

Exercise-induced mobilisation of endothelial progenitor cells in patients with premature coronary heart disease

Maciej Kaźmierski¹, Wojciech Wojakowski¹, Aleksandra Michalewska-Włodarczyk¹, Ewa Podolecka¹, Maciej Kotowski², Bogusław Machaliński², Michał Tendera¹

¹3rd Department of Cardiology, Upper Silesian Cardiology Centre, Medical University of Silesia, Katowice, Poland

²Department of General Pathology, Pomeranian Medical University, Szczecin, Poland

Abstract

Background: Endothelial progenitor cells (EPC) derive from bone marrow and participate in both endothelial regeneration and development of new blood vessels. EPC also play a role in the atherosclerotic process, and their number correlates negatively with the presence of classical risk factors.

Aim: To evaluate circulating EPC count and their exercise-induced mobilisation in patients with premature coronary artery disease (CAD).

Methods: The study group included 60 patients with stable CAD diagnosed before 45 years of age. The control group consisted of 33 healthy age- and gender-matched volunteers. Venous blood was sampled 3 times in order to assess circulating EPC count immediately before an exercise test (EPC 0) and at 15 min (EPC 15) and 60 min (EPC 60) after the exercise test.

Results: Circulating EPC count in the study group at rest and at 15 min after exercise was comparable (2.1 vs. 2.1 cell/ μ L, $p = 0.35$) and increased significantly at 60 min after exercise in comparison to resting values (2.1 vs. 3.2 cell/ μ L, $p < 0.00001$). In the control group, circulating EPC count increased significantly at 15 min after exercise (2.0 vs. 3.5 cell/ μ L, $p < 0.0001$) but later decreased at 60 min after exercise, although it remained greater than at rest (2.7 vs. 2.0 cell/ μ L, $p < 0.0002$). Circulating EPC count at rest and at 60 min after exercise was comparable in the two groups (2.1 vs. 2.0 cell/ μ L, $p = 0.96$; and 3.2 vs. 2.7 cell/ μ L, $p = 0.13$, respectively) but it was significantly lower in the study group compared to the control group at 15 min after exercise (2.1 vs. 3.5 cell/ μ L, $p < 0.00001$). Circulating EPC count at rest and at 15 min after exercise did not correlate with the number of stenosed coronary arteries but at 60 min after exercise it was greater in patients with one-vessel disease compared to those with two- or three-vessel disease (4.2 vs. 3.4 cell/ μ L, $p = 0.01$; and 4.2 vs. 2.3 cell/ μ L, $p = 0.00003$). However, no difference in circulating EPC count was seen at 60 min after exercise between patients with two- or three-vessel disease (3.4 vs. 2.3 cell/ μ L, $p = 0.3$).

Conclusions: 1. Circulating EPC count at rest is comparable between subjects with premature atherosclerosis and healthy volunteers. 2. A single bout of physical exercise causes a significant increase in circulating EPC count in both groups, but the dynamics of exercise-induced EPC mobilisation is different, with delayed exercise-induced EPC mobilisation in subjects with premature CAD. 3. The extent of atherosclerotic coronary lesions does not influence circulating EPC count at rest.

Key words: endothelial progenitor cells, premature coronary heart disease, physical exercise

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INTRODUCTION

Coronary artery disease (CAD) and myocardial infarction (MI) are major causes of mortality and disability. More than 80% of MIs occur in subjects after 50 years of age. Younger subjects, i.e.

those below 40 years of age, account for only 3–10% of all cases of MI [1, 2]. CAD is often considered premature if diagnosed before 55 or 60 years of age in men and before 65 years of age in women [3–5]. Based on Framingham study risk stratification

Address for correspondence:

Ewa Podolecka, MD, 3rd Department of Cardiology, Upper Silesian Cardiology Centre, Medical University of Silesia in Katowice, ul. Ziołowa 45/47, 40–635 Katowice, Poland, e-mail: epodolecka@interia.pl

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tables and multiple data on the incidence of MI, it may be concluded that the incidence of CAD in the general population begins to increase after 40–45 years of age [1, 6, 7].

