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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Does mobilisation of CD34+ stem cells along with VEGF, angiogenin, interleukin 6, interleukin 8, and hsCRP levels allow predicting the direction of left ventricular ejection fraction and wall motion score index changes in patients with myocardial infarction?

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Abstract

Background: Left ventricular (LV) systolic function is a significant prognostic factor in patients after myocardial infarction (MI). Multiple angiogenic and inflammatory factors are involved in postinfarction LV remodelling process. In addition, CD34+ progenitor cells mobilised from bone marrow and tissue niches participate in regeneration of the infarcted myocardium.

Aim: To examine relationships between LV ejection fraction (LVEF) and wall motion score index (WMSI) and the number of CD34+ cells and plasma levels of vascular endothelial growth factor (VEGF), angiogenin and such inflammatory factors as interleukin 6 (IL-6), interleukin 8 (IL-8), and high-sensitivity C-reactive protein (hsCRP) in patients with ST-elevation MI (STEMI).

Methods: The study group included 61 patients with STEMI treated with primary percutaneous coronary intervention (PCI) involving bare metal stent implantation. Plasma levels of the evaluated angiogenic and inflammatory factors were measured by flow cytometry at 4 time points (just before PCI, 24 h later, at hospital discharge, and 30 days after STEMI). LVEF and WMSI were measured by echocardiography at hospital discharge, 1 month later, and 6 months later. We compared angiogenic and inflammatory factor levels in patients with no improvement of the LV systolic function during the follow-up (group 1, n = 22) vs. those with improved LV systolic function (group 2, n = 39).

Results: No differences in the levels of VEGF, angiogenin, IL-6, IL-8, and hsCRP, and the number of CD34+ cells were observed between the two groups. Despite this, we found significant negative correlations between hsCRP level and LVEF, and positive correlations between hsCRP level and WMSI in both patient groups, but these correlations were much stronger in group 1. We also found a significant negative correlation between WMSI at 6 months and the number of CD34+ cells measured 24 h after PCI.

Conclusions: 1. Evaluation of plasma VEGF, angiogenin, IL-6, IL-8, and hsCRP levels and the number of CD34+ cells at different time points in patients with STEMI did not allow predicting the direction of changes in LVEF and WMSI. 2. Observed significant correlations between hsCRP level and LVEF and WMSI may suggest a harmful effect of inflammation on postinfarction myocardial remodelling. 3. A significant negative correlation between the number of CD34+ and WMSI suggests that increased mobilisation of these cells might have a beneficial effect on systolic function after MI.

Key words: myocardial infarction, left ventricular systolic function, CD34+ stem cells, angiogenic and inflammatory factors

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INTRODUCTION

Left ventricular (LV) systolic function after myocardial infarction is an established prognostic factor. Systolic function following infarction depends on multiple factors including duration of ischaemia, extent of myocardial necrosis, flow in the culprit artery after coronary revascularisation, and perfusion of coronary microcirculation [1]. Myocardial necrosis induces an inflammatory response that contributes to further myocardial damage but also underlies regenerative processes. These processes depend on endothelial precursor cells that belong to the pool of bone marrow CD34+ cells, and require actions of multiple angiogenic and growth factors.

The aim of this study was to examine whether plasma levels of selected angiogenic factors such as vascular endothelial growth factor (VEGF) and angiogenin, plasma levels of inflammatory factors including interleukin 6 (IL-6), interleukin 8 (IL-8), and high-sensitivity C-reactive protein (hsCRP), and the number of CD34+ cells at various time points allow predicting the direction of changes of LV systolic function parameters, including LV ejection fraction (LVEF) and wall motion score index (WMSI), in patients with first ST segment elevation myocardial infarction (STEMI).

METHODS

Study group

We studied 61 patients admitted due to first STEMI type 1 according to the European Society of Cardiology (ESC) guidelines. All patients underwent primary percutaneous coronary intervention (PCI) that involved implantation of a bare metal stent. A written informed consent was obtained from all patients before their inclusion into the study. The study was approved by a local ethics committee (approval No. BW 60/2006). Exclusion criteria included cardiogenic shock or pulmonary oedema, concomitant inflammatory or neoplastic disease, chronic anticoagulation, and liver or kidney failure. During 6 months of follow-up, all patients received aspirin, clopidogrel, angiotensin-converting enzyme inhibitor (perindopril or ramipril), beta-blocker (bisoprolol or metoprolol succinate), and statin (simvastatin or atorvastatin).

