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Increasing Physical Tolerance during Cardiac Rehabilitation Helps to Restore Endothelial Function in Patients after Acute Coronary Syndrome

Abstract. In recent years, many studies have been aimed at exploring the possibilities of cardiac rehabilitation as a tool to improve the prognosis in patients after acute coronary syndrome (ACS). Endothelial dysfunction is one of the initiating mechanisms of cardiovascular diseases, and myocardial infarction in particular, so it is important to assess the dynamics of changes in the number of endothelial progenitor cells (EPCs) in patients during cardiac rehabilitation with the increase in physical activity.

The aim. To establish the relationship between the level of recovery of exercise tolerance and the recovery of endothelial function by determining the number of EPCs in patients undergoing cardiac rehabilitation after ACS.

Materials and methods. The study included 44 patients with ST-elevation myocardial infarction who underwent urgent stenting of the infarct-related artery, with a mean age of 59 years (Q_1-Q_3; 51-64). All the study participants underwent laboratory tests (CD45+/CD34+ cell count before and after the exercise test) and instrumental tests (echocardiography, bicycle ergometry, coronary angiography). Statistical processing was carried out using SPSS Statistics 23 (trial version).

Results. According to the results of the exercise test at the first examination, the patients were divided into 2 groups: group 1 with low exercise tolerance (≤50 W) and group 2 with high exercise tolerance (>50 W). The data obtained indicate a link between better recovery of exercise tolerance after ACS and recovery of endothelial function in patients with high exercise tolerance during follow-up compared to the patients whose exercise tolerance did not exceed 50 W, as evidenced by a statistically higher number of EPCs after exercise in patients with a favorable course and high exercise tolerance (3633 vs. 2400 cells/ml) (p=0.006). Patients with low exercise tolerance were more likely to be diagnosed with lesions of left anterior descending coronary artery (96% vs. 70%, p=0.02). More severe coronary vascular lesions with stenosis of 75% of two or more arteries showed lower pre-exercise EPCs, but increased post-exercise EPCs (+228 cells/ml), whereas in the group with stenosis of more than 75% of one vessel, a decrease in post-exercise EPCs (–604 cells/ml) was observed (p=0.004). If patients have more than one stent, there is a 2.5-fold increased risk of decreased exercise tolerance to values of 25-50 W (relative risk = 1.8; 95% confidence interval: 1.3-2.4).

Conclusions. The data obtained indicate that there is an association between a better recovery of exercise tolerance after ACS and recovery of endothelial function in patients with a favorable course at repeated examination, compared to patients whose level of exercise tolerance did not exceed 50 W (low exercise tolerance), as evidenced by a statistically greater number of EPCs after exercise test in patients with favorable course and high exercise tolerance compared with patients with unfavorable course and low exercise tolerance.

Keywords: *circulating progenitor cell, myocardial infarction, exercise test, cardiac rehabilitation, angiogenesis.*

Introduction. Myocardial infarction (MI), also known as a heart attack, is a serious medical condition that occurs when the blood flow to the heart is blocked, leading to damage or death of the heart muscle. The heart is made up of various types of cells, including progenitor cells. In recent years, there has been growing interest in the potential role of progenitor cells in the development and treatment of MI. Progenitor cells are immature cells that have the ability to differentiate into multiple cell types, including heart muscle cells. These cells are present in the heart and can be activated in response to injury or damage, such as that caused by a heart attack [1, 2]. When activated, progenitor cells can migrate to the site of injury and differentiate into heart muscle cells, replacing the damaged tissue and helping to repair the heart [3]. Studies have shown that the activation and migration of endothelial progenitor cells (EPCs) is a critical component of the body's response to MI [4, 5]. These cells play a key role in repairing the heart and preventing further damage. In addition, the number of EPCs in the heart has been shown to be a predictor of the severity of MI and the likelihood of recovery [6, 7]. Despite these promising findings, the use of progenitor cells as a treatment for MI is still at the early stages of development.