Age-related cellular senescence results from accumulating damage due to oxidative stress, and telomere shortening resulting in progressively impaired potential for cell division. Due to intense effects of these factors, vessel regeneration becomes gradually impaired [8, 9]. In the cardiovascular system, cellular senescence is seen as a series of parallel changes that mostly include abnormal vessel wall tone balance related to impaired nitric oxide synthesis and increased angiotensin and endothelin levels [10], impaired angiogenesis and regulation of vessel wall repair mechanisms [11], and a reduced number and impaired function of circulation endothelial progenitor cells (EPC), including their role in neovascularisation [12].

Circulating EPC are a heterogeneous population of cells occurring in a very low number (single cells in 1 μL), with characteristics similar to those of embryonal angioblasts at a varying level of maturity [13]. They mostly derive from bone marrow and are mobilised in response to chemotactic factors released, among others, by the endothelium. Features of EPC include their viability and ability to form colonies *in vitro* and differentiate into mature endothelial cells [13, 14]. The initial report of the role of EPC in ongoing endothelial regeneration was published in 2003 by Hill et al. [15] who showed a relation between the number of circulating EPC and endothelial function. Their studies also showed a clear relation between the number of EPC and the overall risk of cardiovascular events, and a reduction in the number of circulating EPC correlated with progression of cardiovascular disease. EPC mediate regeneration of damaged artery, inhibiting progression of atherosclerosis in experimental models of permanent vascular wall damage [16, 17].

In the present study, we evaluated the hypothesis that premature CAD may be related to a reduced number of circulating EPC and their impaired mobilisation.

METHODS

Study group

The study was conducted at the 3rd Chair and Department of Cardiology, Medical University of Silesia, Katowice, Poland, in 93 subjects who were divided into two subsets: the study group and the control group. The study group included 60 patients who fulfilled the following inclusion criteria: women and men aged 18–50 years, CAD diagnosed before 45 years of age and confirmed by invasive coronary angiography showing the presence of at least one 70% stenosis in at least 1 of the 3 major coronary arteries, the New York Heart Association (NYHA) functional class I, stable Canadian Cardiovascular Society (CCS) class \leq II, and a written consent for participation in the study.

Exclusion criteria included unstable angina; uncontrolled hypertension; NYHA class II–IV; atrial fibrillation; haemodynamically significant valvular heart disease; inflammatory, au-

toimmune or neoplastic disease; use of nitroglycerin or related drugs, growth hormone, erythropoietin, oral antidiabetic drugs from the thiazolidinedione class (rosiglitazone, pioglitazone), and oral contraceptives; haemoglobin level $<$ 10.0 g/dL; creatinine level \geq 1.4 mg/dL; platelet count $<$ 100,000/ μL ; inability to perform an exercise test; pregnancy; and lack of a written consent for participation in the study.

Sixty patients with stable CAD were included into the study. In all participants, coronary angioplasty was performed more than 1 year before inclusion into the study. None of the studied subjects received clopidogrel and antiplatelet drugs other than aspirin.

The control group consisted of 33 healthy volunteers who were matched for gender and age to the patients in the study group. The inclusion criteria for the control group were healthy women and men aged 18–50 years who received no chronic treatment, and a written consent for participation in the study. The exclusion criteria were clinical evidence of ischaemic heart disease, hypertension, NYHA class II–IV, atrial fibrillation, haemodynamically significant valvular heart disease, haemoglobin level $<$ 10.0 g/dL, creatinine level \geq 1.4 mg/dL, platelet count $<$ 100,000/ μL , inability to perform an exercise test, use of oral contraceptives, pregnancy, and lack of a written consent for participation in the study.

Echocardiographic examination

In all patients, transthoracic echocardiography was performed using a Sonos 7500 device with a 2.5 MHz probe (Hewlett-Packard, USA). The following parameters were evaluated: left ventricular (LV) end-diastolic dimension, LV end-systolic dimension, LV end-diastolic volume, LV end-systolic volume, LV ejection fraction (LVEF), and left atrial dimension. Chamber volumes and LVEF were calculated using the Simpson method.

Carotid artery ultrasonography

Carotid artery ultrasonography was performed using a Sonos 7500 device with a 11 MHz probe (Hewlett-Packard, USA). Both common carotid arteries underwent real-time imaging in two opposed planes. Measurements of the intima-media complex were performed within the distal walls of both common carotid arteries, 20 mm below the carotid bulb. Measurements were performed in the longitudinal axis of the vessel at end-diastole. Normal IMT was defined as \leq 0.8 mm [18].