Study protocol

In all patients, blood for laboratory testing was collected immediately before PCI, at 6, 12, and 14 h after PCI, on the day of discharge (between 5 and 7 days after MI), and at 30 days after MI. Blood samples were immediately sent for determination of troponin I level. Fraction of the samples was centrifuged for 15 min at 3000 g/min and the obtained plasma was frozen at –70°C. Plasma levels of VEGF, angiogenin, hsCRP, IL-6, and IL-8 were measured using the FACSArray flow cytometer with the use of Beckton Dickinson kits. Levels of angiogenic and inflammatory factors were determined at 4 time points — immediately before PCI, 24 h after PCI, at discharge, and at 30 days after MI. Complete blood count and the number and proportion of CD34+ cells were evaluated in blood samples collected to tubes containing ethylenediaminetetraacetate (EDTA). Cytometric analysis was performed using the Coulter Cytomics FC-500 cytometer. Peripheral blood samples with EDTA were tagged with monoclonal anti-CD34 antibodies as per manufacturer instructions with simultaneous erythrocyte lysis using UtiLyse (DAKO). Appropriate isotypic immunoglobulins were used as negative control. Each testing involved the use of approximately 30,000 leukocytes. The number of cells with positive antigen expression at the lymphocyte gate was measured, and their proportion in relation to all peripheral blood leukocytes was calculated. These evaluations were performed three times at time points consistent with measurements of angiogenic factors.

Echocardiography

Echocardiographic examinations were performed using a Sonos 7500 machine at discharge, at 30 days after MI, and at 6 months after MI. Full echocardiographic examination was performed at each occasion but only LVEF (Teicholz method) and WMSI measurements were used for the purpose of the present study. Regional wall motion abnormalities were evaluated using the standard 17-segment model of the LV myocardium. Systolic function was categorised as normokinesis, hypokinesis, akinesis, or dyskinesis, with scores of 1 to 4 points, respectively. WSMI was calculated as the mean score for all evaluable segments. Depending on changes in echocardiographic parameters of LV systolic function during 6 months of follow-up, patients were categorised into two groups. Group 1 included 22 patients with no improvement or worsening of LV systolic function during the follow (defined as LVEF reduction by at least 2% and an increase in WMSI), and Group 2 included 39 patients with improvement of LV systolic function during the follow (defined as an increase in LVEF by at least 2% and WMSI reduction).

Statistical analysis

Statistical analysis was performed using the STATISTICA version 7.1 software (StatSoft®). Normally distributed variables were reported as mean values with standard deviation, and non-normally distributed variables as medians and quartiles. Significance of differences between groups was evaluated using the Friedman and Wilcoxon tests for paired samples, and the Kruskal-Wallis and Mann-Whitney test for unpaired samples. $P \leq 0.05$ was considered statistically significant. Calculated Spearman correlation coefficient values were also considered significant at $p \leq 0.05$.

RESULTS

Table 1 shows characteristics of the study group. Most patients were men (73%), and 77.7% of patients were above 50 years of age. Mean delay from the onset of chest pain

to PCI was 278 ± 191 min. At 6 months, 4 patients had symptoms of heart failure (New York Heart Association class II) and 1 patient died due to a recurrent MI. Overall, LV systolic function improved during the follow-up. Mean increase in LVEF was 2.2%, and WMSI decreased by 0.07. Both parameters showed an expected relation to the location of MI, with significantly higher LVEF and significantly lower WMSI in patients with inferior wall infarction compared to those with anterior wall infarction (LVEF 47.8 ± 5.12% vs. 40.6 ± 6.0% and WMSI 1.48 ± 0.18 vs. 1.70 ± 0.19 at discharge, and LVEF 51.5 ± 4.1% vs. 43.7 ± 6.80% and WMSI 1.41 ± 0.16 vs. 1.65 ± 0.22 at 6 months; $p < 0.0001$ for all comparisons). Groups 1 and 2 did not differ significantly in regard to gender proportions and age (both overall and for men and women separately). Anterior and inferior wall infarction proportions were the same in both groups. No significant differences were found between groups in regard to the delay from the onset of chest pain to PCI, and mean peak troponin I levels (Table 2).

