Serum levels of interleukin-6, interleukin-10 and C-reactive protein in relation to left ventricular function in patients with myocardial infarction treated with primary angioplasty

Łukasz Karpiński, Rafał Płaksej, Wojciech Kosmala, Maria Witkowska

Department of Cardiology, Medical University, Wroclaw, Poland

Abstract

Background: Inflammatory factors are involved in the cardiac remodelling process after myocardial infarction (MI). Pronounced and sustained activation of proinflammatory factors is believed to enhance the damage to the myocardium and leads to its dysfunction and heart failure. Anti-inflammatory factors, especially interleukin-10 (IL-10), exert a protective action by reducing excessive inflammatory reactions.

Aim: To asses the relationship between serum levels of IL-6, IL-10, CRP and echocardiographic indices of myocardial function in patients with ST-elevated myocardial infarction (STEMI) treated with primary angioplasty. Prognostic value of IL-6, IL-10 and CRP levels in predicting systolic and diastolic dysfunction 6 months after MI was also assessed.

Methods: We studied 75 patients aged 36-82 (28 women and 47 men) presenting with STEMI treated with primary angioplasty. Blood samples for assesment of IL-6, IL-10 and CRP levels were on days 3 and 7 (3d, 7d) of MI and after 6-month follow-up (6m). Echocardiographic examination was performed on day 7 and 6 months after MI during which the parameters of LV systolic (LVEF, WMSI) and diastolic function (E/A, DT, IVRT, Ep, E/Ep) were evaluated. Twenty four healthy persons served as controls.

Results: Interleukin-6 and CRP levels in consecutive measurements correlated significantly inversely with LVEF (7d) and LVEF (6m). The IL-10 (7d) and IL-10 (6m) level correlated positively with LVEF (6m) (r=0.39, p=0.02; r=0.27, p=0.04). The IL-6 and CRP levels in consecutive measurements correlated significantly positively with E/A and E/Ep and inversely with IVRT, DT and Ep. The IL-10 (3d) level correlated inversely with DT (6m) (r=–0.25, p=0.04), while IL-10 (7d) level correlated positively with DT (6m) (r=0.36, p=0.004). Increased level of IL-6 (3d) and CRP (3d) was an independent prognostic factor of LV systolic (OR=1.27, p=0.02; OR=1.14, p=0.05) and diastolic dysfunction (OR=1.14, p=0.03; OR=1.05, p=0.01) 6 months after MI.

Conclusions: 1. A significant, correlations between increased IL-6, CRP level and impaired LV systolic and diastolic function indicate the possible involvement of these factors in postinfarction cardiac damage. 2. Increased level of IL-6 and CRP in the acute phase of MI is an independent predictor of LV systolic and diastolic dysfunction 6 months after MI. 3. Increased serum level of IL-10 in the acute phase of MI reflects the extension of post-infarction myocardial lesion. 4. Maintenance of increased level of IL-10 for days/months after MI seems to be prognostically beneficial.

Key words: interleukin-6, interleukin-10, C-reactive protein, myocardial infarction, LV dysfunction

Kardiol Pol 2008; 66: 1279-1285

Introduction

In spite of the progress in invasive and pharmacological treatment of myocardial infarction (MI), long-term prognosis is still hampered by the risk of heart failure (HF) due to postinfarction cardiac remodelling [1]. The pathophysiological mechanisms of postinfarction cardiac remodelling still need to be investigated more thoroughly. Recent studies have identified the importance of inflammatory and immunological phenomena, which contribute not only to the healing process of the necrotic area but also to postinfarction cardiac remodelling. It is believed that sustained activation of proinflammatory mediators, including interleukin-6 (IL-6) and C-reactive protein (CRP), may be associated with enhanced myocardial damage and its dysfunction, and may lead to HF. On the other hand, an anti-inflammatory agent, interleukin-10 (IL-10), inhibits an excessive inflammatory response, thus decreasing the extent of infarct-related myocardial necrosis [2]. The gathered data enable one to assume that modifying the activity of pro- and

Address for correspondence:

Łukasz Karpiński MD, Klinika Kardiologii, Akademia Medyczna, ul. L. Pasteura 4, 50-367 Wrocław, tel.: +48 71 784 26 11, fax: +48 71 327 09 61, e-mail: futuredream@poczta.fm

Received: 10 August 2008. **Accepted:** 01 October 2008.

anti-inflammatory factors in the acute MI setting may become a new approach towards therapy reducing expansion of the infarct-related myocardial lesion.

