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Influence of low and moderate grade leg ischaemia on the skin microcirculation parameters in peripheral arterial occlusive disease patients

Wpływ niewielkiego i zaawansowanego niedokrwienia na przepływ w mikrokrążeniu skórnym u pacjentów z miażdżycowym niedokrwieniem kończyn dolnych

Katarzyna Pawlaczyk-Gabriel[1], Marcin Gabriel[2], Zbigniew Krasiński[2], Łukasz Dzieciuchowicz[2], Michał Stanisić[2], Zofia Gabriel[3], Małgorzata Olejniczak-Nowakowska[4], Tomasz Urbanek[5]

[1]Department of Hypertensiology, Angiology and Internal Diseases, Poznan University of Medical Sciences, Poland (Klinika Hipertensjologii, Angiologii i Chorób Wewnętrznych Uniwersytetu Medycznego w Poznaniu)
[2]Department of General and Vascular Surgery, Poznan University of Medical Sciences, Poland (Klinika Chirurgii Ogólnej i Naczyń Uniwersytetu Medycznego w Poznaniu)
[3]Student Research Club at the Department of General and Vascular Surgery, Poznan University of Medical Sciences, Poland (Studenckie Koło Naukowe przy Klinice Chirurgii Ogólnej i Naczyń Uniwersytetu Medycznego w Poznaniu)
[4]Department of Cancer Prevention, Medical University of Silesia in Katowice, Poland (Zakład Profilaktyki Chorób Nowotworowych, Śląski Uniwersytet Medyczny w Katowicach)
[5]Department of General and Vascular Surgery, Medical University of Silesia in Katowice, Poland (Klinika Chirurgii Ogólnej i Naczyniowej Śląskiego Uniwersytetu Medycznego w Katowicach)

Abstract

Introduction. *The aim of the study was to characterize the changes in the microcirculation in patients with varying severity of atherosclerotic ischaemia of the lower limbs (PAOD).*

Material and methods. *The study included 27 healthy subjects, 79 patients with PAOD category 0 and 1 according to the Rutherford classification, and 137 patients with PAOD category 3 and 4. The study evaluated cutaneous blood flow, flowmotion bonds, percutaneous partial pressure of oxygen and flow-mediated vasodilation.*

Results. *Even mild PAOD exhibits a worse systemic vascular function expressed as a reduction in the scope of flow-mediated vasodilation, and locally in $TcpO_2$ decrease. Increase in local changes in advanced forms of PAOD were observed as further reduction in $TcpO_2$ and a drastic reduction or exhaustion of the functional microcirculatory reserve. Among the evaluated risk factors for atherosclerosis only diabetes and smoking significantly modified perfusion, which resulted in a significant decrease in the values of vasodilation and $TcpO_2$.*

Conclusions. *The study revealed the occurrence of adverse changes in microcirculation, also in patients with poorly discernible signs of limb ischaemia. It can be assumed that these may also occur in the patients who underwent a haemodynamically effective revascularization.*

Key words: skin microcirculation, flowmotion, atherosclerotic limb ischaemia, percutaneous partial pressure of oxygen, flow-mediated vasodilation

Streszczenie

Wstęp. *Celem badań było scharakteryzowanie zmian w mikrokrążeniu u pacjentów z różnym stopniem zaawansowania miażdżycowego niedokrwienia kończyn dolnych (PAOD).*

Adres do korespondencji:
dr hab. n. med. Katarzyna Pawlaczyk-Gabriel
Department of Hypertensiology, Angiology and Internal Diseases
Karol Marcinkowski Medical University of Poznan
ul. Długa 1–2, 61–848 Poznań
e-mail: kati2911@poczta.onet.eu