Parameters of left ventricular systolic function (Table 3). At discharge, both LVEF and WMSI did not differ significantly between the two groups. At 6 months, LVEF in Group 1 was lower than at discharge, with a nearly significant difference ($p = 0.051$), and WMSI did not differ significantly. In Group 2, LVEF at 6 months after MI was significantly higher compared to discharge values, and WMSI was significantly lower. Despite different directions of change, LVEF at 6 months after MI did not differ significantly between the two groups, and WMSI was significantly lower in Group 2 compared to Group 1.

CD34+ cells and angiogenic and inflammatory factors. Data for the overall study group are shown in Table 4. The highest number of CD34+ cells was found at 24 h after PCI in Group 1, and at discharge in Group 2, but it did not differ significantly between the two groups at any of the evaluated time points. VEGF and angiogenin levels did not differ significantly between the two groups at any of the time points. In Group 2, IL-6 and IL-8 levels were higher than in Group 1 at all time points, and the difference in IL-8 levels before reperfusion therapy was nearly significant ($p = 0.051$). Levels of hsCRP did not differ significantly between the two groups at any of the time points. In both groups, hsCRP level increased significantly on the second day after MI (reaching peak values in both groups) and remained significantly higher compared to baseline values until discharge (Table 5).

Correlations (Table 5). In the overall study group, no significant correlations were found between VEGF and angiogenin levels and LVEF and WMSI values at any of the time points. A significant negative correlation was found between the number of CD34+ cells at discharge and WMSI at 6 months after MI ($r = –0.31$; $p < 0.05$). In the overall study group, a weak but significant positive correlation was also found between IL-6 level ($r = 0.33$; $p < 0.05$) and IL-8 level ($r = 0.34$; $p < 0.05$) and WMSI at 30 days after MI. Despite no significant differences in the evaluated angiogenic and

Table 1. Characteristics of the study group

Parameter	N (%) or mean ± SD
Study group	61 (100)
Age [years]	59.8 ± 10.1
Men	48 (72.3)
Anterior wall infarction	30 (49.1)
Inferior wall infarction	31 (58.9)
Mean troponin I [ng/mL]	35.44 ± 17.83
LVEF (0) [%]	43.96 ± 0.21
LVEF (6) [%]	46.13 ± 8.52
WMSI (0)	1.60 ± 0.21
WMSI (6)	1.53 ± 0.25

LVEF — left ventricular ejection fraction; WMSI — wall motion score index. Numbers and percentages (in parentheses) of patients or mean values ± standard deviation (SD) are given. LVEF (0) and WMSI (0) denote echocardiographic parameters at discharge, and LVEF (6) and WMSI (6) denote echocardiographic parameters at 6 months after myocardial infarction.

Table 2. Characteristics of patients in Groups 1 and 2

Parameter	Group 1 (n = 22) (LVEF ↓, WMSI ↑)	Group 2 (n = 39) (LVEF ↑, WMSI ↓)	P
Women	8 (36.4)	8 (20.5)	NS
Age	64.5 ± 10.2	60.5 ± 7.0	NS
Men	14 (63.6)	31 (79.5)	NS
Age	55.3 ± 9.8	60.3 ± 10.2	NS
Anterior wall infarction	11 (50)	19 (48.7)	NS
Inferior wall infarction	11 (50)	20 (51.3)	NS
Time from the onset of chest pain to PCI [min]	295 ± 200.5	233.6 ± 175.4	NS
Mean peak troponin I [U/L]	37.18 ± 17.06	35.91 ± 18.33	NS

LVEF — left ventricular ejection fraction; PCI — percutaneous coronary intervention; WMSI — wall motion score index. Numbers and percentages (in parentheses) of patients or mean values ± standard deviation (SD) are given.

Table 3. Comparison of mean left ventricular ejection fraction (LVEF) and wall motion score index (WMSI) values at discharge (0) and at 6 months after myocardial infarction (6) in patients with worsening or no change of LV systolic function during 6-month follow-up (Group 1) and those with improvement of LV systolic function (Group 2). Mean values ± standard deviation (SD) are given

Parameter	Group 1 (n = 22)	Group 2 (n = 39)	P
LVEF 0 (%)	44.91 ± 7.6	43.36 ± 5.54	NS
LVEF 6 (%)	44.08 ± 7.75	48.56 ± 6.15	NS
P	0.051	< 0.0001	
WMSI 0	1.59 ± 0.19	1.61 ± 0.23	NS
WMSI 6	1.64 ± 0.20	1.49 ± 0.22	0.046
P	NS	< 0.0001	

