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THE ROLE OF HOMOCYSTEINE AND HIGH SENSITIVITY C-REACTIVE PROTEIN IN ASSESSING THE RISK OF CARDIOVASCULAR DISEASES

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Resume

Purpose of the study: to evaluate the role of homocysteine (HC) and high-sensitivity C-reactive protein (hs-CRP) in the progression of cardiovascular diseases (CVD).

Material and methods. We examined 401 people who had not previously been observed with cardiovascular pathology, as well as patients with CVD aged from 30 to 70 years. The following studies were carried out: a standard questionnaire survey, determination of lipid spectrum indicators, glucose, creatinine and urea levels, uric acid levels in blood serum, C-reactive protein. Based on the results, patients were divided into groups depending on the level of cardiovascular risk (CVR) according to SCORE2. Group 1 consisted of persons with low and moderate cardiovascular risk according to SCORE2 - 198 patients; group 2 – with high CV risk according to SCORE2 – 69 patients with CV risk; Group 3: persons without coronary diseases (IHD, PICS, CHF) with very high cardiovascular risk according to SCORE2 - 53 patients; Group 4 – 91 patients with diagnosed coronary diseases and very high cardiovascular risk. The control group consisted of 23 healthy individuals, CV risk according to SCORE2 was less than 1% - low CV risk.

Research results. According to the results of our study, there was an increase in the level of total cholesterol, LDL, non-HDL cholesterol, TG, and a decrease in HDL in the study groups. The results of the study showed an increase in the level of GC in the blood serum with significant values in patients with very high cardiovascular risk in groups 3 and 4 with an increase of 71.2% ($p<0.05$) and 108% ($p<0.05$), respectively, compared with the indicators of the control group and in patients with CVD in group 4 was 15.2±6.2 µmol/l. The hsCRP values in the very high CSR groups (groups 3 and 4) were significantly higher by 8 times ($p<0.05$) and 9 times ($p<0.05$), respectively, compared to the values in the control group. There is a correlation between the level of CSR according to SCORE2 and non-HDL cholesterol, HC and hsCRP with a correlation coefficient of $r=0.76$, $r=0.55$ and $r=0.44$.

Conclusions. The role of hyperhomocysteinemia, uric acid, hsCRP>3 mg/l, and non-HDL cholesterol as potential biomarkers of increased cardiovascular risk and atherosclerotic CVD has been demonstrated. The dependence of the level of hyperhomocysteinemia, hsCRP, and non-HDL cholesterol on the risk of developing CVD was revealed.

One of the main risk factors for the development of cardiovascular diseases (CVD) is hypercholesterolemia. An increase in total cholesterol and dyslipoproteinemia cause characteristic atherosclerotic occlusive-ostenotic lesions of the main arteries, which is accompanied by ischemic damage to target organs []. Recently, quite a lot of attention has been paid to other mechanisms of the occurrence and progression of damage to the cardiovascular system: endothelial dysfunction, inflammatory factors, endocrine disorders,

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etc. []. At the same time, the constant search for the possibility of the broadest possible understanding of the mechanisms of CVD remains relevant and is dictated by the need to search for reliable predictors of increased cardiovascular risk (CVR). In this regard, it is of interest to study the role of homocysteine (HC) and high-sensitivity C-reactive protein (hs-CRP) in assessing the prediction of CV risk.

Purpose of the study: to evaluate the role of HC and hs-CRP in the progression of cardiovascular diseases (CVD).

Material and methods. We examined 401 people who had not previously been observed with cardiovascular pathology, as well as patients with CVD aged from 30 to 70 years. The following studies were carried out: a standard questionnaire designed to assess the objective condition of patients; assessment of hemodynamic and anthropometric parameters; electrocardiography. Measurement of lipid spectrum indicators, glucose, creatinine and urea levels, uric acid levels in blood serum, C-reactive protein. Based on the results, patients were divided into groups depending on the level of cardiovascular risk (CVR) according to SCORE2. Group 1 consisted of individuals with low and moderate cardiovascular risk according to SCORE2 - 198 patients; cardiovascular risk was 2.5±1.5%, average age was 43.0±8.56 years; Group 2 – with high CVS according to SCORE2 – 69 patients with CVS, CVS – 7.3±1.7%, average age was 50.3±7.9 years; Group 3: persons without coronary diseases (IHD, PICS, CHF) with very high CV risk according to SCORE2 - 53 patients, CV risk - 17.4 ± 5.9%, average age was 59.3 ± 9.03 years; Group 4 - 91 patients with diagnosed coronary diseases in very high cardiovascular risk, in whom SCORE2 is not used, the average age was 60.6±8.2 years. The control group consisted of 23 healthy individuals, CV risk according to SCORE2 was less than 1% - low CV risk. Clinical characteristics of the patients are presented in Table 1.

