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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Diminished serum paraoxonase activity in patients with coronary artery calcification

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Abstract

Background: Previous studies have shown an association between paraoxonase (PON) activity and the presence and severity of coronary atherosclerosis.

Aim: To demonstrate any association between serum PON activity and the presence and severity of coronary artery calcification (CAC).

Methods: A total of 156 consecutive patients having the suspicion of coronary atherosclerosis or needing risk stratification for cardiovascular events were included in the present study. Peripheral venous blood samples of all participants to measure serum PON activity were collected before undergoing multidetector computed tomography, which was used to determine the presence and quantity of CAC.

Results: Serum PON-1 levels were lower in the CAC group compared to the no CAC group (60 [35–96] U/L vs. 291 [230–371] U/L, respectively, $p < 0.001$). There was a significant negative correlation between total CAC score and PON ($r^2 = 0.335$, $p < 0.001$). In multivariate analysis, the significant and independent predictors of the presence of CAC were male sex, high-sensitive C-reactive protein, and PON. Similarly, increased PON was significantly and independently associated with freedom from CAC. In receiver operating characteristics analysis, PON level < 197 U/L had 87% sensitivity, 91% specificity, 93% positive predictive value, and 85% negative predictive value in predicting CAC.

Conclusions: Diminished serum PON activity is significantly and independently associated with the presence and severity of CAC, and vice versa.

Key words: coronary calcification, multidetector computed tomography, paraoxonase

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INTRODUCTION

An increased level of high density lipoprotein (HDL) has been reported to be associated with a decreased risk for coronary artery disease. This protective effect of HDL against atherosclerosis has been at least partly attributed to enzymes associated with HDL. One of these enzymes is paraoxonase (PON). Studies have shown that HDL-associated PON-1 inhibits lipid peroxidation and degrades biologically active oxidised lipids in low-density lipoprotein (LDL) [1]. PON-1 is recruited with breakdown of lipid peroxides before their accumulation on LDL [2].

The presence and quantity of coronary artery calcium (CAC) detected by computed tomography (CT) correlates with the overall magnitude of the atherosclerotic plaque burden and with the development of subsequent adverse coronary events [3–7]. It has been shown that its increased levels, measured as either percentiles (CAC > 75th percentile for age and sex matched) or absolute scores (i.e. > 100 or > 400)

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are associated with adverse events, and because of that in several guidelines the high CAC score has been proposed as a marker to identify individuals requiring aggressive preventive management [8–10]. It has been also demonstrated that CAC improved risk prediction after taking into account Framingham risk score in four racial or ethnic groups [11].

METHODS

Study population

All patients admitted to our department of cardiology were possible candidates for inclusion in the study. However, among them, patients who were scheduled for multidetector CT as a screening tool for cardiovascular risk assessment of low-intermediate likelihood persons (coronary CT has higher accuracy values when low-likelihood persons are subjected) and patients who underwent coronary CT after a non-diagnostic, non-conclusive stress test to determine coronary atherosclerosis, were candidates for inclusion in the study. A total of 156 consecutive patients (mean age 57 ± 10 years; range 36–87 years; 98 [63%] male and 58 [37%] female) were recruited. Venous blood samples were obtained from all study participants for the measurement of laboratory parameters before multidetector CT. Exclusion criteria included the following: known coronary artery disease; left ventricular dysfunction (left ventricular ejection fraction [LVEF] < 50%) and hypertrophy (defined as increased left ventricular mass index calculated echocardiographically; > 95 g/m^2 for women and > 115 g/m^2 for men); unstable ischaemic conditions (unstable angina pectoris and myocardial infarction); rhythms other than sinus; significant valvular heart disease; current systemic inflammatory conditions; pregnancy; renal or hepatic dysfunction (creatinine > 2.5 mg/dL, AST and ALT > 2 times upper limit of normal, respectively); psychiatric abnormalities requiring drug use; thyroid abnormalities; any drug use affecting measured laboratory parameters including statins, fibrates (any drug for dyslipidaemia), furosemide, antidepressants, anticonvulsants, vitamin supplements, acetylsalicylic acid, non-steroidal anti-inflammatory drugs, antibiotics, alcohol, and refusal to take part in the study. The only permitted drugs and comorbidities were beta-blockers, calcium channel blockers, angiotensin converting enzyme inhibitors/angiotensin receptor blockers, hypertension and diabetes. Written consent was obtained from all patients and our local ethical committee approved the study.

