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Low adiponectin blood concentration predicts left ventricular remodeling after ST-segment elevation myocardial infarction treated with primary percutaneous coronary intervention

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Abstract

Background: *Left ventricular remodeling (LVR), an increase in left ventricular end-diastolic volume index ≥ 20%, is an adverse consequence of myocardial infarction. The aim of this study was to assess the association between LVR and adiponectin, which has been shown to protect against myocardial ischemia-reperfusion injury.*

Methods: *In 75 patients echocardiographic examination was performed one year after ST-segment elevation myocardial infarction, successfully treated with primary percutaneous coronary intervention (pPCI). Two groups of patients were analyzed: those with LVR (n = 15) and those without LVR (n = 60).*

Results: *The predictors of LVR were: anterior myocardial infarction, glucose at admission, baseline C-reactive protein, adiponectin, and echocardiographic parameters: left ventricular end-diastolic and end-systolic volume indices, ejection fraction < 40% and left ventricular wall motion score index (WMSI) at discharge. On multivariable regression analysis, lower adiponectin level (OR = 0.67, 95% CI 0.49–0.91, p < 0.05) and higher WMSI (OR = 20.14, 95% CI 2.62–154.82, p < 0.01) were the only independent negative predictors of LVR. The optimal cut-off for adiponectin for predicting LVR was ≤ 4.7 μg/mL (sensitivity: 73%, specificity: 85%) and this level increased the risk of LVR 15-fold (95% CI 4.05–59.87, p = 0.0001).*

Conclusions: *Baseline low blood adiponectin concentration, along with WMSI, can be considered as a predictor of the LVR in male patients one year after myocardial infarction and pPCI.*
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Key words: adiponectin, myocardial infarction, left ventricular remodeing

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Introduction

Left ventricular remodeling (LVR) after myocardial infarction (MI) is a dynamic process resulting in global enlargement, changes in geometry and mass of the left ventricle. Remodeling is an important determinant of subsequent heart failure: a major source of morbidity and mortality in the post-infarction population. This adverse consequence occurs in response to the loss of myocardium and sudden increase in ventricular loading conditions, subsequent infarct extension and late hypertrophy in the remote ventricular myocardium [1, 2]. Opening of the infarct-related artery is crucial in the prevention of the LVR [3–5], but several other important factors have been recognized. These are infarct size, anterior location, microvascular dysfunction, mitral regurgitation after MI, contractile reserve and inducible ischaemia [6–11]. The association between inflammation [12] and stress hyperglycaemia [13, 14] on the remodeling process have attracted attention recently.

Adiponectin, an adipose tissue-derived hormone that is down-regulated in obese individuals, affects several signaling pathways in skeletal muscles, liver, cardiac myocytes and vascular cells [15]. Adiponectin has a favorable effect on endothelial function and angiogenesis [16, 17] and suppresses the atherogenic process [18, 19]. Several studies suggest that adiponectin has anti-inflammatory properties [20, 21], reduces endothelial cell apoptosis [22] and promotes nitric oxide production [23]. The protective action of adiponectin against myocardial ischemia-reperfusion injury has been shown recently [24, 25]. The value of adiponectin as a prognostic factor of left ventricular function [26] and future adverse cardiac events [27] after MI has been recently suggested. To our knowledge, the association between blood adiponectin concentration and LVR following MI has not been analyzed.

The aim of the study was to assess the impact of adiponectin on the LVR one year after acute MI successfully treated with primary percutaneous coronary intervention (pPCI).

Methods

Study population

From the group of patients with the first ST-segment elevation MI, successfully treated with pPCI, 80 men aged ≤ 65 years were initially selected for the study. Successful PCI was defined as the restoration of TIMI 3 grade flow and residual stenosis < 30% at the end of the procedure. In 99% of patients, bare metal stents were implanted. Significant valvular heart disease, atrial fibrillation, atrioventricular block, temporary or permanent stimulation, acute and chronic inflammation or infection, autoimmune diseases, liver kidney and thyroid diseases were considered as grounds for exclusion.

In 68% of patients, glycoprotein IIb/IIIa inhibitor was administered in the course of MI. In patients with multivessel disease, staged PCI of another significant lesion was performed according to agreement reached by the cardiologist and the interventional cardiologist on an individual basis. The pharmacological treatment according to the current standards was recommended at discharge (aspirin, clopidogrel for at least 30 days and statins in 100% of patients, beta-blockers in 94% of patients, and angiotensin converting enzyme-inhibitors in 66% of patients).