Materiał i metody. *Do badania włączono 27 zdrowych osób, 79 pacjentów z PAOD w 0 i 1 kategorii oraz 137 pacjentów z PAOD w 3 i 4 kategorii według klasyfikacji Rutherforda. Oceniano skórny przepływ krwi, pasma flowmotion, przezskórne ciśnienie parcjalne tlenu i wazodylatację indukowaną przepływem.*
Wyniki. *Już w łagodnej postaci PAOD występuje ogólnoustrojowe pogorszenie funkcji naczyń, wyrażone zmniejszeniem zakresu wazodylatacji indukowanej przepływem, a miejscowo zmniejszeniem $TcpO_2$. W zaawansowanych postaciach PAOD obserwowano pogłębienie zmian miejscowych w postaci dalszego obniżenia $TcpO_2$ i radykalnego zmniejszenia lub też wyczerpania rezerwy czynnościowej mikrokrążenia. Spośród ocenianych czynników ryzyka rozwoju miażdżycy tylko cukrzyca i palenie tytoniu znamiennie modyfikowały perfuzję, istotnie zmniejszając wartości wazodylatacji i $TcpO_2$.*
Wnioski. *W przeprowadzonym badaniu wykazano występowanie niekorzystnych zmian w mikrokrążeniu także u pacjentów ze słabo zaznaczonymi objawami niedokrwienia kończyn. Można przypuszczać, że mogą one występować również u pacjentów po skutecznych hemodynamicznie zabiegach rewaskularyzacji.*

Słowa kluczowe: mikrokrążenie skórne, *flowmotion*, miażdżycowe niedokrwienie kończyn, przezskórne ciśnienie parcjalne tlenu, wazodylatacja indukowana przepływem

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Introduction

Evaluation of the efficacy of peripheral revascularization is mainly based on the subjective experience of the patient, increase in the temperature of the integuments and improvement in the flow within the main arterial trunks [1]. The latter is not always synonymous with an improvement in the degree of integumental perfusion. To date, the parameters of microcirculation have not been characterized in varying degrees of severity for atherosclerotic limb ischaemia, which could otherwise become the basis of objective assessment of the extent of peripheral perfusion impairment.

This condition is derived from three problems. Apart from a few cases of microvascular parameters, the studies related to patients with atherosclerotic limb ischaemia in stage II according to the Fontaine classification [2, 3]. However, considering the qualification criteria for revascularization of patients with PAOD, it seems that despite the difficulty with completing uniform and sufficiently large research groups, it would be more appropriate for the study to consider patients with advanced forms of the disease, as such advanced forms become a clear indication for surgical procedures [4].

On the other hand, the study evaluated only single parameters, e.g., the nature of the flow in large arterial trunks or some aspects of skin perfusion, possibly with vasomotion bonds or flow-mediated endothelium-dependent vasodilation [5–7]. In addition, the studies were carried out on small groups of patients, usually not exceeding 50 subjects.

The difficulty defining explicit and universally recognized standards of flow in the microcirculation makes it hard to develop some useful criteria to assess the impact of revascularization on peripheral perfusion. Therefore it is impossible to divide the changes observed in the postoperative period into the categories of "improvement" or "deterioration".

In order to deal with such a disadvantage, microcirculatory parameters occurring in patients with varying severity of the symptoms of atherosclerotic ischaemia of the lower limbs were compared with those of healthy subjects.

Material and methods

The study included patients with haemodynamically significant lesions or occlusions present in the femoral-popliteal section, with the ankle-brachial index value lower than 0.9. On the basis of the clinical symptoms, patients were included in two study groups:

— Group 1 included 137 patients with symptoms of chronic atherosclerotic ischaemia of the lower limbs in category 3 and 4 according to the Rutherford classification;
— Group 2 included 79 patients with symptoms of chronic atherosclerotic ischaemia of the lower limbs in category 0 and 1 according to the Rutherford classification.

The control group (Group 3) consisted of 27 volunteers with no clinically perceptible presence of atherosclerotic lesions in coronary and peripheral vessels. All subjects underwent electrocardiography at rest, dual Doppler imaging of the carotid and vertebral arteries and of the lower limbs; their ankle-brachial indexes were specified (ABPI > 0.9).

Study exclusion factors included: the presence of haemodynamically significant lesions in the iliac, com-

mon femoral, popliteal, tibial and sagittal arteries; the presence of ulceration or necrotic lesions on the limbs; pregnancy; chronic venous insufficiency; renal failure requiring dialysis; neoplastic, allergic, rheumatic or inflammatory diseases; diffuse dermatological lesions; uncontrolled or untreated arterial hypertension and vasomotor disorders; past ischaemic or haemorrhagic cerebral stroke, spinal or spinal cord injury; past pharmacological treatments or operational sympathectomy; limb oedema, regardless of its aetiology; intake of steroid, immunosuppressant, vasomotor or phlebotropic medications.

