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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

The relation between the levels of osteoprotegerin and the degree of coronary artery disease in patients with acute coronary syndrome and stable angina pectoris

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Abstract

Background: Osteoprotegerin (OPG), an inhibitor of osteoclastogenesis, has recently been under the spotlight in studies regarding the pathophysiology of atherosclerosis.

Aim: To evaluate the value of serum OPG in the diagnosis and severity in patients with stable angina pectoris (SA) and unstable angina pectoris/non ST elevation myocardial infarction.

Methods: This study involved 160 patients, SA (n = 65), acute coronary syndrome (NSTE-ACS; n = 65), and a control group (n = 30). Blood samples were collected in the first hour, after 24 hours and on the fifth day. The prevalence of coronary artery atherosclerotic lesions was determined using the Gensini scoring system.

Results: A statistically significant difference was observed in the first hour OPG levels between the control group and both the SA and NSTE-ACS group ($p < 0.001$). When the cut-off value was determined as 247.71 pg/mL, the sensitivity and specifi city of the first hour OPG levels indicating coronary artery disease were 91.54% and 46.67%, respectively, while the positive predictive value was 88.1% and the negative predictive value was 56%. No correlations were observed between the first, 24th hour and the fifth day OPG levels and the Gensini scores. No relation was denoted between the OPG levels and number of diseased coronary arteries.

Conclusions: In our study, serum OPG level seemed to be unrelated to the severity or the degree of coronary artery disease in patients with SA and unstable angina pectoris/non ST elevation myocardial infarction. OPG may only be accepted as an indicator of coronary artherosclerosis.

Key words: osteoprotegerin, stable angina pectoris, acute coronary syndrome

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INTRODUCTION

Coronary atherosclerosis is the most common form of cardiovascular disease, with high mortality and morbidity rates. Arterial calcification has been found to be related to an increased risk of cardiovascular events, although the predictive value of coronary risk factors remains unclear [1].

Osteoprotegerin (OPG) was discovered in 1997 as a member of the tumour necrosis factor receptor family, and has a role in the inhibition of the differentiation and activation of osteoclasts [2]. Studies regarding physiological or pathological bone resorption have led to the discovery of receptor activator nuclear kappa B (RANK) on osteoclasts, activated by RANK

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ligand and involved in bone resorption [3, 4]. OPG inhibits the destruction of the bone executed by osteoclasts by acting as an antiresorptive and a hypocalcaemic. The biological effects of OPG on bone tissue are opposite to the effects of RANK/RANKL. OPG acts as a decoy receptor, binding with RANKL and blocking RANK. As a result, the differentiation and activation of osteoclasts are inhibited and bone resorption carried out by RANKL is hindered. Besides osteoblasts, OPG is synthesised by many tissues such as the cardiovascular system (including the heart, arteries, and veins), kidneys, spleen, brain, lungs, as well as by the components of the haematopoietic and immune systems [5, 6]. Its secretion is regulated by many cytokines such as transforming growth factor-α, transforming growth factor-β, interleukin-1α, interleukin-17, peptides like bone morphogenetic proteins, hormones such as parathyroid hormone, and drugs [6, 7]. OPG is synthesised in the medial layer of the large arteries and the smooth muscle of the coronary arteries as well as endothelial cells [3, 4, 6].

Recent studies of experimental models have demonstrated that increased activation of osteoclasts in OPG-deficient mice have led to osteoporosis [8]; nevertheless, calcification in large arteries, proliferation in the intimal and medial layers, and aortic dissection were observed, which suggested the protective effects of OPG on the calcification of medial layers of large arteries [8, 9]. On the other hand, OPG has been demonstrated to be associated with cardiovascular disease and arterial calcification in postmenopausal women and elderly patients with osteoporosis [10, 11]. In another study, OPG was shown to be strongly related to cardiovascular risk factors such as smoking, chronic infection, systemic inflammatory markers, diabetes mellitus, and age [12]. Moreover, recent studies have reported a correlation between serum OPG levels and the severity of coronary vessels disease in patients with chronic coronary disease [13, 14].

