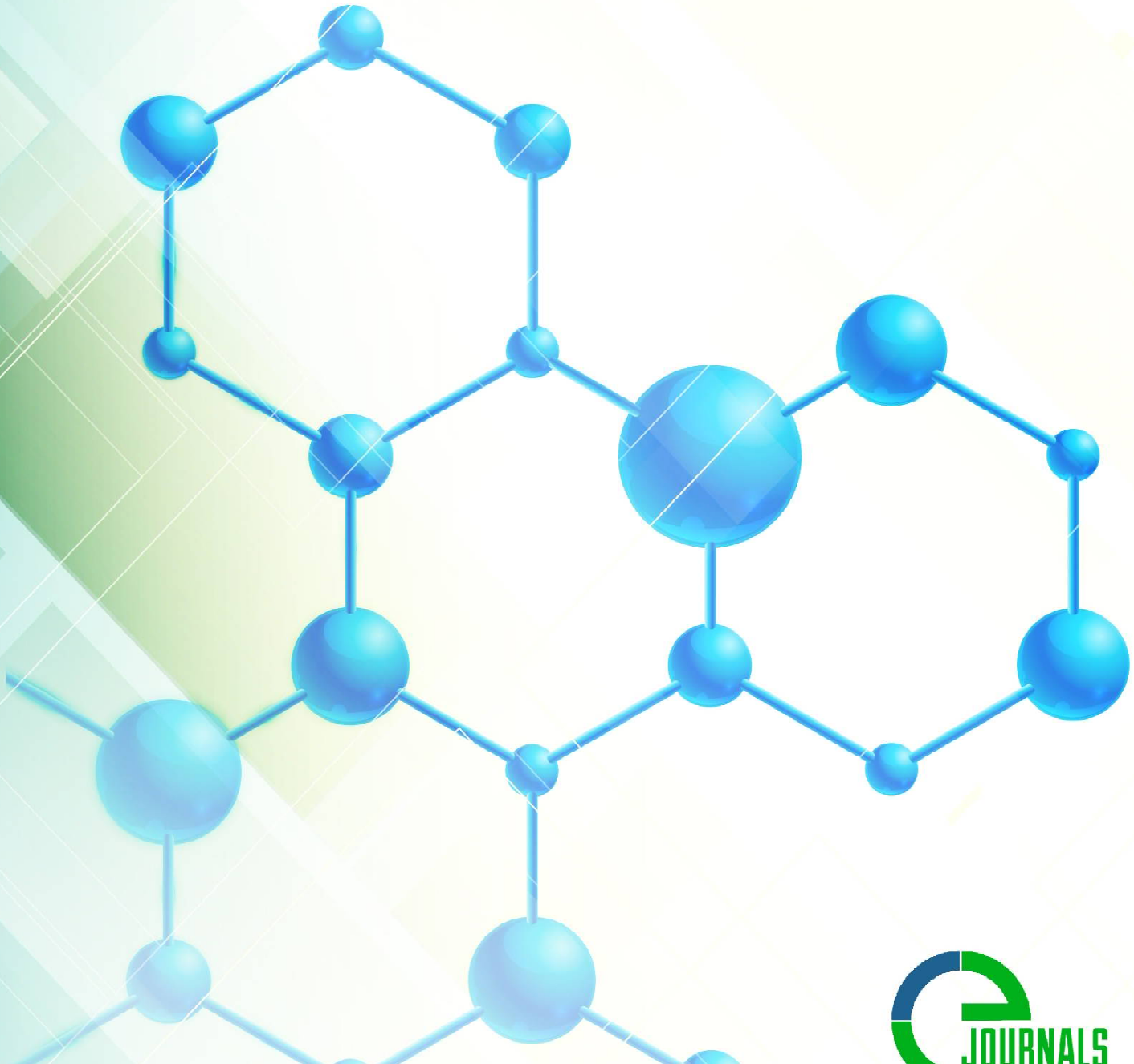
EUROPEAN JOURNAL OF

MOLECULAR MEDICINE



JOURNALS

European Journal of Molecular medicine

Volume 2, No.5, September 2022

Internet address: ttp://ejournals.id/index.php/EJMM/issue/archive
E-mail: info@ejournals.id
Published by ejournals PVT LTD
DOI prefix: 10.52325
Issued Bimonthly
Potsdamer Straße 170, 10784 Berlin, Germany

Requirements for the authors.