Currently, the main challenge is finding a way to effectively deliver the cells to the site of injury and promote their activation and differentiation. However, researchers are actively exploring various strategies, including the use of stem cell transplantation, gene therapy, and pharmacological agents to stimulate the activation of progenitor cells [8, 9]. Further research is needed to fully understand their potential and develop effective treatments that can be used in clinical practice. The response of endocardial progenitor cells to acute myocardial infarction (AMI) is an active area of research in the field of cardiovascular medicine. Endocardial progenitor cells are a type of progenitor cells that are found within the inner lining of the heart, also known as the endocardium. Studies have shown that endocardial progenitor cells can play a role in repairing the heart after AMI [10, 11].

However, the exact mechanisms by which EPCs respond to AMI are not yet fully understood, and more research is needed to determine the best ways to harness their potential for the treatment of heart attacks. In addition to their potential for heart repair and regeneration, EPCs have also been shown to have anti-inflammatory and anti-apoptotic properties, which can help to protect the heart from further damage and promote recovery after injury [12, 13, 14, 15]. Inflammation is a normal response to injury or damage, but if it becomes chronic, it can contribute to further damage and scarring of the heart.

Studies have demonstrated that EPCs can produce growth factors and cytokines that can protect heart muscle cells from apoptosis [16, 17]. For example, EPCs have been shown to secrete factors such as vascular endothelial growth factor and basic fibroblast growth factor, which can stimulate angiogenesis (the growth of new blood vessels) and promote the survival of heart muscle cells [18]. EPCs have also been shown to upregulate anti-apoptotic genes, such as Bcl-2, in response to injury. Bcl-2 is a well-known anti-apoptotic protein that helps to prevent cell death and promote the survival of heart muscle cells [19].

The aim. To establish the relationship between the level of recovery of exercise tolerance and the recovery of endothelial function by determining the number of EPCs in patients undergoing cardiac rehabilitation after acute coronary syndrome (ACS).

Materials and methods. We studied 44 patients with STEMI who underwent urgent stenting of the infarct-related artery with the mean age of 59 years (Q_1-Q_3; 51-64). The exclusion criteria were: left ventricular ejection fraction (LVEF) less than 35, large aneurysm with thrombosis, history of acute cerebrovascular accident, history of cancer, joint diseases, severe rhythm and conduction disorders, recurrent MI. All the patients included in the study underwent laboratory tests (CD45+/CD34+ cell count) and instrumental studies (echocardiography, bicycle ergometry, coronary angiography).

The intracardiac hemodynamics was assessed by echocardiography using Medison SA9900 Prime ultrasound scanner (Korea). We evaluated the volumetric parameters of left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), LVEDV index, LVESV index, LVEF, and also calculated the left ventricular (LV) diastolic wall thickness (posterior wall and interventricular septum), aortic diameter, left atrial size. Diastolic function was assessed by Ve/Va ratio, left ventricular isovolumic relaxation time, DecTime.

The exercise tolerance test was performed in patients in the morning on an empty stomach in a sitting position on a VE-02 bicycle ergometer with electrocardiogram (ECG) recording on a six-channel HeartScreen 112 Clinic electrocardiograph in 12 standard leads. The trial was conducted in a continuous stepwise pattern, starting at 25 Watts (W) with 25 W increments at each step until the development of ischemic ECG changes and/or pain.

Determination of the number of EPCs was performed at the first examination 10-12 days after the MI, and within 7-10 days (after stabilization) in patients with unstable angina. Re-analysis of indicators was performed after 3 months. All the patients had blood drawn before the exercise test and within 30 minutes after the test. The number of EPCs (phenotype CD45+/CD34+) of peripheral blood was determined through the method of flow cytometry with the help of reagents for determining the differentiation clusters of CD34, CD45 manufactured by Beckman Coulter Inc. Calculation of the results was performed on the NAVIOS device (Beckman Coulter Inc.). The results were obtained in the form of absolute values – the number of cells per 1 ml of blood.

