

Elevated levels of 8-iso-prostaglandin F_{2α} in acute coronary syndromes are associated with systemic and local platelet activation

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KEY WORDS

8-iso-prostaglandin F_{2α}, acute coronary syndrome, isoprostanes, platelet activation, soluble CD40 ligand

ABSTRACT

INTRODUCTION Oxidative stress is an important causative factor in atherosclerosis. Isoprostanes are derivatives of arachidonate oxidized by reactive oxygen species (ROS). Oxidized lipids are markers of oxidative stress, important mediators of atherosclerosis, and activators of platelets. 8-iso-prostaglandin F_{2α} (8-iso-PGF_{2α}) is a stable isoprostane and reliable marker of oxidative stress in vivo.

OBJECTIVES The aim of the study was to determine the level of oxidative stress in acute coronary syndromes (ACS) and its correlations with the parameters of hemostasis.

PATIENTS AND METHODS Forty-nine patients aged 46 to 76 years, including 28 with ACS and 25 with stable coronary artery disease (CAD), were enrolled to the study. The levels of 8-iso-PGF_{2α}, soluble CD40 ligand (sCD40L), P-selectin (P-sel), β-thromboglobulin, and the thrombin-antithrombin complex (TAT) in the plasma of venous blood were determined. A microvascular injury model was also used to evaluate TAT generation and sCD40L levels in blood collected every 60 seconds at the site of standardized microvascular injury.

RESULTS 8-iso-PGF_{2α} levels were significantly higher in ACS compared to CAD patients (363.2 ± 45.94 vs. 328.2 ± 31.96 pg/ml, *P* = 0.011) and correlated with venous plasma levels of P-sel and β-thromboglobulin in the ACS (*r* = 0.66; *P* = 0.0005 and *r* = 0.62; *P* = 0.001, respectively) and CAD groups (*r* = 0.46; *P* = 0.02 and *r* = 0.49; *P* = 0.01, respectively). In the microvascular injury model, the maximum concentrations of sCD40L in the ACS group were associated with plasma 8-iso-PGF_{2α} levels (*r* = 0.50, *P* = 0.01). No correlations between 8-iso-PGF_{2α} and markers of thrombin generation in venous blood and microvascular injury model were observed.

CONCLUSIONS Plasma levels of 8-iso-PGF_{2α} are significantly higher in ACS compared with stable CAD and correlate with platelet activation.

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INTRODUCTION Oxidative stress implies increased tissue exposure to reactive oxygen species (ROS) due to either enhanced production of ROS or diminished antioxidant activity. ROS are produced by activated platelets, vascular smooth muscle cells, and various inflammatory cells in a range of conditions, especially tissue hypoxia, as well as risk factors for coronary artery disease (CAD). Oxidative attack, that is interaction of ROS, produces oxidized proteins, lipids, and DNA. Oxidized lipids are products of ROS attack

on lipids of cellular membrane and circulating lipoproteins, especially low-density lipoproteins (LDL).

Oxidative stress is a key factor of myocardial injury associated with atherosclerosis.¹ Large amounts of oxidized lipids, particularly oxidized LDL (ox-LDL), are found within the atherosclerotic plaque.² In addition, oxidation of arachidonate by ROS generates a wide variety of derivatives known as isoprostanes (IsoPs).³ Elevated levels of IsoPs are associated with inflammatory

diseases, hyperthyroidism,^{4,5} and numerous risk factors for atherosclerosis, including hypercholesterolemia, diabetes mellitus, and smoking. IsoPs are not only the markers of oxidative stress but also biologically active substances that enhance atherosclerosis and activate platelets.⁶ As one of the most stable IsoPs, 8-iso-prostaglandin F_{2α} (8-iso-PGF_{2α}) has become a “gold standard” measure of oxidative stress in vivo.⁷ We investigated the intensity of oxidative stress and its impact on coagulation in patients with acute coronary syndromes (ACS).

