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Analysis of plasma myeloperoxidase levels and functional gene –463G>A and –129G>A polymorphisms with early onset of coronary artery disease in South Indian population

Analiza związku stężeń mieloperoksydazy w osoczu i czynnościowych polimorfizmów genów –463G>A i –129G>A z wczesnym początkiem choroby wieńcowej w populacji południowej części Indii

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Abstract

Introduction. The present investigation is pursued to study the possible association of –463G>A and –129G>A polymorphism in MPO gene and assessment of plasma MPO levels with the risk of developing coronary artery disease.

Material and methods. A total of 200 angiographically documented CAD patients and 200 age, gender ethnicity matched healthy controls were recruited for the study. Plasma MPO levels were assessed using enzyme-linked immunosorbent assay (ELISA) kit and genotypes were determined by PCR-RFLP technique.

Results. The MPO levels were found to be significantly increased in CAD patients when compared with controls ($p < 0.04$) but there were no significant effect of –463G>A gene polymorphism on MPO levels. A significant association of –463G>A polymorphism was observed with coronary artery disease. The frequency of recessive genotype "AA" at –463 promoter site was considerably lesser in patients (4%) relative to controls (11%) (odds ratio [OR] = 0.3371, 95% confidence interval [CI] 0.1463–0.7766, $p = 0.012$). However we did not find significant association of –129G>A polymorphism with CAD. Additionally, haplotype analysis revealed that single nucleotide polymorphisms (SNP) 1 of AA genotype and SNP 2 of GG genotype showed significant protective effect with disease (OR = 0.64; 95% CI [0.42–0.96], $p = 0.032$).

Conclusion. The results revealed that –463G>A polymorphism in the MPO gene lowers the CAD related condition in patients by down regulating serum MPO concentration, which is known to aggravate the atherosclerotic events observed in CAD.

Key words: early onset of CAD, myeloperoxidase, gene polymorphism, Atheros

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Introduction

Coronary artery disease (CAD) surfaced as a multifactorial disease with acquired and inherited components and offers significant economic burden to developing countries like India [1]. The prevalence of CAD in Indian subcontinent is typically manifested between the age group of 20–40 years and 20–45 years respectively in young men and women

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[2]. CAD is characterized by atherosclerosis — a chronic inflammatory process involving accumulation of lipoprotein particles in the intima of the coronary artery and deposition of fibrous plaque containing smooth muscle cells, lipids, fibrous tissue and extra cellular matrix proteins [3, 4]. Accumulation of atheroma can limit blood flow to the myocardium resulting in ischemic discomfort and progressively leading to myocardial infarction (MI) [5]. Pioneering studies revealed the pivotal role of myeloperoxidase (MPO) in clinical presentation of atherosclerosis and development of coronary artery disease (CAD) [6]. MPO is an enzyme produced in the bone marrow during myeloid differentiation which accumulates in neutrophils and monocytes before their entry in circulation and is gradually released during inflammation upon leukocytes activation and degranulation [7]. Despite its antimicrobial activity, MPO has a strong pro-inflammatory feature that promotes tissue injury through oxidative damage at inflammatory site [8]. MPO plays an important role in the diagnosis and prognosis of CAD and elevated MPO levels frequently form the predictive marker for cardiovascular diseases [9].

MPO is a heme protein encoded by a single gene approximately 11kb located on chromosome 17q23.1 composed of 11 introns and 12 exons [10]. Elevated levels of MPO has been demonstrated in response to significant polymorphism like, –463G>A, –129G>A, –V53F, –A332V, –638C>A locussed at the promoter region of the MPO gene [11].

A prominent functional polymorphism involving G to A base exchange at –463 (rs2333227) located in the promoter region was documented to positively elevate MPO transcriptional activity by reversible binding of SP1 transcription factor [12]. In addition, the clinical impact of –463G allele has been suggested in several diseases wherein MPO serum concentration were relatively higher to healthy controls activity was significantly elevated [13, 14]. Studies have shown that in myeloid cell lines –463G>A obliterates the binding site for SP1 that results in decreased the expression of MPO enzyme in the cell [12].

Another relevant polymorphism *i.e.*, G>A substitution located at promoter position –129 upstream alters the transcription start site by abolishing SP1 binding efficiency [11, 15]. According to documented medical literature, there are no published reports mentioning the MPO gene polymorphisms in relation to CAD especially in south Indian population. Hence the present study was aimed to evaluate the association of MPO gene (–463G>A and –129G>A) in clinical presentation of CAD.