These studies were conducted on merely asymptomatic and/or stable patients, while no data is available regarding the possible role of OPG in patients with acute coronary syndromes. Data regarding patients with acute coronary syndromes other than ST elevation myocardial infarction is very limited. In the aforementioned studies, as well as in other similar studies, only patients with critical and significant stenosis were taken into account [13–16]. The exclusion of subjects with non-critical lesions has limited the value of these studies.

It is not clearly understood whether the elevated OPG level simply reflects vascular damage, is a counter-regulatory mechanism to confine vascular disease, or mediates the progression of the disease. The aim of our study was to evaluate the role of OPG in the development of critical/non-critical atherosclerotic lesions and to seek possible answers to the above questions.

METHODS

Study groups

Hundred sixty patients who were admitted with chest pain to the Coronary Intensive Care Unit of Trakya University Hospital from June 2006 to March 2009 were enrolled in our study. The Ethical Committee of Trakya University approved our study. Informed consent was obtained from all patients. The patients were divided into three groups. The control group (n = 30) contained patients with normal coronary arteries who underwent coronary angiographies due to suspected coronary artery disease (CAD) with clinical or non-invasive tests (electrocardiogram, exercise testing, myocardial perfusion scintigraphy). The stable angina pectoris (SA) group (n = 65) contained patients with typical angina pectoris after exercise or emotional stress. The non-ST elevation-acute coronary syndrome (NSTE-ACS) group (n = 65) was defined by electrocardiographic (ECG) ST-segment depression, prominent T-wave inversion, and/or positive biomarkers of necrosis (e.g. troponin) in the absence of ST-segment elevation and in a probable clinical setting (chest discomfort or angina equivalent). Myocardial necrosis is defined by an elevation of troponin above the 99th percentile of normal. Myocardial infarction (necrosis related to ischaemia) is defined by the elevation of troponin with at least one of the following criteria: ischaemic ST or T-wave changes.

Participants were instructed to continue taking all their existing medications. Recorded data for each patient included coronary angiography findings and detailed cardiovascular risk factors. A medical history regarding previous myocardial infarction, hypertension, smoking, diabetes mellitus, and hypercholesterolaemia was obtained and recorded for all patients. Arterial hypertension was defined as systolic blood pressure repeatedly greater than 140 mm Hg, diastolic blood pressure greater than 90 mm Hg, or current use of antihypertensive drugs. Patients were considered as diabetic if their fasting glucose was repeatedly above 126 mg/dL or if they were already receiving oral anti-diabetic drugs or insulin. Hyperlipidaemia was defined as having a total cholesterol level above 200 mg/dL, and/or the current use of lipid-lowering treatment. Patients with a history of myocardial infarction, scheduled revascularisation procedures, valvular disease, heart failure, cardiomyopathy, ejection fraction below 45%, malignancies, osteoporosis, renal disease (creatinine levels > 2.0 mg/dL), and patients receiving systemic glucocorticoids or immunosuppressants were excluded from the study.

Coronary angiography

Critical stenosis was defined as stenosis of 50% or more in the main coronary artery, or stenosis of 70% in other coronary arteries, causing narrowing of the lumen. Non-critical stenosis was defined as stenosis of any lesser degree. The prevalence of CAD was determined using the Gensini scoring system [17]. The angiographic appearance of concentric lesions and eccentric plaques resulted in, respectively, 25%, 50%, 75%, 90%, and 99% obstruction, as well as complete occlusion (100%). The relative severity of these lesions used a score of one for 25% obstruction, and doubled that num-

Table 1. Baseline demographic and clinical characteristics of all study patients

	Control group (n = 30)	SA group (n = 65)	NSTE-ACS group (n = 65)
Age [years]	52.5 ± 10.16	59.03 ± 10.14*	59.92 ± 10.35*
Women	17 (56.7%)	18 (27.7%)	17 (26.2%)
Body mass index [kg/m^2]	27.6 ± 3.4	27.5 ± 3.4	26.6 ± 4.8
Diabetes mellitus	1 (3.3%)	27 (41.5%)*	17 (26.2%)*
Hypertension	14 (46.7%)	42 (64.6%)*	27 (41.5%)*
Dyslipidaemia	13 (43.3%)	32 (49.2%)	26 (40.0%)
Family history of CAD	7 (23.3%)	16 (24.6%)	17 (26.2%)
Current smoker	5 (16.7%)	22 (33.8%)*	34 (52.3%)*
< 50% stenosed vessels		9 (13.8%)	7 (10.8%)
Affected coronary arteries:			
One		21 (32.3%)	19 (29.2%)
Two		15 (23.1%)	18 (27.7%)
Three or four		20 (30.8%)	21 (32.3%)
Gensini score		30.5 (13–60)	40 (16.5–59)