Measurement of PON activity

Blood samples were obtained following an overnight fasting period before coronary CT. The serum was separated from the cells by centrifugation at 3,000 r/min for 10 min, and stored at –78°C until measurement of PON activity.

Serum PON activities were measured using the synthetic substrate paraoxon (diethyl-p-nitrophenol, PS610, SUPELCO, USA). The rate of paraoxon hydrolysis was measured by monitoring the increase of absorbency at 415 nm at 37°C. The amount of generated p-nitrophenol was calculated from the molar absorptivity coefficient at pH 8, which was 16,900/M/cm [12]. PON activity was expressed as U/L serum. The most widely available and used method for measuring PON-1 activity is the continuous recording spectrophotometer [13–18].

Other laboratory data

Fasting peripheral venous blood samples were also obtained from all patients in the study for the measurement of total cholesterol, LDL cholesterol, HDL cholesterol, triglyceride, and glucose levels. Blood samples were centrifuged and plasma was obtained. Total cholesterol, HDL cholesterol, triglyceride, and glucose levels were measured enzymatically with an auto analyser. Measurement of LDL cholesterol level was done through application of Friedewald's formula.

Multidetector computed tomography

Computed tomography images were obtained and the quantity of CAC was measured with the 64-slice technique (Toshiba Aquilion 64 scanner, Toshiba Medical, Tochigi, Japan). Slices of 3 mm-thickness were acquired. The score according to the algorithm suggested by Agatston et al. [19] was used by one radiologist blinded to the study protocol. On the basis of the electrocardiography tracing, the software automatically selected a reduced set of diastolic images from each cardiac cycle. All pixels with a density > 130 HU were automatically highlighted in colour on the images. The radiologist assigned one of four locations to each calcified plaque: left main, left anterior descending, circumflex, or right coronary artery. The Agatston method determines the density of the highest density pixel in each plaque and applies a weighting factor to each plaque dependent on the peak density in the plaque: density [HU] of 130–199 = weight of 1; density of 200–299 = weight of 2; density of 300–399 = weight of 3; and density of ≥ 400 = weight of 4. The score for each plaque equals the plaque area X weighting factor X increment/slice width. The score for the entire specimen equals the sum of the scores for each plaque. The original Agatston method used a slice thickness of 3 mm.

Statistical analysis

For an 80% statistical power, a minimum sample size per group (two-tailed hypothesis, two-tailed α of 0.05) of 64 (total of 128) is required. Therefore, the statistical power of our study was 87.3%. Data was analysed with SPSS software version 15.0 for Windows (SPSS Inc., Chicago, IL, USA). Categorical variables were presented as frequency and percentage. The χ^2 test and Fisher's exact test were used to compare categorical variables. The Kolmogorov-Smirnov test was used to assess the distribution of continuous variables. Student's *t*-test was used for variables with normal distribution and the values

Table 1. Baseline demographic, clinical and laboratory parameters of the two study groups

Characteristics	CAC group (n = 86)	No CAC group (n = 70)	P
Male sex	66 (77%)	32 (46%)	< 0.001
Age [years]	60 ± 10	53 ± 8	< 0.001
Diabetes	20 (23%)	12 (17%)	0.427
Hypertension	64 (74%)	36 (51%)	0.004
Hyperlipidaemia	62 (72%)	54 (77%)	0.581
Smoking	22 (26%)	18 (26%)	0.985
Systolic BP [mm Hg]*	120 (117–127)	124 (117–130)	0.314
Diastolic BP [mm Hg]	72 ± 10	75 ± 9	0.046
Pulse pressure [mm Hg]*	50 (45–57)	50 (45–53)	0.364
Heart rate [bpm]*	70 (65–79)	70 (66–80)	0.384
Beta-blocker use	5 (6%)	4 (6%)	0.979
Calcium channel blocker use	9 (11%)	5 (7%)	0.470
ACE-I/ARB use	50 (58%)	27 (39%)	0.015
Diastolic dysfunction	72 (84%)	42 (60%)	0.001
Tomographic LVEF*	64 (54–67)	67 (63–70)	0.003
Fasting plasma glucose [mg/dL]*	99 (93–122)	97 (89–110)	0.214
Total cholesterol [mg/dL]	189 ± 45	208 ± 38	0.008
LDL cholesterol [mg/dL]	111 ± 40	125 ± 37	0.025
HDL cholesterol [mg/dL]*	42 (37–52)	44 (40–57)	0.048
Triglyceride [mg/dL]*	151 (105–195)	137 (107–187)	0.957
Lipid hydroxide [nmol]*	11.79 (4.84–20.63)	10.32 (5.47–14.74)	0.194
Aryl esterase [U/L]	202 ± 27	208 ± 27	0.144
Total thiol [μL]	518 ± 125	570 ± 81	0.004