All patients in all study groups received a single anti-aggregation drug (Acetylsalicylic acid at a dose of 100–150 mg/day or Clopidogrel 1 × 75 mg) and statins (Simvastatin or Atorvastatin at a dose of 20–40 mg/day) as part of pharmacotherapy. Patients with arterial hypertension were treated without the use of beta-blockers or calcium antagonists.

Patients from the study groups and the control group with arterial hypertension, diabetes or hyperlipidaemia were properly treated as part of the pharmacotherapy. Proper treatment was confirmed by inspections carried out in the form of multiple measurements of arterial blood pressure, lipid management profile, blood glucose and glycated haemoglobin levels. The characteristics of patients included in each group are presented in Table 1.

Table 1. Characteristics of treatment groups and the control group
Tabela 1. Charakterystyka grup leczonej i kontrolnej

	Group		
	1	2	3
Number of people	137	79	27
Women/men *number (percent)*	40/97 (29.2/70.8)	25/54 (31.6/68.4)	11/16 (33.3/66.7)
Age — mean ± *SD*	63.3 ± 14.2	66.2 ± 9.9	59.9 ± 12.6
BMI — mean ± *SD*	25.7 ± 5.9	25.9 ± 4.6	24.9 ± 4.3
Dyslipidaemia *number (percent)*	109 (79.6)	55 (69.6)	16 (59.2)
Arterial hypertension *number (percent)*	86 (62.8)	46 (58.2)	13 (48.1)
Smoking *number (percent)*	94 (68.6)	54 (68.4)	19 (70.4)
Diabetes *number (percent)*	39 (26.3)	15 (18.9)	6 (22.2)
Ischaemic heart disease *number (percent)*	95 (69.3)	50 (63.3)	0 (0)
Renal failure *number (percent)*	6 (4.4)	4 (5.1)	2 (7.4)

Testing methodology

All tests were performed in the morning, in air-conditioned room, at a fixed temperature of 21°C, in the supine position, after a 15-minute rest. Patients were advised to abstain from caffeinated beverages and/or theine and alcoholic beverages for at least 2 hours and to avoid physical exercise making them exceed the distance of painless passage within 6 hours prior to testing. The last doses of hypotensive medications were taken by the patients at least 12 hours prior to testing.

All patients had their ankle-brachial indexes measured. The location and extent of atherosclerotic lesions were determined on the basis of imaging results (duplex Doppler, angioCT, angioMRI).

To perform vasomotion analyses, skin blood flow (SBF) (in arbitrary perfusion units; 1 PU = 10 mV) was measured with a laser Doppler probe (PF 457; Perimed, Stockholm, Sweden) at the dorsal side of the foot (in the middle between the second and third metatarsals). Fast-Fourier transform analysis was performed by means of Perisoft dedicated software (PSW version 2.50; Perimed) to determine the contribution of the five frequency components (VFB, vasomotion frequency band) to the variability of the laser Doppler signal [i.e., endothelial, 0,01–0,02 Hz (VFB_E); neurogenic, 0,02–0,06 Hz (VFB_N); myogenic, 0,06–0,15 Hz (VFB_M); respiratory, 0,15–0,40 Hz (VFB_R); and heartbeat, 0,40–1,60 Hz (VFB_H)].

The evaluation was performed at the following 3 times during each measurement: in the resting condition, during the thermal stimulation test (44°C) and after post-ischaemic hyperaemia [8]. The results of the skin flowmotion assessment are presented in Power Density Units [PU/Hz] [9].

Percutaneous O_2 pressure measurement ($TcpO_2$) was performed using a Clark electrode (tc electrode REF 945-605, E 5250-$TcpO_2$, Radiometer Medicals Aps, Denmark) and the PF 5040 $TcpO_2$/pCO_2 module of the Periflux System 5000.

Determination of flow-mediated vasodilation

Determination of flow-mediated vasodilation was performed according to the recommendations of the International Brachial Artery Reactivity Task Force [10]. Calculations related to endothelial-dependent flow-mediated dilation (FMD) and flow-mediated endothelium-independent vasodilation after the administration of nitroglycerin (NMD).

Before the study, approval was obtained from the local bioethics committee of the Medical University of

Poznan. STATISTICA v.9 from StatSoft was used for statistical analysis. The Mann-Whitney test for group comparisons and the Wilcoxon test for measurement comparisons within groups were used. Additionally, the Spearman correlation index was used, and values of $p < 0.05$ were considered statistically significant.