All numerical data is presented as the mean ± standard deviation or median (25–75%); *p < 0.05 compared to controls; CAD — coronary artery disease; NSTE-ACS — non ST elevation acute coronary syndrome; SA — stable angina pectoris

ber as the severity of the obstructions progressed, according to the indicated reduction of lumen diameter. Each of the principal vascular segments of the right coronary artery, the left anterior descending, and the circumflex is followed by a multiplying factor such as X1, X2.5, and so on, depending on the functional significance of the area supplied by that segment artery. This scoring of coronary artery atherosclerotic lesions in a tree illustrated the results obtained from a single value for each patient.

Measurements

Blood samples from the antecubital vein (5cc each) were obtained in the first hour from the SA and control groups. From the NSTE-ACS group, samples were obtained in the first hour, the 24th hour, and on the fifth day. All samples were centrifuged at 3,500 rpm for 5 min and then stored at –80°C. OPG levels were determined by the ELISA method using the Human OPG Instant Elisa Kit (Bender Med Systems GmbH, Austria).

Statistical analysis

All data is presented as mean ± standard deviations (SD). Normality distribution of the variables was tested using one sample Kolmogorov-Smirnov test. Differences among groups were compared using the one-way ANOVA test for normal, and a Bonferroni post-hoc test was used when a significant difference was found. The Kruskal-Wallis test was used for non-normally distributed data which is the number of involved coronary arteries. Dual comparisons between groups exhibiting significant values were evaluated with the Mann-Whitney U-test; p-values (indicating significance) underwent the Bonferroni correction. A p-value of < 0.005 was considered as statistically significant because of the Bonferroni correction.

Descriptive statistics (e.g. the median: 25–75% percentile) were shown. The χ^2 test was used for statistical analysis of categorical variables. Spearman's correlation analysis was performed on OPG levels and continuous variables in the first hour, the 24th hour, and the fifth day. To demonstrate the predictive value of CAD, the OPG level measurements from the first hour, the receiver operating characteristic (ROC) curve drawing, and the area under the curve were calculated. Factors that can impact the diagnosis of CAD and mortality in logistic regression analysis were used to assess the impact. A p-value of < 0.05 was considered as statistically significant.

RESULTS

Demographic and biochemical features of the patients are summarised in Tables 1 and 2. No difference was observed within groups regarding body mass index or gender. Accompanying risk factors were observed to be more frequent in patients with known CAD. Among the acute coronary syndrome group, 41 patients had unstable angina pectoris (63.1%), while 24 had non-ST elevation myocardial infarction (36.9%). The first hour OPG levels in the control, SA, and NSTE-ACS groups are shown in Table 2 and a statistical significance was observed between the results of controls with SA and controls with NSTE-ACS (p < 0.001). No difference was observed between the SA group and the NSTE-ACS group regarding the first hour OPG levels.

As analysed by multivariate logistic regression analysis (Table 3), OPG serum levels were independently and positively associated with the presence of CAD (SA: OR 1.016, 95% CI

Table 2. Biochemical parameters of all study groups

	Control group (n = 30)	SA group (n = 65)	NSTE-ACS group (n = 65)
Urea [mg/dL]	31.5 (25–40.25)	34 (27.5–40)	34 (30–41.5)
Creatinine [mg/dL]	1 (0.8–1)	1 (0.8–1)	1 (0.9–1)
Glucose [mg/dL]	99 (92–105.25)	104 (93–139.5)	107 (98.5–125)
Haemoglobin [g/dL]	13.05 ± 1.50	13.48 ± 1.46	13.51 ± 1.48
White blood cell count [mm^3]	7.91 ± 2.80	8.41 ± 2.32**	9.61 ± 2.61*
LDL cholesterol [mg/dL]	128.97 ± 37.62	108.77 ± 34.23	118.02 ± 39.53
HDL cholesterol [mg/dL]	47.22 ± 13.77	40.95 ± 9.32*	37.47 ± 9.57*
Triglycerides [mg/dL]	112 (84–160)	139 (98.75–200.75)	134 (97.75–180.75)
Cholesterol [mg/dL]	189.52 ± 62.35	184.21 ± 40.47	188.14 ± 45.31
Osteoprotegerin [pg/mL]:			
1 h	266.35 (158.33–328.85)	325.63 (285.83–376.67)***	338.13 (282.92–464.79)***
24 h			376.20 ± 149.19
5 day			359.44 ± 148.04