PATIENTS AND METHODS We studied 49 consecutive patients with ACS or stable CAD admitted to the Department of Haemodynamics and Angiocardiology, Institute of Cardiology, Jagiellonian University School of Medicine, Kraków, Poland, from May to June 2006. The ACS patients were admitted within 12 h (median 6, range 1–12 h) from the onset of symptoms. The inclusion criteria were typical chest pain and either ST-segment elevation ≥ 0.1 mV or ST-segment depression ≥ 0.1 mV in at least 2 contiguous leads. All ACS patients were troponin-positive. Based on electrocardiogram (ECG) findings they were classified as ST-segment elevation myocardial infarction (STEMI) or non-STEMI. All ACS patients received aspirin (75–300 mg) prior to admission.

The diagnosis of CAD (class II or III according to the Canadian Cardiovascular Society or class I with high risk of ischemia in other tests) was confirmed in ECG exercise test or heart imaging studies (coronary calcium scoring or nuclear cardiac imaging). Patients with sustained or recurrent angina after ACS were also enrolled (at least 3 months after ACS). These patients were scheduled for coronary angiography due to unsatisfactory response to medical treatment. Troponin levels in the CAD patients at enrollment were < 0.1 ng/ml. All patients received aspirin (75–300 mg) prior to admission.

The exclusion criteria for ACS and CAD groups were as follows: acute infection; use of oral anticoagulants, heparin or thienopyridines; history of deep vein thrombosis, stroke or ACS within the last 3 months; serious diseases such as malignancies, autoimmune disorders, renal failure, and heart failure (New York Heart Association class III/IV). The study was approved by the Jagiellonian University Bioethical Committee and all patients gave informed consent.

Blood samples were drawn from an antecubital vein with minimal stasis within 15 min from admission in the case of ACS patients and after an overnight fasting between 8 and 9 a.m. in the case of stable CAD patients, before clopidogrel administration in each subject. Serum and citrated plasma samples (9:1 of 3.2% sodium citrate) were centrifuged at 2540 g for 15 min at 4°C within 20 min of collection, immediately frozen, and stored in aliquots at -80°C until further use.

Laboratory methods Commercially available immunoenzymatic assays were used to determine plasma 8-iso-PGF_{2α} levels (Cayman Chemicals, United States), β -thromboglobulin (Diagnostica Stago, France), P-selectin (P-sel) (R&D Systems, United Kingdom). In plasma and supernatant samples, we also measured soluble CD40 ligand (sCD40L) (R&D Systems, United Kingdom) and thrombin-antithrombin complex (TAT) (Dade-Behring, Germany). Serum levels of troponin I were determined using the enzyme-linked fluorescent assay (VIDAS Troponin I Ultra, BioMerieux, France). Serial troponin I measurements were performed and the maximum value was recorded.

A microvascular injury model was performed as described previously.^{8,9} Both sCD40L and TAT levels were measured as a function of time in blood oozing from standardized bleeding-time wounds, performed with a Simplate RI device (Organon Teknika) on the lateral aspect of a forearm 4 to 5 cm below the elbow crease upon inflation of the sphyngomanometer to 40 mmHg placed on the arm above the incision. Oozing blood was collected into heparinized capillary tubes every 60 seconds and then passed into an anticoagulant mixture (NaCl 0.9%, EDTA 50 mmol/l, benzamidine 20 mmol/l, thrombin inhibitor D-Val-Leu-Lyschloromethylketone [V3763 Sigma] 50 μM), centrifuged at 4°C (6000 g by 20 min), and the supernatant was frozen (-70°C). The levels of sCD40L and TAT in oozing blood were determined with enzyme-linked immunosorbent assays (R&D Systems, United Kingdom and Dade Behring, Germany, respectively). As a quantitative measure of TAT and sCD40L we used the mean concentration at each time point (every 60 seconds) and the area under the concentration vs. time curve (AUC). As the average bleeding time was about 6 min, the analysis was performed using samples collected during the first 6 min.

