Plasma adiponectin in patients with acute myocardial infarction treated with percutaneous coronary intervention

Aleksandra Michalewska-Włudarczyk, Maciej Kaźmierski, Tomasz Pawłowski, Iwona Mróz, Wojciech Wojakowski, Michał Tendera

Clinic Hospital no. 7, Medical University of Silesia, Silesian Medical Center, Katowice, Poland

Abstract

Background: Adiponectin is an adipocytokine with anti-inflammatory and anti-atherogenic properties. It has been also shown to protect cardiomyocytes, suppressing their apoptosis.

Aim: Evaluation of changes in plasma adiponectin concentrations in patients with acute myocardial infarction (AMI) and analysis of their correlations with cardiac ischaemic markers.

Methods: Fifty men with AMI treated with primary coronary angioplasty were included in the study. A control group matched for age and sex consisted of patients without AMI who underwent elective coronary angioplasty. Blood samples were obtained on admission, on the 1st, 3rd and 5th day of AMI, and at follow-up visits after 1 and 3 months.

Results: There were no significant differences in plasma adiponectin concentrations between the groups on admission (4.29 vs. 3.64 mg/ml, p = 0.52). In patients with AMI a significant decrease in plasma adiponectin concentration (to 3.64 mg/ml, p < 0.001) was observed. Plasma adiponectin concentrations at follow-up visits were comparable to those on admission in both groups. Plasma adiponectin concentrations did not correlate with creatine kinase (CK), CK-MB, troponin I, blood glucose or left ventricular ejection fraction.

Conclusions: In patients with AMI plasma adiponectin concentrations significantly decrease, with subsequent increase to initial values after one month. No correlation between plasma adiponectin concentrations and cardiac ischaemic markers or blood glucose was found. The decline in plasma adiponectin concentration may reflect its utilisation in the heart for protection of cardiomyocytes against apoptosis and inflammation.

Key words: adiponectin, myocardial infarction, coronary artery disease

Introduction

Adiponectin is an adipocytokine abundant in the peripheral circulation with plasma concentration ranging from 5 to 30 μg/ml, which accounts for approximately 0.01% of total plasma protein [1]. It has been shown to have anti-inflammatory and anti-atherogenic properties. Anti-inflammatory properties of adiponectin include modulation of inflammatory response of endothelium [2], suppression of TNF-α and Il-6 production and induction of Il-10 in macrophages [3]. Moreover, adiponectin adheres to injured vascular walls, accumulates in the subendothelial space, and suppresses macrophage-to-foam cell transformation and vascular smooth muscle cell proliferation and migration [4, 5].

Plasma concentration of adiponectin is decreased in obesity and negatively correlates with body mass index (BMI) and with insulin resistance [1, 6]. Adiponectin secretion is significantly higher in omental adipose cells and negatively correlates with BMI, whereas secretion from subcutaneous cells is not related to BMI [7].

There are many data confirming a close link between adiponectin and lipid as well as glucose metabolism. Plasma adiponectin concentration is decreased in dyslipidaemia and correlates negatively with plasma triglyceride levels and positively with high-density lipoprotein cholesterol (HDL-Ch) [8]. Adiponectin concentration in diabetics is lower than in non-diabetics [9, 10] and correlates negatively with insulin resistance [11].

Plasma adiponectin concentration was found to be lower in patients with hypertension and negatively correlated both with systolic and diastolic blood pressure, independently of other variables associated with metabolic syndrome [12, 13]. Hypoadiponectinaemia was also

observed in patients with coronary artery disease (CAD) [2, 14, 15]. Kumada et al. reported that low plasma adiponectin concentration (< 4.0 µg/ml) was independently correlated with the presence of CAD after adjustment for other well-known CAD risk factors [15]. Further studies showed that high plasma adiponectin levels were associated with decreased risk of myocardial infarction (MI) [16] and cardiovascular events in general [17]. The association of adiponectin with hypertension and CAD is believed to have a genetic background [12, 18].

Both in vitro and in vivo studies suggested that adiponectin has protective properties for cardiomyocytes and endothelial cells, suppressing their apoptosis [19, 20].

A change in plasma adiponectin level in patients with MI was described by Kojima et al. [21], who observed a decline in adiponectin concentration with subsequent increase to previous values. However, there are no literature data indicating whether percutaneous coronary intervention (PCI) can influence adiponectin concentration.

The aim of this study was to evaluate changes in plasma adiponectin concentrations in patients with acute myocardial infarction (AMI), as well as to analyse correlations between plasma adiponectin and cardiac ischaemic markers (creatine kinase – CK, its myocardial fraction – CK-MB, troponin I), and blood glucose.

Methods

Study group

Fifty consecutive male patients with ST-segment elevation MI treated with primary PCI were enrolled in the study.

The following inclusion criteria were used:
• male gender,
• age < 75 years,
• AMI with ST-segment elevation less than 12 h since chest pain onset.

Exclusion criteria were the following:
• known diabetes mellitus or blood glucose on admission 200 mg/dl (random glucose level),
• renal insufficiency (creatinine concentration > 1.4 mg/dl),
• infectious diseases and chronic inflammatory diseases,
• change in body weight exceeding 10% in the last 6 months.