Statistical data processing was performed on a personal computer using SPSS Statistics 23 (trial version) with the determination of the median values, interquartile intervals (Q_1-Q_3), mean values, descriptive statistics, parametric (Student's t-test) and nonparametric (Mann-Whitney, Wilcoxon) statistical criteria; correlations were assessed by the correlation coefficient (Pearson and Spearman in cases of parametric and nonparametric distribution of the studied indicators, respectively, or in case of dichotomous indicators); the difference in the frequency of detection of signs in the groups was assessed by Pearson's χ^2, relative risks (RR) with the corresponding 95% confidence intervals (CI). The level of statistical significance was $p \leq 0.05$.

Results and discussion. As a result of the study, it was established that there is an associative relationship between the better recovery of the level of exercise tolerance in patients in the next 3 months after ACS and the recovery of endothelial function. This is evidenced by a statistically significant increase in the number of EPCs after exercise test in patients with a favorable prognosis. Indicators in the patients with a decrease in the number of EPCs after physical exertion are associated with a trend towards worse prognosis of the disease.

We examined 44 patients, 39 patients with AMI and 5 patients with unstable angina. Thirty-three (84.6%) patients developed Q-wave MI, 6 (15.3%) patients developed non-Q-wave MI, most of them were transferred from the intensive care unit on day 3-7 after MI.

Among comorbid conditions, 42 (95.4%) patients had hypertension with a maximum systolic blood pressure of 160 (Q_1-Q_3; 150-170) mm Hg, and 10 (22.7%) patients had diabetes mellitus. Stage IIA heart failure was diagnosed in 27 (61.3%) patients.

Attention is drawn to the fact of delayed hospitalization, which caused a slight delay in percutaneous coronary intervention (PCI): up to 2 hours after the development of MI in 4 patients (10.2%), from 2 to 6 hours in 12 (30.7%) patients, and after 6 hours from the onset of MI in 18 (46.1%) patients. Median body mass index was 27 (Q_1-Q_3; 19.6-37.6) kg/m^2: 23 patients had normal BMI, 9 were overweight, and 12 were obese (Table 1).

The patients were divided into 2 groups according to the result of the exercise test. Group 1 (low tolerance, LT) included patients who could not reach a power of 50 W on a bicycle ergometer (n=24). Group 2 (high tolerance, HT) included patients who reached a threshold power of more than 50 W during bicycle ergometry (n=20).

According to PCI data, there was hemodynamically significant lesion of one coronary vessel in 8 (20.5%) patients, two vessels in 15 (38.5%), and more than two vessels in 5 (25.0%) patients with AMI. At the time of inclusion in the study 14 (35.9%) patients with AMI had full revascularization.

Thirty-seven patients had lesions of the left anterior descending artery; of these, 25 (67.6%) had volume lesions of 90-100%, and 9 (24.3%) had lesions of 50-89% of this artery.

Right coronary artery lesions were detected in 31 (70.5%) patients; volume lesions of 90-100% of this artery were found in 11 (35.5%) patients, and volume lesions of 50-89% in 15 (48.4%) patients.

Circumflex artery lesions were identified in 24 (54.5%) patients, with volume lesions of 90-100% in 13 (54.2%), and 50-89% lesions in 9 (37.5%) patients.