*Values were presented as median (50th) and interquantile (25th and 75th) ranges; ACE-I/ARB — angiotensin converting enzyme inhibitor/angiotensin receptor blocker; BP — blood pressure; CAC — coronary artery calcium; HDL — high density lipoprotein; LDL — low density lipoprotein; LVEF — left ventricular ejection fraction

were presented as mean ± standard deviation. Continuous variables without normal distribution were analysed using Mann-Whitney U test and the obtained values were presented as median (50th) values and interquantile ranges (25th and 75th). Correlation was investigated among laboratory parameters using Pearson correlation analysis. Multivariate logistic regression analysis was used to evaluate the independent associates of the risk of CAC. Parameters with a p-value of less than 0.1 in univariate analysis were included in the model. Receiver operating characteristics (ROC) analysis was used to determine the cut-off values and the sensitivity/specificity of PON and high-sensitive C-reactive protein (hsCRP). The odds ratios (OR) and 95% confidence intervals (CI) were calculated. Changes in PON levels according to the CAC threshold were analysed using analysis of variance. A two-tailed p-value of < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics

Baseline demographic, clinical and laboratory characteristics of the two study groups are outlined in Table 1. There was a male predominance in the CAC group compared to the no CAC group. The CAC group was also older than the no CAC group. The prevalence of hypertension was more frequent in the CAC group compared to the no CAC group, although the prevalence of diabetes was similar. Diastolic blood pressure level was lower in the CAC group than in the no CAC group, although no systolic blood pressure level difference was present. Echocardiographically determined diastolic dysfunction was more prevalent in the CAC group compared to the no CAC group. LVEF measured by CT was lower in the CAC group than in the no CAC group. Laboratory parameters including total cholesterol, LDL cholesterol and HDL cholesterol were higher in the no CAC group compared to the CAC group.

Main laboratory parameters

The main objective laboratory data of the study is presented in Table 2. Accordingly, PON levels were lower and hsCRP levels were higher in the CAC group compared to the no CAC group. However, in the diabetic subgroup there was no significant difference regarding serum PON-1 activity between the CAC and no CAC groups (115 [90–198] U/L vs. 187 [86–208] U/L,

Table 2. Main laboratory parameters between the two study groups

Parameter	CAC group (n = 86)	No CAC group (n = 70)	P
Paraoxonase [U/L]*	60 (35–96)	291 (230–371)	< 0.001
High-sensitive C-reactive protein [mg/L]*	3.73 (1.88–5.07)	0.97 (0.56–1.48)	< 0.001

*Values were presented as median (50th) and interquantile (25th and 75th) ranges; CAC — coronary artery calcium

Table 3. Univariate analyses for the risk of coronary artery calcium

Characteristics	Odds ratio	95% confidence interval	P
Male sex	3.922	1.972–7.813	< 0.001
Age [year]	1.090	1.047–1.135	< 0.001
Hypertension	2.747	1.401–5.405	0.003
Diastolic blood pressure [mm Hg]	0.966	0.933–1.000	0.049
Pulse pressure [mm Hg]	1.035	0.994–1.077	0.096
ACE-I/ARB use	2.212	1.161–4.213	0.016
Diastolic dysfunction	3.425	1.626–7.246	0.001
Tomographic LVEF [%]	0.923	0.871–0.978	0.006
Total cholesterol [mg/dL]	0.989	0.982–0.997	0.010
LDL cholesterol [mg/dL]	0.990	0.982–0.999	0.028
Lipid hydroxide [nmol]	1.030	0.998–1.063	0.067
Total thiol [μL]	0.995	0.992–0.999	0.005
Paraoxonase [U/L]	0.982	0.977–0.987	< 0.001
High-sensitive C-reactive protein [mg/L]	3.995	2.484–6.427	< 0.001

ACE-I/ARB — angiotensin converting enzyme inhibitor/angiotensin receptor blocker; LDL — low density lipoprotein; LVEF — left ventricular ejection fraction

Table 4. Multivariate analyses for the risk of coronary artery calcium

Characteristics	Odds ratio	95% confidence interval	P
Male sex	4.673	1.080–20.408	0.039
High-sensitive C-reactive protein [mg/L]	2.044	1.056–3.954	0.034
Paraoxonase [U/L]	0.988	0.981–0.996	0.002

respectively, p = 0.436) and no significant correlation was found between PON-1 and CAC (r^2 = 0.095, p = 0.085).