Accordingly, the aim of the study was to determine the relationship between IL-6, IL-10 and CRP levels and echocardiographic parameters in patients with ST segment elevation MI (STEMI) treated with primary coronary angioplasty over a 6-month follow-up. Additionally, we examined the prognostic significance of these factors with respect to predicting systolic and diastolic left ventricular (LV) dysfunction 6 months after MI.

Methods

A total of 74 patients aged 6-82 years (mean age 56.94±11.38 years), including 28 women (mean age 59.28±13.10 years) and 47 men (mean age 55.55±10.11 years) were enrolled in this study. The participants were hospitalised for their first STEMI and were treated with primary coronary angioplasty with insertion of a bare metal stent.

The inclusion criteria were as follows: typical angina, pain to hospital time <12 hours, ST segment elevation at J point in at least two adjacent leads by ≥0.2 mV in V_1-V_3 or by ≥0.1 mV in the remaining leads in the resting 12-lead ECG, serum troponin I increase, infarct-related artery occlusion (TIMI 0), restoration of normal flow in the target artery (TIMI 3).

The exclusion criteria were: acute or chronic inflammatory condition, autoimmune diseases, cancer, history of MI, previous coronary revascularisation, primary cardiomyopathies, significant valvular heart defects, history of stroke, peripheral artery disease, renal failure, surgical procedure or serious injury in the last 6 months.

The control group comprised 24 healthy subjects (mean age 59.35±7.97 years), including 10 females (61.30±7.13 years) and 14 males (57.40±8.65 years). All were free from coronary artery disease, arterial hypertension, diabetes or other diseases which could possibly affect the serum levels of the investigated inflammatory factors. The demographic and clinical characteristics of the study group are presented in Table I.

Table I. Demographic and clinical characteristics of the study group

Variable	Subjects (n=75)
Age [years]	56.94±11.38
Gender [females/males (%)]	37/63
Arterial hypertension (%)	72
Diabetes mellitus (%)	28
Pain to PTCA time [hours]	5.8±3.94
Body mass index [kg/m^2]	26.77±4.06
Infarction location [anterior wall/other (%)]	47/53
Infarct-related artery [LAD/RCA/Cx (%)]	48/45/7
Single-or multi-vessel disease (%)	63/37
No-reflow (%)	15
Troponin I [ng/ml]	82.53±102.83

Abbreviations: PTCA – percutaneous transluminal coronary angiography, LAD – left anterior descending, RCA – right coronary artery, Cx – circumflex

The study protocol was approved by the Bioethical Committee of the Medical Academy in Wrocław. Each patient signed an informed consent form for participation in this study.

Laboratory tests

The blood for IL-6, IL-10 and CRP levels was collected on the 3rd and 7th day of hospitalisation (day 3 and day 7) and 6 months after MI (month 6). The plasma levels of IL-6 and IL-10 were measured by the immunoenzymatic assay ELISA using Bender MedSystems kits (Vienna, Austria). Plasma CRP concentrations were determined using high sensitivity nephelometric method with Dade Behring Marburg GmbH CardioPhase hsCRP kits (Marburg, Germany).

Echocardiography

Transthoracic echocardiography was performed on day 7 and at month 6 after MI using a GE Vingmed System Five scanner (Horten, Norwegia), and 2.5 MHz transducer; standard imaging protocols were applied. The LV systolic function was expressed by LV ejection fraction (LVEF). The LV systolic dysfunction criterion was LVEF <45%. The LV diastolic function was evaluated based on the Doppler spectrum of mitral inflow. The following parameters were assessed: the velocity of early mitral inflow jet to the maximum velocity of the atrial jet ratio (E/A), early mitral inflow deceleration time (DT), LV isovolumetric relaxation time (IVRT), propagation time of early mitral flow (Ep), maximum E wave velocity to E wave propagation velocity ratio (E/Ep). The LV diastolic filling was assessed using the following criteria: normal profile – Ep ≥45 cm/s and DT=140-240 ms; impaired relaxation – Ep <45 cm/s and DT >240 ms; pseudonormalisation – Ep <45 cm/s and DT=140-240 ms; restriction – Ep <45 cm/s and DT <140 ms. Significant LV dysfunction criterion was the presence of pseudonormalisation or restrictive profile of mitral flow.

Statistical analysis

Statistical analysis was performed using Statistica software with Analyse-it extension to obtain the ROC curves (receiver operator characteristic curves). The results are presented as mean ± SD or numbers and percentages. The significance of differences between the analysed parameters depending on the grouping variable were evaluated using Mann-Whitney U test.