A control group matched for age and sex consisted of 50 patients without AMI who underwent elective coronary angioplasty.

Study design and follow-up

The study was divided into two parts: early period (in-hospital evaluation) and late period – 3-month follow-up.

1. Early in-hospital evaluation

At baseline all patients were examined by a physician, and the following information was obtained: medical history, physical examination, measurement of height and weight, waist and hips circumference, resting blood pressure and heart rate; echocardiography; all patients in the study group underwent immediate coronary angiography with subsequent coronary angioplasty with stent implantation and all patients in the control group underwent elective coronary angiography and coronary angioplasty with stent implantation.

Venous blood was drawn on admission (non-fasting), on the 1st, 3rd and 5th day of AMI or on the 1st and 3rd day after PCI (after min. 8 h overnight fast) to measure plasma adiponectin and glucose concentrations, and in the study group additionally troponin I concentrations, and CK and CK-MB activity.

In both groups routine laboratory parameters including lipid profile (total cholesterol, HDL cholesterol, LDL cholesterol, triglycerides) and oral glucose tolerance test (OGTT) were also measured. On the basis of OGTT glucose metabolism was assessed; diabetes was diagnosed when blood glucose 120 min after oral administration of 75 g of glucose exceeded 200 mg/dl and impaired glucose tolerance when glucose level after 120 min was 140-199 mg/dl.

2. Late 3-month follow-up period

All patients were followed for 3 months. Venous blood was drawn at follow-up visits after 1 month and 3 months (after min. 8 h overnight fast) to measure plasma adiponectin and blood glucose concentrations.

The study was approved by the Bioethics Committee of the Medical University of Silesia and all patients provided written informed consent.

Laboratory procedures

Venous blood was drawn into EDTA tubes and centrifuged for 15 min at 1000 × g within 30 min of collection, and plasma was frozen and stored at ≤ –20°C until analysis. Plasma adiponectin was determined using the quantitative sandwich enzyme immunoassay technique (commercially available Human Adiponectin/Acrp30 Quantikine ELISA kit, R&D System).

Statistical analysis

Because for most data distribution was different from normal, they were expressed as median and range. Statistical analysis included Mann-Whitney U test, Kruskal-Wallis test and Spearman's rank correlation, as well as χ^2 test. Differences and correlations with p value < 0.05 were considered significant.

Results

Clinical characteristics of both groups are presented in Table I.

In both groups patients received similar pharmacological treatment: in all subjects double antiplatelet therapy was administered (ASA and clopidogrel or ticlopidine); those with no contraindication were treated with beta-adrenolytics (86% in the study group and 92%

Table I. Clinical characteristics

	Study group (AMI) n = 50	Control group n = 50	p
Age [years]	54.5 (38-73)	57.5 (43-65)	0.1
BMI [kg/m²]	27.5 (20.8-34.8)	28.1 (18.7-38.3)	0.98
Weight [kg]	84.3 (56-104)	85 (57-113)	0.7
Waist circumference [cm]	100.5 (84-116)	97 (72-111)	0.06
Hips circumference [cm]	102 (90-110)	101 (86-114)	0.47
WHR	0.99 (0.85-1.15)	0.96 (0.84-1.09)	0.005
Glucose metabolism, n (%)			0.32
Normal	37 (74)	32 (64)	
Impaired glucose tolerance	9 (18)	9 (18)	
Diabetes mellitus	4 (8)	9 (18)	
Systolic arterial blood pressure [mmHg]	126 (102-142)	105 (88-121)	< 0.000001
Diastolic arterial blood pressure [mmHg]	76 (66-95)	62.5 (56-76)	< 0.000001
Hypertension (%)	29 (58)	40 (80)	0.02
Hyperlipidaemia (%)	42 (84)	36 (72)	0.15
CAD duration [years]	0 (0-18)	1.5 (0-20)	0.00001
Hypertension duration [years]	0.1 (0-25)	4 (0-36)	0.01
Positive family history, n (%)	7 (14)	15 (30)	0.053
Smoking status, n (%)			0.01
Never smokers	8 (16)	6 (12)	
Former smokers (>1 year)	10 (20)	24 (48)	
Current smokers	32 (64)	20 (40)	
Previous MI, n (%)	6 (12)	27 (54)	0.00001
Previous PCI, n (%)	2 (4)	22 (44)	< 0.00001
Previous CABG, n (%)	1 (2)	3 (6)	0.31
Previous MI, PCI or CABG, n (%)	7 (14)	35 (70)	< 0.00001
Number of diseased vessels, n (%)			0.28
1	18 (36)	14 (28)	
2	22 (44)	19 (38)	
3	10 (20)	17 (34)	
LVEF [%]	46 (20-60)	55 (20-63)	0.00004

Abbreviations: BMI – body mass index, WHR – waist-hip ratio, CAD – coronary artery disease, MI – myocardial infarction, PCI – percutaneous coronary intervention, LVEF – left ventricular ejection fraction, AMI – acute myocardiol infarction

in the control group), ACE inhibitors (94% and 84%) and statins (98% and 88%).

There were no significant differences in the baseline adiponectin concentrations between the study group [4.29 (1.25-12.09) μg/ml], and the control group [3.64 (1.29-11.65) μg/ml] (p = 0.52). There was no significant difference between adiponectin concentration and smoking status either in the study group or in the control group (Table II).