According to measured and then calculated Agatston score, 86 (55%) patients had a score ≤ 10, 20 (13%) had a score of 11–100, 20 (13%) had a score of 101–400, 14 (9%) had a score of 401–1,000, and 16 (10%) patients had a score of > 1,000.

Univariate and multivariate analyses

In univariate analysis of demographic, clinical and laboratory parameters, male sex, age, hypertension, pulse pressure, LVEF, diastolic dysfunction, and laboratory parameters including total cholesterol and LDL cholesterol, total thiol, PON, and hsCRP were found to be significant predictors of the presence of CAC (Table 3). Low total cholesterol and LDL cholesterol predict coronary calcium by univariate analysis. This may be a consequence of total cholesterol and LDL cholesterol being used to select patients for CAC screening.

In multivariate analysis, however, after the addition of variables of male sex, age, hypertension, diastolic and pulse pressures, LVEF, diastolic dysfunction, and laboratory parameters including total cholesterol and LDL cholesterol, lipid peroxide, total thiol, PON, and hsCRP, the significant and independent predictors of the presence of CAC were male sex, hsCRP and PON (Table 4).

In addition, in both univariate (OR 1.018; 95% CI 1.013–1.024; p < 0.001) and multivariate (OR 1.012; 95% CI 1.004–1.019; p = 0.002) analyses, serum PON increment (for each 1 U/L) was found to be a significant and independent predictor of the absence of CAC (CAC = 0).

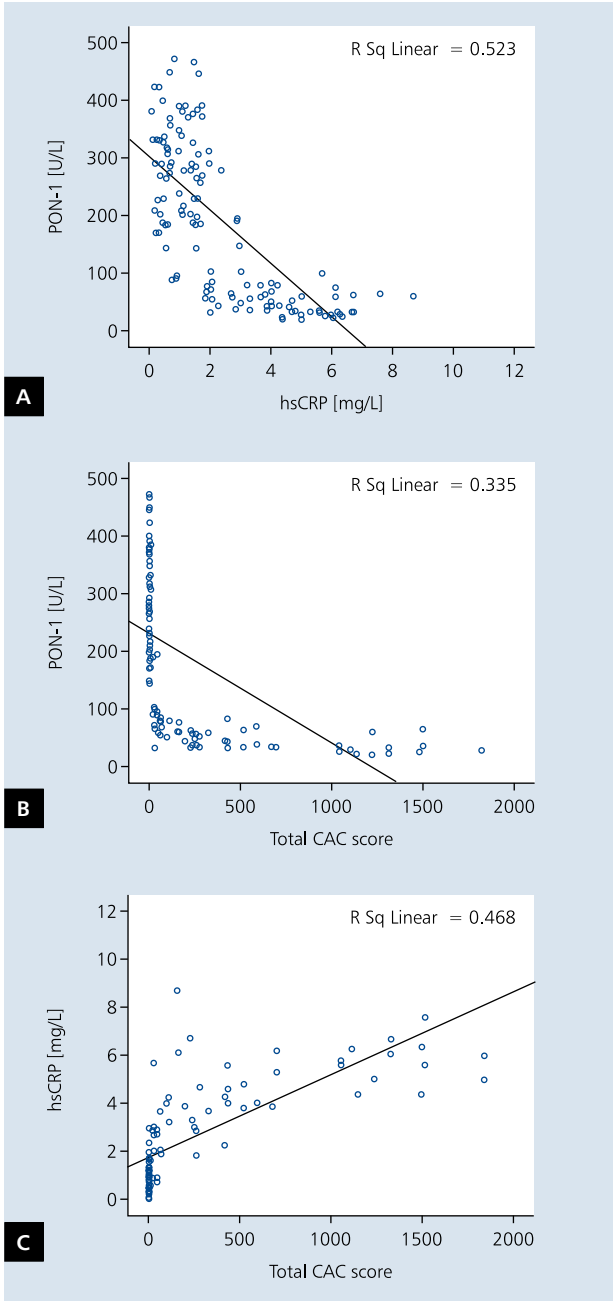

Figure 1. Correlation analyses between paraoxonase (PON-1) and high-sensitive C-reactive protein (hsCRP) (**A**); PON-1 and coronary artery calcium (CAC) (**B**), and hsCRP and CAC (**C**)

Correlation analyses

In addition, there were significant negative correlations between hsCRP and PON ($r^2 = 0.523$, $p < 0.001$), and total CAC score and PON ($r^2 = 0.335$, $p < 0.001$) and a positive correlation between hsCRP and total CAC score ($r^2 = 0.468$, $p < 0.001$) (Fig. 1). Increased CAC thresholds were significantly related with decreased PON levels and with increased hsCRP levels ($p < 0.001$) (Fig. 2).