All numerical data is presented as the mean ± standard deviation or median (25–75%); *p <0.05 compared to controls; **p < 0.05 compared to SA and NSTE-ACS; ***p < 0.001 compared to controls; NSTE-ACS — non ST elevation acute coronary syndrome; SA — stable angina pectoris

Table 3. Association of presence of CAD with CAD risk factors and OPG

Variable	P	OR	95% CI
Age [years]	0.138	1.063	0.981–1.152
Male sex	0.232	2.368	0.576–9.733
Diabetes	0.004	36.104	3.224–404.318
Hypertension	0.844	1.164	0.255–5.321
Hyperlipidaemia	0.986	0.988	0.243–4.022
Current smoking	0.009	11.651	1.861–72.954
Family history of premature CAD	0.643	0.665	0.119–3.729
Body mass index [kg/m^2]	0.992	0.999	0.821–1.216
1 h OPG pg/mL (SA)	**0.002**	**1.016**	**1.006–1.025**
1 h OPG pg/mL (NSTE-ACS)	**0.004**	**1.012**	**1.004–1.020**

CAD — coronary artery disease; CI — confidence interval; OR — odds ratio; OPG — osteoprotegerin; NSTE-ACS — non ST elevation acute coronary syndrome; SA — stable angina pectoris

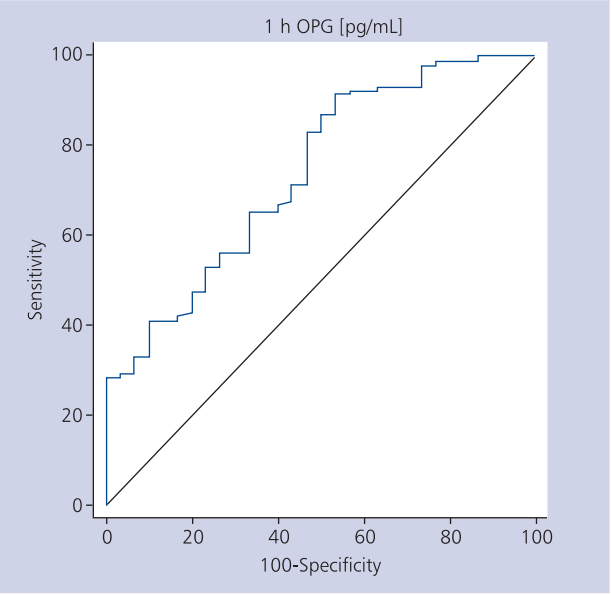

Figure 1. Curve receiver operating characteristics. The area under the curve (AUROC) 0.739, p < 0.001; OPG — osteoprotegerin

1.006–1.025, p = 0.002) and in the NSTE-ACS (OR 1.012, 95% CI 1.004–1.020, p = 0.004).

In patients with SA, together with NSTE-ACS, the area under the curve (AUROC) of the predictive value of the first hour OPG level for CAD was observed to be 0.739, p < 0.001. When the cutoff value was determined as 247.71 pg/mL, the predictive value of the first hour measures beyond this level demonstrated a sensitivity of 91.54% and a specificity of 43.3%, with a positive predictive value of 88.1% and a negative predictive value of 56% (Fig. 1).