There was also no correlation between adiponectin concentration and blood glucose level either in the study group or in the control group at any time point (Table III), as well as no significant difference in the baseline adiponectin concentration between the subgroups with normal glucose metabolism, impaired glucose tolerance (IGT) or diabetes mellitus (diagnosed on discharge) (Table II).

Baseline plasma adiponectin concentration was not associated with previous cardiovascular events (MI, PCI or coronary artery bypass grafts), or with the number of diseased vessels in coronary angiography (Table II).

In the early in-hospital observation plasma adiponectin concentrations in the study group significantly decreased in comparison to the baseline (Figure 1 A). In the control group plasma adiponectin level did not change significantly (Figure 1 B).

There were no significant differences between plasma adiponectin concentrations at 1 month and 3 months after

Table II. Baseline plasma adiponectin and other baseline variables

	Smoking status			
	Never smokers	Former smokers	Current smokers	p
Adiponectin (study group)	3.68 (1.5-8.0)	6.65 (1.25-12.09)	4.28 (1.39-9.88)	0.5
Adiponectin (control group)	4.75 (1.57-10.9)	3.76 (1.29-10.81)	3.52 (1.54-11.65)	0.75
	Glucose metabolism			
	Normal glucose tolerance	IGT	Diabetes mellitus	p
Adiponectin (study group)	4.44 (1.25-12.09)	6.05 (2.63-11.54)	2.58 (1.5-7.13)	0.28
Adiponectin (control group)	3.77 (1.29-10.9)	3.33 (1.57-11.65)	3.86 (1.96-10.71)	0.83
	Previous cardiovascular events			
	No previous MI/PCI/CABG	Previous MI/PCI/CABG		p
Adiponectin (study group)	4.64 (1.39-12.09)	3.2 (1.25-6.0)		0.14
Adiponectin (control group)	3.76 (1.57-10.9)	3.64 (1.29-11.65)		0.8
	Number of diseased vessels			
	1-vessel disease	2-vessel disease	3-vessel disease	p
Adiponectin (study group)	3.88 (1.39-9.51)	4.87 (1.25-11.54)	5.04 (1.59-12.09)	0.43
Adiponectin (control group)	4.07 (1.57-11.65)	3.78 (2.6-10.81)	3.04 (1.29-6.27)	0.17

Table III. Correlation between plasma adiponectin concentration and blood glucose level

	Study group		Control group	
Time point	R Spearman	p	R Spearman	p
On admission	−0.22	0.13	−0.01	0.92
1st day	−0.25	0.08	0.05	0.75
3rd day	0.07	0.63	0.05	0.72
5th day	0.06	0.68	X	X
1 month	−0.28	0.07	0.1	0.58
3 months	−0.2	0.18	0.02	0.91

MI and the baseline values in the study group (Figure 2 A) and in the control group (Figure 2 B).

The changes in the plasma adiponectin concentration in the study group (difference between plasma adiponectin concentrations on the 5th day and the baseline) and in the control group (difference between plasma adiponectin concentrations on the 3rd day and the baseline) differed significantly (Figure 3).

No significant correlation was found between the change in the plasma adiponectin concentration in the study group and cardiac ischaemic markers or left ventricular ejection fraction (LVEF) (Table IV).

We also assessed the correlation between plasma adiponectin level and clinical variables: systolic and diastolic arterial blood pressure at each study time point, total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride concentrations, BMI, waist-hip ratio (WHR) and weight at the baseline and after 3 months, LVEF (%), CAD and hypertension duration on admission.

