Original article

Cigarette smoking, carrier state of A or G allele of 46A>G and 79C>G polymorphisms of beta2-adrenergic receptor gene, and the risk of coronary artery disease

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Abstract

Background: Coronary artery disease (CAD) is a multifactorial disorder which results from the interactions between a number of genetic and non-genetic factors. Beta-adrenergic receptors are cell-surface receptors which activate adenylyl cyclase by coupling to G proteins. The 46A>G and 79C>G polymorphisms of the beta2-adrenergic receptor gene (ADRB2) have been associated with altered response to sympathetic stimulation.

Aim: To assess the relationship between 46A>G and 79C>G polymorphisms of the ADRB2 gene and CAD as well as the associations between these polymorphic variants and traditional risk factors, e.g. cigarette smoking, hypercholesterolaemia, hypertension and overweight or obesity, in determining the risk of CAD.

Methods: The study population consisted of 207 individuals (white Polish Caucasians aged 20-55 years): 98 patients with angiographically documented CAD (with more than 50% diameter stenosis of at least one of the major coronary vessels) and 109 blood donors with no signs of CAD. The analysis of genetic polymorphisms was performed by means of PCR-RFLP.

Results: The genotype frequencies of both analysed genes in the studied groups were compatible with Hardy-Weinberg equilibrium. We observed higher frequency of the 46A allele in CAD patients than in controls. We also found a tendency to higher prevalence of 46A allele carriers (subjects with genotypes AA+AG) in the CAD group compared to the control group. We did not find any differences in the distribution of genotypes and alleles of 79C>G polymorphism between patients and controls. Multivariate analysis showed that smoking and overweight were independent risk factors of CAD in patients. We found a synergistic effect between carrier state of the 46A allele or 79G allele and smoking, which influences the CAD risk. The 46A allele carriers who smoke as well as carriers of the 79G allele who smoke were much more frequent in the CAD group than in controls. The incidence of 46A allele carriers with hypercholesterolaemia is also higher in patients than in the blood donor group.

Conclusion: Obtained results indicate a synergistic effect between cigarette smoking and carrier state of 46A allele or 79G allele of ADRB2 in determining the risk of CAD.

Key words: beta2-adrenergic receptor, polymorphism, coronary artery disease, cigarette smoking

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Introduction

Coronary artery disease (CAD) is a leading cause of death in the developed countries. CAD phenotype results from progressive atherosclerosis of the coronary arteries and interaction of genetic with other risk factors, including environmental ones. Extrinsic risk factors of CAD may enhance disease manifestation, especially in individuals who possess a genetic predisposition. Genetic background of CAD may be created by functional polymorphic genes encoding different variants of proteins with variable biological activities that are involved in processes of key importance in atherogenesis. Interactions between genetic and extrinsic risk factors may produce cumulative, synergic or protective effects.

Beta-adrenoceptors are membrane receptors coupled with protein G acting through adenylate cyclase. Activation of these receptors leads to increased activity of cyclic adenosine monophosphate (cAMP) that induces protein kinase A, phosphorylation of the regulatory muscular proteins and reactions with Ca^{2+} ions [1]. Normally there are a few hundred thousand adrenoceptors on the myocyte surface, although some medications and other factors may

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change their number. Beta2-adrenoceptors (ADRB2) are mainly located in smooth muscle cells located in the vessel walls, bronchi, uterus and also in the liver, adipose tissue and heart. Their activation provokes relaxation of some vascular and bronchial smooth muscle cells.

The gene encoding the *ADRB2* receptor is situated on chromosome 5q31-32 [2]. A few polymorphisms of this gene are known, including Arg16Gly polymorphism with arginine 16 to glycine exchange as a result of A>G substitution in position 46 of the gene and Gln27Glu polymorphism with glutamine 27 to glutamic acid exchange caused by C>G substitution in gene 79 position [3]. It has previously been shown that the 46G variant may lead to a decrease in a receptor number due to their intracellular sequestration and breakdown (a mechanism known as down-regulation) in response to the action of agonists [3], while the 79G variant does not cause any drop in the receptor number and thus acts oppositely to the 46G variant. Epinephrine and norepinephrine are beta adrenoceptor agonists.