Table 4. Evaluation of CD34+ cells and angiogenic and inflammatory factors. Time points for measurements of CD34+ cells, vascular endothelial growth factor (VEGF), angiogenin, interleukin 6 (IL-6), interleukin 8 (IL-8), and high-sensitivity C-reactive protein (hsCRP) were: (1) before primary percutaneous coronary intervention (PCI), (2) one day after primary PCI, (3) at discharge, and (4) 30 days after myocardial infarction. Median, first quartile (Q1), and third quartile (Q3) values are given

	Time point				P
Parameter	(1)	(2)	(3)	(4)	
CD34+ [cells/μL]	15 (Q1 10; Q3 23)	19.5 (Q1 9.5; Q3 33)	20 (Q1 13;Q3 41)	–	0.04[1 vs. 2] 0.01[1 vs. 3]
VEGF [pg/mL]	720.96 (Q1 366.38; Q3 1067.74)	536.57 (Q1 325.6; Q3 906.68)	592.09 (Q1 316.70; Q3 1077.84)	657.38 (Q1 340.73; Q3 956.36)	NS
Angiogenin [ng/mL]	214.63 (Q1 161.4; Q3 285.4)	196.90 (Q1 161.7; Q3 236.5)	204.10 (Q1 159.5; Q3 253.2)	198.3 (Q1 155.2; Q3 259.02)	0.02[1 vs. 4]
IL-6 [pg/mL]	19.17 (Q1 9.38; Q3 34.76)	27.38 (Q1 16.27; Q3 56.50)	18.33 (Q1 8.59; Q3 42.02)	11.74 (Q1 6.07; Q3 25.61)	0.001[1 vs. 2] 0.0007[2 vs. 4]
IL-8 [pg/mL]	24.92 (Q1 17; Q3 42.37)	23.15 (Q1 16.53; Q3 35.58)	19.76 (Q1 11.48; Q3 40.99)	20.44 (Q1 12.23; Q3 27.69)	NS
hsCRP [mg/L]	2.51 (Q1 1.03; Q3 3.86)	11.95 (Q1 6.98; Q3 19.97)	10.72 (Q1 6.64; Q3 18.47)	1.45 (Q1 0.83; Q3 2.91)	0.001[1 vs. 2] 0.001[1 vs. 3]

inflammatory factors between the two groups, significant correlations between hsCRP and LVEF and WMSI were found in both groups, with hsCRP levels at 24 h after PCI and at discharge showing negative correlations with LVEF and positive correlations with WMSI at all time points (at discharge, at 1 month after MI, and at 6 months after MI). In Group 1, these correlations were always stronger than in Group 2, both for LVEF and WMSI (Table 6). WMSI in Group 1 at 1 month after MI also showed positive correlation with the levels of both interleukins at the same time point. In patients with improvement of LV systolic function (Group 2), a significant negative correlation was also found between the number of CD34+ cells on the second day after MI and WMSI at 6 months after MI ($r = –0.38$; $p < 0.05$). The number of CD34+ cells on the second day after MI also showed a negative correlation with IL-8 level at the same time point ($r = –0.36$; $p < 0.05$). No correlations between LVEF and WMSI and VEGF and angiogenin levels were found in any of the study groups.

DISCUSSION

Necrosis and apoptosis of myocardial cells induce an inflammatory state. Cells that migrate to the area of necrosis (macrophages and neutrophils) release interleukins, and CRP is produced by the liver in response to inflammatory stimuli [2, 3]. Inflammation underlies myocardial regeneration which is mediated by such angiogenic factors as VEGF and angiogenin [4–7]. Both VEGF and Il-6 and IL-8 are among factors mobilising CD34+ and CD133+ precursor cells [8–10]. All these factors participate in postinfarction LV remodelling. Effects of the latter may be evaluated by echocardiographic evaluation of the parameters of LV systolic and diastolic function. Mobilisation of CD34+ precursor cells to the peripheral circulation in the peri-infarction period was reported for the first time by Shintani et al. [11] and further confirmed in many other studies [12–14]. The pool of CD34+ cells is heterogeneous and isolating cells that actually participate in neoangiogenesis and regeneration of myocardium would