Results

The mean ABI values were 0.53 ± 0.2 in Group 1; 0.75 ± 0.13 in Group 2 and 1.0 ± 0.05 in the control group. The values differed significantly between the specific groups (Table 2).

When analysing the relationship between the values of the studied parameters and the comorbidities and risk factors, two significant differences were observed:

— diabetic patients from Group 2 showed a significant deterioration in the value of endothelium-dependent flow-mediated vasodilation (FMD) (Table 3);
— smokers from Group 3 showed a significant decrease in the value of transcutaneous partial pressure of oxygen (Table 4).

Except for the above-mentioned situations, the impact of comorbidities and risk factors on microcirculatory parameters was not observed (Tables 3–5).

Comparison of Groups 1 and 3

Significantly lower values than in healthy subjects were observed in the patients with advanced forms of atherosclerotic ischaemia of the lower limbs:
— at rest — power density of the muscular layer bond;

Table 2. Comparison of values and the level of significance for the differences between the distribution of values for the characteristics of microcirculation in the members of treatment groups
Tabela 2. Porównanie wartości i poziomu istotności dla różnic między rozkładem wartości charakteryzującej mikrokrążenie w poszczególnych grupach

Study parameter		Units	Study group			Significance level (p)		
			1	2	3	2 *vs.* 3	1 *vs.* 3	1 *vs.* 2
Conditions at rest	SBF	PU	12.05 ± 3.45	12.05 ± 3.45	12.16 ± 6.80	0.174	0.052	0.271
	VFB_E	PU/Hz	1.06 ± 0.41	1.06 ± 0.41	1.01 ± 0.72	0.173	0.443	0.164
	VFB_N	PU/Hz	1.15 ± 0.69	1.15 ± 0.69	1.28 ± 0.56	0.509	0.159	0.546
	VFB_M	PU/Hz	1.33 ± 0.65	1.33 ± 0.65	1.50 ± 0.91	0.690	0.002	< 0.001
	VFB_R	PU/Hz	0.41 ± 0.17	0.41 ± 0.17	0.41 ± 0.19	0.617	0.918	0.433
	VFB_H	PU/Hz	0.62 ± 0.28	0.62 ± 0.28	0.58 ± 0.39	0.192	0.465	0.328
	VFB	PU/Hz	4.57 ± 1.16	4.57 ± 1.16	4.78 ± 2.13	0.664	0.207	0.001
Thermal stimulation test	SBF	PU	75.05 ± 24.43	75.05 ± 24.43	136.05 ± 58.2	< 0.001	< 0.001	< 0.001
	VFB_E	PU/Hz	6.59 ± 3.39	6.59 ± 3.39	8.61 ± 7.28	0.340	< 0.001	< 0.001
	VFB_N	PU/Hz	2.37 ± 1.53	2.37 ± 1.53	2.75 ± 1.24	0.285	0.012	0.204
	VFB_M	PU/Hz	2.98 ± 1.31	2.98 ± 1.31	4.15 ± 2.16	0.018	< 0.001	< 0.001
	VFB_R	PU/Hz	1.20 ± 0.70	1.20 ± 0.70	1.23 ± 0.61	0.609	0.259	0.580
	VFB_H	PU/Hz	5.38 ± 2.38	5.38 ± 2.38	5.87 ± 4.14	0.728	0.690	0.186
	VFB	PU/Hz	18.51 ± 5.03	18.51 ± 5.03	22.61 ± 11.96	0.498	< 0.001	< 0.001
Ischaemic stimulation test	SBF	PU	62.30 ± 27.93	62.30 ± 27.93	60.88 ± 32.32	0.664	< 0.001	< 0.001
	VFB_E	PU/Hz	2.15 ± 1.06	2.15 ± 1.06	2.45 ± 1.80	0.957	0.014	< 0.001
	VFB_N	PU/Hz	2.85 ± 1.71	2.85 ± 1.71	3.07 ± 1.66	0.977	0.334	0.483
	VFB_M	PU/Hz	2.14 ± 0.99	2.14 ± 0.99	2.25 ± 1.26	0.939	< 0.001	< 0.001
	VFB_R	PU/Hz	0.97 ± 0.58	0.97 ± 0.58	0.92 ± 0.61	0.526	0.951	0.384
	VFB_H	PU/Hz	4.42 ± 1.98	4.42 ± 1.98	4.30 ± 2.53	0.669	0.821	0.224
	VFB	PU/Hz	12.53 ± 3.07	12.53 ± 3.07	13.00 ± 5.57	0.931	0.034	< 0.001
Thermal stimulation test index			3.12 ± 1.30	6.39 ± 1.68	12.60 ± 5.97	< 0.001	< 0.001	< 0.001
Ischaemic stimulation test index			2.17 ± 0.97	5.19 ± 1.77	5.48 ± 3.10	0.627	< 0.001	< 0.001
$TpcO_2$		mm Hg	19.76 ± 12.20	47.54 ± 14.86	64.30 ± 7.25	< 0.001	< 0.001	< 0.001
ABPI		m^2/kg	0.53 ± 0.21	0.75 ± 0.13	1.00 ± 0.05	< 0.001	< 0.001	< 0.001
FMD			4.11 ± 2.02	7.44 ± 2.58	9.33 ± 3.87	0.010	< 0.001	< 0.001
NMD			14.06 ± 3.60	14.03 ± 4.33	19.64 ± 5.99	< 0.001	< 0.001	0.762