At one year follow-up (12 ± 1.2 months) we had lost contact with one patient, two patients had died and two patients had experienced subsequent MI. In the other 75 patients who formed the study group echocardiographic examination was performed. An increase in left ventricular end-diastolic volume index (LVEDVI) ≥ 20% was accepted as a surrogate for remodeling. The data was finally analyzed in groups of patients divided into those with LVR (n = 15; 20%) and those without LVR (n = 60; 80%).

Echocardiographic examination

Echocardiographic study was performed on the second or third day after admission with Sonos 5500, S3 probe. The harmonic option was used to enhance the visualization of the endocardium. LVEDV, left ventricular end-systolic volume (LVESV) and left ventricular ejection fraction (LVEF) was assessed at four-chamber and two-chamber apical views with the biplane Simpson's formula. Left ventricular volumes indexed by body surface area (LVEDVI, LVESVI) were calculated. Impaired systolic function was diagnosed in cases of LVEF below 40%. For each segment of LV, wall motion was scored from one (normal) to four (dyskinetic) and global wall motion score index (WMSI) was calculated as the average over 16 segments. From the pulse-wave Doppler mitral inflow tracings recorded from the four-chamber apical view the following parameters were measured: early (E), and late (A) transmitral peak flow velocities, E/A ratio and E wave deceleration time (DT).

Laboratory measurements

Fasting blood samples for measurements of adiponectin were taken on the next day after ad-

Table 1. Baseline characteristics of the study groups.

	With remodeling (n = 15)	Without remodeling (n = 60)	p
Age (years)	55 ± 5	54 ± 6	NS
Hypertension	9 (60%)	30 (50%)	NS
Diabetes mellitus	5 (33%)	12 (20%)	NS
Dyslipidemia	14 (93%)	46 (77%)	NS
Obesity	7 (46%)	27 (45%)	Ns
Smoking	11 (73%)	37 (62%)	NS
Time since the onset of symptoms to admission [h]	5.0 ± 2.4	4.3 ± 2.8	NS
Anterior infarct localization	10 (67%)	22 (37%)	< 0.05
Multivessel disease	6 (40%)	23 (38%)	NS
Glucose at admission [mg/dL]	166.5 ± 49.7	128.0 ± 34.1	< 0.0001
C-reactive protein [mg/dL]	9.7 ± 6.8	5.1 ± 4.7	< 0.01
Adiponectin [μg/mL]	4.6 ± 2.2	10.1 ± 6.6	< 0.0001

mission for ST elevation myocardial infarction. Plasma for measurements was frozen at –70° until analysis with the quantitative sandwich enzyme immunoassay technique (ELISA) obtained from R&D Systems Inc. Plasma triglicerydes (TG) and total cholesterol (TCH) were measured by enzymatic analytical chemistry. HDL-cholesterol (HDL-CH) was precipitated using dextran-sulphate and measured enzymatically. The LDL-cholesterol (LDL-CH) was calculated using the Friedewald equation: LDL-CH = TCH – (TG/5) – HDL-CH. Hyperlipidemia was diagnosed in case of hypercholesterolemia (TCH > 200 mg/dL) with LDL-CH (LDL > > 100 mg/dL) and/or hypertriglicerydemia (TG > > 150 mg/dL) and low HDL-CH (HDL-CH < < 40 mg/dL).

Statistical analysis

Continuous variables were presented as mean ± ± standard deviation. Variables were log-transformed before statistical analysis if necessary. Comparisons between analyzed groups (with LVR and without LVR) were performed using the two-tailed, non-paired Student t test or Mann-Whitney test, as appropriate. Differences in echocardiographic variables at baseline and at one-year follow-up were assessed with the paired Student's t test. Categorical data were summarized as frequencies and percentages, and comparisons between the groups were performed with χ^2 test or Fisher's exact test. The independent predictors of LVR were assessed using the multivariate logistic regression analysis, including variables that were significantly associated with LVR in univariate analysis. The variables included in the univariate logistic regression analysis were: age, smoking, obesity, diabetes mellitus, hypertension, dyslipidemia, time since the onset of symptoms to admission, anterior myocardial infarction, multivessel disease, glucose at admission, beseline blood levels of adiponectin and C-reactive protein (CRP), baseline LVEDVI, LVESVI, LVEF < 40%, WMSI, E/A and DT. Results were expressed as odds ratio (OR) and confidence interval (CI). A receiver-operating characteristics (ROC) curve analysis was used to determine the cut-off values for adiponectin for predicting LVR. P value < 0.05 was considered statistically significant. Statistical analysis was performed using Statistica software (version 6.0; Tulsa, OK, USA) and MedCalc statistical software (version 7.2.1.0 for Windows; Mariakerke, Belgium).