Electrocardiographic exercise test

Electrocardiographic (ECG) exercise test was performed in all subjects included into the study. The examination was performed on a treadmill (CASE, GE Healthcare, USA) using the standard Bruce protocol, with continuous ECG monitoring and blood pressure measurements. Duration of exercise and workload in the control group were adjusted to these parameters in the study group so as to obtain comparable energy expenditure (in metabolic equivalents [MET]) in both groups.

Invasive coronary angiography

Invasive coronary angiography was performed in all subjects in the study group during previous diagnostic workup for CAD. A finding of at least one significant stenosis in at least one major coronary artery was the inclusion criterion for the study. Coronary angiography procedures were performed in the Department of Invasive Cardiology, Upper Silesian Cardiology Centre in Katowice, in 2004–2009. The procedure was performed via the right femoral artery or the right radial artery approach. Following insertion of a vascular sheath, selective angiography of both coronary arteries was performed by contrast agent injections using standard sets of coronary catheters. The right coronary artery was imaged in at least 2 opposed views, and the left coronary artery was imaged in at least 4 different views. Coronary angiographic images were documented and archived on CD discs. The degree of vessel stenosis was calculated using quantitative coronary angiography.

Evaluation of EPC count

Peripheral venous blood was sampled 3 times to EDTA-containing tubes using a vacuum system in order to assess circulating EPC count immediately before the exercise test (EPC 0) and at 15 min (EPC 15) and 60 min (EPC 60) after the exercise test. Blood samples stored at 4°C were sent for determination of the number of circulating CD34(+)CD133(+)VEGFR-2(+) cell to a laboratory at the Department of General Pathology, Pomeranian Medical University, Szczecin, Poland. The number of circulating CD34(+)CD133(+)VEGFR-2(+) cells was calculated as leukocyte percentage. Peripheral blood mononuclear cells were isolated by centrifugation at density gradient and incubated with antibodies in dark conditions for 20 min at 4°C. Goat anti-rabbit IgG antibodies conjugated with fluorescein isothiocyanate (FITC) were used as secondary antibodies and added to each test tube. Secondary antibodies were also used as a negative control. Cell suspension was incubated in dark conditions for 10 min at room temperature with a mixture of mouse monoclonal anti-human CD34 antibodies conjugated with phycoerythrin (PE) and mouse monoclonal anti-human VEGFR2 (KDR) antibodies conjugated with allophycocyanin (APC), and a mixture of mouse monoclonal anti-human CD133 antibodies conjugated with PE and KDR antibodies conjugated with APC. Following incubation, cells were washed and suspended in paraformaldehyde fixing solution until flow cytometry. Determinations of the cell count were performed

according to the ISHAGE guidelines using a FACS Calibur cytometer (Beckton Dickinson), and the results were expressed as the number of EPC per μL .

Statistical analysis

Statistical analysis was performed using the Statistica 7.1 software (StatSoft Polska) and included simple analyses with evaluation of relations and between-group differences. Quantitative variables were shown as medians and ranges (minimum–maximum). Normal distribution of quantitative variables was verified using the Kolmogorov-Smirnov test. Qualitative variables were expressed as absolute values and percentages. Relations between variables were evaluated using non-parametric Spearman rank correlation analysis. Between-group differences in quantitative variables were evaluated using the Mann-Whitney U test and the Kruskal-Wallis test. If a significant difference was seen by the Kruskal-Wallis test, *post-hoc* analysis was performed using the Mann-Whitney U test. To evaluate differences in qualitative variables between groups, the χ^2 test, the χ^2 test with Yates correction, or the exact Fisher test was used depending on sample size. $P < 0.05$ was considered statistically significant.

The study was performed according to a protocol approved by the Bioethics Committee at the Medical University of Silesia in Katowice (approval No. KNW/0022/KB 1/38/1/09, dated 19.05.2009). Each study participant received, read and personally signed the patient information form (“Informacja dla badanego”) and the patient statement (“Oświadczenie Badanego”), thereby giving an informed consent for participation in the study.