The aim of this study was to determine if there was any association between the *ADRB2* gene 46A>G or 79C>G polymorphism and CAD and if there were any correlations between those genotypes and CAD risk related to traditional CAD risk factors such as cigarette smoking, arterial hypertension and overweight or obesity.

Methods

The study involved 207 Caucasians aged from 20 to 55 years who were divided into 2 groups: group 1 – CAD patients, and group 2 – controls.

Study group

The CAD group comprised 98 individuals (34 women and 64 men) at the mean age of 43.6±6.1 years with atherosclerotic CAD confirmed by coronary angiography documenting stenosis exceeding 50% in at least one of the major coronary arteries. Patients were enrolled in the First Department and Chair of Cardiology in Katowice-Ochojec between 2000 and 2004. Coronary angiography was performed using Judkin's method. Myocardial infarction (MI) was diagnosed according to the recommendations of the European Society of Cardiology [4]. Exclusion criteria were as follows: other than vascular disease aetiology and clinical presentation of cardiomyopathy, connective tissue disease, coagulation disorder and acute poisoning (for example, carbon monoxide or amphetamine intoxication). Patient characteristics were based on medical history regarding the presence or absence of concomitant CAD risk factors such as smoking, hypertension, overweight or obesity, type 1 or type 2 diabetes mellitus and family history of premature cardiovascular disease.

Active smokers were classified as subjects who reported smoking more than five cigarettes per day. Body mass index (BMI) was calculated according to the formula: BMI = body mass (kg)/height $(m)^2$. Presence of risk factors associated with increased body mass in all patients was defined based on increased BMI according to the recommendations (ranges and categories) of the Polish Cardiac Society: BMI <25 – normal weight, BMI 25 ≤BMI <30 – overweight and BMI ≥30 – obesity.

Control group

This group consisted of 109 healthy subjects (7 women and 102 men) at the mean age of 37.5±9.6 years, who were voluntary blood donors free from CAD symptoms. Blood donors were recruited from Regionalne Centrum Krwiodawstwa i Krwiolecznictwa in Katowice in years 2000-2003, on the basis of study inclusion and exclusion criteria. The exclusion criterion was family history of premature MI, CAD or ischaemic stroke declared in the study questionnaire.

This study involved only individuals who expressed informed written consent for participation. The study protocol received a positive opinion and was approved by the Bioethical Committee of the Silesian Medical University in Katowice.

Biochemical analysis

Total cholesterol (TC), HDL cholesterol and triglycerides (TG) fresh serum concentrations were measured by means of enzymatic methods using commercially available kits (Analco; Warsaw, Poland). Concentration of LDL cholesterol was calculated according to the Friedewald's formula [5].

Analysis of polymorphisms

The polymorphic variants were analysed by means of RFLP-PCR (*restriction fragment length polymorphism – polymerase chain reaction*). DNA was isolated from peripheral lymphocytes using MasterPure Genomic DNA Purification Kit (Epicentre Technologies; Madison, WI, USA) according to instructions attached to the kit.

Amplification was performed according to a method reported by Martinez et al. [6] with our own modifications. The following conditions were applied: the DNA was denatured initially at 94°C for 2 minutes, then was subjected to 40 cycles including denaturation at 94°C for 40 s, starters attachment at 61.6°C for 40 s, extension at 72°C for 50 s and final extension at 72°C for 5 minutes. The size of the PCR product generated was 168 bp. In order to analyse 46A>G polymorphism, 8 µl of PCR product was digested with 2.5 U of the restricting enzyme *Nco*I (Fermentas; Burlington, ON, Canada) while in the case of 79C>G polymorphism assessment, 8 µl of PCR product was digested with 1 U of the restricting enzyme *Bse*XI (Fermentas – isoschizomer *Bbv*I). The restriction digests were electrophoresed on 8% polyacrylamide gel with 5% glycerol buffered once in TBE (pH 8.3). DNA was eventually visualised on the electropherograms with 0.4% silver nitrate according to the standard procedure.