Table 5. Number of CD34+ cells and plasma levels of vascular endothelial growth factor (VEGF), angiogenin, interleukin 6 (IL-6), interleukin 8 (IL-8), and high-sensitivity C-reactive protein (hsCRP) in two groups of patients after myocardial infarction. Group 1 included patients with no improvement or worsening of left ventricular systolic function during 6-month follow-up, and Group 2 included patients with improvement of left ventricular systolic function during 6-month follow-up after myocardial infarction. Time points of measurements were: (1) before primary percutaneous coronary intervention (PCI), (2) one day after primary PCI, (3) at discharge, and (4) 30 days after myocardial infarction. Median (Me), first quartile (Q1), and third quartile (Q3) values are given

Parameter	Group 1 (n = 22) Me (Q1; Q3)	Group 2 (n = 39) Me (Q1; Q3)	P
CD34+ (1) [cells/μL]	16 (Q1 11; Q3 30)	13 (Q1 10; Q3 22)	NS
CD34+ (2)	22 (Q1 13; Q3 30)	17.5 (Q1 9; Q3 36)	NS
CD34+ (3)	19 (Q1 14; Q3 35)	21 (Q1 11; Q3 41)	NS
VEGF (1) [pg/mL]	539.4(Q1 262.9; Q3 1120.3)	725.8 (Q1 417.5; Q3 1027.9)	NS
VEGF (2)	566.7 (Q1 296.7; Q3 787.2)	532 (Q1 350.4; Q3 1020.8)	NS
VEGF (3)	820.2 (Q1 389.9; Q3 1372.3)	502.2 (Q1 236.3; Q3 935.6)	NS
VEGF (4)	747.1 (Q1 479.1; Q3 1808.2)	649.4 (Q1 329.2; Q3 826.1)	NS
Angiogenin (1) [ng/mL]	190.5 (Q1 149.0; Q3 279.4)	213.7 (Q1 165.7; Q3 275319.5)	NS
Angiogenin (2)	206.7 (Q1 190.5; Q3246.4)	195.8 (Q1 168.8; Q3 231.1)	NS
Angiogenin (3)	223.1 (Q1 162.5; Q3 272.0)	191.2 (Q1 159.4; Q3 241.1)	NS
Angiogenin (4)	183.7 (Q1 114.1; Q3 263.3)	183.2 (Q1 150.6; Q3 225.2)	NS
IL-6 (1) [pg/mL]	11.14 (Q1 7.8; Q3 33.1)	20.17 (Q1 12.45; Q3 29.65)	NS
IL-6 (2)	20.35 (Q1 12.7; Q3 42.8)	30.25 (Q1 18.1; Q3 55.98)	NS
IL-6 (3)	14.32 (Q1 8.72; Q3 42.7)	21.11 (Q1 8.55; Q3 39.8)	NS
IL-6 (4)	10.65 (Q1 7.1; Q3 24.7)	17.9 (Q1 6.0; Q3 29.3)	NS
IL-8 (1) [pg/mL]	20.0 (Q1 13.9; Q3 26.2)	28.75 (Q1 21.19; Q3 40.4)	0.051
IL-8 (2)	17.86 (Q1 14.7; Q330.9)	23.2 (Q1 17.6; Q3 45.2)	NS
IL-8 (3)	21.52 (Q1 11.53; Q3 39.8)	19.5 (Q1 11.35; Q3 40.5)	NS
IL-8 (4)	17.3 (Q1 7.3; Q3 22.5)	22.9 (Q1 13.8; Q3 36.3)	NS
hsCRP (1) [mg/L]	2.40 (Q1 0.98; Q3 2.88)	3.17 (Q1 1.26; Q3 4.51)	NS
hsCRP (2)	13.4 (Q1 7.6; Q3 22.5)	11.63 (Q1 6.84; Q3 19.57)	NS
hsCRP (3)	7.86 (Q1 6.17; Q3 16.0)	12.2 (Q1 6.99; Q3 25.85)	NS