The manuscript authors must provide reliable results of the work done, as well as anobjective judgment on the significance of the study. The data underlying the work shouldbe presented accurately, without errors. The work should contain enough details andbibliographic references for possible reproduction. False or knowingly erroneous statementsare perceived as unethical behavior and unacceptable.

Authors should make sure that the original work is submitted and, if other authors'works or claims are used, provide appropriate bibliographic references or citations. Plagiarismcan exist in many forms - from representing someone else's work as copyright to copying orparaphrasing significant parts of another's work without attribution, as well as claimingone's rights to the results of another's research. Plagiarism in all forms constitutes unethicalacts and is unacceptable. Responsibility for plagiarism is entirely on the shoulders of theauthors.

Significant errors in published works. If the author detects significant errors or inaccuraciesin the publication, the author must inform the editor of the journal or the publisher aboutthis and interact with them in order to remove the publication as soon as possible or correcterrors. If the editor or publisher has received information from a third party that thepublication contains significant errors, the author must withdraw the work or correct theerrors as soon as possible.

OPEN ACCESS

CHIEF EDITOR

EDITORIAL BOARD

GENETIC FACTORS OF ATHEROSCLEROTIC LESION OF THE CORONARY ARTERIES IN PATIENTS WITH EARLY DEVELOPMENT OF ACUTE CORONARY SYNDROME

Turdiev U.M.
Bukhara State Medical Institute

Abstract: According to the results of many studies, for most people, the inherited risk of CHD is the result of many small effect size genetic factors acting in combination with and along with environmental and lifestyle factors. Common genetic variants associated with CAD have been identified as a result of larger population studies of genomic associations in Genome-Wide Association Studies (GWAS) o'1g'. A number of studies demonstrate the association between polymorphisms rs3825807 of the ADAMTS7 gene, rs699947 of the VEGF-A gene, rs2891168 of the CDKN2B gene, rs1746048 of the CXCL12 gene, and rs3184504 of the SH2B3 gene with the risk of CHD o'3g'.

Key words: acute coronary syndrome, genes and hereditary factor.

According to the results of many central questionnaires, in the world in the period from 2000 to 2016, mortality from cardiovascular diseases (CVD) in the age group of 30-70 years decreased by 19%, becoming the leader in this indicator, claiming 17.7 million lives annually [4] . Not least, with the observed decrease in the number of deaths, the prevalence of CVD is increasing. Globally, by 2030, the prevalence of coronary heart disease (CHD) is expected to increase from 1655 to 1845 per 100,000 population [2].

In the world, in the period from 2000 to 2016, mortality from cardiovascular diseases (CVD) in the age group of 30-70 years decreased by 19%, remaining the leader in this indicator, claiming 17.7 million lives annually [3]. With the observed decrease in the number of deaths, the prevalence of CVD is increasing. Globally, by 2030, the prevalence of coronary heart disease (CHD) is expected to increase from 1655 to 1845 per 100,000 population [3]

Taking into account the expected increase in the prevalence of coronary heart disease worldwide in the next decade [5] and the fact that the onset of coronary artery disease often occurs in the form of ACS, the search for risk factors for developing ACS at a younger age may contribute to the development of personalized approaches to the diagnosis and prevention of cardiovascular complications in patients with an increased risk of developing ACS at a younger age.

The purpose of the study: to study the risk of developing acute coronary syndrome and predicting the severity of coronary artery disease based on an individual genetic profile.

In a clinical study, it associates new data on the contribution of polymorphic variants rs699947 of the VEGFA gene and rs3825807 of the ADAMTS7 gene to the early development of acute coronary syndrome. This information can be used to optimize risk assessment for an acute coronary event in men under 55 and in women under 65 years of age. The study included data on the role of rs2891168 of the CDKN2B gene and rs3184504 of the SH2B3 gene in the development of more severe coronary artery disease.

The study was performed on the basis of the Republican Scientific Center for Emergency Medical Care of the Bukhara branch in the department of "Cardiotherapeutic resuscitation". The study included 88 patients hospitalized with a clinical diagnosis of ACS, including 58 (65.9%) men and 30 (34.0%) women. The mean age was 63.4ё10.3