Grey highlighting indicates the presence of significant differences in the study parameters

Table 3. Relationship between the endothelium-dependent flow-mediated vasodilation (FMD) and the risk factors in individual groups of patients
Tabela 3. Zależność pomiędzy wartością wazodylatacji indukowanej przepływem (FMD) a występowaniem czynników ryzyka w poszczególnych grupach

Risk factor	Group	Yes			No			p
		Number of patients	Mean	Standard deviation	Number of patients	Mean	Standard deviation	
Smoking	1	94	4.07	1.88	43	4.2	2.3	0.82
	2	54	7.4	2.64	25	7.52	2.49	0.62
	3	9	10.08	2.71	18	8.95	4.35	0.17
Diabetes	1	39	3.02	1.57	98	4.54	2.02	<0.05
	2	12	6.43	1.67	67	7.62	2.68	0.16
Arterial hypertension	1	86	4.07	2.06	51	4.17	1.96	0.65
	2	46	7.65	2.81	33	7.14	2.22	0.64
Stroke/TIA	1	28	4.27	2.22	109	4.07	1.97	0.68
	2	15	4.55	2.53	64	4.37	2.09	0.89
Angina pectoris/ /myocardial infarction	1	61	3.94	1.74	76	4.24	2.15	0.59
	2	32	7.58	2.42	47	7.35	2.7	0.51

Table 4. Relationship between the percutaneous measurement of oxygen partial pressure and the risk factors in individual groups of patients
Tabela 4. Zależność pomiędzy przezskórnym ciśnieniem parcjalnym tlenu a występowaniem czynników ryzyka w poszczególnych grupach

Risk factor	Group	Yes			No			p
		Number of patients	Mean	Standard deviation	Number of patients	Mean	Standard deviation	
			mm Hg			mm Hg		
Smoking	1	94	19.55	12.06	43	20.19	12.61	0.78
	2	54	48.11	13.5	25	50.62	17.33	0.21
	3	9	66.54	4.18	18	63.18	8.26	0.04
Diabetes	1	39	19.19	12.49	98	19.98	12.14	0.72
	2	12	44.59	14.72	67	48.06	14.93	0.46
Arterial hypertension	1	86	19.65	12.35	51	19.93	12.06	0.88
	2	46	47.26	12.9	33	47.92	17.42	0.88
Stroke/TIA	1	28	21.14	11.63	109	19.4	12.36	0.3
	2	15	16.14	7.69	64	17.44	10.74	0.88
Angina pectoris/ /myocardial infarction	1	61	18.07	10.73	76	21.09	13.17	0.2
	2	32	47.39	13.33	47	47.31	15.95	0.87

— at thermal stimulation — cutaneous blood flow, power density of the endothelial, neurogenic and myogenic vasomotion frequency bonds and the thermal stimulation test index;
— at ischaemic stimulation — cutaneous blood flow, power density of the endothelial and myogenic vasomotion frequency bonds and the ischaemic stimulation test index;
— flow-mediated endothelium-dependent vasodilation;
— transcutaneous partial pressure of oxygen (Table 2).