As for treatment, it has been administered in accordance with existing treatment protocols and standards based on the 2017 European Society of Cardiology Guidelines for the management of acute myocardial infarction in patients

Table 1

Clinical and anamnestic parameters of patients of two groups at the first examination (12-16 days after MI and 7-10 days after stabilization in patients with unstable angina)

Parameters		Group 1 (LT) n=24	Group 2 (HT) n=20	p
Age, years		63 (57-70)	55 (49-57)	0.001
BMI, kg/m^2		27.3 (24.4-29.0)	28.5 (24.0-31.4)	0.567
Smokers, n (%)		16 (67)	13 (65)	0.908
ACS type, n (%)	Unstable angina	0	1 (5)	0.266
	STEMI	22 (92)	15 (75)	
	Non-STEMI	2 (8)	4 (20)	
MI localization, n (%)	LV anterior wall MI	14 (58)	12 (60)	0.561
	LV posterior wall MI	9 (38)	7 (35)	
	Circumferential MI	1 (4)	0	
Heart failure stage, n (%)	I	11 (46)	6 (30)	0.283
	IIA	13 (54)	14 (70)	

BMI, body mass index; STEMI, ST-elevation myocardial infarction; non-STEMI, non-ST-elevation myocardial infarction; LV, left ventricle.

presenting with ST-segment elevation and 2020 European Society of Cardiology Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation [20, 21].

All the patients included in the study underwent bicycle ergometer test. Eleven patients (25%) performed a submaximal test at a load threshold power (LTP) of 100-125 W, 9 patients (25%) performed at an LTP of 75 W, 18 patients (40.9%) who made up the majority had an LTP of 50 W, and 6 patients (13.6%) had an LTP of 25 W. The duration of the load on four steps was five minutes on each step. The median LTP was 50 W (Q_1-Q_3; 50-87.5). The work (A) was 22.5 kJ (Q_1-Q_3; 22.5-45). The initial heart rate was 70 bpm (Q_1-Q_3; 65-74). The threshold heart rate reached by patients was 100 bpm (Q_1-Q_3; 91.5-110), i.e. did not exceed the limit of 120 bpm (Table 2).

The unit cost of work was determined by the ratio of the difference between the double product (DP) and in the ascending state to the work (ΔDP/A), and it amounted to 2.34 (Q_1-Q_3; 1.27-3.59 conditional units) (Table 3).

The groups were further divided into subgroups according to the exercise tolerance as follows. LT group: 25 W (6 patients); 50 W (18 patients). HT group: 75 W (9 patients); 100 W (10 patients); 125 W (1 patient).

As can be seen from the data presented in Table 4, group 1 patients performed work at the level of 22.5 kJ, group 2 patients at 56.3 kJ (p<0.001). The value of ΔDP/A, reflecting the unit cost of work, was 3.4 conditional units in group 1 vs. 1.3 conditional units in group 2 (p<0.001), which indicates higher energy consumption in group 1 patients to perform a unit of work.

At the same time, the scores of the Borg scale in the groups did not differ and amounted to 13 points in both groups (p=0.935), which indicates the same threshold of load perception, but at different levels.

When studying the hemodynamic parameters of the two groups depending on the level of exercise tolerance during the first examination, it was determined that the groups did not differ either in the size of the left atrium 4.1 (Q_1-Q_3; 3.5-4.4) cm in group 1 and 4.0 (Q_1-Q_3; 3.6-4.2) cm in group 2 (p=0.227) or LVEDV 126.5 (Q_1-Q_3; 109.2-157.8) ml against the 131.3 (Q_1-Q_3; 113.0-149.5) ml (p=0.954), neither for LVEF, which was 49% (Q_1-Q_3; 43-55) in group 1, and 51% (Q_1-Q_3; 46-54) in group 2 (p=0.462), but statistically significantly differed in the left ventricular posterior wall thickness: 1.14 cm (Q_1-Q_3; 1.10-1.20) in group 1 against 1.05 cm (Q_1-Q_3; 1.00-1.10) (p=0.004) in group 2.

Patients with severe disorders of myocardial kinesis in the form of akinesis were more common in group 1, while patients with normal kinesis and dyskinesis were more common in group 2 (Table 5).