years. 39 (44.3%) patients had ST-elevation ECG myocardial infarction, 49 (55.7%) patients had non-ST-elevation ECG myocardial infarction, and 26 (10.9%) patients had unstable angina . All patients were divided into two groups. Group 1 (the group of early development of the first ACS) included 116 patients, including 69 (59%) men with the development of the first ACS before the age of 55 and 47 (41%) women with the development of the first ACS before the age of 65. Group 2 included 122 patients, including 88 (72%) men with the manifestation of the first ACS later than 55 years of age and 34 (28%) women with the manifestation of the first ACS later than 65 years of age. On the first or third day from the moment of admission to the cardiology department, patients with ACS were assessed for compliance with the inclusion and non-inclusion criteriain the study.Informed consent was signed to participate in the study. All included patients underwent history taking, registration of anthropometric data, ECG registration in 12 generally accepted leads, echocardiography, venous blood sampling for a complete blood count, biochemical blood test, and coronary angiography (CAG). The study included patients with at least one narrowing of the lumen of the coronary arteries ?40%, since such a lesion of the coronary artery may be clinically significant. For population genetic control, the material from the database of the central research laboratory of the Kazan State Medical University was used. There were 252 healthy volunteers in the population genetic control group, including 125 men and 127 women (the mean age in the group was 19.9ë5.6 years). In the study group of patients with ACS and in the group of healthy volunteers (population control group), the polymorphisms rs1746048 of the CXCL12 gene, rs699947 of the VEGF-A gene, rs9349379 of the PHACTR1 gene, rs2891168 of the CDKN2B gene, rs3184504 of the SH2B3 gene, and rs3825807 of the ADAMTS gene were determined.

Inclusion Criteria:

- Age 18 and over;
- Hospitalization in the cardiology department for acute coronary syndrome;
- Carrying out coronary angiography during the current hospitalization;
- The presence of at least one narrowing of the lumen of the coronary arteries by 40% or more according to CAG;
- Opportunity to sign informed voluntary consent to participate in the study.
- Inability to sign the informed consent form;
- The patient has aserious illness or condition that limits the possibility of participation in the study.
- Inability to establish contact with the patient.

Exclusion Criteria:

- Withdrawal of informed voluntary consent at any time during the period of hospitalization.

Statistical analysis

Quantitative indicators were assessed for compliance with the normal distribution using the Shapiro-Wilk test (if the number of subjects was less than 50) or the Kolmogorov Smirnov test (if the number of subjects was more than 50). With a normal distribution, the data were described as the arithmetic mean and standard deviation (M ë SD) with a 95% confidence interval (CI), and with an abnormal distribution, using the median (Me) and the lower and upper quartiles (Q1-Q3). Comparison of two groups in quantitative terms with a normal distribution was carried out using the Student's t-test, with an abnormal distribution - using the Mann-Whitney U-test. Categorical data were described with absolute values and percentages. Analysis of multifield contingency tables was performed using Pearson's chi-square test and Fisher's exact test (for small groups).

A predictive model that characterizes the dependence of a quantitative variable on factors represented by quantitative indicators was developed using the method of paired or multiple linear regression.A predictive model that characterizes the dependence of a qualitative variable on factors represented by quantitative or categorical indicators was developed using the logistic regression method. The threshold of significance in the work was $p < 0.05$.