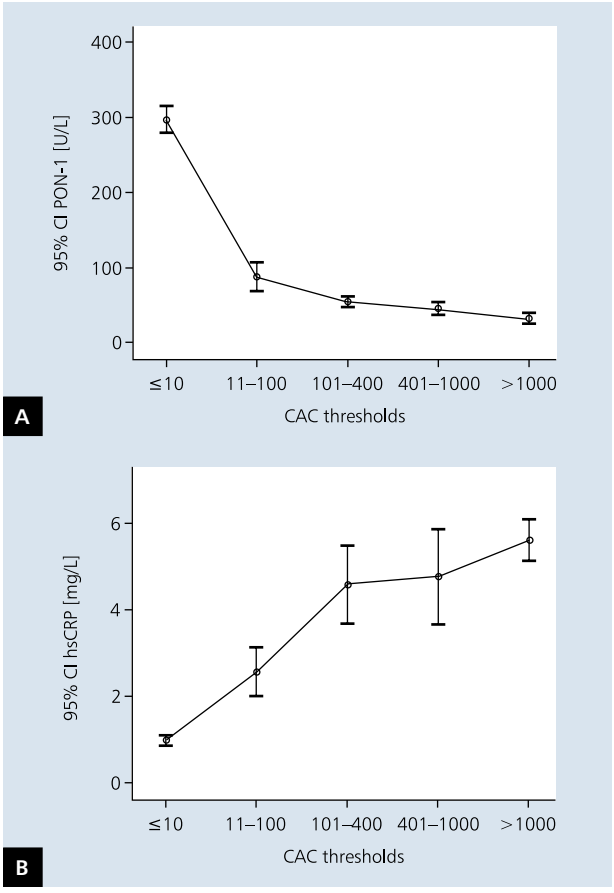

Figure 2. Association between coronary artery calcium (CAC) thresholds with paraoxonase (PON-1) (**A**) and high-sensitive C-reactive protein (hsCRP) (**B**); CI — confidence interval

Sensitivity, specificity, positive and negative predictive values analyses

In ROC analysis, PON level < 197 U/L had 87% sensitivity, 91% specificity, 93% positive predictive value, and 85% negative predictive value in predicting CAC (area under the curve 0.077; 95% CI 0.034–0.119) and hsCRP level > 1.78 mg/dL had 78% sensitivity, 94% specificity, 94% positive predictive value, and 78% negative predictive value in predicting CAC (area under the curve 0.869; 95% CI 0.808–0.929) (Fig. 3).

If three independent parameters of male sex, hsCRP > 1.78 mg/dL and PON < 197 U/L were included in the model, the sensitivity, specificity, positive predictive value, and negative predictive value were 64%, 100%, 100%, and 69%, respectively.

Risk estimate of CAC and no CAC for binary value (197 U/L) of PON

Lastly, 75 patients had a PON level < 197 U/L in the CAC group (11 patients with ≥ 197 U/L) compared to six patients in the no CAC group (64 patients with ≥ 197 U/L) (87%

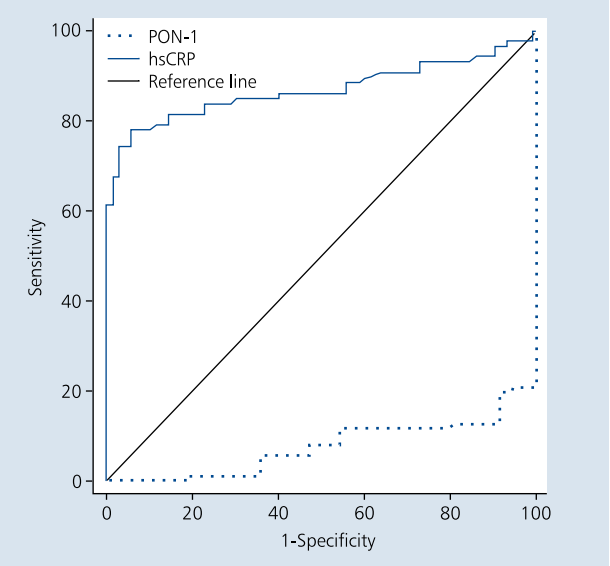

Figure 3. Receiver operating characteristics analysis curves for both paraoxonase (PON-1) and high-sensitive C-reactive protein (hsCRP)

vs. 9%, $p < 0.001$). PON level < 197 U/L increased the risk of presence of CAC (or ≥ 197 U/L increased the predictive value for freedom from CAC) by 73 times (OR 72.727; 95% CI 25.472–207.652; $p < 0.001$).