Comparison of Groups 1 and 2

Significantly lower values than in Group 2 subjects were observed in Group 1 patients:
— at rest – power density of the muscular layer bond;
— at thermal stimulation — cutaneous blood flow, power density of the endothelial and myogenic vasomotion frequency bonds and the thermal stimulation test index;
— at ischaemic stimulation — cutaneous blood flow, power density of the endothelial and myogenic vasomotion frequency bonds and the ischaemic stimulation test index;

Table 5. Relationship between the flow-mediated non-endothelium dependent vasodilation (NMD) and the risk factors in individual groups of patients
Tabela 5. Zależność pomiędzy wazodylatacją niezależną od śródbłonka (NMD) a występowaniem czynników ryzyka w poszczególnych grupach

Risk factor	Group	Yes			No			p
		Number of patients	Mean	Standard deviation	Number of patients	Mean	Standard deviation	
Smoking	1	94	14.29	3.52	43	13.55	3.74	0.36
	2	54	13.97	4.15	25	14.16	4.76	0.86
	3	9	20.63	5.63	18	14.14	6.26	0.79
Diabetes	1	39	14.81	4.18	98	13.76	3.31	0.12
	2	12	15.42	4.63	67	13.78	4.25	0.23
Arterial hypertension	1	86	14.05	3.73	51	14.06	3.37	0.99
	2	46	14.14	3.62	33	13.88	5.2	0.6
Stroke/TIA	1	28	14.62	3.59	109	13.91	3.59	0.35
	2	15	14.04	3.24	64	13.76	3.38	0.78
Angina pectoris/	1	61	14.13	3.73	76	13.99	3.51	0.82
/myocardial infarction	2	32	14.5	4.07	47	13.71	4.5	0.42

— both the endothelium-dependent and endothelium--independent flow-mediated vasodilation;
— transcutaneous partial pressure of oxygen (Table 2).

Comparison of Groups 2 and 3

The values of perfusion at rest and in ischaemic stimulation test were comparable between the groups. Significant differences were revealed during the thermal stimulation test. Cutaneous blood flow was lower in healthy people, and power density of the muscular layer bonds and the thermal stimulation test index were lower in Group 2 (Tables 2–4).

FMD, NMD, $TcpO_2$ and ABPI values were significantly lower in patients from Group 2. All other values of perfusion were comparable in the study populations (Table 2).

Discussion

Including subjects with risk factors for atherosclerosis into the control group, which was adopted in this study, is not a routine procedure. In most studies related to microcirculation in patients with atherosclerosis, the reference system is formed by healthy people with no risk factors [11, 12]. However, we considered that to be inappropriate, as the modifying influence of risk factors, particularly of diabetes and smoking, on the parameters of the flow in microcirculation has been already confirmed. Please note that the only possible effect of revascularization is to restore the normal flow in the main arterial trunks. Therefore, after a haemodynamically successful revascularization, the newly-formed group, a population comparable to our Groups 2 and 3, includes patients with no significant disturbances in the flow but with risk factors present.

We did not observe significant differences in the value of cutaneous flow at rest or in stimulation tests; no significant differences were also observed in the power density of individual vasomotion bonds in patients with and without diabetes. Such a relationship only occurred in relation to the value of endothelium-dependent flow-mediated vasodilation.

However, it should be noted that correct results observed in laser-Doppler flowmetry do not confirm the absence of changes in the microciculatory function. According to Jorneskog, evaluation of microcirculatory flow only on the basis of laser-Doppler flowmetry is insufficient for PAOD stage II patients with diabetes. Cutaneous blood flow, both at rest and in ischaemic stimulation test, often assumes values falling within the broad range of standards, despite the clinically observed tendency to form skin ulcerations. A flattened congestion phase wave in the ischaemic stimulation test was observed only in some cases. In this case, it may be helpful to perform videometric capillaroscopy, allowing to demonstrate that the normal amount of blood reaching the feet passes through the arterio-venous anastomoses and does not reach the capillaries [13].

Isolated abnormalities of the vasomotion bond, dependent on sympathetic fibres, were found in relation to the patients with diabetes [14]. It turned out then that the analysis of the vasomotion bonds is a tool more accurate to study the risk of developing diabetic foot than neu-

rological tests [15]. Diabetes-related impairment of the sympathetic nerve function (neuropathy) may determine the increase in the microcirculatory flow, especially on the feet and lower legs during longer periods of standing. Clinically, this condition may result in the development of persistent knee joint oedema [16].