The analysis of correlation was carried out after determination of Spearman rank correlation coefficient. The

prognostic importance of concentrations of the analysed inflammatory factors was evaluated using multivariable logistic regression. The estimation was performed with Rosenbrock and quasi-Newton methods, while the prognostic value was expressed as odds ratio (OR) ±95% CI. In addition, a diagnostic test value was verified by area under ROC. The results were found statistically significant if p was <0.05.

Results

Concentration of the analysed inflammatory factors

The IL-6, IL-10 and CRP levels were significantly higher on days 3 and 7 of MI in the patient group than in the controls. However, at month 6 after STEMI the IL-6 and IL-10 levels normalised, while CRP levels remained elevated (Table II).

Echocardiographic parameters of LV function

In patients with MI both on day 7 and at month 6 after infarction, LVEF was significantly reduced compared to the control group. Within 6 months, an increase of LVEF was noted of borderline significance (Table III). The LV diastolic function, both on day 7 and at month 6 was impaired as confirmed by prolonged IVRT, decreased Ep and increased E/Ep in comparison with the controls. At 6 months also significant prolongation of DT was observed without noticeable changes of the other parameters (Table III). At month 6, LV dysfunction was present in 21 (28%) patients, while significant impairment of LV diastolic function was found in 29 (38.5%) patients.

Relationship between IL-6, IL-10 and CRP levels and LV systolic function indices

The IL-6, CRP (3d) and CRP (7d) levels were significantly negatively correlated with LVEF (7d) and LVEF (7m). Moreover, IL-6 (6m) and CRP (6m) levels were significantly negatively correlated with LVEF (M 6). The most significant correlations were observed between CRP (3d) and LVEF (6m) (r=–0.61, p=0.000) (Figure 1) and between CRP (7d) levels and LVEF (6m) (r=–0.55, p=0.000). In addition, there was a significant negative correlation between IL-10 (3d) concentration and LVEF (7d) (r=–0.42, p=0.000) and LVEF (6m) (r=–0.46, p=0.000) (Figure 2). On the other hand, IL-10 (7d) and IL-10 (6m) levels were significantly positively correlated with LVEF (6m) (r=0.39, p=0.02; r=0.27, p=0.04, respectively) (Figure 3).

The concentrations of IL-6 (3d), IL-10 (3d) and CRP (3d) were significantly negatively correlated with ΔLVEF

Table II. Serum IL-6 and CRP levels in patients with MI and controls

Variable	Patients with MI (n=75)			Controls (n= 20)	p		
	Measurement						
	3d	7d	6m		3d/C	7d/C	6m/C
IL-6 [pg/ml]	12.62±22.58	4.12±4.03	3.5±4.68	1.67±0.24	p=0.000	p=0.006	NS
IL-10 [pg/ml]	6.19±6.96	4.64±2.83	4.13±2.41	3.08±0.71	p=0.009	p=0.008	NS
CRP [mg/l]	29.22±36.64	19.76±22.88	2.99±4.89	0.91±0.79	p=0.000	p=0.002	p=0.02

Abbreviations: IL-6 – interleukin-6, IL-10 – interleukin-10, CRP – C-reactive protein, 3d – third day of MI, 7d – seventh day of MI, 6m – six months after MI

Table III. Left ventricular systolic and diastolic function parameters in patients with MI and controls

Variable	Patients with MI (n=75)		Controls (n=20)	p		
	Measurement					
	7d	6m		7d/C	6m/C	7d/6m
LVEF [%]	53.58±10.40	55.08±13.91	70.90±5.08	p=0.000	p=0.000	p=0.08
E/A	1.05±0.36	1.08±0.49	1.09±0.35	NS	NS	NS
DT [ms]	198.19±50.99	214.28±58.95	195.75±53.36	NS	NS	p=0.05
IVRT [ms]	111.51±27.84	116.66±32.76	98.50±18.99	p=0.05	p=0.02	NS
EP [cm/s]	42.82±8.71	42.98±10.93	61.10±17.66	p=0.000	p=0.000	NS
E/Ep	1.80±0.46	1.74±0.71	1.10±0.20	p=0.000	p=0.000	NS

Abbreviations: LVEF – left ventricular ejection fraction, E/A – velocity of early mitral inflow jet to maximum velocity of atrial jet ratio, DT – early mitral inflow deceleration time, IVRT – isovolumetric relaxation time, Ep – propagation time of early mitral flow, E/Ep – maximum E wave velocity to E wave propagation velocity ratio