Gensini scoring was used for coronary angiographic evaluation. No relation was observed in the first hour OPG levels of the SA and NSTE-ACS groups, nor in the 24th hour and fifth day OPG levels and Gensini scores (Gensini score first hour OPG: r = –0.062, p = 0.485; Gensini score 24th hour OPG: r = –0.014, p = 0.912; Gensini score fifth day OPG: r = –0.160, p = 0.211). No difference was observed in patients with SA and NSTE-ACS regarding the number of involved coronary arteries. Non-critical CAD was observed in 16 patients from both groups (10%), single-artery disease was found in 40 (25%) patients, two-artery involvement was found in 33 (20.6%) patients, and three- or multiple-vessel

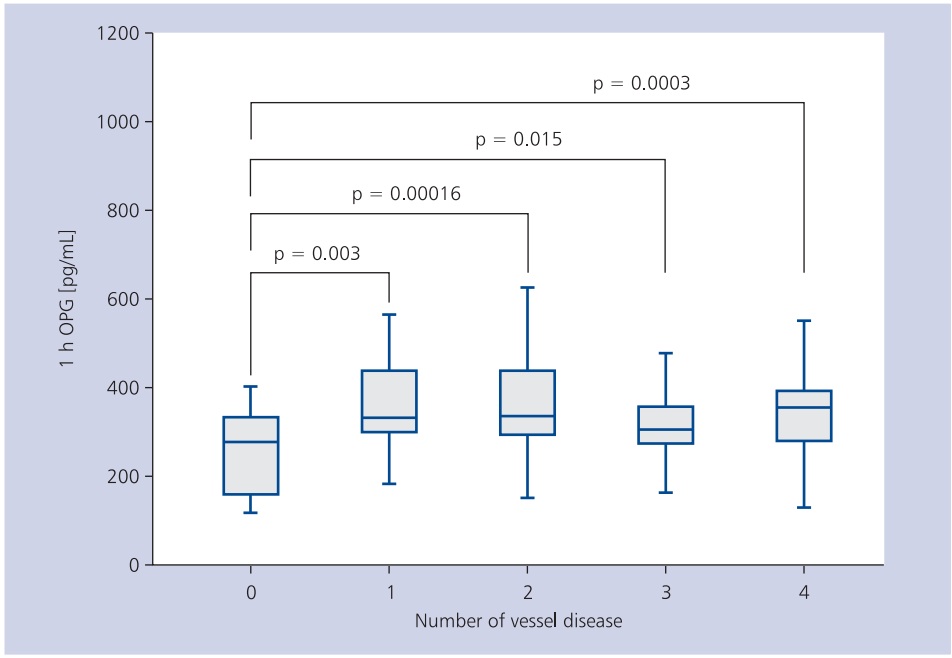

Figure 2. The relationship between the number of diseased coronary arteries and osteoprotegerin (OPG) levels after 1 h; 0 — normal coronary arteries; 1 — non-critical coronary artery disease; 2 — single-vessel disease; 3 — two-vessel disease; 4 — three/four-vessel disease; $p < 0.005$. Boxes represent the 95% confidence intervals, with the mean superimposed as a horizontal line. Error bars indicate ranges of OPG serum levels

disease was found in 41 (25.6%) patients. The mean OPG level in patients with non-critical CAD was 331.46 (296.04–439.79) pg/mL. In patients with single-vessel disease, it was 338.33 (292.40–443.54) pg/mL. In double-vessel disease patients, it was 307.708 (275–369.583) pg/mL. In three- or multiple-vessel disease patients, it was 333.96 (276.67–413.96) pg/mL. In the control group, the mean OPG level was 266.35 (158.33–328.85) pg/mL.

A statistical significance was found between the first hour OPG levels of the control group and non-critical, single-vessel, and three- or multiple-vessel disease patients ($p = 0.003$, $p = 0.00016$, $p = 0.0003$, respectively). Thus, the first hour OPG levels in patients with double-vessel disease were observed to be higher than the controls, though statistically insignificant ($p = 0.015$). Furthermore, no significance was observed in the first hour OPG levels of non-critical CAD with single-, double-, and three- or multiple-vessel disease patients (Fig. 2).

DISCUSSION

In this study, we demonstrated that OPG is an indicator of CAD. No relation was observed between OPG levels and the severity and diffusiveness of CAD in terms of Gensini scores. We observed higher OPG levels in patients with SA and NSTE-ACS (unstable angina pectoris/non ST elevation myocardial infarction) than in patients without CAD.