Statistical analysis Data are expressed as mean and standard deviation or mean and standard error of mean. The Shapiro-Wilk test was used to determine normal distribution. The Mann-Whitney U test was used to test differences between groups. Spearman's or Pearson's tests were used to determine correlations in normal or non-normal distribution data. Analyses were performed using the Statistica 7.1 PL software (StatSoft, Inc., 2005). The level of significance was set at $P < 0.05$.

RESULTS The study group comprised 49 patients aged 46 to 76 years. There were 24 subjects with ACS, including 14 with STEMI and 10 with non-STEMI. The control group comprised 25 subjects with stable CAD. The ACS and CAD patients did not differ significantly in terms of demographic parameters, cardiovascular risk factors, medication, and platelet count. Activated partial thromboplastin time was normal in all study subjects included in the analysis. Five

TABLE 1 Characteristics of the patients with acute coronary syndromes (ACS) and those with stable coronary artery disease (CAD)

	Mean (range)		P
	ACS	CAD	
subjects, n	24	25	
STEMI/non-STEMI, n (%)	14 (58)/10 (42)	0	
age, years	61 (46–76)	61 (47–73)	0.9
males, n (%)	19 (79)	20 (83)	0.96
BMI (kg/m ²)	27.3 (21–40)	26.2 (21–31)	0.93
hypertension, n (%)	18 (75)	16 (64)	0.52
diabetes, n (%)	3 (13)	2 (8)	0.79
family history of CVD, n (%)	13 (54)	22 (73)	0.86
history of MI, n (%)	7 (30)	5 (20)	0.7
smoking, n (%)	9 (38)	12 (48)	0.53
platelet count, (/μl) ±SEM	243,000 ±49,900	245,000 ±61,500	0.67
medication			
aspirin, n (%)	24 (100)	25 (100)	1.0
statins, n (%)	5 (21)	5 (20)	0.96
β-blockers, n (%)	10 (42)	14 (56)	0.4
ACE inhibitors, n (%)	8 (33)	13 (52)	0.27
CCB, n (%)	3 (13)	7 (28)	0.38
diuretics, n (%)	3 (13)	4 (16)	0.98
ARB, n (%)	0 (0)	1 (4)	0.82

Abbreviations: ACE – angiotensin-converting enzyme, ARB – angiotensin II receptor blockers, BMI – body mass index, CCB – calcium channel blockers, CVD – cardiovascular disease, MI – myocardial infarction, SEM – standard error of mean, STEMI – ST-segment elevation MI

TABLE 2 Characteristics of the ACS group

	STEMI	non-STEMI	P
patients, n (%)	14 (58)	10 (42)	
time from the onset of pain, median (range) [h]	4 (1–7)	6 (1–12)	0.1
troponin I on admission (ng/ml)	1.55 ±1.51	5.57 ±9.34	0.6
maximum troponin I (ng/ml)	33.84 ±53.01	11.22 ±14.1	0.4
coronary artery occlusion			
LAD, n (%)	6 (43)	4 (40)	0.95
RCA, n (%)	3 (21)	2 (20)	0.97
Cx, n (%)	4 (29)	4 (40)	0.8
no changes, n (%)	1 (7)	0	0.8

Abbreviations: Cx – circumflex artery, LAD – left anterior descending artery, RCA – right coronary artery, others – see [TABLE 1](#)

patients in each group received statins on a regular basis prior to the study ([TABLE 1](#)). Because only 4 CAD patients were enrolled based on the coronary artery calcium score, no further analysis of this parameter was performed.

The STEMI and non-STEMI groups did not differ significantly in terms of the time from the onset of pain, baseline and maximum serum troponin I levels or the type of coronary artery occlusion ([TABLE 2](#)).

8-iso-prostaglandin F_{2α} in plasma from venous blood

We found that the levels of 8-iso-PGF_{2α}

were significantly higher in ACS compared with CAD patients (363.2 ±45.94 vs. 328.2 ±31.96 pg/ml, $P = 0.011$, [FIGURE 1](#)). No correlations between 8-iso-PGF_{2α}, troponin I or the type of coronary artery occlusion were noted. We did not observe any influence of statins on 8-iso-PGF_{2α} in any of the groups.

