smoking cigarettes were assessed.

Treadmill testing

In all subjects, pain-free walking distance was measured on the treadmill (Woodway Standard, Woodway, Germany) at a constant speed of 3.2 km/h and 12° inclination angle. The treadmill was calibrated prior to the tests. Each time, the subject walked on the treadmill until the onset of claudication pain. The distance to the onset of claudication pain (pain-free walking distance) was recorded when the patient first noticed calf pain during the treadmill test – level of 2 on a 1–5 pain scale (1 = no pain, 2 = onset of pain, 3 = mild pain, 4 = moderate pain and 5 = maximal pain) [2,15,19]. Data from the first walking test following randomisation to two groups was not collected, and on the next day pain-free walking distance was reassessed as an initial value.

Blood flow assessment

Arterial blood flow in lower extremity was measured using a Doppler flow detector with fast Fourier signal analysis system[4] (Transcranial-Peripheral Doppler Spectrograph TDS–4; Sonomed, Poland). The measurement was performed in supine position on posterior tibialis, popliteal, and dorsalis pedis arteries in the more advanced arteriosclerotic leg (early pain symptoms during treadmill test). Pencil probe (8MHz) was placed (angle 60°) in typical places. In the assessment of arterial blood flow velocity the pulsation index (P_I) was determined:

$$P_I = (V_{max} - V_{min}) / V_{av}$$

V_{max} – maximal blood flow velocity, V_{min} – minimal blood flow velocity, V_{av} – average blood flow velocity

The P_I determines the elasticity of vessels and decrease subsequently with the progression of arteriosclerotic process. This method has been recommended as objective and independent of ultrasound frequency and wave angle[20]. The Doppler examination was performed twice in both groups: on entry in to the study and day after the end of program by the specialist blinded as to which group the patients belonged.

Training program

Patients in the treatment group participated in 12 weeks of supervised treadmill training. The exercise training sessions were conducted 3 times a week on a treadmill (Woodway Standard, Woodway Germany) during the morning hours. Treadmill speed was set at 3.2 km/h and an inclination on 12°. The session consisted of intermittent walking to 85% of the previously individually determined pain-free walking distance. The goal of such a workload was not to produce a claudication pain. After 6 weeks patients were reassessed, as described above, and in case of any increase in pain-free walking distance, a new workload was individually determined (85% of pain-free walking distance).

After the treadmill effort, the subject stepped off the treadmill and rested until fatigue subsided from the lower limbs and he/she was able to undertake the next treadmill effort. Exercise to 85% of pain-free walking distance and rest periods to subsidence of fatigue were repeated 3 times throughout each training session.

Training sessions were supervised and heart rate was monitored using telemetry (Polar Sport Tester, Polar, Finland).

Smoking status

The amount of average number of cigarettes per day and the total number of years of smoking were recorded to determine smoking status of all patients. Cigarette consumption per day was assessed on entry and day after the end of program. The data were collected anonymously and recorded on 1—3 scale (1 – 1–5 cigarette/day; 2 – less than 1 pack/day; 3 – more than 1 pack/day).

Statistical analysis

The data are expressed as means ± SD. Statistical significance was set as $P < 0.05$. The distribution of all variables was tested for normality with the Shapiro-Wilk test. The data were not normally distributed. Changes in claudication distances and P_I within groups after 12 weeks were examined by the Wilcoxon signed rank test. Differences between the two groups on entry were determined with the Mann-Whitney U-test. The results were analysed on a personal computer using a commercial statistical program (*STATISTICA 95*).

Results

Out of 98 eligible patients, 80 completed the full 12-weeks program. Ten subjects in the control group did not return for following examinations, eight subjects in the exercising group refused to continue. The cause of this refusal was not connected with health problems. The clinical characteristics of 80 patients completing the program are shown in Table 1. There were no significant differences noted in baseline variables between the training and control group.

Twelve weeks of program resulted in an 119.6% increase of pain free walking distance in the training group and 16.9% in the control group (Table 2). There were no significant differences in pain-free walking distance between groups at the beginning of the program. In both groups significant decrease of the amount of smok-

Table 1

Baseline clinical data of the studied patients

	Experimental group (n=41)	Control group (n=39)	P
Sex, men/women	35 : 6	31 : 8	
Age (years)	61,4 ±6,5	60,9 ±5,4	n.s.
Mean claudication time (years)	4,8 ±3,7	5,5 ±2,8	n.s.
Smoking (years)	32,3 ±8,5	31 ±9,4	n.s.
Smoking (n)	36	32	
ABI (ankle/brachial index)			
rest	0,68 ±0,12	0,69 ±0,15	n.s.
after exercise	0,49 ±0,17	0,48 ±0,16	n.s.