Types of intervention and completeness of revascularization in patients of the examined groups are given in Table 6. The presented data indicate that patients of both groups did not differ in the type of intervention (urgent or non-urgent stenting or angioplasty) and the completeness of revascularization (complete or incomplete). Two or more installed stents were statistically significantly more common in group 1 patients: in 12 out of 24 (50%) versus 4 of 20 (20%), (p=0.060).

The correlation analysis showed that exercise tolerance is statistically significantly dependent on the number of stents (χ^2=4.24, p=0.04, φ=0.31).

If patients have more than 1 stent, there is a 2.5-fold increased risk of decreased exercise tolerance to 25-50 W (RR = 1.8; 95% CI: 1.3-2.4). In patients treated in the first two hours of AMI, there was no increase in EPCs after the exercise test (RR = 2.5; 95% CI: 1.0 to 6.5) (Table 7).

Data on the dynamics of serum EPCs of the examined patients are given in Table 8. As can be seen from the data presented in the table, the number of EPCs did not differ statistically between the groups. Thus, serum EPCs lev-

Table 2

The results of bicycle ergometer test

Parameters (n=44)	Median	Q_1	Q_3
LTP, W	50	50	87.5
A, kJ	22.5	22.5	45
Borg score	13	13	14

Q_1, mean number that lies between the smallest value of the data set and the median; Q_3, mean number that is between the median and the largest number of the distribution.

Table 3

The cost of a unit of work was determined by the ratio of the difference between the double product

Parameters	Me	Q_1	Q_3
DP_1 conditional units	78	71.4	87.5
DP_2 conditional units	142.6	127.5	168
ΔDP, conditional units	61.2	47.8	82.7
ΔDP/A, conditional units	2.34	1.27	3.59

DP_1, double product for group 1 calculated as (heart rate under exercise × systolic blood pressure under exercise) / 100; DP_2, double product for group 2.

Table 4

Indicators of the exercise test at the first examination

Parameters	Group 1 (LT) (n=24)	Group 2 (HT) (n=20)	p
A, kJ	22.5 (10.5-22.5)	56.3 (45.0-75.0)	<0.001
ΔDP/A, conditional units	3.4 (2.6-5.3)	1.3 (1.0-1.5)	<0.001
Borg score	13 (13-14)	13 (13-14)	0.935

Table 5

Some hemodynamic parameters of the two examined groups

Indicators		Group 1 (LT) (n=24)	Group 2 (HT) (n=20)	p
LA, cm		4.1 (3.5-4.4)	4.0 (3.6-4.2)	0.227
LVPWT, cm		1.20 (1.10-1.24)	1.14 (1.00-1.25)	0.583
IVS thickness, cm		1.14 (1.10-1.20)	1.05 (1.00-1.10)	0.004
LVEDV, ml		126.5 (109.2-157.8)	131.3 (113.0-149.5)	0.954
LVEDV index, ml/m^2		62.8 (56.1-73.5)	65.6 (56.1-73.4)	0.825
LVESV, ml		60.8 (50.0-79.0)	65.0 (48.0-73.7)	0.954
LVESV index, ml/m^2		29.8 (23.1-40.3)	29.3 (25.1-37.0)	0.972
LVEF, %		49 (43-55)	51 (46-54)	0.62
LVEF %, n (%)	≥50%	11 (46)	11 (55)	0.258
	40-49%	10 (42)	9 (45)	
	<40%	3 (12)	0	
E/A		0.97 (0.65-1.27)	0.93 (0.74-1.04)	0.825
IVRT, ms		110 (90-114)	114 (75-130)	0.332
DT, ms		186 (150-230)	172 (150-240)	0.800
Kinesis, n (%)	Normal	1 (4)	5 (25)	**0.008**
	Hypokinesis	10 (42)	9 (45)	
	Akinesis	13 (54)	3 (15)	
	Dyskinesis	0	3 (15)	

LA, left atrium; LVPWT, left ventricular posterior wall thickness; IVS, interventricular septum; E, peak velocity of early diastolic transmitral flow; A, peak velocity of late transmitral flow; IVRT, isovolumic relaxation time; DT, deceleration time of early diastolic transmitral flow.