Materials and methods

The study group included 200 patients (20–40 yrs.) with angiographically diagnosed clinical presentation of acute myocardial infarction admitted at the Department of Cardiology, Gandhi Hospital and Nizams Institute of Medical Sciences, Hyderabad, India. Patients presenting with systemic inflammatory disease, liver disease, cardiomyopathy, malignancy or any other heart diseases were excluded from the study. The control group consisted of 200 age, gender and ethnicity matched healthy individuals with no clinical or family history of CAD or clinical symptoms of any other systemic disease. The epidemiological variables like age, gender, nativity, occupation, life style habits, family history and clinical symptoms were recorded in the form of structured questionnaire. The study was approved from the institutional ethics committee for biomedical research. An informed consent was taken from the patients prior to the study and the objectives of the study were clearly explained.

Overnight fasting venous blood (5 ml) was drawn from fasting subjects with 0.1% EDTA. Blood from each subject was assayed for serum concentrations of total cholesterol (TC), triglycerides (TG), LDL-cholesterol (LDL-C), HDL-cholesterol (HDL-C), and VLDL-cholesterol (VLDL-C) by commercially available assay kits (ERBA, diagnostics, Mannheim GMBH, Germany) using CHEM-7 semi auto analyzer (ERBA Mannheim ,Germany). Further sample was centrifuged (2,000 rpm for 15 min) and stored in micro-tubes –80°C for genomic DNA extraction by salting out procedure (TKM) [16].

MPO measurement

Plasma MPO levels were assessed using enzyme-linked immunosorbent assay (ELISA) kit (Hycult biotech, Catalog number HK324, The Netherlands) based on the sandwich principle and the detection range of the samples was 0.4 to 100 ng/ml. The absorbance of the samples was measured by using a microplate reader at 450 nm.

Analysis of myeloperoxidase –463G/A and –129G>A gene polymorphisms: the –463G>A and –129G>A polymorphic sites were analyzed using PCR and RFLP technique (Table 1).

Statistical analysis

Hardy-Weinberg equilibrium was tested for the MPO gene polymorphism and the association between genotypes and CAD was examined by odds ratio and chi-square analysis with threshold confidence interval (CI) of 95% using open EPI6 software (Open Epi Version 2.3.1, Department of Epidemiology, Rollins School of Public Health, Emory University, Atlanta, GA 30322, USA). The demographic and clinical data were expressed as mean ± standard deviation (SD) value and p values were calculated using Students' paired *t*-test. Haplotype association of MPO gene polymorphism and CAD was examined by odds ratio with 95% CI employing single nucleotide polymorphisms (SNP) stats web server [17]. The coefficient (D') of pairwise linkage disequilibrium (LD) between the SNPs was calculated using the software

Table 1. Sequences of primers and digestion fragment lengths used for myeloperoxidase (MPO) genotyping

MPO promoter	Primers	Restriction enzyme	Genotype (characterized by fragments in bp)
–463G>A	F:5'CGGTATAGGCACACAATGGTGAG3' R:5' GCAATGGTTCAAGCGATTCTTC 3'	AciI	GG(168,121,61) GA(289,168,121,61) AA(289,61)
–129G>A	F:5'CCTCCACAGCTCACCTGATAT3' R:5' CGCTTGAACCATTGCACATCA3'	ApaI	GG(278) GA(278,124,154) AA(124,154)

Table 2. The demographic and clinical characteristics of coronary artery disease (CAD) patients and controls

Characteristics	CAD patients	Controls	p value
Mean age	37.0 ± 3.6	36.0 ± 5.8	NS
Male:female	161:39	159:41	NS
BMI [kg/m^2]	25.02 ± 1.40	23.54 ± 1.29	NS
TC [mg/dl]	194.14 ± 40.5	155.23 ± 20.6	< 0.001*
LDL [mg/dl]	133.8 ± 42.4	90.14 ± 21.9	< 0.001*
HDL [mg/dl]	31.66 ± 9.53	42.67 ± 14.15	< 0.001*
TG [mg/dl]	139.34 ± 29.58	112.85 ± 33.79	< 0.001*
SBP [mm Hg]	129.28 ± 9.48	112.66 ± 9.06	< 0.001*
DBP [mm Hg]	84.63 ± 8.42	79.8 ± 6.58	< 0.001*
Smoking	85 (42.5%)	44 (22%)	< 0.001*
Alcoholism	73 (36.5%)	26 (13%)	<0.001*
Family history	58 (29%)	3 (1.5%)	<0.001*

*p values were calculated using Students' paired *t*-test; NS — not significant; BMI — body mass index; TC — total cholesterol; LDL — low-density lipoprotein; HDL — high-density lipoprotein; TG — triglycerides; SBP — systolic blood pressure; DBP — diastolic blood pressure

haploview version 4,2 ref. All the p values were two sided, and the level of significance was considered at $p < 0.05$.