Values are expressed as mean ± SD
n.s. = non significant

Table 2

Changes in pain-free walking distance after 12 weeks in the training group and the control group

Pain-free waking distance (m)	Experimental group	Control group	
Baseline	87,4 ±38	86,9 ±40	p>0,05
6 weeks	135,4 ±63,9	96,7 ±45,2	p<0,01
12 weeks	191,6 ±94,8	102,3 ±56,6	p<0,001
	p^1<0,001	p^1<0,05	

Values are expressed as mean ± SD
p^1 – after 12 weeks to baseline

Table 3

Smoking status of the patients studied before and after 12 weeks of the program

Amount of cigarettes / day	Experimental group	Control group	
baseline	3 ±0,5	2 ±0,5	p>0,05
12 weeks	0 ±0,5	0 ±1	p>0,05
	p<0,001	p<0,001	

Values are expressed as median ± quartile range
0 – nothing
1 – 1 to 5
2 – less than one pack
3 – more than one pack

ing cigarettes after 12 weeks of program ($p<0.001$) was observed. The dimensions of changes were the same in both groups. There were no significant differences between groups in smoking status both at the beginning and at the end of the program (Table 3).

Three months of treadmill exercise resulted in a significant increase in P_I measured on popliteal (43%), posterior tibialis (50.9%) and dorsalis pedis (78.8%) arteries (Figure 1). In the control group small but significant increase in P_I (11.4%) we noted only on popliteal artery (Figure 2). There were no significant differences between groups in the entry values of P_I.

We did not observe any significant correlation between improvement in walking distance and P_I. Also no significant changes in ABI were observed after 12 weeks both in the training and in the control group.

Discussion

After 12 weeks of treadmill training we achieved significant increase of P_I measured on posterior tibialis, popliteal and dorsalis pedis arteries.

There is disagreement between studies as to the influence of exercise training on leg blood flow. In general, it is indicated that exercise training is not associated with significant changes in limb blood flow[16]. Larsen and Lassen in 1966 [21] for the first time used xenon–-133 clearance technique to measure the maximal blood flow in the anterior tibial muscle. Despite of significant improvement in walking distance (155%) they did not observe any significant change in blood flow in the group of 7 claudication patients after 6 months of training. Three years later Alpert et al[22] using the same technique on the group of 19 patients with claudication reported 6% increase in calf muscle blood flow also after 6 months of training. Following studies using venous occlusion pletysmography technique demonstrated increase between 18–122% [15,23–25] or very often no increase in blood flow despite a significant improvement in walking distance ranged 58–150%[26–31]. Johnson et al.[32] used duplex scanner[4] to demonstrate that in claudication patients the common femoral artery blood flow reminds similar to pre-exercise levels despite a claudication distance increase of over 80% after 5 months of training. What is important, the method used in the study was very sensitive, but small group of 10 patients was a week point of this research. Sorlie and Myhre[33] who used a termodilution technique to measure blood flow reported similar results. They observed 79% increase in walking distance with no change in blood flow.

However, initial studies on animals with ligated femoral arteries demonstrated that following exercise training blood flow returned to preligation values within a year[34–35]. Therefore it has been suggested that an increase in absolute blood flow may be secondary to the development of a collateral circulation[10], and the changes in this circulation after physical training may be caused by development of new or widening of present collateral vessels[11]. However, American Heart Association [4] did not confirm the influence of physical exercise on development of a collateral circulation in patients with claudication. Despite of this standpoint it is indicated that elevated blood flow causes the increase of vessel wall shear stress. This physiologic factor may improve endothelial vasoreactivity[36–38]. The improvement of endothelial-dependent vasodilatation connected with lowering of vascular resistance may increase blood flow. It is also suggested that long-lasting elevated shear stress may mediate release of different growth factors leading to stimulation of vascular adaptation process and therefore to increase of total diameter of collateral vessels[12,37,39].