DISCUSSION

We have demonstrated for the first time that there was a notable decrease in PON activity in patients with CAC when compared to control subjects without CAC, and vice versa. We further demonstrated a significant and independent association between PON activity and the presence/severity of CAC.

There are three known PON subtypes: PON-1, PON-2 and PON-3. The most abundant, PON-1, is primarily synthesised in the liver and transported to the HDL in the plasma [20]. PON-1 activity is a readily detectable and measurable process in human plasma. Most reported HDL protective effects have been believed to be mediated by PON-1. PON-1 is by far the most abundant of all PONs within the vasculature. Oxidative modification of LDL plays a major role in the pathogenesis of atherosclerosis [21], and PON-1 directly protects LDL from oxidative modification [22]. In other words, HDL-associated PON-1 prevents lipid peroxidation and inhibits biologically active oxidised lipids in the LDL [1]. Specifically, the genes related to PON have been demonstrated to be associated with measures of arterial calcification. These PON genes have been shown to be associated with calcified plaques in both the carotid and the coronary arteries [23].

In addition, total plasma thiols have been the focus of great interest because previous studies have reported that even a mild degree of hyperhomocysteinaemia was associated with an elevated risk of stenotic vascular disease [24–28]. There is conflicting data regarding the pathophysiologic mechanism behind the vascular injury.

Previous studies have shown that PON-1 polymorphism genotypes were associated with increased carotid intima–media thickness in various populations [29, 30]. It has been suggested that this serum marker can be used as an additional risk factor for subclinical atherosclerosis.

Similarly to the study by Kaya et al. [31], a lower serum PON activity in patients with CAC compared to no CAC, and a significantly negative correlation between CAC quantity and PON activity, were found in our study. However, unlike Kaya et al. [31], we used multidetector CT to determine the presence and quantity of CAC.

In a study performed by Kopp et al. [32], multi-detector CT has yielded better information for the detection and quantification of CAC than electron-beam CT, with low inter-observation variability. Because the volumetric method with isotropic interpolation has improved the reproducibility of CAC score, this has resulted in a statistically significant improvement over the standard calcium scoring method [33]. An observational study in regard to mortality data of approximately 10,000 asymptomatic persons has demonstrated that with increasing calcium scores, five-year survival from all-cause mortality worsens [34].

Lastly, Mackness et al. [35] demonstrated that there was no association between PON-1 activity and CAC in patients with type 2 diabetes. Similarly, we found no significant difference regarding serum PON-1 activity between CAC and no CAC groups, and no correlation between serum PON-1 activity and CAC in diabetic patients in our study.

Limitations of the study

Some important limitations should be mentioned about the current study: firstly, this was a cross-sectional case-control study which has inherent disadvantages including no randomisation, blindness and follow-up outcome data. Secondly, the sample size of the study population was small, which means that the results have to be confirmed by a larger study. Lastly, because serum PON levels were only measured at a single time-point we were unable to examine the variability and prognostic value of level changes over time or the impact of different therapeutic strategies such as drugs or interventional procedures on serum PON activity.

CONCLUSIONS

In patients with CAC, decreased serum activity levels of the antioxidant HDL-associated enzyme PON-1 was significantly and independently associated with the presence and severity of CAC. This serum marker can be used in predicting which patients might be at risk for increased and severe CAC presence. In addition, patients requiring more preventive measures such as more aggressive antiatherosclerotic drug

regimens or interventional procedures can be determined. In addition, with increased PON levels one can predict with a high ratio that the patient with low-intermediate likelihood cardiovascular risk is free from CAC.