Statistical analysis

Data are presented as means ± standard deviation or number and percentage Collected data were analysed using *STATISTICA* 6.0 (STATSOFT; Statistica, Tulsa, OK, USA) and

Table I. Demographic, biochemical and clinical characteristics of the examined groups of patients

Parameter	CAD group (n=98)	Control group (n=109)
Age [years]	43.6±6.1	37.5±9.6*
Body mass index [kg/m^2]	26.7±4.6	25.3±3.3*
Cigarette smoking	61 (62.2%)	32 (29.4%)*
Biochemical characteristics of the examined groups		
Total cholesterol [mmol/l]	5.7±1.3	5.4±1.5
LDL – cholesterol [mmol/l]	3.7±1.0	3.6±1.3
HDL – cholesterol [mmol/l]	0.8±0.6	1.1±0.4*
Triglycerides [mmol/l]	1.8±0.9	1.5±0.7*
Myocardial infarction	76 (77.5%)	–
Occlussion of the infarct-related artery	58 (59.2%)	–
Single-vessel disease	34 (34.7%)	–
Multi-vessel disease	64 (65.3%)	–
Arterial hypertension	62 (63.3%)	–

** p <0.05*
Abbreviations: CAD – patients with coronary artery disease

EpiInfo-6 [Centers for Disease Control and Prevention (CDC), Atlanta, GA, USA] software. In case of quantitative variables, normal distribution was verified using the Shapiro-Wilk W test. The means of the variables following a normal distribution were compared with Student's T test; otherwise the Mann-Whitney U test was applied. The incidence of the alleles was determined on the basis of genotype prevalence. In all patient groups conformity of genotype distribution with Hardy-Weinberg equilibrium was evaluated using χ^2 test. Prevalence of the genotypes and alleles was compared between the examined groups by means of χ^2 test with Fisher's correction if the number of collected data was less than 10. The results of statistical analysis with p values <0.05 were considered significant. The power of association between individual alleles, genotypes and CAD was determined based on odds ratios (OR) within confidence intervals (CI) calculated by means of a univariate as well as multivariate logistic regression model including also traditional CAD risk factors. Correlations between specific genetic and traditional risk factors were analysed based on calculation of the synergy indices according to the following formula:

$$SIM = OR_{GT}/(OR_T \times OR_G)$$

where:
OR_{GT} means odds ratio of disease among individuals with both genetic and traditional risk factor
OR_G means odds ratio of disease among subjects with only genetic factor
OR_T means odds ratio of disease among individuals with only traditional factor
A synergy index, SIM, value >1 indicates synergic effect between genetic and traditional risk factor [7].

Results

Demographic and biochemical characteristics of the examined group (Table I)

The group of CAD patients had significantly higher serum TG concentration (p=0.01) as well as higher BMI (p=0.03) and number of active smokers (p <0.0001, OR=3.97 95% CI 2.13-7.41) compared with controls. In the control group significantly higher HDL cholesterol concentration was seen (p=0.0004) than in CAD patients.

Clinical patient characteristics

In the CAD group approximately 78% of patients had prior MI and 16% had repeated infarctions. Total occlusion of the infarct-related artery was noted in more than a half of patients (59%). In approximately two thirds of patients multi-vessel disease defined as stenosis in 2 or more coronary arteries was observed, and single-vessel disease in the remaining subjects. Hypertension was detected in 63% of patients. Comorbidities such as diabetes mellitus, ischaemic stroke and peripheral artery disease were seen in a small number of patients (in 5%, 1%, and 11%, respectively).