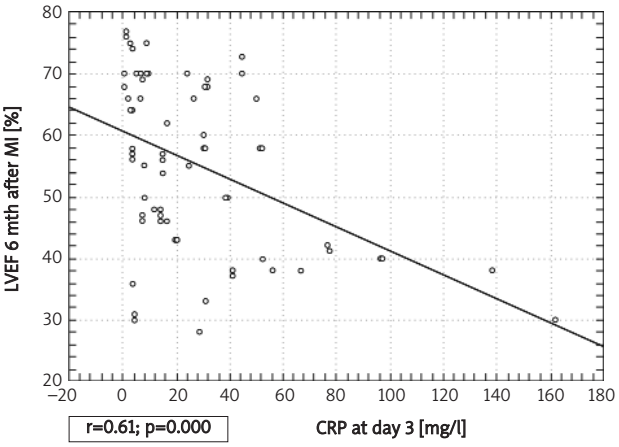

Figure 1. Correlation between CRP levels at day 3 of MI and LVEF at month 6 after MI

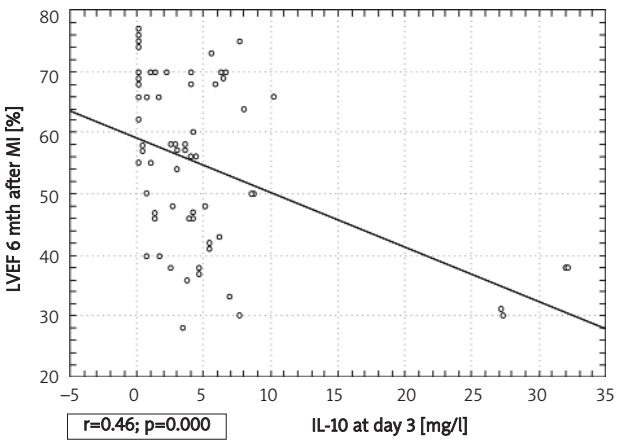

Figure 2. Correlation between IL-10 levels at day 3 of MI and LVEF at month 6 after MI

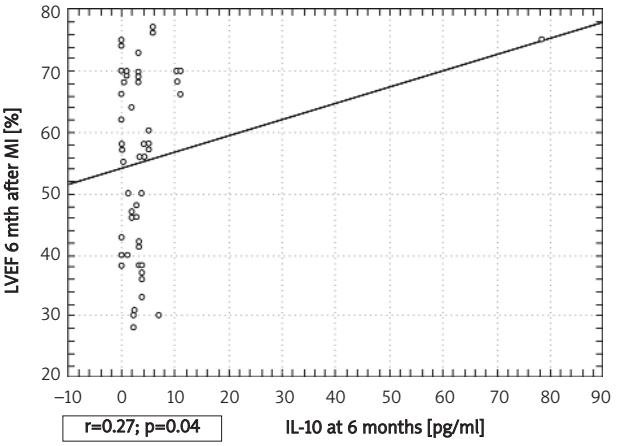

Figure 3. Correlation between IL-10 levels and LVEF at month 6 after MI

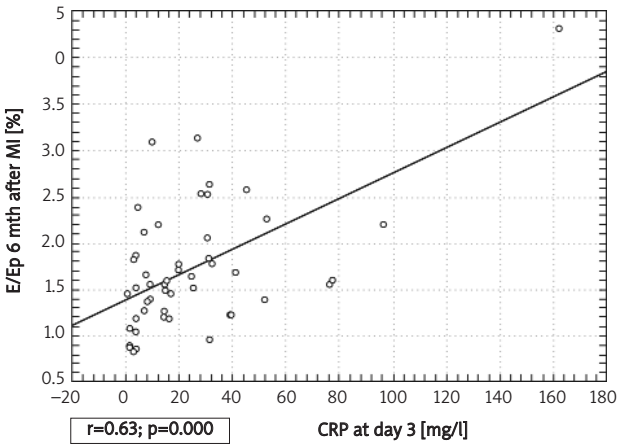

Figure 4. Correlation between CRP levels at day 3 of MI and E/Ep at month 6 after MI

(r=–0.53, p=0.000; r=–0.34, p=0.002; r=–0.51, p=0.000, respectively). Also, the higher was the CRP concentration (7d), the more notable was the reduction in the LVEF at month 6 (r=–0.47, p=0.000).