Results

The demographic and clinical data of the CAD patients and controls is summarized in Table 2. The mean age of CAD patients was 37.0 years and that for controls was 36.0 years. The differences between CAD patients and control subjects were statistically significant in all measures of established risk factors such as hypertension, smoking, alcohol and family history of CAD. The clinical data on TC, LDL-C and TG was found to be significantly elevated in patients than in healthy controls ($p < 0.001$) on the contrary HDL-C was higher in controls than their patient counterparts ($p < 0.001$). Myeloperoxidase levels were found to be significantly increased in patients when compared with controls ($p < 0.04$, Table 3) and there was no statistically significant difference found in distribution of –463G>A gene polymorphism in patients when compared with controls ($p = 0.7$, Table 4).The frequency distribution of different genotypes in cases and controls are shown in Table 5 and 6. A significant association was observed

Table 3. Plasma myeloperoxidase (MPO) levels in coronary artery disease (CAD) patients and controls

Subjects (n= 200)	MPO ng/ml Mean ± SD	p value
CAD cases	44.5 ± 21.2	< 0.04*
Healthy controls	28.3 ± 18.4	

*$p < 0.05$; SD — standard deviation

Table 4. Distribution of plasma myeloperoxidase (MPO) levels in relation to MPO –463G>A gene polymorphism

MPO levels (ng/ml)	MPO genotype –463G>A			ANOVA
Healthy controls	GG (n = 103)	GA (n = 75)	AA (n = 22)	
	42.3 ± 19.6	34.5 ± 21.7	28.4 ± 12.3	< 0.01
CAD cases	GG (n = 108)	GA (n = 84)	AA (n = 08)	0.7
	43.38 ± 20.3	45.6 ± 21.4	42.20 ± 28.6	

CAD — coronary artery disease

Table 5. Distribution of myeloperoxidase (MPO) –463G>A and –129G>A genotype and allelic frequencies in patients and controls

		G–463A					G–129A				
Inheritance model	Genotype	Controls n = 200 n (%)	Patients n = 200 n (%)	OR 95% (CI)	χ^2	p value	Controls n = 200 n (%)	Patients n = 200 n (%)	OR 95% (CI)	χ^2	p value
Co-dominant	GG	103 (51.5)	108 (54)	ref			112 (56)	103 (51.5)	ref		
	GA	75 (37.5)	84 (42)	1.068 (0.707–1.613)	0.043	0.835	75 (37.5)	80 (40.0)	1.160 (0.767–1.753)	0.358	0.550
	AA	22 (11)	8 (4)	0.346 (0.148–0.814)	5.381	< 0.018*	13 (6.5)	17 (8.5)	1.422 (0.658–3.071)	0.496	0.481
Dominant	GG	103 (51.5)	108 (54)	ref			112 (56.0)	103 (51.5)	ref		
	GA/AA	97 (48.5)	92 (46)	0.904 (0.610–1.341)	0.160	0.688	88 (44.0)	97 (48.5)	1.199 (0.809–1.776)	0.644	0.422
Recessive	GG/GA	178 (89)	192 (96)	ref			187 (93.5)	183 (91.5)	ref		
	AA	22 (11)	8 (4)	0.337 (0.146–0.776	6.090	< 0.013*	13 (6.50)	17 (8.5)	1.336 (0.31–2.83)	0.324	0.569
Allele frequencies	G	281 (70.2)	300 (75)	ref			299 (74.7)	286 (71.5)	ref		
	A	119 (29.7)	100 (25)	0.787 (0.576–1.075)	2.037	0.153	101 (25.2)	114 (28.5)	1.18 (0.863–1.614)	0.916	0.330

OR — odds ratio; CI — confidence interval; ref = 1

Table 6. Haplotype association of myeloperoxidase (MPO) –463G>A and –129G>A genotype and allelic frequencies in patients and controls (n = 400)

SNP 1 (–463G>A)	SNP 2 (–129G>A)	Frequency	OR (95%CI)	P value
G	G	0.517	1	–
A	G	0.214	0.64 (0.420–0.960)	0.032*
G	A	0.208	0.91 (0.600–1.380)	0.650
A	A	0.062	1.77 (0.850–3.690)	0.130

*p value < 0.05; SNP — single nucleotide polymorphisms; OR — odds ratio; CI — confidence interval

for genetic variation at MPO (–463G>A) and CAD. The GG genotype was found to be most frequent in both cases (54%) and controls (51.5%) and the frequency of AA genotype was 4% among cases while 11% among the controls. The recessive genotype was significantly more frequent in the CAD patients than in controls, implying lower levels of serum MPO concentrations (odds ratio [OR] = 0.3371, 95% CI [0.1463–0.7766], p = 0.012).