Analysis of association between ADRB2 gene polymorphisms and CAD

The distribution of genotypes of *ADRB2* gene 46A>G and 79C>G polymorphisms were consistent with Hardy-Weinberg equilibrium. Individuals who were either heterozygotic or homozygotic for a given allele were defined as its carrier. The prevalence of genotypes and alleles of both analysed polymorphisms is outlined in Table II. In the group of patients with CAD, incidence of the A allele of *ADRB2* gene 46A>G polymorphism was significantly higher (51 vs. 39%, p=0.018, OR=1.60, 95% CI 1.06-2.41) than in controls. There was also a tendency for more frequent A allele carrier state (individuals with AA+AG genotypes) among CAD patients than in control subjects (68 vs. 56%). This difference was close to significance in both univariate and multivariate logistic regression models after inclusion of traditional CAD risk factors (NS, p=0.067 and p=0.07, respectively). No significant differences between CAD patients and the control group were observed with respect to genotype and alleles of 79C>G polymorphism.

Analysis of correlation between carrier state of a given polymorphic variant and traditional CAD risk factors

Univariate analysis of the traditional risk factors revealed that smoking, overweight and triglyceride concentration may be considered CAD risk factors in the examined patient group (Table III). After taking into account all traditional CAD risk factors, the multivariate logistic regression model confirmed that the independent CAD risk factors in the examined group of patients were smoking (p <0.0001, OR=4.39) and overweight (p=0.029, OR=1.09).

Thus, it was followed by an *analysis* to determine if there were any correlations between *ADRB2* gene polymorphisms and cigarette smoking or overweight in CAD development.

A synergic association between the A allele of 46A>G polymorphism as well as between the G allele of 79C>G polymorphism and smoking in determination of CAD risk was observed (Table IV). Synergy index (SIM) was 1.82 and 1.46, respectively. It indicates that synergic effects of both coexisting factors (genetic and traditional) are approximately 2 and 1.5 times stronger than effects caused by these individual factors evaluated as isolated variables.

It was also noted that smoking carriers of the A allele of *ADRB2* gene 46A>G polymorphism are more frequently represented in patients group than in the control group (43.9 vs. 14.7%, p <0.0001, OR=4.54, 95% CI 2.23-9.34). Similarly, smoking carriers of the G allele of *ADRB2* gene 79C>G polymorphism are more frequent among CAD patients than healthy subjects (39.8 vs. 20.2%, p=0.002, OR=2.61, 95% CI 1.35-5.09). Although in the CAD patient group an increased total cholesterol concentration was not found to be an independent risk factor, prevalence of the A allele of 46A>G polymorphism carriers with high cholesterol level was significantly higher in the CAD group than in the control group (Table V). No significant differences regarding distribution of genotypes and alleles of the analysed polymorphisms were observed in the subgroup of patients with hypertension as compared with the CAD patient subset without hypertension or the control group.

Discussion

Increased stimulation of beta adrenoceptors may be one of the main causes of acute MI resulting from CAD [8]. Thus polymorphisms in the gene encoding beta2-adrenoceptor can be speculated to be associated with elevated CAD risk.

In this study, a significantly higher prevalence of the A allele of 46A>G polymorphism in CAD patients than healthy controls was observed. Moreover, a tendency (although insignificant) to higher incidence of A allele carriers among patients than in control subjects was also found. In the case of *ADRB2* gene 79C>G polymorphism no significant correlation between 79G allele carrier state and CAD in the examined patient population of Upper Silesia was found.

Table II. Prevalence of genotypes and alleles of *ADRB2* gene 46A>G and 79C>G polimorphisms in the examined groups of patients

GENE /polimorphism	Genotypes/allels	CAD group (n=98)	Control group (n=109)
ADRB2 /46 A>G	AA	33 (33.7%)	25 (23.0%)
	AG	34 (34.7%)	36 (33.0%)
	GG	31 (31.6%)	48 (44.0%)
	AA+AG	67 (68.4%)	61 (56.0%)
	A	100 (51.0%)	86 (39.4%)*
	G	96 (49.0%)	132 (60.6%)
ADRB2 /79 C>G	CC	37 (37.7%)	31 (28.4%)
	CG	48 (49.0%)	61 (56.0%)
	GG	13 (13.3%)	17 (15.6%)
	CG+GG	61 (62.2%)	78 (71.6%)
	C	122 (62.2%)	123 (56.4%)
	G	74 (37.8%)	95 (43.6%)