Relationship between IL-6, IL-10 and CRP levels and LV diastolic function indices

The concentrations of IL-6 and CRP on days 3 and 7 and at month 6 were significantly correlated with all LV diastolic function indices analysed 6 months after infarction: positively with E/A and E/Ep, and negatively with IVRT, DT and Ep. The most potent correlations were found between CRP levels (3d) and E/Ep (6m) (r=0.63, p=0.000) (Figure 4) and between IL-6 levels (6m) and E/Ep (6m) (r=0.57, p=0.000). In addition, there was a significant negative correlation between IL-10 (3d) concentration and DT (7d) (r=–0.36, p=0.005; r=–0.25, p=0.04, respectively; Figure 5). Furthermore, a significant positive correlation was found between IL-10 level (7d) and DT (6m) (r=0.36, p=0.004).

Prognostic significance of IL-6, IL-10 and CRP levels – multivariable analysis

Elevated IL-6 (3d) and CRP (3d) levels were independent prognostic factors of LV systolic dysfunction 6 months after MI (Table IV). The prognostic value was additionally confirmed by the area under ROC, which for IL-6 (3d) was 0.842 (CI ±0.737-0.946, p <0.0001) and for CRP (3d) – 0.812 (CI ±0.691-0.933, p <0.0001). Similarly, elevated IL-6 (3d) and CRP (3d) levels were independent prognostic factors of significant LV diastolic dysfunction 6 months after MI (Table V). The prognostic value obtained was additionally confirmed by the area under ROC, which for IL-6 (3d) was 0.884 (CI ±0.806-0.963, p <0.0001) and for CRP (3d) – 0.764 (CI ±0.654-0.875, p <0.0001).

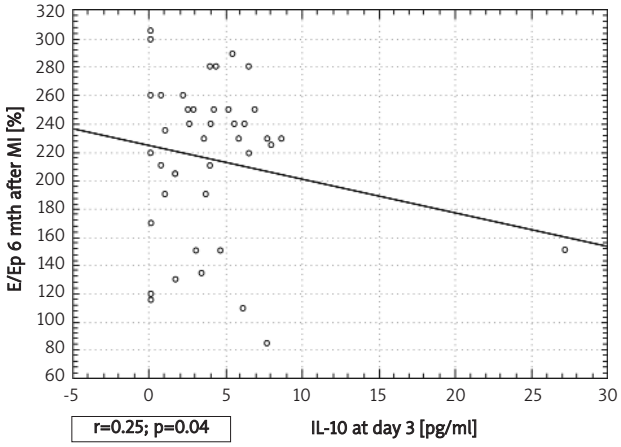

Figure 5. Correlation between IL-10 levels at day 3 of MI and DT at month 6 after MI

Table IV. Prognostic factors of LV systolic dysfunction 6 months after MI – multivariable logistic regression

Variable	p <0.0001			
	OR	–95% CI	+95% CI	p
LVEDD [mm] (7d)	1.908	0.998	3.647	0.05
IL-6 [pg/ml] (3d)	1.277	1.040	1.567	0.02
LVEF [%] (7d)	0.776	0.620	0.972	0.03
CRP [mg/l] (3d)	1.141	0.997	1.305	0.05

Table V. Prognostic factors of significant LV diastolic dysfunction 6 months after MI– multivariable logistic regression

Variable	p <0.00001			
	OR	–95% CI	+95% CI	p
P/R profile (7d)	7.026	1.82	27.03	0.005
IL-6 [pg/ml] (3d)	1.14	1.02	1.27	0.03
CRP [mg/l] (3d)	1.05	1.01	1.10	0.01

Discussion

Concentration of the analysed inflammatory factors and LV systolic function

The experimental studies provide evidence for the contribution of inflammatory factors in the development of systolic myocardial dysfunction. Some of the proinflammatory interleukins, including IL-6, show cardiodepressive properties [3], while C-reactive protein, by binding with the extracellular matrix components that have been changed by the ischaemia, may activate the local complement system and add to the myocardial lesion [4].

In our studies a correlation was found between LV systolic function and activation of proinflammatory factors. Increased IL-6 and CRP levels correlated with impairment of LV systolic function and was an independent predictor of LV systolic dysfunction 6 months after MI.

The studies of other authors also found a relationship between the activation of proinflammatory interleukins and LV systolic function in MI survivors. In none of the available reports was there undertaken such an in-depth evaluation of how much the increased activation of proinflammatory factors is an independent predictor of impairment of LV function, and the follow-up period was less than 3 months.