Table 6

Types of intervention and completeness of revascularization in patients of the examined groups

Indicators		Group 1 (LT) (n=24)	Group 2 (HT) (n=20)	p
Type of interventions, n (%)	Urgent	19 (79)	15 (75)	0.948
	Non-urgent	4 (17)	4 (20)	
	Angioplasty	1 (4)	1 (5)	
Type of revascularization, n (%)	Complete	11 (46)	7 (35)	0.467
	Incomplete	13 (54)	13 (65)	
Number of stents, n (%)	Without stents	1 (4)	1 (5)	0.049
	1	11 (46)	15 (75)	
	2	10 (42)	1 (5)	
	3 and more	2 (8)	3 (15)	
Number of stents 2 or more, n (%)		12 (50)	4 (20)	0.060

Table 7

Correlation analysis between the number of stents and the level of exercise tolerance after ACS (first examination)

Group	Number of stents		Total number of patients	χ^2; ϕ; p; RR (95% CI)
	2 or more stents	1 stent		
LT (25-50 W), n	12	12	24	4.24; 0.31; 0.04; 1.8 (CI 1.3-2.4) 2.5 (CI 1.0-6.5)
HT (75-125 W), n	4	16	20	
Total number of patients	16	28	44	

els were 3491 per ml (Q_1-Q_3; 2084-4541) in group 1 and 2514 per ml (Q_1-Q_3; 1665-5622) in group 2, p=0.616. Attention is drawn to the significant variability of EPCs values, which reflects the minimum and maximum values of the indicator. After exercise test serum EPCs levels were 3278 per ml (Q_1-Q_3;1990-5297) in LT group and 2740 per ml (Q_1-Q_3; 2030-5477) in HT group, which was not statistically significant when comparing the indicators between the groups (p=0.880) after physical exertion. The difference between the number of EPCs before and after exercise test ($\Delta EPCs_{1-2}$/ml) was –186 (–944-350) in LT group and 87 (–766-617) in HT group, p=0.599. A statistically insignificant difference was associated with significant variability in the indicators.

The number of patients who had EPCs increase in LT group was 7 (29%) versus 12 (55%) in HT group (p=0.125 according to Fisher's exact test, but the difference in χ^2 was 3.012; p=0.083), which obviously requires a larger sample to obtain statistical differences between the comparison groups.

An analysis of the dependence of the number of EPCs before and after physical activity was carried out depending on the number of affected vessels. The number of EPCs in serum ml was analyzed in patients with stenosis of 75% or more of one coronary vessel and 2 or more coronary vessels.

As can be seen from the data presented in Table 9, serum EPCs levels per ml before exercise test when 75% or more of one coronary vessel was affected was 3696 (Q_1-Q_3; 2633-6565) versus 2222 (Q_1-Q_3; 1584-3637) cells in ml with stenosis of 75% or more of two or more arteries (p=0.004), that is, when more severe stenosis of 75% or more of 2 arteries or more was detected, there was a statistically significantly lower number of EPCs in ml of serum before physical exertion.

After physical activity with damage to one vessel with stenosis of 75% or more, the number of EPCs/ml was 3616 (Q_1-Q_3; 2196-6600) (p=0.011), while ΔEPC_{1-2}/ml was negative (–604) (Q_1-Q_3; –1059-(–19)), that is, after physical activity the number of EPCs decreased, while in the HT group there was an opposite relationship and ΔEPC_{1-2}/ml was 228 (Q_1-Q_3; –365-1090), which was statistically significant (p=0.004).

Therefore, the number of patients who had an increase in EPCs after exercise test was higher in patients with stenosis of 75% or more of more than two vessels (22% vs. 62% in group 2; p=0.007).