The study was approved by the Internal Ethics Committee of the Medical University of Łódź, and each patient gave informed consent.

Results

Baseline clinical, biochemical, angiographic and echocardiographic characteristics are presented in Table 1. In the group with remodeling, the number of patients with anterior localization of MI, glucose at admission and beseline levels of CRP were significantly higher and adiponectin concentration lower than in the group without remodeling.

Mean values of several echocardiographic parameters measured at baseline and at one year follow-up differed between the analyzed groups: LVEDVI, LVESVI, LVEF and WMSI were significantly higher in patients with LVR. Systolic dysfunction (LVEF < 40%) was detected in more patients in this group (Table 2).

Table 2. Echocardiographic parameters at baseline and at one year follow-up in the study groups.

	With remodeling (n = 15)	Without remodeling (n = 60)	p
Baseline			
LVEDVI [mL/m^2]	57 ± 14	50 ± 11	< 0.05
LVESVI [mL/m^2]	27 ± 11	22 ± 7	< 0.05
LVEF (%)	46 ± 8	58 ± 9	< 0.0001
LVEF < 40% — number of patients (%)	4 (27%)	1 (2%)	< 0.001
WMSI	1.81 ± 0.39	1.33 ± 0.31	< 0.0001
E/A	1.09 ± 0.31	1.01 ± 0.29	NS
DT [ms]	195 ± 41	202 ± 38	NS
One-year follow-up			
LVEDVI [mL/m^2]	70 ± 15	49 ± 12	< 0.0001
LVESVI [mL/m^2]	30 ± 12	22 ± 8	< 0.01
LVEF (%)	44 ± 9	59 ± 8	< 0.0001
WMSI	1.79 ± 0.40	1.26 ± 0.27	< 0.0001
E/A	1.00 ± 0.35	1.03 ± 0.28	NS
DT [ms]	226 ± 48	212 ± 42	NS

LVEDVI — left ventricular end-diastolic volume index; LVESVI — left ventricular end-systolic volume index; LVEF — left ventricular ejection fraction; WMSI — wall motion score index; DT — deceleration time

In univariate logistic regression analysis, predictors of LVR were: anterior myocardial infarction, glucose at admission, beseline blood levels of adiponectin and CRP, baseline LVEDVI, LVESVI, LVEF < 40% and WMSI. The final model of multivariable regression analysis demonstrated that lower adiponectin levels and higher WMSI were the independent negative predictors of LVR (Table 3).

Figure 1 shows the area under the ROC curves for adiponectin concentration for predicting LVR (AUC = 0.842; 95% CI = 0.740–0.916). The optimal value of adiponectin for predicting LVR was defined as the concentration with the largest sum of sensitivity plus specificity for each of the curve. The optimal cut-off for adiponectin was ≤ 4.7 μg/mL; the sensitivity and specificity were 73% and 85%, respectively.

LVEDVI, LVESVI, LVEF and WMSI significantly differed between the group of patients with blood adiponectin level ≤ 4.7 μg/mL (20 patients) and > 4.7 μg/mL (55 patients) both at baseline (58 ± ± 11 *vs* 48 ± 11; 27 ± 10 *vs* 21 ± 7; 50 ± 10 *vs* 57 ± ± 9; 1.69 ± 0.43 *vs* 1.33 ± 0.31, respectively) and at follow up (65 ± 11 *vs* 49 ± 12; 30 ± 11 *vs* 22 ± 8; 51 ± 11 *vs* 58 ± 9; 1.65 ± 0.45 *vs* 1.26 ± 0.27, respectively). LVEDVI significantly increased from baseline until the follow-up only in the group of patients with blood adiponectin level ≤ 4.7 μg/mL and WMSI significantly decreased at follow-up in both groups (Fig. 2A–F). Blood adiponectin level below 4.7 μg/mL 15.5-fold increased the risk of LVR (95% CI 4.05–59.87, p = 0.0001).