In the study group a significant positive correlation between baseline plasma adiponectin concentration and total cholesterol and LDL cholesterol concentrations, and a negative correlation with triglyceride concentration, BMI and body weight was observed. At the 3-month follow-up
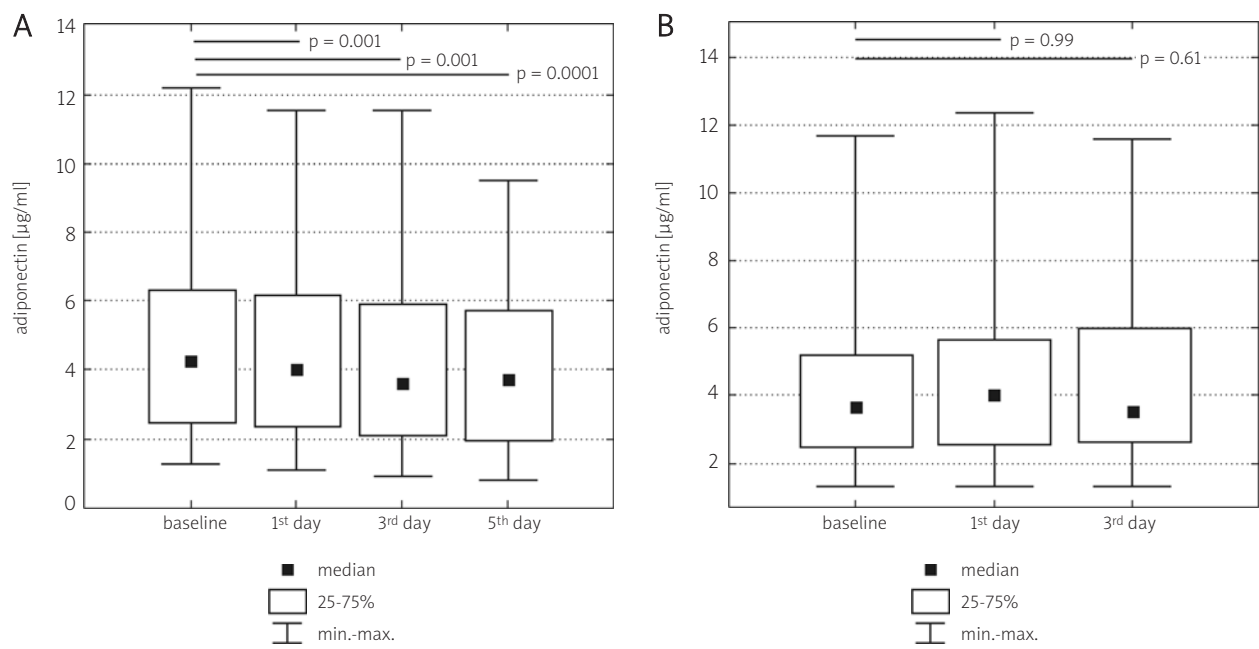
Figure 1. Plasma adiponectin concentration during in-hospital period in the study group (**A**) and control group (**B**)
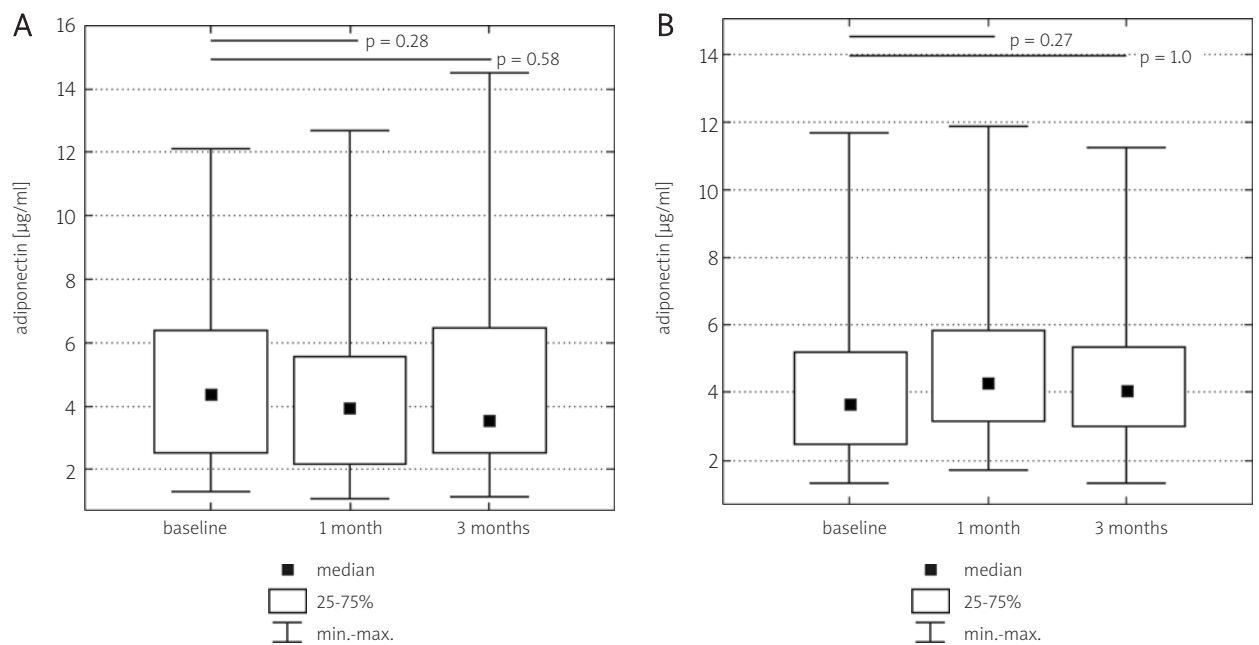

Figure 2. Plasma adiponectin concentration during follow-up in the study group (**A**) and control group (**B**)
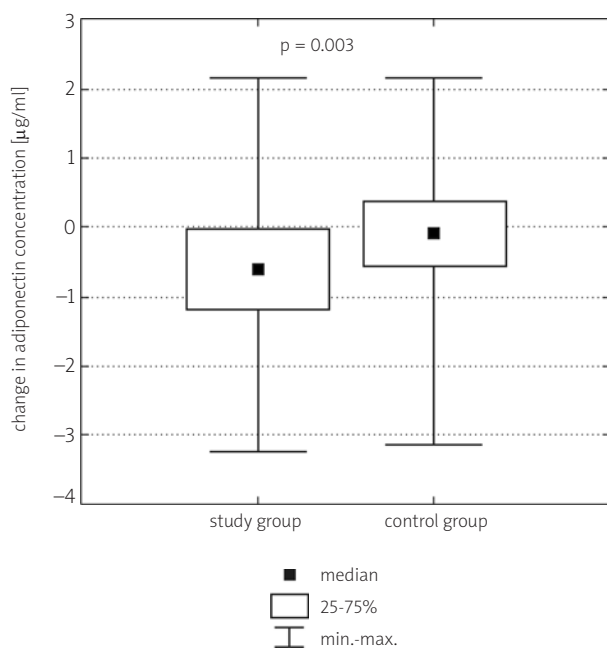
Figure 3. Change in the plasma adiponectin concentration in the study group and in the control group