** p <0.05*

A few studies reported the results of analyses searching for an association between *ADRB2* gene 46A>G and 79C>G polymorphisms and CAD [9, 10]. A significant correlation between 79G allele carrier state and CAD was noted in the CAD patient population in Saudi Arabia [9]. It has also been shown that prevalence of the 79G allele is higher among CAD patients in Belgium and should be considered an independent disease risk factor [10]. Barbato et al. [10] observed 47% incidence of the 79G allele in a patient group, which was higher than revealed in our study (38%). Other studies suggest that prevalence of the G allele of *ADRB2* gene 79C>G polymorphism may be associated with decreased risk of cardiovascular events in the elderly population [11].

Several earlier studies analysed the association between *ADRB2* gene polymorphism and hypertension. However, their findings were often contradictory [12-16].

Table III. Contribution of traditional risk factors in determination of CAD risk in patients vs. control group

Traditional CAD risk factors	Univariate analysis			Mutivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Incerased TC concentration TC ≥5 mmol/l	1.15	0.94-1.41	0.167		NS	
Incerased LDL level LDL ≥3 mmol/l	1.10	0.87-1.39	0.411		NS	
Increased TG level TG >1.7 mmol/l	1.56	1.08-2.25	0.016*		NS	
Overweight or obesity BMI ≥25 kg/m^2	1.09	1.01-1.18	0.021*	1.09	1.01-1.18	0.029*
Nicotinism	3.97	2.21-7.11	<0.0001*	4.39	2.38-8.11	<0.0001*

** p <0.05*

Table IV. Synergic associations between carrier-state of A allele of 46A>G polymorphism or G allele of 79C>G polymorphism of *ADRB2* gene and cigarette smoking in CAD risk determination

Genotype variant	Traditional risk factor	CAD group (n=98)	Control group (n=109)	OR	95% CI	p
Carrier-state of A allele of *ADRB2* gene 46A>G polymorphism	Nicotinism					
0	0	13	32	1		
0	1	18	16	2.77	0.99-7.86	0.03
1	0	24	45	1.31	0.54-3.21	0.51
1	1	43	16	6.62	2.58-17.34	<0.0001
SIM = 6.62/(2.77 · 1.31) = 1.82						
Carrier-state of G allele of *ADRB2* gene 79C>G polymorphism	Nicotinism					
0	0	15	21	1		
0	1	22	10	3.08	1.02-9.52	0.025
1	0	22	56	0.55	0.22-1.36	0.153
1	1	39	22	2.48	0.98-6.31	0.033
SIM = 2.48/(3.08 · 0.55) = 1.46						

0 – a lack of either genetic or traditional risk factor, 1 – a presence of either genetic or traditional risk factor
Abbreviations: SIM – synergy index

Table V. Specific genotype and enviromental variants differentating the examined groups

Genotype and enviromental variant	CAD group (n=98)	Control group (n=109)	OR	95% CI	p
46A allele carrier-state + smoking	43 (43.9%)	16 (14.7%)	4.54	2.23-9.34	<0.0001*
79G allele carrier-state + smoking	39 (39.8%)	22 (20.2%)	2.61	1.35-5.09	0.002*
46A allele carrier-state + hypercholesterolemia	50 (51.0%)	35 (32.1%)	2.20	1.21-4.03	0.006*

** p <0.05*

Timmermann et al. [12] revealed a significant correlation between the A allele of 46A>G polymorphism and hypertension. In another report, Bray et al. [13] showed higher prevalence of the 46G and 79G alleles of the *ADRB2* gene among individuals with hypertension than in subjects with normal blood pressure. However, some reports did not confirm the presence of any association between both *ADRB2* gene polymorphisms and hypertension [14-16], which is consistent with our findings. It has been suggested that there is a significant imbalance of coupling between 46A>G and 79C>G polymorphisms in the gene encoding beta2 adrenoceptor. It has been shown that the 79C allele of 79C>G polymorphism almost always is coupled with the 46G allele of 46A>G polymorphism while the 79G allele of 79C>G polymorphism can be coupled with both 46A and 46G alleles of 46A>G polymorphism [11, 17]. However, our study did not confirm such a correlation.