Discussion

At present, despite the introduction of pPCI into the treatment of MI and recommended widespread use of 'anti-remodeling' medications, LVR remains an important late complication. It is related to microvascular dysfunction and the no-reflow phenomenon within the risk area [11, 28] and with the reduced coronary flow reserve [29].

The most interesting finding of our study is that low baseline blood adiponectin concentration is an independent predictor of the LVR after MI. The efficacy of adiponectin as a prognostic factor of left ventricular function following successful reperfusion has been shown by Shibata et al. [30]. These authors, using the scintigraphic imaging, have revealed that adiponectin levels were negatively associated with changes in LVEF at six months observation. This finding, together with the detected association of adiponectin with myocardial salvage parameters, inclined the authors to suggest that adiponectin could be indicative of long-term myocardial remodeling after MI. Our study confirms this suggestion in a one year follow-up. There are several potential explanations of the protective function of adiponectin. The possible molecular mechanisms mediating metabolic and vascular activity of

Table 3. Univariate and multivariate logistic regression analysis for the predictors of left ventricular remodeling.

	Odds ratio	–95% CI	+95% CI	p
Univariate logistic regression analysis				
Age	1.0426	0.9490	1.1454	0.3851
Hypertension	1.5000	0.4748	4.7388	0.4896
Diabetes mellitus	2.0000	0.5753	6.9532	0.2756
Dyslipidemia	4.2609	0.5139	35.3265	0.1792
Obesity	1.0694	0.3438	3.3264	0.9077
Smoking	1.7095	0.4863	6.0096	0.4032
Time since the onset of symptoms to admission	1.0756	0.8906	1.2990	0.4491
Anterior infarct localization	3.4545	1.0456	11.4131	0.0420
Multivessel disease	1.0725	0.3373	3.4098	0.9056
C-reactive protein	1.1451	1.0373	1.2641	0.0072
Glucose at admission	1.0228	1.0080	1.0378	0.0024
Adiponectin	0.6252	0.4498	0.8414	0.0024
LVEDVI baseline	1.0521	1.0005	1.1062	0.0476
LVESVI baseline	1.0738	1.0050	1.1473	0.0351
LVEF < 40% baseline	21.4545	2.1858	210.5807	0.0085
WMSI baseline	23.0276	4.7862	164.1286	0.0002
E/A baseline	2.3322	0.3712	14.6518	0.3664
DT baseline	0.9948	0.9795	1.0104	0.5123
Multivariate logistic regression analysis				
WMSI baseline	20.1389	2.6210	154.8126	0.0017
Adiponectin	0.6680	0.4889	0.9080	0.0098

LVEDVI — left ventricular end-diastolic volume index; LVESVI — left ventricular end-systolic volume index; LVEF — left ventricular ejection fraction; WMSI — wall motion score index; DT — deceleration time; CI — confidence interval

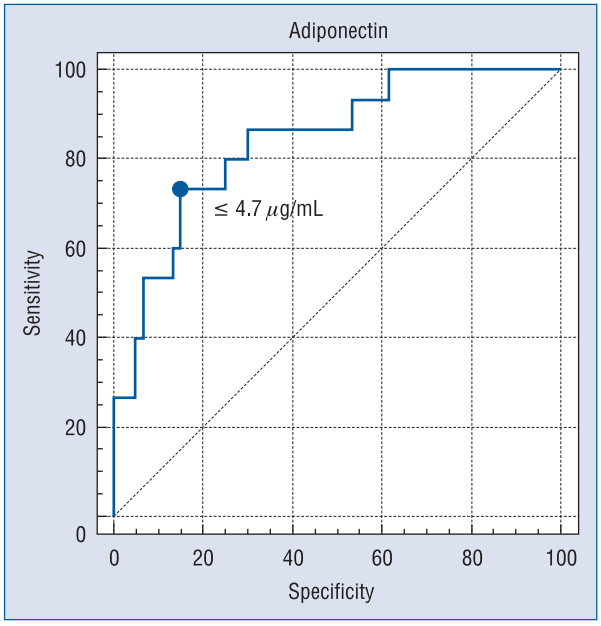

Figure 1. ROC curve for adiponectin for predicting left ventricular remodeling.

adiponectin involve stimulation of AMP kinase activity and cyclooxygenase (COX)-2-dependent synthesis of prostaglandin E2 that inhibits TNF-alpha production [20, 24].