Table IV. Correlation between change in plasma adiponectin concentrations and other variables

	R Spearman	p
CK max	0.08	0.62
CK-MB max	−0.03	0.83
Troponin max	0.06	0.7
LVEF [%]	0.14	0.36

plasma adiponectin concentration still correlated negatively with weight; additionally a positive correlation between plasma adiponectin concentration and HDL cholesterol was found (Table V). Such correlations were not observed in the control group at any time point.

Discussion

There is still no definite cut-off point for normal plasma adiponectin concentration. In clinical studies in healthy subjects it remains within the limits of 5-30 µg/ml [1] and is significantly lower in patients with CAD [2, 14]. Plasma adiponectin level < 4 µg/ml is reported to be associated with a two-fold increase in CAD risk [15] and hypoadiponectinaemia is seen as a risk factor for acute coronary syndrome (ACS) [16, 22]. However, other data suggest that high plasma adiponectin level is an independent predictor of all-cause mortality, cardiac mortality and MI in subjects with CAD and in the group of NSTEMI patients [9]. This discrepancy may be caused by different population size and number of subjects with heart failure (HF), in which adiponectin concentrations are increased and correlate positively not only with other biochemical markers, such as BNP, NT-proBNP and TNF-α, but also with HF severity (NYHA class) [23, 24]. Recent studies have suggested that in patients with HF high plasma adiponectin level is an independent predictor of death due to HF [23].

There are discrepancies concerning plasma adiponectin concentration in patients with MI. Some authors [14, 25] observed that plasma adiponectin levels were lower in patients with ACS compared to subjects with stable angina or a healthy control group; however, others did not confirm these findings [26]. These differences can be explained by different time points of blood collection for

Table V. Correlation between plasma adiponectin concentration and some clinical variables

Plasma adiponectin		R Spearman	p	R Spearman	p
On admission (baseline)	TCh	0.28	**0.049**	0.02	0.88
	LDL Ch	0.34	**0.02**	−0.02	0.89
	HDL Ch	0.28	0.06	0.22	0.14
	TG	−0.33	**0.02**	−0.12	0.43
	BMI	−0.38	**0.007**	−0.13	0.38
	WHR	−0.1	0.47	−0.16	0.28
	Weight	−0.47	**0.0006**	−0.07	0.63
3 months	TCh	0.2	0.18	0.12	0.49
	LDL Ch	0.19	0.19	0.09	0.61
	HDL Ch	0.43	**0.002**	0.25	0.15
	TG	−0.11	0.47	0.04	0.82
	BMI	−0.21	0.15	0.06	0.74
	WHR	−0.14	0.35	0.05	0.76
	Weight	−0.33	**0.02**	0.11	0.51

Abbreviations: TCh – total cholesterol, LDL Ch – LDL cholesterol, HDL Ch – HDL cholesterol, TG – triglycerides. Other abbreviations see Table I

plasma adiponectin measurement. Our data, as well as the data of Kojima et al. [21], show that a significant decrease in plasma adiponectin concentration can be seen after 24 h at the earliest from the onset of chest pain.

Another reason for these differences could be the lack of homogeneity of the groups. In the studies mentioned above, the study groups consisted of both men and women. There is evidence that plasma adiponectin concentration is sex-dependent and is significantly lower in men [6]. Therefore in our study only male subjects were enrolled.

Despite the reports of a negative correlation of plasma adiponectin and blood pressure [27], in our study we have observed such a correlation only for systolic blood pressure at 3 months. However, an influence of pharmacotherapy on this association cannot be excluded, as most patients received beta-adrenolytics and ACE inhibitors, which can increase adiponectin concentrations [28, 29]. The negative correlation between plasma adiponectin level and the amount of adipose tissue and BMI is well known [1, 6, 9, 14, 18]. In our study this relationship for baseline adiponectin concentration was seen only in the study group, where WHR was significantly higher. Central obesity is known to be associated with lower adiponectin concentrations in comparison to peripheral obesity [30].

The association of adiponectin with lipid metabolism is well documented [8, 14, 16, 26]. In our study, only in the study group did baseline adiponectin concentrations correlate positively with total and LDL cholesterol, and negatively with triglycerides; at the 3-month follow-up a positive correlation of plasma adiponectin with HDL cholesterol was observed. The use of statins has to be taken into account, which could alter lipid values and influence adiponectin concentrations, although literature data concerning the effects of statins on adiponectin concentration are inconsistent [28, 31].

The association of adiponectin with glucose metabolism is well documented. Plasma adiponectin level shows a negative correlation with insulin resistance [11] and hypoadiponectinaemia can be seen in diabetics [9, 10]. It is reported that in patients with CAD blood glucose level is negatively correlated not only with plasma adiponectin concentration [14], but also with the concentration of adiponectin in atherosclerotic plaques in the coronary arteries [32].