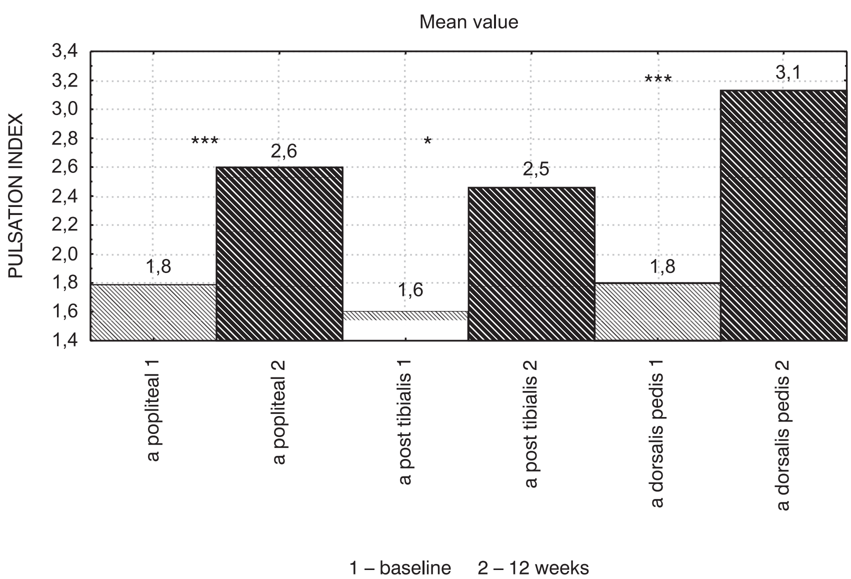

Figure 1

Changes in artery blood flow (pulsation index) after 12 weeks in the patients undergoing exercise training (*p<0,05; ***p<0,001)

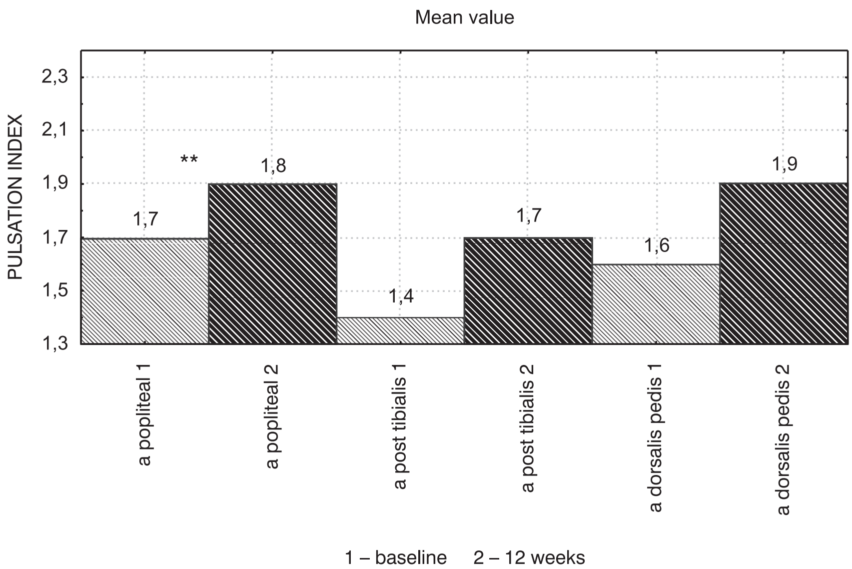

Figure 2

Changes in artery blood flow (pulsation index) after 12 weeks in the control group (p<0,01)**

The results of this study confirm the improvement in arterial wall elasticity determined by P_I (Figure 1). Based on present findings we may hypothesize that vascular resistance was decreased and therefore arterial blood flow consequently improved according to Poiseuill law[40,41]

$Q = P\, r^4\, \Pi / 8\, L\, \eta$

Q – intensity of blood flow, P –change in blood pressure from entry to the end of the vessel; r – radius of the vessel; L – vessel length; η – blood viscosity.

The intensity of blood flow understand as a total value of vascular blood flow in the amount of time is directly proportional to pressure changes and the 4-th power of radius and inversely proportional to the length of the vessel and blood viscosity. Therefore, vasodilatation is the most important factor leading to improvement in the blood perfusion. Also, the bigger are changes in the pressure and the smaller is the vascular resistance, the bigger is blood volume (Q = P/R; R – vascular resistance). The improvement in blood perfusion may be achieved by increase in blood pressure or by lowering vascular resistance. Consequently we can say that minimal vasodilatation can significantly decrease vascular resistance and increase blood flow: $R = 8L\, \eta / \Pi r^4$

This finding makes the problem of vascular elasticity very important. This issue, evaluated in present study, may be connected with improvement in endothelial function and increased flow-dependent dilation mediated by the endothelium[36,37]. It has been suggested that enhanced endothelial release of nitric oxide may be responsible for the increased endothelial vasoreactivity[1,38].