RESULTS

The two study groups did not differ in regard to age, gender distribution, and body mass index (Table 1). In the study group, hypertension was present in 48% of subjects, carbohydrate metabolism disturbances in 18% of subjects, hypercholesterolaemia in 37% of subjects, and hypertriglyceridaemia in 25% of subjects. History of smoking was reported by 82% of subjects, positive family history for cardiovascular disease by 32% of subjects, and 40% subjects were obese. The mean number of risk factors per subject was 2.8 (Table 2). All subjects in the study group received a statin, aspirin, and a beta-blocker. Angiotensin-converting enzyme inhibitors were used by 85% of patients, and angiotensin receptor antagonists by 7% of patients (Table 2).

Table 1. Overall comparison of the study and control groups

	Study group (n = 60)	Control group (n = 33)	P
Age [years]	43 (35–49)	42 (34–49)	0.06
Gender (male/female)	49 (72%)/11 (28%)	27 (82%)/6 (18%)	0.99
Body mass index [kg/m^2]	28.7 (19.6–43.4)	27.4 (19.8–37.7)	0.49

Table 2. Characteristics of the study group (n = 60)

Risk factors for atherosclerosis	
1. Hypertension	29 (48%)
2. Carbohydrate metabolism disturbances, including:	11 (18%)
Impaired glucose tolerance	4 (7%)
Diabetes type 2	4 (7%)
Diabetes type 1	3 (5%)
3. Hypercholesterolaemia	22 (37%)
4. Hypertriglyceridaemia	15 (25%)
5. History of smoking	49 (82%)
Current smoking	7 (12%)
6. Family history of CAD:	19 (32%)
Father	12 (20%)
Mother	4 (7%)
Both father and mother	3 (5%)
7. Obesity	24 (40%)
Number of risk factors per patient	
0 risk factors	3 (5%)
1 risk factor	10 (17%)
2 risk factors	11 (18%)
3 risk factors	15 (25%)
4 risk factors	11 (18%)
5 risk factors	9 (15%)
6 risk factors	1 (2%)
7 risk factors	0 (0%)
Mean number of risk factors per patient	2.8
Medications	
Statin	60 (100%)
Aspirin	60 (100%)
Beta-blocker	60 (100%)
ACE	51 (85%)
Angiotensin receptor antagonist	5 (7%)
Patient age at the time of CA [years]	39.6 (32–45)
ACS as the indication for CA	60 (100%)

ACE — angiotensin-converting enzyme; ACS — acute coronary syndrome; CA — coronary angiography; CAD — coronary artery disease

All subjects in the study group underwent previous coronary angiography due to an acute coronary syndrome. Coronary angiography showed a significant left anterior descending coronary artery stenosis in 27% of patients and a complete occlusion in 23% of patients. Left circumflex coronary artery stenosis was found in 30% of patients and occlusion in 7% of patients. A significant stenosis of the right coronary artery was noted in 23% of patients and a complete occlusion in 28% of patients (Table 3). Overall, single-vessel disease was found in 52% of subjects, two-vessel disease in 30% of sub-

Table 3. Coronary angiographic findings in the study group

Left anterior descending coronary artery	
No lesions	10 (17%)
Stenosis:	
< 50%	17 (28%)
50–70%	3 (5%)
71–99%	16 (27%)
100%	14 (23%)
Left circumflex coronary artery	
No lesions	27 (45%)
Stenosis:	
< 50%	10 (17%)
50–70%	1 (2%)
71–99%	18 (30%)
100%	4 (7%)
Right coronary artery	
No lesions	17 (28%)
Stenosis:	
< 50%	9 (15%)
50–70%	3 (5%)
71–99%	14 (23%)
100%	17 (28%)
Number of stenosed vessels	
Single-vessel disease	31 (52%)
Two-vessel disease	18 (30%)
Three-vessel disease	11 (18%)

jects, and three-vessel disease in 18% of subjects (Table 3). In the study group, all LV dimensions and left atrial dimension were significantly higher, and LVEF was significantly lower compared to the control group (Table 4). Ultrasonography showed significantly higher IMT in the study group compared to the control group (0.55 vs. 0.44 mm, $p < 0.00001$, Table 5).