Although known diabetes was one of the exclusion criteria, on the basis of OGTT diabetes or IGT was newly diagnosed in 26% of patients in the study group and in 36% in the control group, confirming that previously undiagnosed diabetes or IGT is common in patients with AMI [11]. Patients with newly diagnosed diabetes mellitus showed non-significant trend towards lower adiponectin concentrations, and no correlation between plasma adiponectin and blood glucose at any study time point was seen. Our findings are different from the literature data,

emphasising the relationship of adiponectin with glucose metabolism, although Stejskal et al. reported results similar to ours [26].

Despite the reports on the relationship of adiponectin with CAD, there are limited data on the effects of previous cardiovascular events on adiponectin concentration. In our study no association of plasma adiponectin level with previous cardiovascular events (MI, PCI, CABG) was found, which is consistent with the results of Cavusoglu et al. [9].

Also, not much is known about the variability of plasma adiponectin concentration in AMI. Shibata et al. in an experimental study on mice reported a decrease of plasma adiponectin after myocardial ischaemia-reperfusion injury [19]. In our study we also observed a significant decrease in plasma adiponectin concentration, which reached the lowest values on the 3rd day after AMI and returned to the baseline level after 1 month of follow-up. Our data are consistent with those of Kojima et al., who described a decline in plasma adiponectin concentration in patients with AMI, although in their group it did not reach the baseline value after 1 month [21].

The reasons for adiponectin decrease in patients with AMI remain unknown. It has been shown that adiponectin accumulates in atherosclerotic plaques with injured vascular wall but not in plaques with intact endothelium [5]. Its presence has also been reported in atherosclerotic plaques in human coronary arteries taken during CABG [32]. Therefore we can speculate that PCI itself can influence adiponectin concentration due to mechanical injury of the arterial wall during balloon inflation and stent implantation, but there are no literature data confirming it. It cannot be confirmed either on the basis of the study of Kojima et al. [21], in which the control group consisted of subjects with atypical chest pain who had no stenosis on coronary angiography. In our study the control group consisted of patients with stable angina who underwent elective PCI, which allowed us to estimate the effects of coronary intervention on plasma adiponectin concentration and excluded any influence of pharmacotherapy on differences in plasma adiponectin level between the groups. Our results showed no decrease in plasma adiponectin concentration in the control group and a significant difference in the change in adiponectin concentration between the groups, which proves that the observed variation in adiponectin concentration is associated with AMI.

Adiponectin also has cardioprotective properties. It protects heart muscle cells against ischaemia-reperfusion injury and inhibits cardiomyocyte and endothelial cell apoptosis, as well as TNF-α expression in cardiomyocytes [19, 20]. While TNF-α concentration is increased in HF and MI patients and in experimental studies, TNF-α infusion induces LV dysfunction and dilatation [33]. Adiponectin, as an inhibitor of TNF-α expression, could protect against post-infarction cardiomyopathy. Another positive role of adiponectin in injured heart is inhibition of ET-1, AT-II and

IGF-1 – induced cardiomyocyte hypertrophy, which is one of the compensation mechanisms after focal injury leading to LV remodelling and HF [34].

Takahashi et al. reported that adiponectin accumulates in damaged cardiomyocytes. Adiponectin accumulation seems to be a non-specific mechanism as it was observed in autopsied patients with MI and dilated cardiomyopathy [35], and could explain the decrease of adiponectin concentration in AMI. Such a hypothesis is consistent with the results of Furuhashi et al., who, based on the difference in adiponectin concentration in blood samples collected simultaneously from the aortic root and coronary sinus, reached the conclusion that adiponectin is utilised in the coronary arteries and/or the heart [10]. Moreover, in their study adiponectin concentration in the coronary sinus correlated with the stenosis score in the coronary arteries. Stejskal et al. [26] did not observe any difference in adiponectin concentration between blood samples from coronary arteries and peripheral veins or from infarct – related or infarct non-related in patients with MI. This may not be inconsistent with the hypothesis of adiponectin accumulation in injured heart, as blood samples in the study mentioned above were taken during the angiography done 3 h after symptoms onset, and in other studies the decrease of adiponectin level in peripheral blood was reported only after 24 h.

Our results showed no correlation of plasma adiponectin concentration change either with cardiac ischaemic markers which indirectly indicate infarction size, or with LVEF, which is similar to the reports of other authors [9, 11, 26]. However, the number of subjects in our study groups may be too small to draw general conclusions about correlation of adiponectin concentration and ischaemic injury size in patients with AMI.