We also analysed whether there were any associations between traditional CAD risk factors and *ADRB2* gene polymorphisms in determination of CAD development. We found that among traditional CAD risk factors only smoking and overweight are independent risk factors of disease development in the analysed group of CAD patients. Synergic correlations between prevalence of the 46A or 79G allele of the *ADRB2* gene and smoking were seen that impacted CAD risk (SIM 1.82 and 1.46, respectively). There were more smoking 46A and 79G allele carriers in the group of CAD patients than in the control one. We are not aware of any studies investigating the association between polymorphisms of the gene encoding beta2-adrenoceptors and smoking with respect to the risk of CAD. Only in a group of patients with bronchial asthma was a correlation of *ADRB2* gene polymorphisms and smoking analysed [18]. Wang et al. [18] showed that AA homozygotes and active smokers had increased risk of asthma development in comparison to non-smoking GG homozygotes with regard to *ADRB2* 46A>G polymorphism. The impact of smoking on beta2 adrenoceptor characteristics was studied among ten pairs of male monozygous twins [19]. Laustiola et al. [19] showed that in smoking twins density of beta2 adrenoceptors on the lymphocyte surface was lower and these cells presented weaker ligand binding, leading in consequence to decreased amount of generated second messenger (cAMP) and impaired response to catecholamines as compared to non-smoking twins. The authors suggested that long-term cigarette smoking acted on beta2--adrenoceptors, down-regulating them. Our previous studies documented synergic relations between polymorphisms

of other genes such as *APOE* or *CYBA* and smoking in determination of CAD risk [20, 21].

We have also found that in the CAD group the incidence of 46A allele carriers with abnormally high TC level is significantly higher than in the control group even though TC concentration per se failed to reach the status of a significant risk factor in the examined group of patients. The most recent studies reported that AA homozygotes of 46A>G polymorphism (as compared to GG homozygotes of this polymorphism) manifested elevated levels of lipids, especially TG and LDL cholesterol [22]. Similar associations were observed in subjects that were CC homozygotes of 79C>G polymorphism in comparison to GG homozygotes of this polymorphism [22]. In our CAD patients no correlations between *ADRB2* polymorphisms and overweight in CAD risk determination were observed. Examined subjects did not manifest significant overweight or obesity. Some reports suggest associations between 46A>G or 79C>G polymorphism and obesity [23], including gender-dependent ones [24, 25].

The results presented in this report indicate that analyses of genetic factors in interaction with traditional CAD risk factors such as smoking, hypercholesterolaemia, hypertension and overweight may be useful in predicting the risk of disease development in a particular population.

Conclusions

The results of our study suggest a synergic association between smoking and carrier state of the 46A or 79G allele of the gene encoding beta2 adrenoceptors in determination of the risk of CAD in the patient population of the Silesian region.

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Związek między nikotynizmem i nosicielstwem allela A lub allela G polimorfizmów 46A>G i 79C>G genu receptora beta2-adrenergicznego a ryzyko choroby niedokrwiennej serca

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Streszczenie

Wstęp: Fenotyp choroby niedokrwiennej serca (CAD) jest następstwem postępującej miażdżycy tętnic wieńcowych i wynika z interakcji czynników genetycznych i pozagenetycznych. Genetyczne podłoże CAD mogą współtworzyć funkcjonalne geny polimorficzne, kodujące warianty białek o odmiennej aktywności biologicznej, zaangażowane w procesy istotne z punktu widzenia patogenezy miażdżycy. Receptory beta-adrenergiczne są receptorami błonowymi sprzężonymi z białkiem G, działającymi poprzez cyklazę adenylanową. Ich aktywacja powoduje wzrost cyklicznego AMP, indukującego kinazę białkową A, fosforylację regulatorowych białek mięśniowych i reakcje z udziałem jonów Ca^{2+}. Na powierzchni każdej komórki mięśnia sercowego występuje kilkaset tysięcy receptorów adrenergicznych, jednak ich liczba i wrażliwość może ulegać zmianom m.in. pod wpływem stosowanych leków. Wariant 46G polimorfizmu 46A>G genu kodującego receptor beta2-adrenergiczny (*ADRB2*) może wpływać na zmniejszenie liczby receptorów przez ich wewnątrzkomórkową sekwestrację i degradację (mechanizm *down-regulation*) w odpowiedzi na działanie agonistów. Z kolei wariant 79G polimorfizmu 79C>G genu *ADRB2* wykazuje działanie przeciwstawne do wariantu 46G. Agonistami receptorów beta-adrenergicznych są adrenalina i noradrenalina.