Platelet activation markers in venous blood Significantly higher levels of all platelet activation markers were observed in venous blood of ACS subjects compared with the CAD group ([TABLE 3](#)).

In ACS patients there were significant correlations of 8-iso-PGF_{2α} with the markers of platelet activation in venous blood, namely P-sel ($r = 0.66$, $P = 0.0005$) and β-thromboglobulin ($r = 0.62$, $P = 0.001$).

Similar, though less distinct correlations were found in the CAD group for P-sel ($r = 0.46$, $P = 0.02$) and β-thromboglobulin ($r = 0.49$, $P = 0.01$).

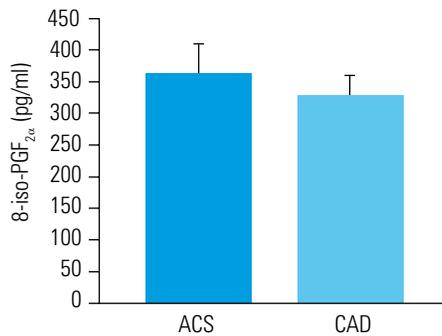
Thrombin generation markers in venous blood

The levels of TAT complexes in venous blood were significantly higher in the ACS group compared to CAD (6.93 ±1.33 vs. 3.19 ±0.64 μg/l; $P < 0.0001$). No correlations between 8-iso-PGF_{2α} and the parameters of thrombin generation in plasma from venous blood were observed.

Vascular injury model In the model of vascular injury, the levels of sCD40L in blood oozing from skin incisions at all time points and the AUC were significantly higher in ACS patients compared with CAD ([TABLE 4](#)). A significant correlation between 8-iso-PGF_{2α} levels in venous blood and maximum sCD40L concentrations (at 6 min) in blood oozing from skin incisions was found in patients with ACS ($r = 0.50$, $P = 0.01$) but not in the CAD group. Thrombin generation in the microvascular injury model was significantly more enhanced in the ACS group ([TABLE 5](#)), however no correlations with 8-iso-PGF_{2α} levels in venous blood were observed in either group.

DISCUSSION It is widely known that oxidative stress plays an important role in various inflammatory diseases and atherosclerosis.¹⁰ ROS are released from different types of cells, including erythrocytes, phagocytes, platelets, and vascular smooth muscle cells where they are produced intracellularly by mitochondrial electron transport chain, nitric oxide synthase (NOS), NADPH oxidase, xanthine oxidase, cytochrome P450, and lipoxygenase/cyclooxygenase (COX) pathways.¹¹ Endogenous free radical scavenging enzymes include superoxide dismutase, catalase, and glutathione peroxidase. Additionally, a number of natural antioxidants, such as ascorbic acid, tocopherol, carotenoids, and flavonoids, inhibit oxidative activity of free radicals.¹¹ Oxidative stress plays an important role in ischemic myocardial injury and elevated levels of ROS have been detected in ischemic myocardium. Particularly high levels of ROS have been observed in the ischemia-

FIGURE 1 8-iso-PGF_{2α} levels in venous blood of ACS and CAD subjects. Data are presented as mean ± SEM. Abbreviations: see TABLE 1



-reperfusion phenomenon.¹¹ In myocardial infarction, prolonged ischemia leads to severe ATP deficit resulting in an inability to scavenge free radicals. Increased levels of ROS are observed despite low partial pressure of O₂ due to ischemia. Reperfusion of the myocardium with a sudden increase of O₂ generates even higher levels of ROS because of impaired antioxidant mechanisms.¹²