Table 6. Summary of significant correlations (r) between high-sensitivity C-reactive protein (hsCRP) at 24 h after primary percutaneous coronary intervention (PCI) and at hospital discharge and left ventricular ejection fraction (LVEF) and wall motion score index (WMSI) at hospital discharge (0), 1 month after myocardial infarction (1), and 6 months after myocardial infarction (6) in patients with no echocardiographic improvement of LV systolic function (Group 1) and patients with improvement of LV systolic function during 6 months of follow-up (Group 2)

	hsCRP (24 h after PCI)		hsCRP (at discharge)	
	Group 1	Group 2	Group 1	Group 2
LVEF (0)	r = –0.76	r = –0.38	X	r = –0.49
LVEF (1)	r = –0.80	r = –0.40	X	r = –0.51
LVEF (6)	r = –0.69	X	X	r = –0.44
WMSI (0)	r = 0.73	r = 0.43	r = 0.42	X
WMSI (1)	r = 0.78	r = 0.41	r = 0.47	r = 0.51
WMSI (6)	r = 0.79	r = 0.44	r = 0.50	r = 0.49

require much more precise determination of surface markers (CD34+, CD133+, CD117+, CXCR4+, c-met+) [12]. Some studies showed that increased mobilisation of precursor cells in the peri-infarction period was associated with improved LV systolic function during long-term follow-up [12]. These observations were the basis for about 10 years of research on

the use of cellular therapy in cardiac regeneration. However, results of these works are conflicting, with some studies showing improvement of LV systolic function and patients outcomes (REPEAR-AMI, REGENT, BALANCE, SCIPIO) [15–19] but others not confirming these benefits (ASTAMI, FINCELL, HEBE) [20–23]. Physiological role of precursor cell mobilisation in the peri-infarction period has not been clearly defined. Based on the results of the BOOST study that showed improvement in LVEF but no change in LV volume among patients who received intracoronary injections of bone marrow cells, it was suggested that the observed increase in LVEF resulted from improved inotropic properties of cardiomyocytes and not from an increase in their number [24]. In our study, we found an increase in the number of CD34+ cells in the peri-infarction period but no evidence of their greater mobilisation among patients with improvement of LV systolic function during 6 months of follow-up (Group 2) compared to patients with no observed improvement of LVEF and WMSI. However, we found a negative correlation between WMSI at 6 months after MI and the number of CD34+ cells on the second day after MI among patients with improvement of LV systolic function ($r = 0.38$). This may suggest that at least in some patients, larger mobilisation of precursor cell may result in improved LV systolic function. In our study, we also did not find statistically significant differences in the levels of evaluated angiogenic and inflammatory factors between patients with improvement of LV systolic function (Group 2) and those with no such improvement (Group 1). Although inflammation in the area of myocardial necrosis underlies repair processes, many studies showed that acutely increased IL-6 and CRP levels in the peri-infarction period contribute to worse patient outcomes. Higher IL-6 and CRP levels were associated with a higher risk of death, recurrent MI or readmission [25]. An increase in IL-6 level in MI was observed early (within hours from the onset of myocardial ischaemia) and simultaneously with rapid mobilisation of CD34+ and CD133+ precursor cells into the circulation [8]. In our study, peak IL-6 levels were observed on the second day after MI in both patient groups, parallel to changes in the number of CD34+ cells, but no significant differences in IL-6 level and the number of CD34+ cells were found between the two groups. We also did not find correlations between IL-6 level and the number of CD34+ cells in any of the two patient groups. IL-8 was shown to be one of signals initiating angiogenesis, associated with mobilisation of CD133+ precursor cells in MI and homing of CD34+ cells in ischaemic myocardial tissue [8–10]. A negative correlation between IL-8 level on the second day after MI and the number of CD34+ cells at the same time may indicate increased homing of these cells in the myocardium. Unfortunately, there are no morphological data to confirm this. Our findings also indicate an unfavourable association between hsCRP level and LV systolic function after MI, as hsCRP level showed a significant negative correlation with LVEF and a positive correlation with WMSI. These correlations were observed in both patient groups but they were much stronger among patients with no improvement of LV systolic function.

Limitations of the study

Study limitations included small numbers of patients and a relatively preserved LV systolic function immediately after MI in both study groups. Patients in Group 2, i.e. those with improvement of LV systolic function during follow-up, presented to hospital earlier than patients in Group 1. This difference in time to admission did not reach statistical significance but was as much as 60 min, which might have affected the size of myocardial necrosis. No significant difference in troponin I levels between the two groups might have reflected a suboptimal sensitivity of the laboratory method used (peak measurable value was 50 ng/mL, with higher values reported as > 50 ng/mL) and not the actual lack of difference.