The clinical characteristics of the studied group of patients are presented in tables 1 and 2. The age of patients and the age of onset of ACS in the first group were less than in patients of the second group. Also, a statistically significantly higher body weight was in patients with earlier onset of ACS, but the body mass index did not significantly differ in patients of both groups. Group 2 patients had a significantly higher blood creatinine level and a lower estimated glomerular filtration rate (GFR), which may be due to a greater average age and the associated decrease in kidney function in this group. The frequency of occurrence of generally accepted cardiovascular risk factors, such as: male sex, diabetes mellitus (DM), hypertension, obesity, smoking, the presence of a aggravated family cardiovascular history, hyperlipidemia, did not differ significantly in patients with different ages of development of the first ACS. like many other factors and diseases, but atrial fibrillation was less common in patients of the first group than in patients of the second group (3% vs. 12%, respectively, $p = 0.006$). The frequency of occurrence of various genotypes of rs699947 of the VEGF-A gene, rs9349379 of the PHACTR1 gene, rs2891168 of the CDKN2B gene, rs3825807 of the ADAMTS7 gene, rs1746048 of the CXCL12 gene, rs3184504 of the SH2B3 gene in the 1st and 2nd groups of patients, and the control population was studied. The distribution of the genotypes of the studied genes corresponded to the Hardy-Weinberg equilibrium distribution law in all the studied groups. The frequency of occurrence of the CC genotype rs699947 of the VEGF-A gene in patients with early development of ACS was significantly higher than in patients of the second group (38% versus 25%; $p=0.03$). The chance of earlier development of ACS among carriers of CC of the rs699947 genotype of the VEGF-A gene is 1.77 times higher than among carriers of the AC and AA genotypes (OR=1.77; 95% CI 1.02-3.08). The frequency of occurrence of genotypes AA and AC rs699947 of the VEGF-A gene in patients with early development of the first ACS and in patients with a later development of the first ACS does not differ significantly. The frequency of genotypes CC, AC, and AA rs699947 of the VEGF-A gene did not differ significantly among population controls and in patients of groups 1 and 2. than in patients in group 2 (15% vs. 7%; $p=0.04$). The chance of earlier development of ACS is 2.58 times higher among carriers of the SS genotype rs3825807 of the ADAMTS7 gene than among carriers of the CT and TT genotypes (OR=2.58; 95% CI 1.07-6.16). The frequency of occurrence of the TT and CT rs3825807 genotypes of the ADAMTS7 gene in patients of groups 1 and 2 did not differ significantly. The frequency of genotypes CC, CT, and TT rs3825807 of the ADAMTS7 gene did not differ significantly in the population control group and in both study groups. than in patients in group 2 (15% vs. 7%; $p=0.04$). The chance of earlier development of ACS is 2.58 times higher among carriers of the CC genotype rs3825807 of the DAMTS7 gene than among carriers of the CT and TT genotypes (OR = 2.58; 95% CI 1.07-6.16) (Table 4). The frequency of occurrence of the TT and CT rs3825807 genotypes of the ADAMTS7 gene in patients of groups 1 and 2 did not differ significantly. The frequency of genotypes CC, CT, and TT rs3825807 of the ADAMTS7 gene did not differ significantly in the population control group and in both study groups. A multivariate analysis of variance (ANOVA) was carried out to assess the significance of various factors studied in this work on the sum of scores on the SYNTAX and Gensini scales. Gender, age, presence of hypertension, presence of

diabetes mellitus, presence of hyperlipidemia, smoking, burdened heredity, as well as the carriage of various genotypes of the genes studied in the work were taken as the studied factors. In the constructed model, significant factors influencing the severity of coronary artery disease in patients with earlier development of ACS, assessed by the Gensini scale, were age (an increase in age by 1 year significantly increased the severity of coronary artery disease by 0.6 ë 0.3 points on this scale) carriage of the TT genotype rs3184504 of the SH2B3 gene, which is associated with a less pronounced lesion of the CA, by an average of 10.1ë5.8 points on the Gensini scale, carriage of the TT genotype rs2891168 of the CDKN2B gene, which is associated with a less severe lesion of the CA, by an average of 5 .8ë4.9 points on the Gensini scale (Table 6). The contribution of age, carriage of the TT genotype rs3184504 of the SH2B3 gene and the TT genotype of the CDKN2B gene determine the severity of CA lesions according to the Gensini scale by 12.1%. When assessing the severity of coronary artery disease on the SYTNTAX scale in patients with early development of ACS, the greatest role was noted in such factors as the age of the patient and the carriage of TT rs2891168 of the CDKN2B gene (again, its protective role is noted, the carriage of this genotype is associated with less severity of coronary injury, regardless of age) . Carriage of the TT genotype rs2891168 of the CDKN2B gene is associated with a 1.4-fold lower severity of coronary lesions as assessed by the SYNTAX scale. The frequency of occurrence of the genotypes of the genes presented in this work was studied in patients with early onset of ACS with different localization of CA lesions. The presence of stenosis was determined by the narrowing of the vessel lumen by 40% or more. Less significant narrowings were taken into account only when calculating the total score for Gensini. Statistically significant differences in the frequency of occurrence of the genotypes of the genes presented in the work in patients with early onset of ACS were found in patients with damage to the LCA trunk: the frequency of occurrence of the CT rs3184504 genotype of the SH2B3 gene in patients with LCA stenosis ?40% was almost twice as high (82% versus 42%; p=0.012) than in patients without LCA stenosis (OR=6.34; 95% CI 1.31-30.79); the frequency of occurrence of the TT genotype rs2891168 of the CDKN2B gene was significantly lower (7% vs. 28%; p=0.035) than in patients without DV stenosis (OR=0.21; 95% CI 0.05-0.94); the frequency of occurrence of TT genotype rs3825807 of the ADAMTS7 gene in patients with PV/PMVA stenosis is significantly higher (78% versus 35%, p=0.027) than in patients without such severe stenosis (OR=6.36; 95% CI 1.27-32 .59).