Halawa et al. [5] found in patients with MI a significant negative correlation between IL-6 level and LVEF in the echocardiography performed on days 3 and 7 of hospitalisation. On the other hand, Gabriel et al. [6] found that patients with impaired LV systolic function 12 weeks after MI were characterised by elevated IL-6 levels in comparison to patients with normal LV systolic function. Similarly to our findings, the studies of other authors revealed that maximum CRP concentration in MI patients (on the third day of hospitalisation) was significantly negatively correlated with LVEF assessed in the echocardiography and ventriculography at discharge [7, 8]. The relationship between the CRP levels on the third day of hospitalisation and LVEF after 2 weeks from MI was also documented by Takahashi et al. [9].

Due to MI, the increased activation of proinflammatory interleukins is associated with increased local secretion of anti-inflammatory interleukins, of which the most important is IL-10. It has been shown that it contributes to restoration of the infarction zone, in particular in degradation and remodelling of the extracellular matrix [10]. Moreover, this interleukin decreases synthesis of proinflammatory cytokines and inhibits cellular apoptosis, which counteracts post-reperfusion myocardial damage [11].

There are no reports available on the relationship between IL-10 and LV function in patients with MI. Our results indicate that the prognostic value of IL-10 levels may depend on the time of measurement. As we have documented, the directly proportional correlation between IL-10 levels on the 3rd day of hospitalisation and parameters reflecting LV systolic impairment may indicate that elevated IL-10 concentration in the acute phase of infarction, accompanying the increased activation of proinflammatory interleukins, reflects a higher degree of postinfarction damage and systolic dysfunction. However, the directly proportional relationship between IL-10 level on the 7th day of infarction and 6 months after the MI episode and LVEF 6 months after MI speaks for the fact that after resolution of a potent stimulus, such as acute myocardial ischaemia and reperfusion, maintenance of elevated levels of this interleukin seems beneficial. This is supported by the experimental and clinical studies. Kaur et al. [12] on the basis of experimentally induced MI in rats found that the lower

the IL-10 expression in the myocardium in the 4th, 8th, and 16th weeks of follow-up, the more impaired was the LV systolic function assessed in echocardiography and invasive methods. Heeschen et al. reported in MI patients that higher IL-10 level at discharge was associated with a lower risk of death and re-infarction in the 6-month follow-up [13].

Inflammatory factor levels and LV diastolic function

So far there have been few data on participation of inflammatory factors in the development of diastolic dysfunction of the heart, unlike the documented characteristics of these factors as contributors to LV systolic dysfunction [14]. However, taking into account the close relationship between systole and diastole as well as their interdependence (and some cardiodepressive mechanisms of cytokines may also play a role in the diastolic phase) it cannot be excluded that those factors add to the development of myocardial diastolic dysfunction. Undoubtedly, the common denominator for those relationships between LV diastolic function and inflammatory factor levels is myocardial ischaemia.

There are no reports in literature on the correlations between LV diastolic function and immuno-inflammatory activation in patients with MI. The results of our study support such a relationship. This has been indicated by a significant correlation between IL-6 and CRP levels and impairment of Doppler parameters of diastolic LV filling. The IL-6 and CRP levels on the 3rd day of MI were also found to be independent predictors of considerable LV diastolic dysfunction 6 months after MI.

In the case of IL-10, based on our results it can be concluded that the time of IL-10 level measurement may affect its prognostic value in the assessment of LV diastolic dysfunction similarly to systolic impairment. It can be assumed that increased IL-10 concentration in the early phase of MI is a measure of immuno-inflammatory myocardial damage and reflects a higher degree of postinfarction myocardial damage and diastolic dysfunction. However, after resolution of a potent stimulus, such as acute myocardial ischaemia and reperfusion, maintained elevated levels of interleukin-10 seem prognostically favourable.

Conclusions

1. Significant correlation between increased serum IL-6 and CRP levels and LV systolic as well as diastolic dysfunction suggests possible input of those factors into the postinfarction myocardial damage.
2. Increased IL-6 and CRP levels during an acute phase of MI are independent predictors of LV systolic and diastolic dysfunction 6 months post MI.
3. Significant correlation between increased serum IL-10 levels in the first days of MI and LV systolic and diastolic impairment implicate major enhancement of the damaging factor, stimulating a protective action of IL-10.
4. Increased IL-10 levels maintained in the subsequent days/months after MI seem to be beneficial, as indicated by a correlation between IL-10 levels measured at that specific time and both LVEF and DT.