Conflict of interest: *none declared*

References

1. Barter PJ, Nicholls S, Rye KA et al. Antiinflammatory properties of HDL. Circ Res, 2004; 95: 764–772.
2. Mackness MI, Arrol S, Durrington PN. Paraoxonase prevents accumulation of lipoperoxides in low-density lipoprotein. FEBS Lett 1991;286:152–4.
3. Arad Y, Goodman KJ, Roth M et al. Coronary calcification, coronary risk factors, and atherosclerotic cardiovascular disease events. The St. Francis Heart Study. J Am Coll Cardiol, 2005; 46: 158–165.
4. Taylor AJ, Bindeman J, Feuerstein I et al. Coronary calcium independently predicts incident premature coronary heart disease over measured cardiovascular risk factors. J Am Coll Cardiol, 2005; 46: 807–814.
5. Budoff MJ, Shaw LJ, Liu ST et al. Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. J Am Coll Cardiol, 2007; 49: 1860–1870.
6. Javadrashid R, Salehi A, Tarzamni MK et al. Diagnostic efficacy of coronary calcium score in the assessment of significant coronary artery stenosis. Kardiol Pol, 2010; 68: 285–291.
7. Konieczyńska M, Tracz W, Pasowicz M et al. Use of coronary calcium score in the assessment of atherosclerotic lesions in coronary arteries. Kardiol Pol, 2006; 64: 1073–1079.
8. Budoff MJ, Achenbach S, Blumenthal RS et al. Assessment of coronary artery disease by cardiac computed tomography, a scientific statement from the American Heart Association Committee on Cardiovascular Imaging and Intervention, Council on Cardiovascular Radiology and Intervention, and Committee on Cardiac Imaging, Council on Clinical Cardiology. Circulation, 2006; 114: 1761–1791.
9. Greenland P, Bonow RO, Brundage BH et al. Coronary artery calcium scoring: ACCF/AHA 2007 Clinical Expert Consensus Document on Coronary Artery Calcium Scoring by Computed Tomography in Global Cardiovascular Risk Assessment and in Evaluation of Patients With Chest Pain. J Am Coll Cardiol, 2007; 49: 378–402.
10. Wong ND, Budoff MJ, Pio J et al. Coronary calcium and cardiovascular event risk: evaluation by age- and gender-specific quartiles. Am Heart J, 2002; 143: 456–459.
11. Detrano R, Guerci AD, Carr JJ et al. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. N Engl J Med, 2008; 358: 1336–1345.
12. Eckerson HW, Wyte CM, La Du BN. The human serum paraoxonase/arylesterase polymorphism. Am J Hum Genet, 1983; 35: 1126–1138.
13. Furlong CE, Richter RJ, Seidel SL, Motulsky AG. Role of genetic polymorphism of human plasma paraoxonase/arylesterase in hydrolysis of the insecticide metabolites chlorpyrifos oxon and paraoxon. Am J Hum Genet, 1988; 43: 230–238.
14. Abbott CA, Mackness MI, Kumar S et al. Serum paraoxonase activity, concentration, and phenotype distribution in diabetes mellitus and its relationship to serum lipids and lipoproteins. Arterioscler Thromb Vasc Biol, 1995; 15: 1812–1818.
15. Mackness B, Mackness MI, Arrol S et al. Serum paraoxonase (PON1) 55 and 192 polymorphism and paraoxonase activity and concentration in non-insulin dependent diabetes mellitus. Atherosclerosis, 1998; 139: 341–349.
16. James RW, Leviev I, Ruiz J et al. Promoter polymorphism T(107) C of the paraoxonase gene PON1 gene is a risk factor for coronary heart disease in type 2 diabetic patients. Diabetes, 2000; 49: 1390–1393.
17. Evelson P, Gambino G, Travacio M et al. Higher antioxidant defenses in plasma and low density lipoproteins from rugby players. Eur J Clin Invest, 2002; 32: 818–825.
18. Lee M-K, Park E-M, Bok S-H et al. Two cinnamate derivatives produce similar alteration in mRNA expression and activity of antioxidant enzymes in rats. J Biochem Mol Toxicol, 2003; 17: 255–262.
19. Agatston AS, Janowitz WR, Hildner FJ et al. Quantification of coronary artery calcium using ultrafast computed tomography. J Am Coll Cardiol, 1990; 15: 827–832.
20. Bergmeier C, Siekmeier R, Gross W. Distribution spectrum of paraoxonase activity in HDL fractions. Clin Chem, 2004; 50: 2309–2315.
21. Berliner JA, Heinecke JW. The role of oxidised lipoprotein in atherogenesis. Free Radic Biol Med, 1996; 20: 707–27.
22. Mackness MI, Mackness B, Durrington PN. Paraoxonase and coronary heart disease. Atheroscler Suppl, 2002; 3: 49–55.
23. Burdon KP, Langefeld CD, Beck SR et al. Association of genes of lipid metabolism with measures of subclinical cardiovascular disease in the Diabetes Heart Study. J Med Genet, 2005; 42: 720–724.
24. Silverman LM, Christenson RH. Amino acids and proteins. In: Burtis CA, Ashwood ER eds. Tietz textbook of clinical chemistry. 2nd ed. WB Saunders, Philadelphia 1994: 625–734.
25. Albumin test methodology. Publication no. MP2-17. Johnson & Johnson Clinical Diagnostics, Rochester, NY 1996.
26. Leerink CB, Winckers EK. Multilayer-film bromcresol green method for albumin measurement significantly inaccurate when albumin/globulin ratio is less than 0.8. Clin Chem, 1991; 37: 766–768.
27. Keyser JW. Standardization of dye-binding methods for the estimation of serum albumin. Clin Chim Acta, 1965; 11: 477–479.
28. Blaaberg O, Hyltoft Petersen P. Effect of aggregates on albumin standardization. Scand J Clin Lab Investig, 1979; 39: 751–757.
29. Fortunato G, Rubba P, Panico S et al. A paraoxonase gene polymorphism, PON 1 (55), as an independent risk factor for increased carotid intima-media thickness in middle-aged women. Atherosclerosis, 2003; 167: 141–148.
30. Leus FR, Wittekoek ME, Prins J et al. Paraoxonase gene polymorphisms are associated with carotid arterial wall thickness in subjects with familial hypercholesterolemia. Atherosclerosis, 2000; 149: 371–377.
31. Kaya Z, Salih Aydin M, Hazar A et al. Association of serum paraoxonase activity and coronary artery calcification. Eur Rev Med Pharmacol Sci, 2013; 17: 2121–2126.
32. Kopp AF, Ohnesorge B, Becker C et al. Reproducibility and accuracy of coronary calcium measurements with multi-detector row versus electron-beam CT. Radiology, 2002; 225: 113–119.
33. Callister TQ, Cooil B, Raya SP et al. Coronary artery disease: improved reproducibility of calcium scoring with an electronbeam CT volumetric method. Radiology, 1998; 208: 807–814.
34. Shaw LJ, Raggi P, Schisterman E et al. Prognostic value of cardiac risk factors and coronary artery calcium screening for all-cause mortality. Radiology, 2003; 228: 826–833.
35. Mackness B, Marsillach J, Elkeles RS et al. Paraoxonase-1 is not associated with coronary artery calcification in type 2 diabetes: results from the PREDICT study. Dis Markers, 2012; 33: 101–112.