Circulating EPC count at rest and at 60 min after exercise did not differ significantly between the two groups (2.1 vs. 2.0 cell/ μ L, $p = 0.96$; and 3.2 vs. 2.7 cell/ μ L, $p = 0.13$, respectively) but it was significantly lower in the study group compared to the control group at 15 min after exercise (2.1 vs. 3.5 cell/ μ L, $p < 0.00001$) (Table 6). In the study group, circulating EPC count was comparable at rest and at 15 min after exercise (2.1 vs. 2.1 cell/ μ L, $p = 0.35$) but it increased significantly at 60 min after exercise in comparison to resting values (2.1 vs. 3.2 cell/ μ L, $p < 0.00001$, Table 6). In the control group, circulating EPC count increased significantly at 15 min after exercise (2.0 vs. 3.5 cell/ μ L, $p < 0.0001$) but later decreased at 60 min after exercise, although it remained greater than at rest (2.7 vs. 2.0 cell/ μ L, $p < 0.0002$, Table 6).

The number of stenosed coronary arteries in the study group did not correlate with circulating EPC count at rest and at 15 min after exercise but at 60 min after exercise it was greater in patients with one-vessel disease compared to those with two- or three-vessel disease (4.2 vs. 3.4 cell/ μ L, $p = 0.01$;

Table 4. Transthoracic echocardiography

Parameters (N: normal values)	Study group (n = 60)	Control group (n = 33)	P
Left ventricular ejection fraction (N: $\geq 50\%$)	51 (25–70)	61 (55–73)	< 0.00001
Left ventricular end-diastolic diameter (N: 35–57 mm)	55 (40–71)	50 (41–63)	0.0005
Left ventricular end-systolic diameter (N: 22–40 mm)	36 (23–59)	30 (22–49)	< 0.00001
Left ventricular end-diastolic volume (N: 104 ± 25 mL)	143 (71–310)	117 (68–260)	0.01
Left ventricular end-systolic volume (N: 33 ± 13 mL)	71 (20–150)	46 (21–116)	< 0.00001
Left atrium (N: 19–40 mm)	40 (30–53)	36 (30–43)	0.0001

Table 5. Intima–media thickness (IMT) in the study and control groups

	Study group (n = 120)	Control group (n = 66)	P
IMT common carotid artery [mm]	0.55 (0.36–1.49)	0.44 (0.28–0.79)	< 0.00001
IMT common carotid artery > 0.8 [mm]	13 (11%)	0 (0%)	< 0.04

Table 6. Number and post-exercise mobilisation of endothelial progenitor cells (EPC)

	Study group (n = 60)	Control group (n = 33)	P
Workload [METs]	9.9 (2.7–12)	10.1 (5.2–10.2)	0.07
EPC 0*	2.1 (0–6.3)	2.0 (0–5.1)	0.96
EPC 15*	2.1 (0.5–4.9)	3.5 (1.3–5.6)	< 0.00001
EPC 60*	3.2 (0.6–7.4)	2.7 (1–4.8)	0.13
EPC 15 – EPC 0**	0.2 (–1.6 to 2)	1.5 (–1.1 to 4.1)	< 0.00001
EPC 60 – EPC 0***	1.1 (–1.4 to 4.3)	0.8 (–3.4 to 3.1)	0.17
	EPC 0*	EPC 15*	P
Study group (n = 60)	2.1 (0–6.3)	2.1 (0.5–4.9)	0.35
Control group (n = 33)	2.0 (0–5.1)	3.5 (1.3–5.6)	0.00001
	EPC 0*	EPC 60*	P
Study group (n = 60)	2.1 (0–6.3)	3.2 (0.6–7.4)	< 0.00001
Control group (n = 33)	2.0 (0–5.1)	2.7 (1–4.8)	0.0002

MET — metabolic equivalent; Quantitative variables are expressed as medians and ranges; *EPC count in cells/ μ L; **Difference between EPC count [cells/ μ L] at baseline and at 15 min after exercise; ***Difference between EPC count [cells/ μ L] at baseline and at 60 min after exercise

and 4.2 vs. 2.3 cell/ μ L, $p = 0.00003$, Fig. 1). However, no difference in circulating EPC count was seen at 60 min after exercise between patients with two- or three-vessel disease (3.4 vs. 2.3 cell/ μ L, $p = 0.3$, Fig. 1). No effect of hypertension, carbohydrate metabolism disturbances, hypercholesterolaemia, obesity, positive family history, gender, and age was found on the EPC count at rest and EPC mobilisation during exercise ($p > 0.05$).