References

1. Cohn JN, Ferreri R, Sharpe N, on behalf of an International Forum on Cardiac Remodeling. Cardiac Remodeling – Concepts and Clinical Implications: a consensus paper from an International Forum on Cardiac Remodeling. *J Am Coll Cardiol* 2000; 35: 569-82.
2. Shan K, Kurrelmeyer K, Seta Y, et al. The role of cytokines in disease progression in heart failure. *Curr Opin Cardiol* 1997; 12: 218-23.
3. Finkel MS, Oddis CV, Jacob TD, et al. Negative inotropic effects of cytokines on the heart mediated by nitric oxide. *Science* 1992; 257: 387-9.
4. Griselli M, Herbert J, Hutchinson WL, et al. C-reactive protein and complement are important mediators of tissue damage in acute myocardial infarction. *J Exp Med* 1999; 190: 1733-40.
5. Halawa B, Salomon P, Jołda-Mydłowska B, et al. Stężenia czynnika martwicy nowotworów (TNF-alfa) i interleukiny-6 (IL-6) w surowicy chorych na świeży zawał mięśnia serca. *Pol Arch Med Wewn* 1999; 101: 197-203.
6. Gabriel AS, Martinsson A, Wretlind B, et al. IL-6 levels in acute and post myocardial infarction: their relation to CRP levels, infarction size, left ventricular systolic function, and heart failure. *Eur J Intern Med* 2004; 15: 523-8.
7. Dedobbeleer C, Melot C, Renard M, et al. C-reactive protein increase in acute myocardial infarction. *Acta Cardiol* 2004; 59: 291-6.
8. Anzai T, Yoshikawa T, Shiraki H, et al. C-reactive protein as a predictor of infarct expansion and cardiac rupture after a first Q-wave acute myocardial infarction. *Circulation* 1997; 96: 778-84.
9. Takahashi T, Anzai T, Yoshikawa T, et al. Serum C-reactive protein elevation in left ventricular remodeling after acute myocardial infarction – role of neurohormones and cytokines. *Int J Cardiol* 2003; 88: 257-65.
10. Mostafa Mtairag E, Chollet-Martin S, Oudghiri M, et al. Effects of interleukin-10 on monocyte/endothelial cell adhesion and MMP-9/TIMP-1 secretion. *Cardiovasc Res* 2001; 49: 882-90.
11. Opal SM, DePalo VA. Anti-inflammatory cytokines. *Chest* 2000; 117: 1162-72.
12. Kaur K, Sharma AK, Singal PK. Significance of changes in TNF-alpha and IL-10 levels in the progession of heart failure subsequent to myocardial infarction. *Am J Physiol Heart Circ Physiol* 2006; 291: H106-13.
13. Heeschen C, Dimmeler S, Hamm CW, et al. The CAPTURE Study Investigators. Serum level of the anti-inflammatory cytokine interleukin-10 is an important prognostic determinant in patients with acute coronary syndromes. *Circulation* 2003; 107: 2109-14.
14. Kosmala W, Derzhko R, Przewłocka-Kosmala M, et al. Plasma levels of TNF-alpha, IL-6 and IL-10 and their relationship with left ventricular diastolic function in patients with stable angina pectoris and preserved left ventricular systolic performance. *Coron Artery Dis* 2008; 19: 375-82

Stężenie interleukiny 6, interleukiny 10 i białka C-reaktywnego a funkcja lewej komory u chorych z zawałem mięśnia sercowego leczonych pierwotną angioplastyką

Łukasz Karpiński, Rafał Płaksej, Wojciech Kosmala, Maria Witkowska

Klinika Kardiologii, Akademia Medyczna, Wrocław

Streszczenie

Wstęp: Badania ostatnich lat wskazują, że w procesie przebudowy serca po zawale biorą udział czynniki zapalno-immunologiczne. Uważa się, że zwiększona i przetrwała aktywacja czynników prozapalnych może potęgować uszkodzenie mięśnia sercowego i przyczyniać się do wystąpienia niewydolności serca. Z kolei czynniki przeciwzapalne, hamując nadmierną reakcję zapalną, wykazują działanie ochronne.

Cel: Poszukiwanie związków między stężeniem interleukiny 6 (IL-6), interleukiny 10 (IL-10) i białka C-reaktywnego (CRP) a echokardiograficznymi parametrami funkcji serca u chorych z zawałem mięśnia sercowego z uniesieniem odcinka ST (STEMI) leczonych pierwotną plastyką tętnic wieńcowych w obserwacji 6-miesięcznej. Oceniano także znaczenie prognostyczne stężenia tych czynników w przewidywaniu dysfunkcji skurczowej i rozkurczowej lewej komory (LV) 6 miesięcy po zawale serca.