The relation between coronary atherosclerosis and OPG has also been demonstrated in recent studies [4, 18]. If atherosclerotic calcification fails, it can cause the vessels to break as a result of plaque rupture [4, 19]. In autopsy series, thrombotic coronary death and acute coronary syndromes have been shown to be caused by plaque rupture, which is the most common type of plaque complication [5, 20]. Recent studies have shown that the OPG/RANK/RANKL system is involved in plaque instability and rupture because it induces plaque calcification [21]. Caidahl et al. [3] and Venuraju et al. [4] demonstrated that this system plays a role in the pathogenesis of atherosclerosis. The expression of OPG is up-regulated in endothelial cells by proinflammatory cytokines; therefore, the increasing expression of endothelial cell adhesion molecules helps monocytes and lymphocytes into the intima of the vessel wall. The inflammatory cells up-regulate expression of RANKL and form vascular smooth muscle cells. OPG together with RANKL at higher RANKL/OPG ratios increases activity of matrix metalloproteinase. Increased matrix metalloproteinase activity leads to degradation of the extracellular matrix and reduced thickness of the fibrous cap. The plaque rupture due to erosion causes thrombus formation and promotion of osteogenesis, leading to synthesis of bone proteins and matrix calcification within the arterial vessel.

Although several larger studies have addressed the role of OPG in the progression of cardiovascular disease, they have provided differing results. Some studies have demonstrated the increased serum level of OPG in coronary artery calcification, while other results have reported inhibitory effects

of OPG on vascular calcification [22, 23]. Recent studies have found that OPG is part of a complex mechanism in the RANKL/OPG/RANK axis [3, 4, 21].

We think that this complex mechanism is not fully understood in all aspects of the OPG, although OPG may undertake the role of maestro in atherosclerosis and plaque stabilisation. In reality, OPG as a soluble scavenger presents the RANKL/RANK binding, inhibiting the RANKL function [19]. Some reports indicated that in the cardiovascular system, the serum concentration of OPG was increased in the clinical cases that were susceptible to atherosclerosis and unstable vascular calcification [19]. OPG secretion is not probably enough to cause a compensatory mechanism that is responding to an increase of RANKL secretion; it could not prevent calcification and atherosclerosis [24]. Therefore, the serum OPG level is only a biomarker for CAD. In our findings, the lack of correlation between the severity of the disease and OPG may be explained by this speculation. The RANKL/OPG ratio may be a better diagnostic indicator for intensity of vascular calcification that leads to coronary disorders.

Jono et al. [13] found that OPG was increased in patients with SA. However, after a series of follow-ups over 10 years, OPG was determined to be an independent risk factor for progressive atherosclerosis and cardiovascular disease in the population [12]. In two independent studies, increased OPG levels were found in asymptomatic CAD and diabetes patients [15, 25]. OPG was shown to be an indicator for coronary atherosclerosis in our study as well. Atherosclerotic risk factors such as old age, male gender, hypertension, diabetes mellitus, and smoking were more prevalent in patients with atherosclerotic disease. With the multivariate logistic regression analysis, OPG indicated the presence of CAD independently from the mentioned risk factors. Also, we found a cutoff level of OPG in CAD. Morena et al. [18] reported that the cutoff level of OPG was best able to predict the presence of significant CAD. But, the cutoff level of OPG could act as a predictor in CAD patients, since this attribute was found in chronic kidney disease patients.

Schoppet et al. [14] observed a relation between the OPG levels and the Gensini score in male patients with SA (only the lesions of the proximal segments were taken into account since the distal segments are difficult to evaluate). Palazzuoli et al. [16] evaluated the severity and extent of CAD using the Duke Jeopardy score in patients with NSTE-ACS and observed a positive correlation between the extent of CAD and serum levels of OPG. The Duke Jeopardy score system evaluates the six segments of the coronary tree and stenosis of only 50% of the left descending coronary artery; 75% of the other segments are taken into account. For this reason, we used the Gensini score system for its high sensitivity, and did not observe a relation between the serum levels of OPG and the extent of CAD in patients with SA and NSTE-ACS.