The next fragment of the work was follow-up examination of the patients. Of the 17 patients examined within 3 to 6 months, 9 patients had high exercise tolerance (75-125 W) and a favorable course of the disease (without destabilization of coronary artery disease during the observation period, and 8 patients had unfavorable course, because their level of exercise tolerance did not exceed 50 W during a three-month examination. These data are shown in Table 10.

Table 8

Dynamics of EPCs in serum in patients of two groups before and after exercise test (first examination)

Parameters	Group 1 (LT) (n=24)	Group 2 (HT) (n=20)	p
EPC_1/ml	3491 (2084-4541)	2514 (1665-5622)	0.616
EPC_2/ml	3278 (1990-5297)	2740 (2030-5477)	0.880
ΔEPC_{1-2}/ml	–186 (–944-350)	87 (–766-617)	0.599
(+)ΔEPC_{1-2}/ml, n (%)	7 (29) 95% CI 12-50	12 (55) 95% CI 32-77	0.125

EPC_1, the number of EPCs before the exercise test; EPC_2, the number of EPCs after the exercise test; (+)ΔEPC_{1-2}, the number (n) and percentage (%) of patients who had an increase in EPC after the exercise test.

Table 9

EPC values depending on the number of affected vessels at the first examination

	Stenosis ≥75% of coronary arteries diameter		
Indicators	1 vessel (n=23)	2 or more vessels (n=21)	p
EPC_1/ml	3696 (2633-6565)	2222 (1584-3637)	0.004
EPC_2/ml	3616 (2196-6600)*	2612 (1936-3964)**	0.160
ΔEPC_{1-2}/ml	–604 (–1059-(–19))	228 (–365-1090)	0.004
(+)ΔEPC_{1-2}/ml, n (%)	5 (22)	13 (62)	0.007

*p=0.011 (against EPC_1 in the same group).
**p=0.911 (against EPC_1 in the same group).

Table 10

EPC values in patients examined within 3 to 6 months

Parameters	Patients with favorable course (n=9)	Patients with unfavorable course (n=8)	p
Examination 1			
EPC_1/ml	4062 (1746-6564)	3460 (1989-4246)	0.888
EPC_2/ml	3867 (2228-6455)*	3006 (1977-4294)**	0.606
ΔEPC_{1-2}/ml	148 (–812-492)	–376 (–842-149)	0.541
Examination 2			
EPC_1/ml	3057 (2147-4468)	2309 (1637-3850)	0.424
EPC_2/ml	3633 (3172-5349)#	2400 (1504-2729)##	**0.00**6
ΔEPC_{1-2}/ml	492 (56-1144)	–233 (–1170-366)	0.200

*p=0.953 (vs. EPC_1 in the same group – initially).
**p=0.161 (against EPC_1 in the same group – initially).
#p=0.213 (against EPC_1 in the same group – after 3 months).
##p=0.484 (against EPC_1 in the same group – after 3 months).

And although the number of EPCs during the initial examination did not differ statistically, during the re-examination when determining the EPCs in ml of serum in patients with high exercise tolerance and favorable course was statistically significantly higher than in patients with low exercise tolerance and unfavorable course: 3633 (Q_1-Q_3; 3172-5349) vs. 2400 (Q_1-Q_3; 1504-2729), (p=0.006).

These data may indicate that there is an association between better recovery of exercise tolerance after acute coronary syndrome and recovery of endothelial function in patients with a favorable post-infarction period at follow-up, compared to patients whose exercise tolerance did not exceed 50 W (low exercise tolerance), as evidenced by a statistically higher number of EPCs after physical activity in patients with favorable course, compared to patients with unfavorable course.