DISCUSSION

Numerous studies indicate that bone marrow-derived EPC mobilised to peripheral blood play a role in neovascularisation of ischaemic tissues and arterial regeneration [17]. A reduction in the number of circulating EPC and their impaired function may negatively affect regeneration of vascular endothe-

lium [19]. Results of the first studies showing EPC mobilisation to peripheral blood induced by a single bout of intensive exercise were reported by Rehman et al. [20] in 2004 and a year later by Laufs et al. [21]. Both these studies were performed in healthy volunteers at about 55 years of age. The maximal observed effect was a nearly fourfold increase in EPC count at 10 to 30 min after exercise. In the study by Laufs et al. [21], a significant increase in EPC count was seen in healthy subjects at both 10 and 30 min after exercise compared to resting conditions, with no difference in the mean EPC count in the two measurements after exercise. A similar result was noted by Jenkins et al. [22] in healthy men following a single session of submaximal exercise. A significant increase in EPC count at 30 min after exercise was seen only in previously physically active men ($p = 0.04$) but not in those who were

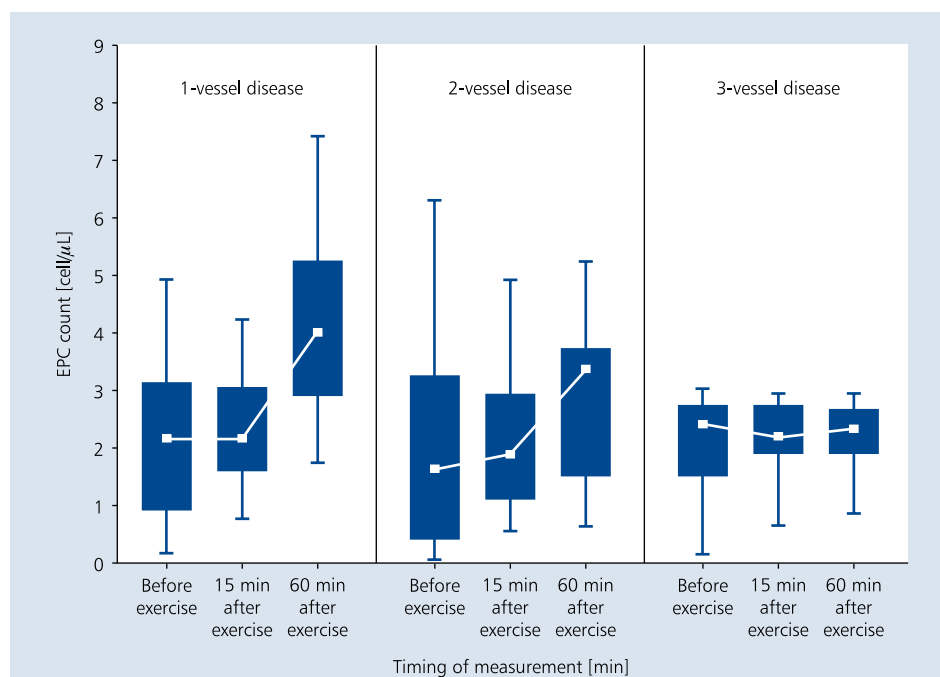


Figure 1. Post-exercise endothelial progenitor cells (EPC) mobilisation in relation to the number of stenosed coronary arteries

not active physically. Van Craenenbroeck et al. [23] studied a group of healthy subjects at varying age before a single bout of exercise and 10, 30, and 60 min and 2, 4, and 8 h afterwards, showing a significant increase in CD34(+)/KDR(+) EPC cells already at 10 min after exercise that was maintained at a similar level until 2 h after exercise.

In our study, a significant increase in EPC count was seen in the control group as early as at 15 min after exercise. At 60 min after exercise, EPC remained significantly higher compared to resting conditions. Our study varies from others in that we observed a different dynamics of post-exercise changes in healthy subjects. At 1 h after exercise, EPC count was still higher compared to resting conditions but decreased compared to the maximum value seen at 15 min after exercise.