Clinical use of ROS as the markers of oxidative stress is very limited due to their short half-life. Hence, other useful markers of oxidative stress are needed. Asymmetric dimethylarginine (ADMA), a potent endogenous inhibitor of endothelial NOS, is an example of a marker related to oxidative stress. Elevated levels of ADMA were found in oxidative stress and are associated with impaired nitric oxide production and endothelial dysfunction.¹³ Serum ADMA levels are associated with endothelial dysfunction in young healthy subjects,¹⁴ in patients with coronary atherosclerosis,^{15,16} and in individuals with multiple risk factors of atherosclerosis.^{15,17} They are also associated with increased cardiovascular risk in the general population.¹⁸

An oxidative attack results in the production of oxidized DNA, proteins, and lipids. Oxidized lipids are useful markers of oxidant stress in vivo. Large amounts of oxidized lipids have been detected within the atherosclerotic plaque.² Increased levels of oxidized lipids are also associated with various risk factors of atherosclerosis, i.e., diabetes, renal failure, and smoking. ox-LDL is not only a marker of oxidation but also an important factor promoting atherosclerosis and activating platelets.^{19,20} A number of studies demonstrated that plasma ox-LDL levels are elevated in patients with stable CAD^{21,22} and ACS^{23,24} and correlate directly with CAD confirmed angiographically.²⁵ Statins increase the clearance of oxidized phospholipids and reduce the impact of oxidative stress by inhibiting NADPH oxidase, a major source of ROS in human vasculature.²⁶ Similarly, fibrates were demonstrated to reduce the levels of oxidative stress markers.²⁷

Oxidative modification of phospholipids generates a wide spectrum of biologically active compounds – IsoPs.³ IsoPs including iso-prostaglandins, iso-leukotrienes, and iso-thromboxanes were confirmed to be produced predominantly by nonenzymatic oxidation of lipids, while irrelevant quantities are the product of COX.⁷ IsoPs are

formed in situ, bind to phospholipids and are subsequently cleaved by an undefined phospholipase, while prostaglandins are generated only from free arachidonic acid.⁷ The results of the Biomarkers of the Oxidative Stress Study proved that IsoPs are reliable markers of oxidative injury in an animal model.²⁸ F_{2α}-IsoPs are the most stable IsoPs and are currently recognized as a “gold standard” marker of oxidant stress in vivo. 8-iso-PGF_{2α} can be measured in situ in all tissues and in biological fluids, i.e., in serum and in urine, which makes it a particularly useful clinical marker.⁷ Recent studies have demonstrated that 8-iso-PGF_{2α} is not only a marker of oxidative stress but also a biologically active molecule. It promotes atherosclerosis and attenuates angiogenesis by activating thromboxane receptor.^{29,30} Furthermore, 8-iso-PGF_{2α} contributes to platelet activation.⁶ The levels of F_{2α}-IsoPs are increased in atherosclerotic plaques.³¹ Persistently enhanced formation of F_{2α}-IsoPs has been described in association with a number of cardiovascular risk factors including smoking,³² diabetes mellitus,³³ and hypercholesterolemia.³⁴ Moreover, increased levels of 8-iso-PGF_{2α} were found to be an independent risk factor of atherosclerosis.³⁵

Considering an undisputed role of oxidative stress and IsoPs in atherosclerosis and their influence on platelet function, we decided to investigate the levels of 8-iso-PGF_{2α} in ACS and their impact on platelet activation. Our results confirm enhanced production of 8-iso-PGF_{2α} in myocardial infarction compared with CAD, indicating high intensity of oxidative stress generated by coronary artery occlusion. High levels of 8-iso-PGF_{2α} in ACS were correlated with enhanced platelet activation in circulating blood and in the microvascular injury model, thus reflecting systemic impact of oxidative stress associated with myocardial infarction on local hemostasis. Increased levels of sCD40L in venous blood of ACS patients compared with CAD were confirmed by earlier studies.³⁶ Interestingly, no influence of oxidative stress on thrombin generation was observed. Use of statins prior to the study had no influence on 8-iso-PGF_{2α} levels in venous blood.