References

1. Arita Y, Kihara S, Ouchi N, et al. Paradoxical decrease of an adipose-specific protein, adiponectin, in obesity. *Biochem Biophys Res Commun* 1999; 257: 79-83.
2. Ouchi N, Kihara S, Arita Y, et al. Novel modulator for endothelial adhesion molecules: adipocyte-derived plasma protein adiponectin. *Circulation* 1999; 100: 2473-6.
3. Wulster-Radcliffe M, Ajuwon K, Wang J, et al. Adiponectin differentially regulates cytokines in porcine macrophages. *Biochem Biophys Res Commun* 2004; 316: 924-9.
4. 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: 1057-63.
5. Okamoto Y, Arita Y, Nishida M, et al. An adipocyte-derived plasma protein, adiponectin, adheres to injured vascular walls. *Horm Metab Res* 2000; 32: 47-50.
6. Shand BI, Scott RS, Elder PA, et al. Plasma adiponectin in overweight, nondiabetic individuals with or without insulin resistance. *Diabetes Obes Metab* 2003; 5: 349-53.
7. Motoshima H, Wu X, Sinha M, et al. Differential regulation of adiponectin secretion from cultured human omental and subcutaneous adipocytes: effects of insulin and rosiglitazone. *J Clin Endocrinol Metab* 2002; 87: 5662-7.
8. Matsubara M, Maruoka S, Katayose S. Decreased plasma adiponectin concentrations in women with dyslipidemia. *J Clin Endocrinol Metab* 2002; 87: 2764-9.
9. Cavusoglu E, Ruwende C, Chopra V, et al. Adiponectin is an independent predictor of all-cause mortality, cardiac mortality, and myocardial infarction in patients presenting with chest pain. *Eur Heart J* 2006; 27: 2300-9.
10. Furuhashi M, Ura N, Moniwa N, et al. Possible impairment of transcardiac utilization of adiponectin in patients with type 2 diabetes. *Diabetes Care* 2004; 27: 2217-21.
11. Choi K, Lee K, Kim S, et al. Inflammation, insulin resistance, and glucose intolerance in acute myocardial infarction patients without a previous diagnosis of diabetes mellitus. *J Clin Endocrinol Metab* 2005; 90: 175-80.
12. Iwashima Y, Katsuya T, Ishikawa K, et al. Hypoadiponectinemia is an independent risk factor for hypertension. *Hypertension* 2004; 43: 1318-23.
13. Adamczak M, Więcek A, Furuhashi T, et al. Decreased plasma adiponectin concentration in patients with essential hypertension. *Am J Hypertens* 2003; 16: 72-5.
14. Nakamura Y, Shimada K, Fukuda D, et al. Implications of plasma concentrations of adiponectin in patients with coronary artery disease. *Heart* 2004; 90: 528-33.
15. Kumada M, Kihara S, Sumitsuji S, et al. Association of hypoadiponectinemia with coronary artery disease in men. *Arterioscler Thromb Vasc Biol* 2003; 23: 85-9.
16. Pischon T, Girman CJ, Hotamisligil GS, et al. Plasma adiponectin levels and risk of myocardial infarction in men. *JAMA* 2004; 291: 1730-7.
17. Schulze M, Shai I, Rimm E, et al. Adiponectin and future coronary heart disease events among men with type 2 diabetes. *Diabetes* 2005; 54: 534-9.
18. Ohashi K, Ouchi N, Kihara S, et al. Adiponectin I164T mutation is associated with the metabolic syndrome and coronary artery disease. *J Am Coll Cardiol* 2004; 43: 1195-200.
19. Shibata R, Sato K, Pimentel D, et al. Adiponectin protects against myocardial ischemia-reperfusion injury through AMPK- and COX-2-dependent mechanisms. *Nat Med* 2005; 11: 1096-103.
20. 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.
21. 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: 667-8.
22. Wolk R, Berger P, Lennon R, et al. Association between plasma adiponectin levels and unstable coronary syndromes. *Eur Heart J* 2007; 28: 272-98.
23. Tsutamoto T, Tanaka T, Sakai H, et al. Total and high molecular weight adiponectin, haemodynamics, and mortality in patients with chronic heart failure. *Eur Heart J* 2007; 28: 1723-30.
24. Von Eynatten M, Hamann A, Twardella D, et al. Relationship of adiponectin with markers of systemic inflammation, atherogenic dyslipidemia, and heart failure in patients with coronary heart disease. *Clin Chem* 2006; 52: 853-9.
25. Otsuka F, Sugiyama S, Kojima S, et al. Plasma adiponectin levels are associated with coronary lesion complexity in men with coronary artery disease. *J Am Coll Cardiol* 2006; 48: 1155-62.
26. Stejskal D, Bartek J. Adiponectin in patients with various stages of coronary heart disease – comparison of its concentration in

coronary arteries and peripheral venous circulation. *Biomed Papers* 2003; 147: 161-6.

27. Huang K, Chen Ch, Chuang L, et al. Plasma adiponectin levels and blood pressures in nondiabetic adolescent females. *J Clin Endocrinol Metab* 2003; 88: 4130-4.

28. Koh KK, Quon MJ, Han SH , et al. Additive beneficial effects of losartan combined with simvastatin in the treatment of hypercholesterolemic, hypertensive patients. *Circulation* 2004; 110: 3687-92.

29. Celik T, Iyisoy A, Kursaklioglu H, et al. Comparative effects of nebivolol and metoprolol on oxidative stress, insulin resistance, plasma adiponectin and soluble P-selectin levels in hypertensive patients. *J Hypertens* 2006; 24: 591-6.

30. Tanko LB, Bruun JM, Alexandersen P, et al. Novel associations between bioavailable estradiol and adipokines in elderly women with different phenotypes of obesity: implications for atherogenesis. *Circulation* 2004; 110: 2246-52.