Experimental studies by Tao et al. [25] demonstrated that adiponectin protects against ischemia/reperfusion injury by inhibition of nitric oxide, superoxide and their cytotoxic reaction product formation. In animal models, Shibata at al. [26] showed that adiponectin administered into the created myocardial zone suppressed cardiac hypertrophy and interstitial fibrosis, protected against myocyte apoptosis and increased capillary density in the infarct border zone that was associated with decreased left ventricular dilatation and improved left ventricular function.

In our study group, including relatively young men with the first, mostly inferior MI, successful treatment with pPCI remodeling was observed in 20% of patients. Some other studies performed on comparable groups of patients show similar results to ours [6, 31]. Savoye et al. [8] reported the inci-

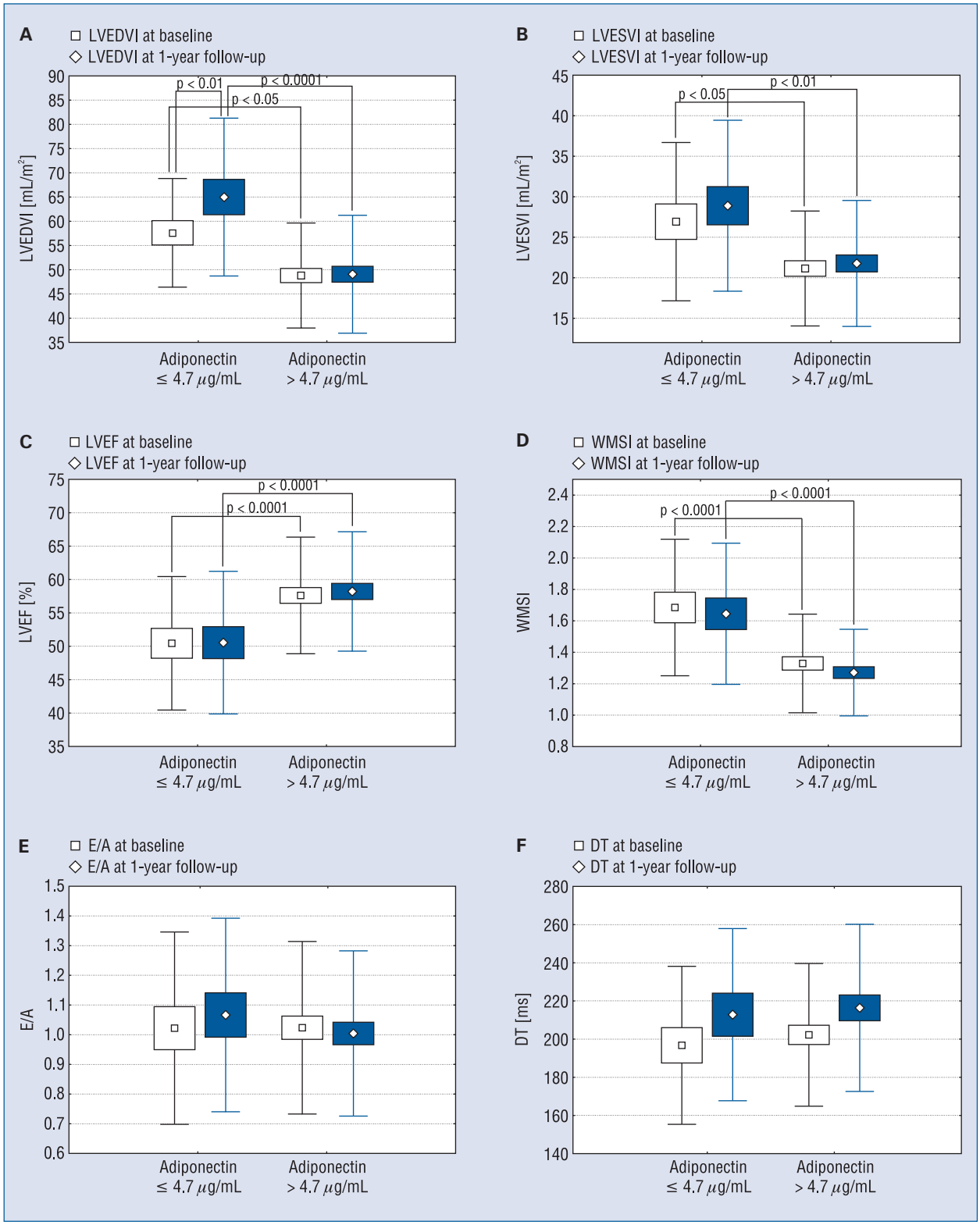

Figure 2. Changes in echocardiographic parameters from baseline to follow-up in patients with blood adiponectin level below and above the optimal cut-off value for predicting left ventricular remodeling: 4.7 μg/mL; **A.** Left ventricular end-diastolic volume index (LVEDVI); **B.** Left ventricular end-systolic volume index (LVESVI); **C.** Left ventricular ejection fraction (LVEF); **D.** Left ventricular wall motion score index (WMSI); **E.** Early (E) to late (A) transmitral peak flow velocities ratio (E/A); **F.** Early transmitral wave deceleration time (DT).

dence of LVR in 31% of the study group including exclusively patients with at least three akinetic left ventricular segments at discharge. This observation indicates that infarct size is an important determinant of subsequent changes in left ventricular volume. Our results and some other previous studies [8, 32, 33], which identify WMSI as an independent predictor of remodeling, confirm such a notion. However, in our study group the relation between decreased LVEF below 40% and LVR was not confirmed in multivariate analysis, suggesting that LVR is not related to the deterioration of global left ventricular function. Similar results were shown by Łoboz-Grudzień et al. [6] but disparate observations come from papers [4, 32] published before the widespread application of pPCI and abciximab, a protector against microvascular disfunction [34].

It has been shown that in patients with MI, stress hyperglycemia may be related to the no-reflow phenomenon [35], reduce collateral flow to the area at risk [36], abolish the effect of preconditioning [37] and result in high one-year mortality [38]. The interesting observation came from the study of Carrabba et al. [39] who showed that more frequent progression to heart failure in diabetics after MI cannot be explained by a greater propensity for LVR. Recently, a significant and independent impact of stress hyperglycemia on LVR after MI has been revealed in non-diabetic patients [13, 14]. This observation was not confirmed in our study group, quite possibly due to the inclusion of both diabetic and non-diabetic patients, and a very small subset of non-diabetic patients with hyperglycemia on admission. It has been shown in some other studies that stress hyperglycemia is associated with a more adverse outcome, expressed as an increased risk of congestive heart failure and one-year mortality only in non-diabetics [40].