Metody: Badanie przeprowadzono u 75 chorych w wieku 36–82 lat, w tym 28 kobiet i 47 mężczyzn, hospitalizowanych z powodu pierwszego w życiu STEMI, leczonych pierwotną przezskórną angioplastyką. W celu oznaczenia stężenia IL-6, IL-10 i CRP pobierano krew w 3. i 7. dobie zawału (3d, 7d) oraz 6 miesięcy po incydencie (6m). Badanie echokardiograficzne przeprowadzano w 7. dobie zawału i po pół roku, oceniając parametry funkcji skurczowej LV: frakcja wyrzutowa LV (LVEF), oraz rozkurczowej: stosunek maksymalnej prędkości fali wczesnego napływu mitralnego do maksymalnej prędkości fali przedsionkowej (E/A), czas deceleracji fali wczesnego napływu mitralnego (DT), czas rozkurczu izowolumetrycznego LV (IVRT), prędkość propagacji fali wczesnego napływu mitralnego (Ep), stosunek maksymalnej prędkości fali wczesnego napływu mitralnego do prędkości jego propagacji (E/Ep). Za kryterium dysfunkcji skurczowej LV przyjęto LVEF <45%. Jako kryterium istotnej dysfunkcji rozkurczowej LV przyjęto obecność profilu pseudonormalizacji lub restrykcji napływu mitralnego.

Wyniki: Stężenie IL-6 i CRP w kolejnych badaniach korelowało istotnie ujemnie z LVEF (7d) i LVED (6m). Stężenie IL-10 (3d) korelowało istotnie ujemnie z LVEF (6m) (r=–0,46, p=0,000). Natomiast stężenie IL-10 (7d) i IL-10 (6m) korelowało znamiennie dodatnio z LVEF (6m) (r=0,39, p=0,02; r=0,27, p=0,04). Stężenie IL-6 i CRP w kolejnych badaniach korelowało istotnie dodatnio z E/A, E/Ep oraz ujemnie z IVRT, DT i Ep. Stężenie IL-10 (3d) korelowało istotnie ujemnie z DT (6m) (r=–0,25, p=0,04), natomiast stężenie IL-10 (7d) korelowało znamiennie dodatnio z DT (6m) (r=0,36, p=0,004). W analizie wieloczynnikowej regresji logistycznej podwyższone stężenie IL-6 (3d) i CRP (3d) było niezależnym wskaźnikiem prognostycznym dysfunkcji skurczowej (odpowiednio: OR=1,27, p=0,02; OR=1,14, p=0,05) oraz rozkurczowej LV (OR=1,14, p=0,03; OR=1,05, p=0,01) 6 miesięcy po zawale.

Wnioski: 1. Istotne wprost proporcjonalne związki pomiędzy podwyższonym stężeniem w surowicy IL-6 i CRP a upośledzeniem funkcji skurczowej i rozkurczowej LV wskazują na możliwy udział tych czynników w pozawałowym uszkodzeniu serca. 2. Podwyższone stężenie IL-6 i CRP w ostrej fazie zawału jest czynnikiem o niezależnej mocy prognostycznej dysfunkcji skurczowej i rozkurczowej LV 6 miesięcy po zawale. 3. Istotne wprost proporcjonalne związki między podwyższonym stężeniem IL-10 w pierwszych dniach zawału a upośledzeniem funkcji skurczowej i rozkurczowej LV przemawiają za znacznym stopniem nasilenia czynnika uszkadzającego, pobudzającego ochronne działanie IL-10. 4. Wydaje się, że utrzymywanie się podwyższonego stężenia IL-10 w kolejnych dniach/miesiącach po zawale ma znaczenie korzystne, na co wskazuje wprost proporcjonalna korelacja między mierzonym wówczas stężeniem IL-10 a LVEF i DT.

Słowa kluczowe: interleukina 6, interleukina 10, białko C-reaktywne, zawał mięśnia sercowego, dysfunkcja LV

Kardiol Pol 2008; 66: 1279-1285

Adres do korespondencji:

dr n. med. Łukasz Karpiński, Klinika Kardiologii, Akademia Medyczna, ul. L. Pasteura 4, 50-367 Wrocław, tel.: +48 71 784 26 11, faks: +48 71 327 09 61, e-mail: futuredream@poczta.fm

Praca wpłynęła: 10.08.2008. **Zaakceptowana do druku:** 01.10.2008.