31. Sakamoto K, Sakamoto T, Ogawa H. Kumamoto Joint Research on Hypercholesterolemia Investigators: The effect of 6 months of treatment with pravastatin on serum adiponection concentrations in Japanese patients with coronary artery disease and hypercholesterolemia: a pilot study. *Clin Ther* 2006; 28: 1012-21.

32. Karaduman M, Sengul A, Oktenli C, et al. Tissue levels of adiponectin, tumor necrosis factor-alpha, soluble intercellular adhesion molecule-1 and heart-type fatty acid-binding protein in human coronary atherosclerotic plaques. *Clin Endocrinol* (*Oxf*) 2006; 64: 196-202.

33. Yousef Z, Redwood S, Marber M. Postinfarction left ventricular remodeling: a pathophysiological and therapeutic review. *Cardiovasc Drugs Ther* 2000; 14: 243-52.

34. Fujioka D, Kawabata K, Saito Y, et al. Role of adiponectin receptors in endothelin-induced cellular hypertrophy in cultured cardiomyocytes and their expression in infracted heart. *Am J Physiol Heart Circ Physiol* 2006; 290: 2409-16.

35. Takahashi T, Saegusa S, Sumino H, et al. Adiponectin, T-cadherin, and tumor necrosis factor-á in damaged cardiomyocytes from autopsy specimens. *J Inter Med Res* 2005; 33: 236-44.

Stężenie adiponektyny w osoczu chorych z zawałem mięśnia sercowego poddanych zabiegowi przezskórnej angioplastyki wieńcowej

Aleksandra Michalewska-Włudarczyk, Maciej Kaźmierski, Tomasz Pawłowski, Iwona Mróz, Wojciech Wojakowski, Michał Tendera

Samodzielny Publiczny Szpital Kliniczny nr 7, Śląski Uniwersytet Medyczny, Górnośląskie Centrum Medyczne, Katowice

Streszczenie

Wstęp: Adiponektyna jest cytokiną o właściwościach przeciwmiażdżycowych, przeciwzapalnych i kardioprotekcyjnych, a jej niskie stężenia są czynnikiem ryzyka choroby wieńcowej.

Cel: Zbadanie zmian stężenia adiponektyny w osoczu chorych z ostrym zawałem serca i ich korelacji ze wskaźnikami uszkodzenia mięśnia sercowego.

Metody: Grupę badaną stanowiło 50 mężczyzn w wieku 38–73 lat (średnio 54,4 roku) z ostrym zawałem mięśnia sercowego z uniesieniem odcinka ST, u których przeprowadzono skuteczny zabieg angioplastyki wieńcowej z wszczepieniem stentu. Kryteria wyłączenia stanowiły: rozpoznana cukrzyca lub stężenie glukozy przy przyjęciu (glikemia przygodna) > 200 mg%, niewydolność nerek, choroby infekcyjne i przewlekłe stany zapalne, zmiana masy ciała o ponad 10% w ciągu ostatniego pół roku. Grupę kontrolną stanowiło 50 mężczyzn w wieku 43–75 lat (średnio 57,5 roku), u których przeprowadzono planowy zabieg angioplastyki wieńcowej. Przy przyjęciu oraz w 1., 3. i 5. dobie zawału serca oznaczano stężenia adiponektyny, glukozy, troponiny I, aktywność kinazy kreatynowej (CPK) i jej frakcji sercowej (CK-MB), a podczas wizyt kontrolnych po 1 i po 3 miesiącach od zawału serca – stężenia adiponektyny i glukozy.

Wyniki: Wyjściowe stężenia adiponektyny w grupie badanej i kontrolnej nie różniły się istotnie (4,29 *vs* 3,64 mg/ml, p = 0,52). W przebiegu zawału serca obserwowano znamienny spadek stężenia adiponektyny (do 3,64 μg/ml, p < 0,001). Stężenia adiponektyny po 1 i 3 miesiącach w obu grupach były porównywalne ze stężeniem wyjściowym. Nie stwierdzono korelacji stężenia adiponektyny z aktywnością CPK, CK-MB, stężeniem troponiny I, glukozy, a także z frakcją wyrzutową lewej komory.

Wnioski: U chorych z ostrym zawałem serca obserwuje się znamienny spadek stężenia adiponektyny, które powraca do wartości wyjściowych po miesiącu, co może wskazywać na jej zużycie w mięśniu sercowym dla ochrony kardiomiocytów przed czynnikami zapalnymi czy apoptozą. Nie stwierdzono zależności pomiędzy stężeniami adiponektyny a wskaźnikami uszkodzenia mięśnia sercowego lub stężeniem glukozy.

Słowa kluczowe: adiponektyna, zawał serca, choroba wieńcowa

Adres do korespondencji:

dr n. med. Aleksandra Michalewska-Włudarczyk, Samodzielny Publiczny Szpital Kliniczny nr 7, Śląski Uniwersytet Medyczny, Górnośląskie Centrum Medyczne, ul. Ziołowa 45/47, 40-635 Katowice, tel.: +48 32 359 80 00, faks: +48 32 202 87 54, e-mail: aleksam@poczta.onet.pl