Limitations of the study

Unfortunately we have not performed serial measurements of adiponectin in the course of MI, whereas plasma adiponectin concentrations decline significantly at 24 hours compared to the concentrations on admission and remains relatively stable only between 24 and 72 hours [41]. Moreover, we have measured CRP levels at admission, not the peak values which have been shown to predict LVR [12]. We have not performed coronary angiography at follow-up, so the condition of the infarct related artery and the late potency of the implanted stents is not known.

The results of our study concern only male patients, so the conclusions cannot be generalized for the whole population as there are sex-related differences in plasma adiponectin concentration [42].

Long-term clinical studies in large number of patients are warranted to fully elucidate the impact of several factors on LVR and consider the action of the cluster of these factors.

Conclusions

Baseline low blood adiponectin concentration, along with WMSI, can be considered as a predictor of LVR in male patients one year after MI and pPCI.

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References

1. Cohn JN, Ferrari 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: 569–582.
2. French BA, Kramer CM. Mechanisms of post-infarct left ventricular remodeling. Drug Discov Today Dis Mech, 2007; 4: 185–196.
3. Tani S, Nagao K, Watanabe I et al. Increasingly well-preserved left ventricular function in hospital survivors with acute myocardial infarction: Effect of early and complete reperfusion strategy on left ventricular remodeling. Circ J, 2007; 71: 180–185.
4. Gaudron P, Eilles C, Kugler I, Ertl G. Progressive left ventricular dysfunction and remodeling after myocardial infarction. Potential mechanisms and early predictors. Circulation, 1993; 87: 755–763.
5. Yang Y, Gao R, Tian J et al. Beneficial effects of early coronary reperfusion on left ventricular remodeling and systolic function in patients with acute myocardial infarction. Chin Med J (Engl), 1998; 111: 142–146.
6. Łoboz-Grudzień K, Kowalska A, Brzezińska B, Sokalski L, Jaroch J. Early predictors of adverse left ventricular remodelling after myocardial infarction treated by primary angioplasty. Cardiol J, 2007; 14: 238–245.
7. Chareonthaitawee P, Christian TF, Hirose K, Gibbons RJ, Rumberger JA. Relation of initial infarct size to extent of left ventricular remodeling in the year after acute myocardial infarction. J Am Coll Cardiol, 1995; 25: 567–573.
8. Savoye C, Equine O, Tricot O et al.; REmodelage VEntriculaire Study Group. Left ventricular remodeling after anterior wall acute myocardial infarction in modern clinical practice (from the REmodelage VEntriculaire [REVE] study group). Am J Cardiol, 2006; 98: 1144–1149.
9. Ennezat PV, Darchis J, Lamblin N et al.; REVE Investigators. Left ventricular remodeling is associated with the severity of mitral regurgitation after inaugural anterior myocardial infarction-optimal timing for echocardiographic imaging. Am Heart J, 2008; 155: 959–965.