Our study has several limitations. The most important one was the small size of the study population, which limited statistical power of the results and precluded evaluation of any influence of statins on oxidative stress in ACS. The small size of our study group resulted from a study design, which excluded patients receiving thienopyridines prior to enrollment. However, use of other antiplatelet agent along with aspirin may have resulted in a potent attenuation of platelet activity precluding observation of any variability of platelet function. Another possible limitation was the fact that all study subjects received aspirin. Apart from inhibition of platelet function, aspirin diminishes the production of ROS and inhibits COX. It has been demonstrated that aspirin suppresses NADPH oxidase-mediated ROS generation in endothelial cells.³⁷ However, Cipollone et al.³⁸

TABLE 3 Levels of platelet activation markers in venous blood plasma of ACS and CAD patients

	ACS	CAD	P
sCD40L (pg/ml)	807.1 ± 295.6	226.2 ± 52.3	<i>P</i> < 0.0001
P-sel (ng/ml)	158.1 ± 37.3	102.7 ± 13.5	<i>P</i> < 0.0001
β-thromboglobulin (IU/ml)	65.8 ± 11.4	55.1 ± 6.8	<i>P</i> = 0.0009

Data are presented as mean ± SEM.

Abbreviations: P-sel – P-selectin, sCD40L – soluble CD40 ligand, others – see TABLE 1

TABLE 4 Soluble CD40 ligand levels in blood oozing from skin incisions in ACS and CAD patients

	ACS (ng/ml)	CAD (ng/ml)	P
1 min	2.14 ± 0.06	0.58 ± 0.02	<i>P</i> < 0.001
2 min	7.34 ± 0.10	4.43 ± 0.16	<i>P</i> < 0.001
3 min	12.74 ± 0.20	7.42 ± 0.22	<i>P</i> < 0.001
4 min	18.73 ± 0.27	8.30 ± 0.24	<i>P</i> < 0.001
5 min	20.09 ± 0.35	8.74 ± 0.24	<i>P</i> < 0.001
6 min	20.68 ± 0.43	8.78 ± 0.25	<i>P</i> < 0.001
AUC	31.58 ± 0.46	16.58 ± 0.51	<i>P</i> < 0.001

Data are presented as mean ± SEM.

Abbreviations: AUC – area under the curve, others – see TABLE 1

TABLE 5 Thrombin-antithrombin complex levels in blood oozing from skin incisions in ACS and CAD patients

	ACS (nmol/l)	CAD (nmol/l)	P
1 min	19.60 ± 1.32	4.60 ± 0.60	<i>P</i> < 0.001
2 min	34.97 ± 1.74	10.12 ± 2.56	<i>P</i> < 0.001
3 min	53.40 ± 2.55	17.12 ± 3.18	<i>P</i> < 0.001
4 min	72.98 ± 3.08	26.08 ± 5.38	<i>P</i> < 0.001
5 min	81.04 ± 2.95	32.74 ± 3.51	<i>P</i> < 0.001
6 min	84.16 ± 2.29	36.46 ± 2.94	<i>P</i> < 0.001
AUC	144.46 ± 6.80	44.88 ± 8.90	<i>P</i> < 0.001

Data are presented as mean ± SEM.

Abbreviations: see TABLES 1 and 4

demonstrated that in patients with unstable angina treated with low-dose aspirin, despite almost complete suppression of platelet COX-1 activity, urinary 8-iso-PGF_{2α} excretion remained significantly higher than in matched patients with stable angina or in healthy subjects. Davi et al.³³ observed no change in urinary 8-iso-PGF_{2α} excretion in patients with diabetes despite a 2-week treatment with aspirin or indobufen. Yin et al. demonstrated that most of 8-iso-PGF_{2α} in smoking subjects and healthy individuals was produced in vivo by COX-independent mechanisms, and inhibition of COX with ibuprofen yielded no significant decrease in 8-iso-PGF_{2α} urinary levels.³⁹