CONCLUSIONS

1. Levels of angiogenic factors such as VEGF and angiogenin, and inflammatory factors such as IL-6, IL-8, and hsCRP levels determined at 1, 2, 5–7 and 30 days after MI do not allow predicting the direction of changes of LV systolic function parameters during 6 months of follow-up
2. Observed significant correlations between hsCRP level and LVEF and WMSI, and between IL-6 and IL-8 levels and WMSI may suggest a harmful effect of inflammation in the peri-infarction period on LV remodelling after MI.
3. A significant negative correlation between the number of CD34+ and WMSI suggests that increased mobilisation of these cells might have a beneficial effect on LV systolic function during long-term follow-up.

Conflict of interest: *none declared*

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Czy wielkość mobilizacji komórek CD34+ i stężenia VEGF, angiogeniny, interleukiny 6, interleukiny 8 oraz hsCRP pozwalają przewidywać kierunek zmian parametrów funkcji skurczowej lewej komory po przebytym zawale serca?

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Streszczenie

Wstęp: Funkcja skurczowa lewej komory po przebytym zawale serca jest istotnym czynnikiem rokowniczym. Jest ona efektem pozawałowej przebudowy serca, na którą składają się procesy martwicy i regeneracji mięśnia sercowego. W procesie przebudowy pozawałowej biorą udział czynniki angiogenne, zapalne, a także komórki macierzyste mobilizowane ze szpiku oraz z nisz tkankowych.

Cel: Celem pracy było zbadanie powiązań między parametrami funkcji skurczowej lewej komory u chorych po pierwszym w życiu zawale serca a wielkością mobilizacji komórek CD34+ oraz osoczowymi stężeniami takich czynników angiogennych, jak VEGF i angiogenina oraz stężeniami takich czynników zapalnych, jak interleukina 6 i 8 (IL-6, IL-8) oraz białko C-reaktywne (hsCRP).

Metody: U 61 pacjentów (30 z zawałem ściany przedniej i 31 z zawałem ściany dolnej) oznaczano metodą cytometrii przepływowej stężenia osoczowe VEGF, angiogeniny, IL-6, IL-8, hsCRP. Badania wykonywano przed leczeniem reperfuzyjnym, 24 h później, w dniu wypisu ze szpitala oraz w 30. dobie po zawale serca. W tych samych punktach czasowych metodą znakowania przeciwciałami monoklonalnymi oznaczano liczbę komórek CD34+, a w dniu wypisu ze szpitala, po 1 i 6 miesiącach od zawału, określano za pomocą echokardiografii frakcję wyrzutową lewej komory (LVEF) i wskaźnik kurczliwości (WMSI). Zachowanie się czynników angiogennych i zapalnych porównywano między grupą pacjentów, u których w okresie 6 miesięcy parametry funkcji skurczowej lewej komory nie uległy poprawie (grupa 1, n = 22), a grupą, u której obserwowano poprawę LVEF i WMSI (grupa 2, n = 39).

Wyniki: Stężenia badanych czynników angiogennych i zapalnych oraz liczba komórek CD34+ nie różniły się istotnie między grupą 1 a grupą 2 w żadnym punkcie czasowym. Stwierdzono znamienne korelacje pomiędzy hsCRP, IL-6 i IL-8 a LVEF i WMSI w obydwu grupach badanych, ale w grupie 1 były to korelacje silniejsze. Zanotowano również znamienną ujemną korelację między liczbą komórek CD34+ w 2. dobie zawału a WMSI 6 miesięcy po zawale serca.

Wnioski: 1. Na podstawie zachowania się badanych czynników angiogennych, zapalnych i komórek CD34+ nie można przewidzieć kierunku zmian LVEF oraz WMSI u pacjentów po przebytym zawale serca. 2. Znamienne korelacje między stężeniami hsCRP a LVEF oraz WMSI wskazują na niekorzystny wpływ nasilenia zapalenia w okresie okołozawałowym na przebudowę lewej komory. 3. Ujemna korelacja pomiędzy liczbą komórek CD34+ a WMSI może sugerować korzystny wpływ większej ich mobilizacji w okresie okołozawałowym na lepszą funkcję skurczową lewej komory w obserwacji odległej.

Słowa kluczowe: zawał serca, funkcja skurczowa lewej komory, komórki CD34+, czynniki angiogenne i zapalne

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