In further analysis we found, no significant association of MPO (–129G>A) with CAD. The frequencies of 'GG' (51.5%), 'GA' (40%) and 'AA' (8.5%) genotype were not significantly different in cases with reference to controls GG (56%), GA (37.5%) and AA (6.5%). We further performed haplotype analysis by considering SNP 1(–463G>A) and SNP 2 (–129G>A) for which we did not find any significant association of either genotype/alleles of [SNP 1 GG/G and SNP 2 AA/A; SNP 1 AA/A and SNP 2 AA/A], whereas on the other hand AA/A of SNP 1 and GG/G of SNP 2 showed significant protective effect with disease (OR = 0.64, 95% CI [0.42–0.96], p = 0.032). Linkage disequilibrium analysis (LD), defined by the delta coefficient (D'), was determined for both patients and controls for two SNPs, –463G>A and –129G>A. No linkage disequilibrium was observed between the two SNP polymorphisms (Figure 1).

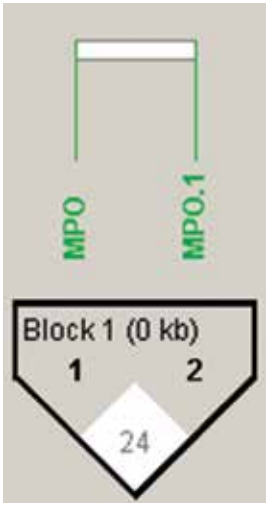

Figure 1. Linkage disequilibrium pattern of the genomic region in chromosome 17q located between single nucleotide polymorphisms (SNP) –463G>A and –129G>A; MPO — myeloperoxidase

Discussion

In recent years, several studies have confirmed that elevated concentrations of MPO are independently associated with increased risk of CAD [18–20]. Both the polymorphic variants MPO –463G>A and MPO –129G>A are located upstream of the translation initiation codon of MPO gene. These two variants have been reported to disrupt the SP1-binding site in an Alu hormone-responsive element and subsequently induce the down regulation of MPO expression, which in turn likely decreases the enzyme levels [21].

In the present study, we investigated the association of –463G>A polymorphism and MPO levels but we did not observe any significant difference between MPO genotypes and patients. A study carried out by Duzguncınar et al., (2008) [22] showed that MPO levels were elevated in Turkish patients with CAD and this increase is correlated with extent and severity of atherosclerosis. In our study we observed that increased MPO levels in CAD cases when compared with controls as similar to previous studies.

Several studies have reported the association of –463G>A and –129G>A polymorphism with CAD. However these results may vary depending upon the ethnicity of the study population. Therefore we evaluated the association between –463G>A and –129G>A promoter polymorphisms of the MPO gene with risk of CAD in South Indian population and this is the first study reporting the variation in association with CAD in South Indian cohorts.

Our study is in coherence with investigation by Nikpoor et al., in French Canadian population (2001) [23] who reported recessive allele "A" being statistically associated with less probability of developing CAD. Another study carried out by Zhang et al., (2008) [24] suggested that the risk of premature CAD was significantly reduced with –463AA genotype and the similar results were observed in the present study.

In a recent meta-analysis carried out by Chen et al., (2013) [25] including 3,449 cases and 3,082 controls

from 15 case-control studies including both Asians and Caucasians revealed strong association of MPO –463G>A polymorphism with CAD. The pooled OR for genotypes AA vs AG + GG were significantly associated with reduced risk of CAD (OR = 0.38, 95% CI [0.26–0.57], p = 0.001) and this study suggested that the MPO –463G>A variant is associated with decreased risk of CAD. In the present study we found that there was no significant association between MPO –129G>A gene polymorphism and risk of CAD. Our study is supported by observation that pooled OR for genotypes GG vs AA + AG in MPO –129G>A gene polymorphism, was not significantly associated (OR = 0.91; 95% CI [0.74–1.10], p = 0.32) [24].