Cel: Wyjaśnienie, czy istnieją związki między polimorfizmami 46A>G i 79C>G genu *ADRB2* a CAD oraz czy istnieją korelacje między określonymi genotypami a ryzykiem wystąpienia choroby związane z współwystępowaniem tradycyjnych czynników ryzyka CAD, m.in. nikotynizmu, hipercholesterolemii, nadciśnienia tętniczego oraz nadwagi lub otyłości.

Metodyka: Badaniami objęto 207 osób rasy kaukaskiej (w wieku 20–55 lat) – 98 z potwierdzoną koronarograficznie CAD (ze zwężeniem przynajmniej jednego głównego naczynia wieńcowego >50%) i 109 dobrowolnych dawców krwi, którzy nie mieli objawów CAD. Polimorficzne warianty analizowano techniką RFLP-PCR. DNA izolowano z limfocytów krwi obwodowej. Stężenia cholesterolu całkowitego, frakcji HDL cholesterolu i trójglicerydów analizowano metodami enzymatycznymi. Stężenie frakcji LDL cholesterolu obliczano wg wzoru Friedewalda. Uzyskane dane analizowano przy użyciu programów STATISTICA 6.0 oraz EpiInfo-6.

Wyniki: Rozkłady genotypów polimorfizmów 46A>G i 79C>G genu *ADRB2* były zgodne z równowagą Hardy'ego-Weinberga. W grupie chorych z CAD stwierdzono znamiennie częstsze występowanie allela A polimorfizmu 46A>G genu *ADRB2* w porównaniu z grupą kontrolną oraz tendencję (bliską granicy istotności statystycznej) do częstszego występowania nosicieli allela A (osoby o genotypach AA+AG). W rozkładzie genotypów i alleli polimorfizmu 79C>G nie stwierdzono znaczących różnic pomiędzy grupą badaną a grupą kontrolną. Analiza wieloczynnikowa wykazała, że niezależnymi czynnikami ryzyka CAD u badanych chorych są nikotynizm i nadwaga. Zaobserwowano synergiczny związek między występowaniem allela 46A oraz allela 79G i nikotynizmem, który ma wpływ na ryzyko CAD. Wartości indeksu synergii SIM wskazują, że efekty współdziałania obu czynników (genetycznego i tradycyjnego) są znacznie silniejsze od efektów wywoływanych przez te czynniki rozpatrywane pojedynczo. Palących nosicieli allela 46A oraz palących nosicieli allela 79G było istotnie więcej wśród chorych niż w grupie kontrolnej. Odsetek nosicieli allela 46A z hipercholesterolemią jest znamiennie wyższy w grupie CAD niż w grupie kontrolnej. Nie wykazano znamiennych różnic w rozkładzie genotypów i alleli analizowanych polimorfizmów w podgrupie chorych z nadciśnieniem tętniczym w porównaniu z podgrupą chorych bez nadciśnienia oraz z grupą kontrolną.

Wnioski: Powyższe badania wskazują na synergiczny związek między nikotynizmem i nosicielstwem alleli 46A lub 79G genu kodującego receptor beta2-adrenergiczny w determinowaniu ryzyka choroby niedokrwiennej serca w populacji osób z CAD z Górnego Śląska.

Słowa kluczowe: receptor beta2-adrenergiczny, polimorfizm, choroba niedokrwienna serca, palenie papierosów

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