It is also indicated that changes in blood flow observed in some studies may be due simply to a redistribution of blood flow from less to more active muscles during physical effort[11,16,22]. This idea was supported by a study showing reduced femoral venous oxygen saturation during exercise in claudicants after training program[10]. However, the increased lower limb oxygen uptake may not be due to redistribution of blood flow. It may be mediated by metabolic capabilities of muscle fibers change after exercise training as an increase in the number of mitochondria per muscle fiber or higher level of oxidative enzymes[10,11].

The following, often observed, problem is poor or no correlation between lower limb blood flow and walking performance in patient with claudication[15,16]. Also in present study we did not note significant correlation between improvement in walking distance and elevation in P_I. Some study indicated that there may be a relationship between this variables[42]. Alpert et al.[22] after 6 months of physical training observed that increased maximal blood flow correlated with increased walking distance.

There is also disagreement between studies as to the influence of exercise training on ABI. Womac et al.[14] observed increase of ABI from 0,36 to 0,43 after 4 months of training, but Gardner et al.[19] did not note any changes in ABI after 6 months of training, while increase in calf blood flow was observed. The study of Brendle et al.[1] also indicated on increase in blood flow after 6 months of training connected with improved endothelial-dependent vasodilation. The small increase of ABI observed in this study was not significant. The result of our study is in agreement with previous researches. We did not note any change in ABI, despite observed increase in P_I.

Gardner and Poehlman[9] reviewed studies of exercise training for claudicants and concluded that the increase in lower limb blood flow was small, while exercise tolerance regularly increased by over 100%. They indicated that the Pearson correlation between the improvement blood flow and walking distance lies between 0,23 and 0,55 and suggested that the flow increase could account for only 5–30% of the improvement in walking distance.

In our study we observed almost 120% increase in claudication distance, 43–79% increase of P_I (Figure 1), but we did not note any correlation between these variables. Therefore an improvement in blood flow is not the main factor leading to an increase in walking ability in patients with claudication.

In non-exercised control group the improvement in claudication distance (16.9%) and increase in P_I (11.4%) measured on popliteal artery has been also observed (Figure 2). The reduction of smoking may be responsible for these changes. In treatment of patients with PAOD cessation of smoking is a standard procedure[4,8,43]. The nicotine stimulates adrenal medulla and increase catecholamine secretion leading to vasocontraction and therefore to increase of peripheral vascular resistance. Additionally, carbon monoxide released during smoking causes endothelial injury. It is also known that smokers have increased blood viscosity – one of the factors of increased blood flow resistance[2]. The Framingham study[44] shows that smoking is a key risk factor for the development and progression of PAOD. It has been indicated that cessation of smoking can significantly increase walking distance in patients with claudication[45]. Therefore reduction of smoking observed in our study in the control group may be the reason of positive changes in walking distance and blood flow. Additionally, the same range of smoking reduction observed in exercising group could add to the improvement (in part) in walking distance and P_I. These observations confirm the importance of smoking cessation in treatment of claudication.

In summary, the results of this study indicate that treadmill training may improve lower limb blood flow in patient with claudication. These changes may be related to elastic properties of blood vessels and decreased vascular resistance. The improvement in blood flow may be one of the factors leading to improvement in walking ability in patients with claudication. Future investigations evaluating changes in lower limb blood flow with treadmill training, measured with more precise devices, should be planned.

Conclusions

1. The increase in P_I after 3 months of treadmill training may confirm improvement in lower limb blood flow velocity. These changes may lead to the increase in walking distance in patients with claudication.
2. The absence of correlation between increase in P_I and improvement in walking distance may suggest that changes in lower limb blood flow are not the main factor of improvement in walking ability in patients with claudication.
3. The smoking cessation may cause significant improvement in lower limb blood flow and walking distance in patients with claudication.