According to Nikpoor et al., (2001) [23] MPO gene –463G/A polymorphism is related with changes in lipid levels and it is involved in the oxidation of low density lipoprotein, the high levels of MPO increasing the brittleness of artery plaque, there by converting the plaque from stable to unstable state, thus increasing the risk of Acute coronary syndrome. The MPO –463A allele could interfere with the binding sites of sp1 transcription factor, by reducing the level of MPO gene expression and its role in plaque formation, thus having a definite impact on risk of CAD. Meanwhile MPO may promote the oxidation of HDL-C and affect the reverse cholesterol transport, thereby interfering in the development of disease. In the present study family history, smoking, alcohol, TC, LDL-C and TG are independent predictors for early onset of CAD, thus conforming they are traditional risk factors contributing independently to disease.

Conclusion

In summary, in the present study we found that MPO levels were increasing in CAD but there was no effect of –463G>A gene polymorphism on MPO levels and in our study there was significant association of –463G>A recessive allele as well as genotype in the clinical condition of CAD. The presence of recessive allele offers a benign effect by down regulating the levels of circulatory MPO enzyme thereby implying lower oxidation of LDL and reducing atherosclerotic events occurring CAD. The haplotype analysis of our study revealed that SNP 1 of AA genotype and SNP 2 of GG genotype has a protective role in clinical condition of CAD. However there was no significant association observed for –129G>A polymorphism and CAD pathophysiology. However, there is no strong LD between the two promoter polymorphisms in both patients and controls. The study underscores the importance of MPO polymorphism and its associated down regulation as a protective confounder in atheroprotection in CAD.

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Conflict of interest(s)

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Streszczenie

Wstęp. Badanie przeprowadzono w celu oceny potencjalnych zależności między polimorfizmem genów mieloperoksydazy (MPO) –463G>A i –129G>A oraz stężeniami MPO w osoczu a ryzykiem rozwoju choroby wieńcowej (CAD).

Materiał i metody. Do badania włączono 200 chorych z potwierdzoną w badaniu angiograficznym CAD oraz 200 zdrowych osób dobranych pod względem wieku, płci i pochodzenia etnicznego tworzących grupę kontrolną. Stężenie MPO w osoczu mierzono metodą immunoabsorpcyjną (ELISA), a do genotypowania zastosowano technikę PCR-RFLP.

Wyniki. Stężenia MPO były istotnie wyższe u chorych z CAD niż u osób z grupy kontrolnej (p < 0,04), jednak nie stwierdzono, by polimorfizm genu –463G>A miał istotny wpływ na stężenie tego enzymu. Zaobserwowano natomiast statystycznie istotny związek polimorfizmu genu –463G>A z występowaniem CAD. Recesywny genotyp „AA" w obrębie promotora –463 występował znacznie rzadziej u chorych z CAD (4%) niż w grupie kontrolnej (11%) (iloraz szans [OR] = 0,3371; 95-procentowy przedział ufności [CI] 0,1463–0,7766; p = 0,012). Jednak nie stwierdzono istotnych zależności między polimorfizmem genu –129G>A a CAD, a ponadto dodatkowa analiza haplotypu wykazała, że polimorfizmy pojedynczego nukleotydu (SNP) (SNP 1 genotypu AA oraz SNP 2 genotypu GG) miały istotny ochronny wpływ na wystąpienie choroby [OR = 0,64; 95% CI 0,42–0,96; p = 0,032].

Wnioski. Wyniki badania dowiodły, że polimorfizm –463G>A genu MPO ma ochronny wpływ na występowanie CAD przez obniżenie osoczowego stężenia MPO — enzymu nasilającego rozwój zmian miażdżycowych u chorych z CAD.

Słowa kluczowe: wczesny początek choroby wieńcowej, mieloperoksydaza, polimorfizm genów, *Atheros*