Few reports of EPC mobilisation following a single bout of exercise in subjects with ischaemic heart disease have been reported in the literature. Adams et al. [24] studied EPC mobilisation at 10 time points after a single exercise session, i.e. before an exercise test, at 2, 4, 6, and 8 h afterwards, and at every 24 h until 6 days after exercise. Patients with CAD were compared to healthy subjects. Patients were divided into two groups based on coronary angiography and ECG exercise test findings. The first group included patients with a documented > 75% stenosis of a major epicardial vessel and evidence of ischaemia on exercise testing. The other group included patients after coronary angioplasty, without significant coronary stenoses and with no evidence of ischaemia on exercise testing. The study was performed

in subjects aged more than 60 years with LVEF > 60% and showed a significant increase in EPC count only in subjects with angiographically confirmed CAD in whom exercise induced ischaemic changes on ECG. An increase in EPC count was seen at 8 h after exercise, and maximum EPC count was noted at the second day. During the first 8 h after exercise and on the third and subsequent days, EPC count did not differ from baseline values. The highest observed EPC count was increased threefold compared to baseline. Adams et al. [24] showed no significant difference in EPC count between subjects after coronary revascularisation and healthy subjects both at rest and during post-exercise EPC mobilisation.

Our study is the first to evaluate the number of circulating CD34(+)/CD133(+)/KDR(+) cells before and at 15 and 60 min after a single session of controlled exercise in subjects with premature CAD and healthy subjects.

CONCLUSIONS

Circulating EPC count at rest is comparable between subjects with premature atherosclerosis and healthy volunteers.

Patients with premature CAD are characterised by delayed exercise-induced EPC mobilisation.

The extent of stenotic coronary lesions does not influence circulating EPC count at rest. In patients with single- or two-vessel disease, circulating EPC count increases significantly after a single bout of exercise, while no increase in circulating EPC count is seen after exercise in patients with multivessel disease.

Conflict of interest: none declared

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Wysiłkowa mobilizacja komórek progenitorowych śródbłonka u osób z przedwczesną chorobą wieńcową

Maciej Kaźmierski¹, Wojciech Wojakowski¹, Aleksandra Michalewska-Włodarczyk¹, Ewa Podolecka¹, Maciej Kotowski², Bogusław Machaliński², Michał Tendera¹

¹III Oddział Kardiologii, Górnośląski Ośrodek Kardiologii, Śląski Uniwersytet Medyczny, Katowice

²Zakład Patologii Ogólnej, Pomorski Uniwersytet Medyczny, Szczecin

Streszczenie

Wstęp: Komórki progenitorowe śródbłonka (EPC) uczestniczą zarówno w regeneracji śródbłonka, jak i w powstawaniu nowych naczyń. Ponadto odgrywają rolę w procesie miażdżycowym; ich liczba koreluje ujemnie z obecnością klasycznych czynników ryzyka (hipercholesterolemia, cukrzyca, nadciśnienie tętnicze), a regularna aktywność fizyczna znacząco zwiększa liczbę EPC krążących we krwi. Wydaje się, że przedwczesne występowanie choroby wieńcowej (CAD) może być uwarunkowane zmniejszeniem liczby krążących we krwi obwodowej EPC i upośledzeniem ich zdolności do mobilizacji.

Cel: Celem pracy była analiza liczby krążących we krwi obwodowej EPC i ocena ich powysiłkowej mobilizacji wśród osób z przedwczesną CAD.

Metody: Grupę badaną stanowiło 60 osób (49 mężczyzn i 11 kobiet, średni wiek 43 lat) ze stabilną CAD (CCS ≤ II), u których CAD rozpoznano przed 45. rż. Grupę kontrolną utworzono z 33 zdrowych ochotników, dobranych pod względem płci i wieku w stosunku do osób z grupy badanej. Przeprowadzono badania: podmiotowe i przedmiotowe, echokardiograficzne i ultrasonograficzne tętnic szyjnych z pomiarem grubości kompleksu błony środkowej i błony wewnętrznej (IMT), elektrokardiograficzny test wysiłkowy oraz w grupie badanej również angiografię tętnic wieńcowych. Krew żylną do oceny liczby krążących we krwi EPC pobierano 3-krotnie: na czczo bezpośrednio przed próbą wysiłkową (EPC 0), w 15. minucie (EPC 15) oraz w 60. minucie po zakończonym wysiłku (EPC 60).