The research was supported by grant 6 PO5D 081 20 from KBN, Poland

References

1. Brendle D.C., Joseph L.J., Corretti M.C., Gardner A.W., Katzel L.I.: Effects of exercise rehabilitation on endothelial reactivity in older patients with peripheral arterial disease. Am J Cardiol. 2001; 87: 324–329
2. Brzostek T., Mika P., Bromboszcz J.: Miażdżyca tętnic kończyn dolnych – patofizjologia, klinika, leczenie i rehabilitacja. Rehabilitacja Medyczna 2004; 8(1): 38–50
3. Ernst E., Fialka V.: A review of the clinical effectiveness of exercise therapy for intermittent claudication. Arch Intern Med. 1993; 153: 2357–2360
4. Weitz J.I., Byrne J., Clagett P., Farkouh M.E., Porter J.M., Sackett D.L. et al.: Diagnosis and treatment of chronic arterial insufficiency of the lower extremities: a critical review. Circulation 1996; 94: 3026–3049
5. TransAtlantic Inter-Society Consensus (TASC). Management of peripheral arterial disease (PAD). Section B: intermittent claudication. European Journal of Vascular and Endovascular Surgery 2000; 19: S47-S66
6. Cencora A.: Chromanie przestankowe: objaw czy czynnik ryzyka? Pol. Przegl. Chirurg. 1995; 67: 875–884
7. Kaseja K., Ciechanowski K.: Chromanie przestankowe – patogeneza i skutki ogólnoustrojowe. Pol. Przegl. Chirurg. 1997; 69: 430–435
8. Housley E.: Treating claudication in five words. BMJ 1988; 296: 1483
9. Gardner A.W., Poehlman E.T.: Exercise rehabilitation programs for the treatment of claudication pain. A metaanalysis. JAMA 1995; 274: 975–80
10. Tan K.H., de Cossart L., Edwards P.R.: Exercise training and peripheral vascular disease. Br J Surg 2000; 87: 553–562
11. Remijnse-Tamerius H.C., Duprez D., De Buyzere M., Oeseburg B., Clement D.L.: Why is training effective in the treatment of patients with intermittent claudication? International Angiology 1999; 18: 103–112
12. Huonker M., Halle M., Keul J.: Structural and functional adaptations of the cardiovascular system by training. Int J Sports Med.1996; 17(Suppl 3): 164–172
13. Cimminiello C., Arpaia G., Aloisio M., Uberti T., Rossi F., Pozzi F.: Platelet-derived growth factor (PDGF) in patients with different degrees of chronic arterial obstructive disease. Angiology 1994; 45: 289–293
14. Womack C.J., Sieminski D.J., Katzel L.I., Yataco A., Gardner A.W.: Improved walking economy in patients with peripheral arterial occlusive disease. Med Sci Sports Exerc. 1997; 29: 1286–1290
15. Hiatt W.R., Regensteiner J.G., Hargarten M.E., Wolfel E.E., Brass E.P.: Benefit of exercise conditioning for patients with peripheral arterial disease. Circulation 1990; 81: 602–609
16. Nehler M.R., Hiatt W.R.: Exercise therapy for claudication. Ann of Vasc Surg. 1999; 13: 109–114
17. Regensteiner J.G., Meyer T.J., Krupski W.C., Cranford L.S., Hiatt W.R.: Hospital versus home-based exercise rehabilitation for patients with peripheral arterial occlusive disease. Angiology 1997; 48: 291–300
18. Hiatt W.R., Regensteiner J.G., Wolfel E.E., Carry M.R., Brass E.P.: Effect of exercise training on skeletal muscle histology and metabolism in peripheral arterial disease. J Appl Physiol. 1996; 81: 780–788
19. Gardner A.W., Katzel L.I., Sorkin J.D., Killweich L.A., Rayan A., Flinn W.R. et al.: Improved functional outcomes following exercise rehabilitation in patients with intermittent claudication. J Gerontol. 2000; 55A: M570–7
20. Nowicki A.: Sposoby obliczania krzywych przepływu krwi mierzonych metodą Dopplera. Ulrtason Pol. 1992; 2: 554
21. Larsen O.A., Lassen N.A.: Effect of daily muscular exercise in patients with intermittent claudication. Lancet 1966; ii: 1093–1096
22. Alpert J.S., Larsen O.A., Lassen N.A.: Exercise and intermittent claudication. Blood flow in the calf muscle during walking studied by the xenon–133 clearance method. Circulation 1969; 39: 353–359
23. Ericsson B., Haeger K., Lindell S.E.: Effect of physical training of intermittent claudication. Angiology 1970; 21: 188–192
24. Fitzgerald D.E., Keates J.S., Macmillan D.: Angiographic and pletysmographic assessment of garduated physical exercise in the treatment of chronic occlusive arterial disease of the leg. Angiology 1971; 22: 99–106
25. Lundgren F., Dahllof A.G., Schersten T., Bylund-Fellenius A.C.: Muscle enzyme adaptation in patients with peripheral arterial insufficiency. Clin Sci 1989; 77: 485–943
26. Zetterquist S.: The effect of active training on the nutritive blood flow in exercising ischemic legs. Scand J Clin Lab Invest 1970; 25: 101–111
27. Dahllof A.G., Bjorntorp B., Holm J., Schersten T.: Metabolic activity of skeletal muscle in patients with peripheral arterial insufficiency. Effect of physical training. Eur J Clin Invest. 1974; 4: 9–15
28. Ekroth R., Dahllof A.G., Gundevall B., Holm J., Schersten T.: Physical training of patients with intermittent claudication: indications, methods, and result. Surgery 1978; 84: 640–643
29. Mannarino E., Pasqualini L., Menna M., Maragoni G., Orlandi U.: Effects of physical training on peripheral vascular disease: a controlled study. Angiology 1989; 40: 5–10
30. Mannarino E., Pasqualini L., Innocente S., Scricciolo V., Rignanese A., Ciuffetti G.: Physical training and antiplatelet treatment in stage II peripheral arterial occlusive disease: alone or combined? Angiology 1991; 42: 513–521
31. Pancera P., Prior M., Zannoni M., Lucchese L., DeMarchi S., Arosio E.: Micro- and macrocirculatory, and biohumoral changes after a month of physical exercise in patients with intermittent claudication. Scand J Rehabil Med 1995; 27: 73–76
32. Johnson E.C., Voyles W.F., Atterbom H.A., Pathak D., Sutton M.F., Greene E.R.: Effects of exercise training on common femoral artery blood flow in patients with intermittent claudication. Circulation 1989; 80(Supl III): III–59–72
33. Sorlie D., Myhre K.: Effects of physical training in intermittent claudication. Scand J Clin Lab Invest 1978; 38: 217–222
34. Weiss Th., Fujita Y., Kreimeier U., Messmer K.: Effect of intensive walking exercise on skeletal muscle blood flow in intermittent claudication. Angiology 1992; 43: 63–71
35. Nicholson C.D., Angersbach D., Wilke R.: The effect of physical training on rat calf muscle, oxygen tension, blood flow, metabolism and function in an animal model of chronic occlusive peripheral vascular disease. Int J Sports Med 1992; 13: 60–64
36. Horning B, Maier V, Drexler H. Physical training improves endothelial function in patients with chronic heart failure. Circulation 1996; 93: 210–214
37. Laughlin M.H., McAllister R.M., Jasperese J.L., Crader S.E., Williams D.A., Huxley V.H.: Endothelium-mediated control of the coronary circulation. Exercise training-induced vascular adaptations. Sports Med 1996; 22: 228–250
38. Arosio E., Cuzzolin L., De Marchi S., Minuz P., Degan M., Crivellente F.: Increased endogenous nitric oxide production induced by physical exercise in peripheral arterial occlusive disease patients. Life Sci 1999; 65: 2815–2822
39. Varin R., Mulder P., Richard V., Tamion F., Devaux C., Henry J.P. et al.: Exercise improves flow-mediated vasodilation of skeletal muscle arteries in rats with chronic heart failure. Circulation 1999; 99:2951–2957