Gas chromatography/mass spectroscopy is still the most reliable method of IsoP quantification. It offers high sensitivity and specificity even in a very low concentration range. In recent years, commercially available immunoassays have been

extensively used to measure the levels of IsoPs due to their low cost and relative ease of use. However, their accuracy has not yet been fully determined by mass spectroscopy.⁷ Furthermore, immunoassays have not been tested for cross-reactivity with isoprostane metabolites.⁴⁰ Nevertheless, 8-iso-PGF_{2α} levels in plasma from venous blood of CAD subjects in our study corresponded to the levels of sCD40L in the CAD group, which were measured using the original method with monoclonal antibodies.⁴¹

In summary, we have demonstrated for the first time that enhanced levels of oxidative stress in ACS measured by 8-iso-PGF_{2α} in venous blood were associated with systemic and local platelet activation but not with thrombin generation.

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Podwyższone stężenia 8-izo-prostaglandyny $F_{2\alpha}$ w ostrych zespołach wieńcowych są związane z ogólnoustrojową i miejscową aktywacją płytek

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SŁOWA KLUCZOWE

8-izo-prostaglandyna $F_{2\alpha}$, aktywacja płytek, izoprostany, ostry zespół wieńcowy, rozpuszczalny ligand CD40

STRESZCZENIE

WPROWADZENIE Stres oksydacyjny jest istotnym czynnikiem sprzyjającym rozwojowi miażdżycy. Izoprostany powstają z kwasu arachidonowego pod wpływem działania aktywnych postaci tlenu. Oksydowane lipidy stanowią nie tylko marker stresu oksydacyjnego, ale są również ważnymi mediatorami rozwoju miażdżycy oraz aktywują płytki krwi. 8-izo-prostaglandyna $F_{2\alpha}$ (8-izo-PGF_{2α}) jest izoprostanem o stabilnej cząsteczce oraz wiarygodnym markerem stresu oksydacyjnego *in vivo*.

CELE Celem niniejszego badania była ocena nasilenia stresu oksydacyjnego u chorych z ostrym zespołem wieńcowym (*acute coronary syndrome* – ACS) oraz jego korelacji z parametrami hemostazy.

PACJENCI I METODY U 49 chorych w wieku 46–76 lat, w tym u 24 z ACS oraz u 25 ze stabilną dławicą piersiową (*coronary artery disease* – CAD), oznaczano stężenia 8-izo-PGF_{2α}, rozpuszczalnego ligandu CD40 (sCD40L), P-selektyny (P-sel) i β-tromboglobuliny oraz kompleksów trombina–antytrombina (TAT) w osoczu krwi żyłnej. Przeprowadzono także badanie krzepnięcia w modelu uszkodzenia mikrokrążenia, w którym co 60 s oznaczano generację TAT oraz uwalnianie sCD40L we krwi zbieranej z wystandaryzowanych nacięć skóry.

WYNIKI Stężenie 8-izo-PGF_{2α} we krwi żyłnej było znacznie większe u chorych z ACS w porównaniu z CAD (363,2 ± 45,94 vs 328,2 ± 31,96 pg/ml; $P = 0,011$) i korelowało ze stężeniami w osoczu krwi żyłnej P-sel i β-tromboglobuliny w grupie ACS (odpowiednio $r = 0,66$; $P = 0,0005$ i $r = 0,62$; $P = 0,001$) oraz w grupie CAD (odpowiednio $r = 0,46$; $P = 0,02$ i $r = 0,49$; $P = 0,01$). Stężenia 8-izo-PGF_{2α} wiązały się z maksymalnym stężeniem sCD40L w grupie ACS w modelu uszkodzenia mikrokrążenia ($r = 0,50$; $P = 0,01$). Nie zaobserwowano korelacji między stężeniami 8-izo-PGF_{2α} i markerami generacji trombiny we krwi żyłnej oraz w modelu uszkodzenia mikrokrążenia.

WNIOSKI Stężenia 8-izo-PGF_{2α} są znacznie większe u chorych z ACS w porównaniu z osobami z CAD i korelują z aktywacją płytek.

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