Conclusions. The obtained data suggest that there is an association between better recovery of exercise tolerance after ACS and recovery of endothelial function in patients with favorable post-infarction period at follow-up, compared to patients whose exercise tolerance did not exceed 50 W (low exercise tolerance), as evidenced by a statistically higher number of EPCs after physical exertion in patients with favorable course and high tolerance to physical activity compared to those with unfavorable course and low tolerance to physical activity. In patients, a decrease in recovery of exercise tolerance is associated with a worse disease prognosis. Inhibition of bone marrow function to produce EPCs underlies the formation of progressive systemic endothelial dysfunction, which can affect the repair of the structural and functional properties of the heart after ACS.

Conflict of interest. The authors have no conflicts of interest to declare.

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Збільшення фізичної толерантності під час кардіореабілітації сприяє відновленню функції ендотелію у пацієнтів після гострого коронарного синдрому

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Резюме. Останніми роками багато досліджень спрямовані на вивчення можливостей кардіореабілітації як інструменту для покращення прогнозу пацієнтів після гострого коронарного синдрому. Дисфункція ендотелію є одним з ініціюючих механізмів серцево-судинних захворювань, і зокрема інфаркту міокарда, тому важливо оцінити динаміку зміни кількості клітин попередників ендотеліоцитів (КПЕ) у пацієнтів під час кардіореабілітації на тлі підвищення рівня фізичного навантаження.

Мета – встановити зв'язок між рівнем відновлення толерантності до фізичного навантаження (ТФН) та відновленням ендотеліальної функції шляхом визначення кількості КПЕ у пацієнтів, які проходять кардіореабілітацію після гострого коронарного синдрому.

Матеріали та методи. До дослідження було включено 44 пацієнти зі STEMI, які перенесли ургентне стентування інфаркт-обумовлюючої артерії, середній вік яких становив 59 років (Q_1–Q_3; 51–64). Усім пацієнтам, що були включені в дослідження, проводили лабораторні дослідження (підрахунок клітин CD45+/CD34+ до та після тесту з фізичним навантаженням) та інструментальні дослідження (ехокардіографія, велоергометрія, коронарографія). Статистичну обробку проводили за допомогою програмного забезпечення SPSS Statistics 23 (trial version).

Результати. За результатами тесту з фізичним навантаженням під час першого обстеження пацієнти були розподілені на 2 групи: група I – низької ТФН (≤ 50 Вт) та група II – високої ТФН (> 50 Вт). Отримані дані свідчать про наявність зв'язку між кращим відновленням ТФН після гострого коронарного синдрому та відновленням ендотеліальної функції у пацієнтів з високою ТФН під час спостереження порівняно з пацієнтами, у яких ТФН не перевищувала 50 Вт. Про це свідчить статистично більша кількість КПЕ після фізичного навантаження в пацієнтів зі сприятливим перебігом і високою ТФН (3633 проти 2400 кл./мл), (p = 0,006). У пацієнтів з низькою ТФН частіше діагностували ураження передньої міжшлуночкової гілки лівої коронарної артерії, ніж у групі з високою ТФН (96 проти 70 %, p = 0,02). Якщо пацієнти мають більше одного стента, збільшується ризик зниження ТФН до значень 25–50 Вт у 2,5 раза (відношення ризику = 1,8; 95 % довірчий інтервал 1,3–2,4).

Висновки. Отримані дані свідчать про те, що існує асоціативний зв'язок між кращим відновленням рівня ТФН після гострого коронарного синдрому і відновленням ендотеліальної функції у пацієнтів зі сприятливим перебігом під час повторного обстеження порівняно з пацієнтами, в яких рівень ТФН не перевищував 50 Вт (низька ТФН). Про це свідчить статистично більша кількість КПЕ після фізичного навантаження у пацієнтів зі сприятливим перебігом і високою ТФН порівняно з пацієнтами з несприятливим перебігом та низькою ТФН.

Ключові слова: *циркулюючі прогеніторні клітини, інфаркт міокарда, тест з фізичним навантаженням, ендотеліальна функція, кардіореабілітація, толерантність до фізичного навантаження, ангіогенез.*

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