40. Turczyński B., Sroczyński J., Matyszczyk B., Szczęsny S.: Lepkość krwi i osocza a dystans chromania przestankowego u chorych na zarostową miażdżycę tętnic kończyn dolnych. Pol Arch Med Wewn 1991; 85: 41–49
41. Jarrett F.: Chromanie przestankowe. Chirurg Wsp 1993; 1: 322–326
42. Ernst E., Matrai A.: Intermitted claudication, exercise, and blood rheology. Circulation 1987; 76: 1110–1114
43. Tornwall M.E., Virtamo J., Haukka J.K., Aro A., Albanes D., Huttungen J.K.: Prospective study of diet, lifestyle, and intermittent claudication in male smokers. Am J Epidemiol 2000; 151: 892–901
44. Murabito J.M., D'Agostino R.B., Silbershatz H., Wilson P.W.: Intermittent claudication. A risk profile from the Framingham Heart Study. Circulation 1997; 96: 44–49
45. De Felice M., Gallo P., Masotti G.: Current therapy of peripheral obstructive arterial disease. Angiology 1990; 41: 1–11

Address for correspondence

Piotr Mika, PhD
Chair of Clinical Rehabilitation Academy
of Physical Education in Cracow
Al. Jana Pawła II 78, 31–571 Kraków, Poland
Tel.: (4812) 683 11 34
e-mail: piotrmika@poczta.fm