Zmniejszona aktywność paraoksonazy w surowicy u chorych ze zwapnieniem tętnic wieńcowych

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Streszczenie

Wstęp: Wcześniejsze badania wykazały związek między aktywnością paraoksonazy (PON) a występowaniem i nasileniem zwapnień w tętnicach wieńcowych (CAC).

Cel: Celem badania było wykazanie zależności między aktywnością PON w surowicy a występowaniem i nasileniem CAC.

Metody: Do badania włączono 156 kolejnych pacjentów z podejrzeniem miażdżycy tętnic wieńcowych lub wymagających stratyfikacji ryzyka zdarzeń sercowo-naczyniowych. Od wszystkich uczestników badania pobrano próbki obwodowej krwi żylnej w celu wykonania pomiaru aktywności PON w surowicy przed badaniem metodą multidetektorowej tomografii komputerowej, które zastosowano do wykrycia obecności zwapnień i ich oceny ilościowej.

Wyniki: Stężenia PON-1 w surowicy były niższe w grupie z CAC niż u osób, u których nie stwierdzono CAC (odpowiednio 60 [35–96] j./l i 291 [230–371] j./l; $p < 0,001$). Wykazano istotną ujemną korelację między całkowitą punktacją w skali oceny CAC oraz PON ($r^2 = 0,335$; $p < 0,001$). W analizie wieloczynnikowej silnymi i niezależnymi czynnikami predykcyjnymi występowania CAC były: płeć męska, stężenia PON i białka C-reaktywnego mierzonego metodą wysokoczułą. Zwiększona aktywność PON była istotnie i niezależnie związana z brakiem zmian typu CAC. W analizie krzywych ROC stężenie PON wynoszące poniżej 197 j./l pozwalało prognozować wystąpienie CAC, przy czym oznaczenie tego parametru cechowało się 87-procentową czułością, 91-procentową swoistością, wartością predykcyjną dodatnią — 93% i wartością predykcyjną ujemną — 85%.

Wnioski: Zmniejszona aktywność PON w surowicy była istotnie i niezależnie związana z obecnością oraz nasileniem CAC i odwrotnie — mała aktywność CAC korelowała z brakiem CAC.

Słowa kluczowe: zwapnienie tętnic wieńcowych, multidetektorowa tomografia komputerowa, paraoksonaza

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