10. Coletta C, Sestili A, Seccareccia F et al. Influence of contractile reserve and inducible ischaemia on left ventricular remodelling after acute myocardial infarction. Heart, 2003; 89: 1138–1143.
11. Bolognese L, Carrabba N, Parodi G et al. Impact of microvascular dysfunction on left ventricular remodeling and long-term clinical outcome after primary coronary angioplasty for acute myocardial infarction. Circulation, 2004; 109: 1121–1126.
12. Uehara K, Nomura M, Ozaki Y et al. High-sensitivity C-reactive protein and left ventricular remodeling in patients with acute myocardial infarction. Heart Vessels, 2003; 18: 67–74.
13. Bauters C, Ennezat PV, Tricot O et al.; REVE Investigators. Stress hyperglycaemia is an independent predictor of left ventricular remodeling after first anterior myocardial infarction in non-diabetic patients. Eur Heart J, 2007; 28: 546–552.
14. Nicolau JC, Maia LN, Vitola JV, Mahaffey KW, Machado MN, Ramires JA. Baseline glucose and left ventricular remodeling after acute myocardial infarction. J Diabetes Complications, 2007; 21: 294–299.
15. Guerre-Millo M. Adiponectin: An update. Diabetes Metab, 2008; 34: 12–18.
16. Okui H, Hamasaki S, Ishida S et al. Adiponectin is a better predictor of endothelial function of the coronary artery than HOMA-R, body mass index, immunoreactive insulin, or triglycerides. Int J Cardiol, 2008; 126: 53–61.
17. Yang H, Zhang R, Mu H, Li M, Yao Q, Chen C. Adiponectin promotes endothelial cell differentiation from human peripheral CD14+ monocytes *in vitro*. J Cell Mol Med, 2006; 10: 459–469.
18. Ouchi N, Kihara S, Arita Y et al. Adipocyte-derived plasma protein, adiponectin, suppresses lipid accumulation and class A scavenger receptor expression in human monocyte-derived macrophages. Circulation, 2001; 103: 1057–1063.
19. Liang KW, Sheu WH, Lee WL et al. Decreased circulating protective adiponectin level is associated with angiographic coronary disease progression in patients with angina pectoris. Int J Cardiol, 2008; 129: 76–80.
20. Chandrasekar B, Boylston WH, Venkatachalam K, Webster NJ, Prabhu SD, Valente AJ. Adiponectin blocks interleukin-18-mediated endothelial cell death via APPL1-dependent AMPK activation and IKK/NF-kappaB/PTEN suppression. J Biol Chem, 2008; 283: 24889–24898.
21. Ouchi N, Kihara S, Arita Y et al. Adiponectin, an adipocyte-derived plasma protein, inhibits endothelial NF-kappaB signaling through a cAMP-dependent pathway. Circulation, 2000; 102: 1296–1301.
22. Kobayashi H, Ouchi N, Kihara S et al. Selective suppression of endothelial cell apoptosis by the high molecular weight form of adiponectin. Circ Res, 2004; 94: e27–e31.
23. Chen H, Montagnani M, Funahashi T, Shimomura I, Quon MJ. Adiponectin stimulates production of nitric oxide in vascular endothelial cells. J Biol Chem, 2003; 278: 45021–45026.
24. Shibata R, Sato K, Pimentel DR et al. Adiponectin protects against myocardial ischemia-reperfusion injury through AMPK- and COX-2-dependent mechanisms. Nat Med, 2005; 11: 1096–1103.
25. Tao L, Gao E, Jiao X et al. Adiponectin cardioprotection after myocardial ischemia/reperfusion involves the reduction of oxidative/nitrative stress. Circulation, 2007; 115: 1408–1416.
26. Shibata R, Izumiya Y, Sato K et al. Adiponectin protects against the development of systolic dysfunction following myocardial infarction. J Mol Cell Cardiol, 2007; 42: 1065–1074.
