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Genetic effects of *PPARG1C* and *TNF1* gene variants related to cardiovascular disorders

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Introduction: Study was aimed to investigate the associations between the SNPs in *PPARG1C* (Gly482Ser), *TNF* (-308G-A) genes and coronary heart disease (CHD) and hypertension and their relations to leukocyte profile and plasma lipid composition in Russian population. **Materials and Methods:** 124 participants older than 55 years were divided into groups according to the anamnesis data. All participants were genotyped for SNPs *PPARG1C* (Gly482Ser) and *TNF* (-308G-A) by allele-specific real-time polymerase chain reaction method using commercial kits. Lipid profiling was measured by homogeneous enzymatic colorimetric test. **Results:** The results of this study suggested the presence of the mutation *PPARG1C* (Gly482Ser) increases the risk of coronary heart disease by 2.4 times (OR 1.17–4.97), but is not associated with arterial hypertension. *TNF* -308A t allele has demonstrated a protective effect, reducing the risk of developing hypertension (OR 0.01–0.84), but is not associated with CHD. The relationship between genotypes and the average values of leukocyte and lipid profiles remained non-significant in our population. However the heterozygous genotype of *TNF* was related to an increased level of drumstick neutrophil, compared to the control group. **Conclusion:** Thus, the investigated polymorphic variant (Gly482Ser) of *PPARG1C* gene is a reliable marker of CHD, whereas in the case of hypertension the association with (-308G-A) of *TNF* gene was identified. This research supported by the grant of the Russian Science Foundation №. 15-15-10022.

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Polymorphisms of TNFA in hypertensive patients

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Introduction: Hypertension is a complex, multifactorial and polygenic disease. This descriptive study analyzed whether there are differences in TNFA -238 G>A and TNFA -308 G>A polymorphisms that encode molecules involved in inflammation among hypertensive patients, refractory hypertensive patients and controls. **Materials and methods:** We performed a case-control study with 444 subjects: 234 hypertensive patients (HTA), 50 refractory hypertensive patients (HTA-R) and 160 controls. The DNA was amplified by PCR and TaqMan trials allowed allelic discrimination. There were no statistically significant differences in either age or sex between all 3 study groups. **Results:** In the analysis of the polymorphisms of TNFA -308 G>A, the distribution of the allele AA for HTA and HTA-R groups was 0% and 2.4%, respectively ($p = 0.02$). No other significant differences were found in the study groups or in the analysis of TNFA -238 G>A genotypes. **Conclusion:** Variations in the polymorphism TNFA -238 G>A do not affect the chances of having refractory hypertension. For the first time, we describe the association between the AA genotype of TNFA -308 G>A and refractory HTA. Individuals carrying the allele A will have an increase in the levels of TNF α which causes endothelial damage. This endothelial alteration could justify the severity of hypertension and the poor response to drugs. This could lead to future therapeutic opportunities in these patients.

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SERPINE1 gene polymorphic variant in the predisposition to cardiovascular diseases

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Genes of predisposition to cardiovascular diseases are actively studied worldwide, including the plasminogen activator inhibitor gene (*SERPINE1*). However, its role in the development of hypertension, atherosclerosis, coronary artery disease, myocardial infarction is poorly understood, and the results of the studies tend to be contradictory. In this regard, the aim of this work was to analyze the association of *SERPINE1* gene polymorphism (-675 5 G/4 G, rs587776796) with the risk of hypertension, atherosclerosis, coronary heart disease (CHD), myocardial infarction development in Russian population. The study involved 121

people aged 55 to 79 years divided into age- and sex-matched groups according to anamnestic data. The informed consent was obtained from all patients. Genotyping of polymorphic locus was carried out by allele-specific real-time polymerase chain reaction method using commercial kits (Litech, Russia). Statistical data processing was performed using MS Excel and the online calculator (http://gen-exp.ru/calculator_or.php). Individuals with homozygous 4G/4G genotype have CHD development increased risk (OR = 2.67; 95% CI 1.11–6.42) and increased total cholesterol, triglycerides and atherogenicity index. Despite some changes in the distribution of alleles and genotypes frequencies of the *SERPINE1* gene between the studied groups of patients diagnosed with hypertension, atherosclerosis, myocardial infarction and control statistically significant differences were not found. Thus, the investigated polymorphic 4G/4G genotype of *SERPINE1* gene is a reliable marker of CHD, whereas in the case of hypertension, atherosclerosis, myocardial infarction development the association was not found. The study was performed with the support of Russian science Foundation grant No. 15-15-10022.

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The association of single nucleotide variations of the *HDAC9* (rs13246896), *CAMK2B* (rs35089892), *GACAT3* (rs62116755) with sudden cardiac death

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Introduction: Single nucleotide variations (SNVs) of the *HDAC9* (rs13246896), *CAMK2B* (rs35089892), *GACAT3* (rs62116755) were identified in own genome-wide association study (GWAS) as associated with sudden cardiac death (SCD). The aim of this work is confirm the association of rs13246896, rs35089892, rs62116755 with SCD in a case-control study. **Materials and Methods:** A sample of SCD cases (n = 383, mean age 53.3 ± 8.8 years, men - 70.9%, women - 29.1%) was formed using the WHO criteria; the control sample (n = 385, mean age 53.1 ± 8.3 years, men - 68.3%, women - 31.7%) was selected according to sex and age. DNA was isolated by phenol-chloroform extraction. The groups were genotyped for the

selected SNVs by RFLP-analysis according to original methods. The data were statistically processed using χ^2 test according to Pearson, two-sided Fisher's exact test with Yates' correction for continuity. **Results:** No statistically significant differences in the genotype and allelic frequencies of rs13246896 (*HDAC9*), rs62116755 (*GACAT3*) between SCD cases and control were detectable. Genotype TT of rs35089892 (*CAMK2B*) is associated with protective effect against SCD (p = 0.01, OR = 0.49, 95%CI 0.28–0.84). **Conclusions:** rs13246896 (*HDAC9*) and rs62116755 (*GACAT3*) are not associated with SCD. rs35089892 (*CAMK2B*) is associated with protective effect against SCD.

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Polymorphism - 634 G/C (rs 2010963) of VEGF-A gene in the development of hypertension in perimenopausal women

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One of the major endothelial factors stimulating angiogenesis is a vascular endothelial growth factor (VEGF). One of the possible mechanisms of increasing of the VEGF concentration in blood may be a genetic predisposition to an increased VEGF synthesis. The aim was to determine the effect of genetic polymorphism -634G/C (rs2010963) of the VEGF-A gene and formation of AH combined with obesity in premenopausal women. In study were 115 women with stage II of AH, aged 45 to 53 years in perimenopausa included. According to menopausal status: 45 premenopausal and 50 menopausal women. The control group was consisted of 20 healthy premenopausal women. The VEGF concentration was determined by ELISA. The study of the allelic polymorphism -634 G/C (rs 2010963) VEGF-A gene was performed by polymerase chain reaction. The VEGF level was also significantly higher in women with the GG genotype (436,4[315,2; 772,8]) pg/ml comparing with the genotype CG (314,6[222,9; 449,4]) pg/ml and the genotype CC (261,8[127,5; 268,8]) pg/ml, there were any significant differences among women with the CG and CC genotypes in the premenopausal group. The VEGF level was significantly higher in the menopause group with the GG genotype (535,2[290,5; 726,8]) pg/ml comparing with the genotype CG (252,4[217,0; 363,8]) pg/ml and the genotype CC (226,9[197,9; 252,8]) pg/ml. The VEGF level was significantly higher among women with the genotype GG comparing to the CC. The relationship between the