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References

1. Libby P. Inflammation in atherosclerosis. Nature 2002; 420: 868–874.
2. Enas E.A., Senthilkumar A. Coronary artery disease in Asian Indians: an update and review. Int. J. Cardiol. 2001; 1 DOI: 10.5580.
3. Lusis A.J. Atherosclerosis. Nature 2000; 407: 233–241.
4. Libby P. What have we learned about the biology of atherosclerosis? The role of inflammation. Am. J. Cardiol. 2001; 88: 3J–6J.
5. Podrez E.A., Febbraio M., Sheibani N. et al. Macrophage scavenger receptor CD36 is the major receptor for LDL modified by monocyte-generated reactive nitrogen species. J. Clin. Invest. 2000; 105: 1095–1108.
6. Zhang R., Brennan M.L., Fu X. et al. Association between myeloperoxidase levels and risk of coronary artery disease. JAMA 2001; 286: 2136–2142.
7. Zhang Z.L., Brennan M.L., Fu X. et al. Association between myeloperoxidase levels and risk of coronary artery disease. JAMA 2001; 286: 2136–2142.
8. Borges F.K., Stella S.F., Souza J.F. et al. Serial analyses of C-reactive protein and myeloperoxidase in acute coronary syndrome. Clin. Cardiol. 2009; 32: E58–E62.
9. Vita J.A., Brennan M.L., Gokce N. et al. Serum myeloperoxidase levels independently predict endothelial dysfunction in humans. Circulation 2004; 110: 1134–1139.
10. Zakhi S.R., Austin G.E. Chan W.C. et al. Chromosomal localization of the human myeloperoxidase gene by in situ hybridization using oligonucleotide probes. Genes Chromosomes Cancer 1990; 2: 266–270.
11. Nikpoor B., Turecki G., Fournier C. et al. A functional myeloperoxidase polymorphic variant is associated with coronary artery disease in French-Canadians. Am. Heart J. 2001; 142: 336–339.
12. Piedrafita F.J., Molander R.B., Vansant G. et al. An Alu element in the myeloperoxidase promoter contains a composite SP1-thyroid hormone-retinoic acid response element. J. Biol. Chem. 1996; 271: 14 412–14 420.
13. Nagra R.M., Becher B., Tourtellotte W.W. et al. Immunohistochemical and genetic evidence of myeloperoxidase involvement in multiple sclerosis. J. Neuroimmunol. 1997; 78: 97–107.
14. Reynolds W.F., Rhees J., Maciejewski D. et al. Myeloperoxidase polymorphism is associated with gender specific risk for Alzheimer's disease. Exp. Neurol. 1999; 155: 31–41.
15. Pecoits-Filho R., Stenvinkel P., Marchlewska A. et al. A functional variant of the myeloperoxidase gene is associated with cardiovascular disease in end-stage renal disease patients. Kidney Int. Suppl. 2003; 84: S172–S176.
16. Lahiri D.K., Schnabel B. DNA isolation by a rapid method from human blood samples: effects of MgCl2, EDTA, storage time, and temperature on DNA yield and quality. Biochem. Genet. 1993; 31: 321–328.
17. Sole X., Guino E., Valls J. et al. SNPStats: a web tool for the analysis of association studies. Bioinformatics 2006; 22: 1928–1929.
18. Karakas M., Koenig W., Zierer A. et al. Myeloperoxidase is associated with incident coronary heart disease independently of traditional risk factors: results from the MONICA/KORA Augsburg study. J. Intern. Med. 2012; 271: 43–50.
19. Loria V., Dato I., Graziani F. et al. Myeloperoxidase: a new biomarker of inflammation in ischemic heart disease and acute coronary syndromes. Mediators Inflamm. 2008; 2008: 135625.
20. Meuwese M.C., Stroes E.S., Hazen S.L. et al. Serum myeloperoxidase levels are associated with the future risk of coronary artery disease in apparently healthy individuals: the EPIC-Norfolk Prospective Population Study. J. Am. Coll. Cardiol. 2007; 50: 159–165.
21. Piedrafita F.J., Molander R.B., Vansant G. et al. An Alu element in the myeloperoxidase promoter contains a composite SP1-thyroid hormone-retinoic acid response element. J. Biol. Chem. 1996; 271: 14 412–14 420.
22. Duzguncınar O., Yavuz B., Hazirolan T. Plasma myeloperoxidase is related to the severity of coronary artery disease. Acta Cardiol. 2008; 63: 147–152.
23. Nikpoor B., Turecki G., Fournier C. et al. A functional myeloperoxidase polymorphic variant is associated with coronary artery disease in French-Canadians. Am. Heart J. 2001; 142: 336–339.
24. Zhang H. Association between the myeloperoxidase gene –463 G/A polymorphism and coronary heart disease. Lanzhou University, Lanzhou 2006.
25. Chen L., Zhao S., Cheng G. et al. Meta-analysis of myeloperoxidase gene polymorphism and coronary artery disease susceptibility. Zhong Nan Da Xue Xue Bao Yi Xue Ban 2014; 39: 217–231.