As genotyping techniques spread and become cheaper, as well as the development of modern technologies for processing big data, studies to identify genetic risk factors for diseases will play an increasingly important role in predicting their occurrence and, possibly, will help to choose the right tactics for managing patients, taking into account their genetic features.

CONCLUSIONS

1.Among patients with early development of acute coronary syndrome, compared with the group of patients with the development of ACS at an older age, there was a higher frequency of occurrence of genotypes CC rs699947 of the VEGF-A gene (0.38 and 0.25, respectively, p=0.038) and CC rs3825807 ADAMTS7 gene (0.15 and 0.07, respectively, p=0.04). Simultaneous carriage of SS rs3825807 of the ADAMTS7 gene and SS rs699947 of the VEGF-A gene is associated with a 10-fold increase in the risk of early ACS;

2.Patients with early onset of ACS with simultaneous carriage of the C allele rs3184504 of the SH2B3 gene and the C allele rs2891168 of the CDKN2B gene have a 2.6 times greater severity of coronary artery lesions according to the Gensini scale (p=0.016). The carriage of the allele C rs2891168 of the CDKN2B gene is associated with a 1.4 times

greater (p=0.023) severity of coronary artery lesions as assessed by the SYNTAX scale. The TT genotype rs2891168 of the CDKN2B gene is protective in relation to the severity of coronary artery lesions;

3.In patients with early onset of ACS and LCA stenosis ?40%, the CT genotype rs3184504 of the SH2B3 gene was more common than in patients with a lesser lesion of the LCA trunk (0.82 and 0.42, respectively; p=0.012), TT genotype rs2891168 of the gene CDKN2B was significantly less common in patients with DV stenosis ?40% than in patients with less DV lesion (0.07 and 0.28, respectively; p=0.035); 40% than in patients with OA stenosis <40% (0.26 and 0.46, respectively; p = 0.033), the TT rs3825807 genotype of the ADAMTS7 gene was significantly more common in patients with stenosis of the MVA and MVA ?40% than in patients with less damage to the coronary arteries of this localization (0.78 and 0.35, respectively; p=0.21);

4.Early development of ACS is associated with the carriage of CC genotypes rs699947 of the VEGF-A gene and CC genotype rs3825807 of the ADAMTS7 gene. Diabetes mellitus, obesity, arterial hypertension, and hyperli pidemiaare equally common among patients with the development of ACS at any age, but in the early development group, ACS are observed 12 years earlier in men (p <0.001) and 17.5 years earlier in women (p <0.001).

Used literature.

1.Кенжаев М.Л., Ахмедов Л.А., Пўлатова Ш.Х. Бобоева М.М. Кардиоген шок билан асоратланган ўткир миокард инфаркти давосида вазопрессор терапияни такомиллаштириш // Вестник терапевтов. Ташкент, 2017.- №1 - С.31

2.Ахмедов Л.А., Пўлатова Ш.Х. Ўткир миокард инфаркти давосини такомиллаштириш // Ўзбекистон кадиологияси. Ташкент, 2019. - №3 (30). - С.105-108 (14.00.00; №22)

3.Пўлатова Ш.Х. Особенности ТЛТ у больных острым инфарктом миокарда // Шошилинч тиббиёт ахборотномаси. Тошкент, 2019. - №6. - С.89-92 (14.00.00; № 11)

4.Pulatova Sh.H. Method of improving vasopressor therapy for acute myocardial infarction complied with cardiogenetic shock // American Journal Of Medicine And Medical Sciences. 2020.- Vol. 10 (11). - - P. 911-913

5.Pulatova Sh.H. Improvement of treatment of patients with acute heart failure, a comparative evaluation of the effectiveness of dobutamine and levosimendan// World Journal Of Pharmaceutical Research. 2020. Vol 9 (6). -P. 2283-2288

6.Rizaeva, M. Z. (2022). The clinical course of atrial fibrillation in patients with coronary heart disease. European journal of molecular medicine, 2(1).

7.Кенжаев, М. Л., & Ризаева, М. Ж. (2020). Клиническое течение фибрилляции предсердий у больных ишемической болезнью сердца. In Наука и инновации-современные концепции (pp. 103-109).

8.Кенжаев, М. Л., & Ризаева, М. Ж. (2020). Выявление предикторов фибрилляции предсердий у больных ишемической болезнью сердца. Новый день в медицине, (2), 403-406.