OPG levels have been thought to increase proportionally with the severity of CAD [14, 16]. Schoppet et al. [14] demonstrated a significant relation between OPG levels and the number of diseased coronary arteries in male patients with SA (single, double, and multiple vessels). Likewise, Palazzuoli et al. [16] demonstrated a relation between the number of involved arteries and the levels of OPG in patients with NSTE-ACS.

In our study, we did not observe such a relation between the levels of OPG and the severity of CAD in patients with SA and NSTE-ACS. High serum OPG levels with diabetes mellitus have been reported [12, 14]. Similarly to our study, Schoppet et al. [14] found that in male patients with SA and without diabetes mellitus, the serum OPG levels in single- or multi-vessel CAD were higher than the control group; however, they did not find significant differences in the two-vessel disease. Nevertheless, they have claimed that there is a correlation between serum OPG levels and the number of affected coronary arteries. We think that the OPG level is neither an indicator of the number of affected coronary arteries nor of the severity of CAD, but only an indicator of the presence of CAD.

Limitations of the study

Our study lacks tested levels of RANKL or OPG/RANKL ratios, but we do speculate that OPG appears as an indicator of the presence of atherosclerosis/vascular calcification, rather than its severity or progression. Another limitation is that we did not study the OPG vs. the RANKL polymorphism of the patients included in this study. The OPG polymorphism is known to be associated with cardiovascular disease [26, 27]. Further, the OPG polymorphism carrier state may become a valuable molecular marker of the risk of CAD [28]. An association between the RANKL polymorphism and CAD has been reported [29]. The lack of correlation between the severity of the disease and OPG may be associated with serum levels in the OPG and/or RANKL relationship, the OPG and/or RANKL polymorphism, or the yet undetermined epistasis of these polymorphic variations in the genes.

CONCLUSIONS

Serum OPG levels are not correlated with the severity and extent of coronary atherosclerosis in patients with SA and NSTE-ACS, and may only be regarded as an indication of the presence of CAD.

Conflict of interest: *none declared*

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Zależność między stężeniem osteoprotegeryny a zaawansowaniem choroby wieńcowej u pacjentów z ostrym zespołem wieńcowym i stabilną dławicą piersiową

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Streszczenie

Wstęp: Osteoprotegeryna (OPG), inhibitor osteoklastogenezy, jest ostatnio przedmiotem badań dotyczących patofizjologii miażdżycy.

Cel: Celem niniejszego badania była ocena stężenia OPG w surowicy u osób ze stabilną dławicą piersiową (SA) i niestabilną dławicą piersiową/zawałem serca bez uniesienia odcinka ST.

Metody: Badaniem objęto 160 pacjentów, w tym chorych z SA (n = 65) lub z ostrym zespołem wieńcowym (NSTE-ACS) (n = 65) oraz osoby stanowiące grupę kontrolną (n = 30). Próbki krwi pobrano w 1. godzinie, 24. godzinie i w 5. dniu. Występowanie zmian miażdżycowych w naczyniach wieńcowych określono, stosując skalę Gensiniego.

Wyniki: Stwierdzono statystycznie istotne różnice między grupą kontrolną a grupami SA i NSTE-ACS w stężeniach OPG w 1. godzinie ($p < 0,001$). Po przyjęciu wartości progowej wynoszącej 247,71 pg/ml czułość i swoistość stężeń OPG w 1. godzinie w odniesieniu do wykrywania choroby wieńcowej wynosiły odpowiednio 91,54% i 46.67%, a wartości prognostyczne dodatnia i ujemna — 81,1% i 56%. Nie stwierdzono korelacji między stężeniami OPG w 1. godzinie, 24. godzinie ani w 5. dniu a punktacją w skali Gensiniego. Nie zanotowano żadnych zależności między stężeniami OPG a liczbą zmienionych miażdżycowo tętnic wieńcowych.

Wnioski: W niniejszym badaniu nie wykazano zależności między stężeniem OPG w surowicy a ciężkością lub zaawansowaniem choroby wieńcowej u pacjentów z SA i z niestabilną dławicą piersiową/zawałem serca bez uniesienia odcinka ST. Można jedynie uznać OPG za wskaźnik miażdżycy tętnic wieńcowych.

Słowa kluczowe: osteoprotegeryna, stabilna dławica piersiowa, ostry zespół wieńcowy

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