However, the presence of diabetes did not have any impact on the changes in the peripheral perfusion in patients undergoing haemodialysis in the course of chronic renal failure. The range of changes observed during dialysis and related to significant decrease in peri-ankle tension, thermal stimulation test index and transcutaneous partial pressure of oxygen was comparable in both groups of patients, i.e. with and without diabetes [12].

Our analysis showed no differences in the distribution of power density of individual vasomotion bonds between the patients with newly diagnosed and persistent arterial hypertension, as compared with healthy subjects. Also, other authors did not observe any significant differences in the values of skin flow at rest or after stimulation tests between subjects with and without arterial hypertension [17–19]. Such differences were demonstrated during studies on vasomotion bonds. In the case of newly diagnosed arterial hypertension, increase in the power density for the endothelial bond, with no changes in the power density values for the myogenic and neurogenic bonds, was observed in thermal stimulation test. In contrast, patients with persistent arterial hypertension exhibited increases in the power density of the myogenic bond and no simultaneous increase in the value of power density for the endothelial or neurogenic bonds [18]. Such a distribution of results indicates a progressive impairment of endothelial function under the influence of persistent arterial hypertension. The restoration of the muscle function to generate vasomotion observed in a later period is interpreted as a positive effect of hypotensive therapy, with no simultaneous improvement, even after the endothelial bond fades out [17].

The third risk factor that could affect microcirculatory parameters is smoking. Decrease in the value of transcutaneous partial pressure of oxygen in smokers was observed only in the group of healthy subjects. We did not find any differences between smokers and non-smokers, regardless of the severity of their clinical symptoms.

Similar observations were also reported by Edvinsson [20]. However, Rossi did not observe any significant differences in skin flow values or power density of individual vasomotion bonds under resting conditions but he found a significant reduction in the value and power density of the endothelial, myogenic and neurogenic bonds in smokers, as compared to non-smokers [21]. Such a change in the perfusion parameters serves as evidence of significant impairment of the endothelial and muscular functions and the way in which human sympathetic system works under the influence of smoking. The decisive role of impaired endothelial function by nicotine was confirmed by Celermajer [22]. Examining a group of male subjects under the age of 30, who were active or passive smokers, he showed a decrease of flow-mediated endothelium-dependent vasodilation with no significant changes during a test with nitroglycerin which is a factor decontracting the vessels independently of the endothelium.

In respect of the clinical assessment of limb perfusion, it was interesting to observe a comparable value of resting skin blood flow in the limbs of healthy subjects (Group 3) and smaller (Group 2) and advanced (Group 1) atherosclerotic lesions. The phenomenon of similar values of skin blood flow can be explained by the important role which is played by the skin vessels in the creation of collateral circulation in patients with advanced forms of atherosclerotic lesions in subfascial arterial trunks. Despite muscle ischaemia, the appearance and warmth of the skin may remain unchanged, which can make it difficult to decide about the need/recommendation to perform revascularization in patients with short-distance claudication but appropriate limb warmth [23]. Therefore it would be advisable to perform provocative tests, e.g. thermal stimulation test and ischaemic stimulation test, which indicate the impairment of the functional microcirculatory reserve. The scope of impairment increases in proportion to the severity of clinical symptoms of ischaemia.

Conclusions

The occurrence of mild forms of PAOD is associated with a worse systemic vascular function expressed as a reduction in the scope of flow-mediated vasodilation and locally in $TcpO_2$ decrease. The occurrence of advanced forms of ischaemia was accompanied by a significant severity of local symptoms, mainly in the form of further reduction in $TcpO_2$ and a drastic reduction or exhaustion of the functional microcirculatory reserve.

Among the evaluated risk factors for atherosclerosis only diabetes and smoking significantly modified perfusion, which resulted in a significant decrease in the values of flow-mediated vasodilation and $TcpO_2$.

Microcirculation characteristics in patients with varying severity of atherosclerotic lesions may be helpful in evaluating revascularization procedures effective-

ness. Cutaneous blood flow maintenance in patients with advanced forms of PAOD indicates that clinical assessment of ischaemic limbs may be insufficient at the initial qualification of PAOD patients to surgical treatment.

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