Wyniki: W grupie badanej wymiary lewej komory i lewego przedsionka były znamienne statystycznie większe, a frakcja wyrzutowa lewej komory istotnie niższa niż w grupie kontrolnej ($p < 0,05$). Wyniki ultrasonografii wykazały w grupie badanej istotne pogrubienie IMT (0,55 vs. 0,44 mm, $p < 0,00001$). W grupie badanej liczba EPC w spoczynku nie różniła się od obserwowanej w 15. minucie po wysiłku (2,1 vs. 2,1 kom/μl; $p = 0,35$), natomiast istotnie wzrosła w 60. minucie po wysiłku w porównaniu z badaniem spoczynkowym (2,1 vs. 3,2 kom/μl; $p < 0,00001$). W grupie kontrolnej liczba EPC w 15. minucie po wysiłku zwiększyła się znamienne (2,0 vs. 3,5 kom/μl; $p < 0,0001$), a liczba EPC w 60. minucie po wysiłku była mniejsza niż w 15. minucie po wysiłku, choć pozostawała nadal większa w porównaniu z wynikiem sprzed wysiłku (2,7 vs. 2,0 kom/μl; $p < 0,0002$). Liczba EPC w spoczynku i 60 minut po wysiłku nie różniła się istotnie między badanymi grupami (odpowiednio 2,1 vs. 2,0 kom/μl; $p = 0,96$ i 3,2 vs. 2,7 kom/μl; $p = 0,13$), natomiast 15 minut po wysiłku liczba EPC w grupie badanej była znamienne mniejsza w porównaniu z grupą kontrolną (2,1 vs. 3,5 kom/μl; $p < 0,00001$). Liczba zwężonych tętnic wieńcowych w grupie badanej nie korelowała z liczbą EPC w badaniu spoczynkowym oraz w 15. minucie po wysiłku, natomiast w 60. minucie po wysiłku liczba EPC u osób z jednonaczyniową CAD była większa w porównaniu z osobami z dwunaczyniową i trójnaczyniową CAD (odpowiednio 4,2 vs. 3,4 kom/μl; $p = 0,01$ i 4,2 vs. 2,3 kom/μl; $p = 0,00003$). Nie wykazano różnic w liczbie EPC w 60. minucie po wysiłku, porównując osoby z dwunaczyniową i trójnaczyniową CAD (3,4 vs. 2,3 kom/μl; $p = 0,3$). W grupie badanej nie stwierdzono również zależności między pomiarem IMT a liczbą EPC w spoczynku i ich mobilizacją 15 minut po wysiłku, natomiast zanotowano ujemną korelację między IMT a liczbą EPC w 60. minucie po wysiłku ($R = -0,37$; $p = 0,003$).

Wnioski: 1. Liczba krążących we krwi obwodowej EPC w spoczynku nie różni się między pacjentami z przedwczesną miażdżycą a osobami zdrowymi. 2. Chorych z przedwczesną CAD charakteryzuje opóźnienie powysiłkowej mobilizacji EPC. 3. Nasilenie zmian zwężających w naczyniach wieńcowych nie wpływa na liczbę krążących we krwi EPC w spoczynku. W grupie osób z jedno- i dwunaczyniową CAD liczba EPC po jednorazowym wysiłku fizycznym istotnie wzrasta. U osób z wielonaczyniową CAD po wysiłku fizycznym nie obserwuje się zwiększonej liczby EPC we krwi.

Słowa kluczowe: komórki progenitorowe śródbłonka, przedwczesna choroba wieńcowa, wysiłek fizyczny

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Adres do korespondencji:

dr n. med. Ewa Podolecka, III Oddział Kardiologii, Górnośląski Ośrodek Kardiologii, Śląski Uniwersytet Medyczny w Katowicach, ul. Ziołowa 45/47, 40–635 Katowice, e-mail: epodolecka@interia.pl

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