27. Kojima S, Funahashi T, Otsuka F et al. Future adverse cardiac events can be predicted by persistently low plasma adiponectin concentrations in men and marked reductions of adiponectin in women after acute myocardial infarction. Atherosclerosis, 2007; 194: 204–213.
28. Morishima I, Sone T, Okumura K et al. Angiographic no-reflow phenomenon as a predictor of adverse long-term outcome in patients treated with percutaneous transluminal coronary angioplasty for first acute myocardial infarction. J Am Coll Cardiol, 2000; 36: 1202–1209.
29. Takahashi T, Hiasa Y, Ohara Y et al. Usefulness of coronary flow reserve immediately after primary coronary angioplasty for acute myocardial infarction in predicting long-term adverse cardiac events. Am J Cardiol, 2007; 100: 806–811.
30. Shibata R, Numaguchi Y, Matsushita K et al. Usefulness of adiponectin to predict myocardial salvage following successful reperfusion in patients with acute myocardial infarction. Am J Cardiol, 2008; 101: 1712–1715.
31. Bolognese L, Neskovic AN, Parodi G et al. Left ventricular remodeling after primary coronary angioplasty: Patterns of left ventricular dilation and long-term prognostic implications. Circulation, 2002; 106: 2351–2357.
32. Modena MG, Rossi R, Sgura FA, Muia N Jr, Molinari R, Mattioli G. Early predictors of late dilation and remodeling after thrombolized anterior transmural myocardial infarction. Modena Clin Cardiol, 1997; 20: 28–34.
33. Giannuzzi P, Temporelli PL, Bosimini E et al. Heterogeneity of left ventricular remodeling after acute myocardial infarction: Results of the Gruppo Italiano per lo Studio della Sopravvivenza nell'Infarto Miocardico-3 Echo Substudy. Am Heart J, 2001; 14: 131–138.
34. Sejersten M, Maynard C, Clemmensen P; DANAMI-2 Investigators. Effects of abciximab as adjunctive therapy in primary percutaneous coronary intervention patients (results from the DANAMI-2 trial). Acute Card Care, 2006; 8: 75–82.
35. Iwakura K, Ito H, Ikushima M et al. Association between hyperglycemia and the no-reflow phenomenon in patients with acute myocardial infarction. J Am Coll Cardiol, 2003; 41: 1–7.
36. Kersten JR, Toller WG, Tessmer JP, Pagel PS, Warltier DC. Hyperglycemia reduces coronary collateral blood flow through a nitric oxide-mediated mechanism. Am J Physiol Heart Circ Physiol, 2001; 281: H2097–H2104.
37. Kersten JR, Schmeling TJ, Orth KG, Pagel PS, Warltier DC. Acute hyperglycemia abolishes ischemic preconditioning *in vivo*. Am J Physiol. 1998; 275: H721-725.
38. Lavi S, Kapeliovich M, Gruberg L et al. Hyperglycemia during acute myocardial infarction in patients who are treated by primary percutaneous coronary intervention: Impact on long-term prognosis. Int J Cardiol, 2008; 123: 117–122.
39. Carrabba N, Valenti R, Parodi G, Santoro GM, Antoniucci D. Left ventricular remodeling and heart failure in diabetic patients treated with primary angioplasty for acute myocardial infarction. Circulation, 2004; 110: 1974–1979.
40. Kadri Z, Danchin N, Yaur L et al. Major impact of admission glycaemia on 30-day and one year mortality in non-diabetic patients admitted for myocardial infarction: Results from the nationwide French USIC 2000 study. Heart, 2006; 92: 910–915.
41. Kojima S, Funahashi T, Sakamoto T et al. The variation of plasma concentrations of a novel, adipocyte derived protein, adiponectin, in patients with acute myocardial infarction. Heart, 2003; 89: 667–668.
42. Nishizawa H, Shimomura I, Kishida K et al. Androgens decrease plasma adiponectin, an insulin sensitizing adipocyte-derived protein. Diabetes, 2002; 51: 2734–2741.