Table 1. Clinical characteristics of patients included in the study protocol

Groups	**n (%)**
Control	23
Total patients	401
Average age of patients, years	51,8±8,3
Men	92 (22,9%)
Women	309 (75,2%)
Group 1 - persons with low and average CVR	188 (46,9%)
Group 2 – persons with high CVR	69 (17,2%)
Group 3 – persons with very high CVR	53 (13,2%)
Group 4 – patients with CVD (very high risk)	91 (22,7%)
Obesity + overweight (AO, BMI more than 25, % fat content)	389 (98,8%)
Overweight (BMI 25-29.9)	96 (23,9%)
Obesity 1st degree (BMI 30-34.9)	151 (37,7%)
Obesity 2 degrees (BMI 35-39.9)	93 (23,2%)
Obesity 3 degrees (BMI 40 or more)	50 (12,5%)
AH	124 (30,2%)
Increased fasting glucose, DM	24 (5,8%)
Smoking	40 (9,7%)
Hyperlipidemia and/or dyslipidemia	245 (59,1%)

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Physical inactivity	71 (17,3%)
High stress levels	91 (22,1%)
Severe QL impairments	162 (39,4%)

In the examined 401 patients, the presence of abdominal obesity (AO) was determined in 389 individuals (98.8%), while overweight was observed in 96 individuals (23.9%), obesity of 1 st in 151 individuals (37.7%), obesity of 2 st in 93 individuals (23.2%), obesity of 3 st in 50 (12.5%); AH with blood pressure greater than 140/90 mmHg in 124 patients (30.9%); fasting glucose and diabetes mellitus (DM) in 24 patients (6%), dyslipidemia and hyperlipidemia in 235 individuals (58.6%), smoking in 40 patients (10%), physical inactivity was observed in 151 individuals (37.7%); A high level of stress was observed in 91 patients (22.7%), aggravated CVD in one parent in 131 patients (32.7%), and on the part of both parents in 79 patients (19.7%).

The results of the study. In order to identify risk factors for the development of CVD and CVR, indicators of lipid metabolism (total cholesterol (TH), triglycerides (TG), high density lipoprotein cholesterol (HDL) and low density lipoprotein cholesterol, atherogenicity coefficient) were determined using a biochemical analyzer, calculated by the method of HC-non-HDL=OHC-HDL, determination of serum glucose, creatinine, urea, serum uric acid level, highly sensitive C-reactive protein (hf-CRP), homocysteine (HC) on a biochemical analyzer. The obtained indicators in 4 groups are presented in Table 2.

Table 2. Laboratory data (M±SD)

№ п/п	Indicators	Control (n=23)	Group 1 (n=188)	Group 2 (n=69)	Group 3 (n=53)	Group 4 (n=91)
1	Blood glucose, mmol/l	5,2±0,4	5,1±1,57	5,5±0,7*	5,74±0,8*	6,4±2,1***
2	Creatinine, µmol/l	61,3±17,33	69,4±15,8	72,6±17	73,02±17,03*	72,7±19,3*
3	Uric acid, µmol/l	181,9±52,2	263,0±100,0***	299,0±104,0***	294±92,0***	317±111,0***
4	TC mmol/l	4,74±0,82	4,8±0,8	5,4±0,9*	5,73±1,3**	5,59±1,4**
5	TG, mmol/l	0,80±0,42	1,4±0,9*	1,8±0,9***	1,87±0,79***	1,91±1,04***
6	LDL, mmol/l	2,51±0,72	2,9±0,73	3,4±0,9*	3,62±1,1***	3,56±1,2***
7	HDL, mmol/l	1,35±0,27	1,1±0,2*	1,08±0,2	1,2±0,3	1,01±0,2**
8	Non-HDL cholesterol, mmol/l	3,24±1,1	3,8±0,9	4,3±1,18*	4,52±1,1***	4,51±1,3***
9	Homocysteine, µmol/l	7,3±5,7	7,34±3,9	9,5±2,3	12,5±3,8*	15,2±6,2*
10	hsCRP, mg/l	0,5±0,8	1,3±0,7	2,5±1,5*	4,5±2,1**	5±1,8***

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*Note: where * - reliability p<0.05; ** - reliability p<0.01, *** - reliability p<0.001 in relation to the control group*

When assessing CVR, the updated SCORE algorithm was used - SCORE2 - and SCORE2-RR in patients over 40 years of age estimates the 10-year risk of death and fatal cases of CVD (documented ischemic heart disease, including anamnestic indications of acute coronary syndrome, coronary revascularization, revascularization of other arterial systems, stroke , transient ischemic attack, aortic aneurysm, peripheral arterial disease).

It is known that the most important risk factor for the development and progression of various cardiovascular pathologies associated with atherosclerosis are lipid metabolism disorders (atherogenic dyslipidemia). According to the results of our study, an increase in the level of total cholesterol, LDL, non-HDL cholesterol, TG, and a decrease in HDL in the studied groups were noted: in individuals with low and moderate risk, there was a significant increase in TG levels and a decrease in HDL by 45% (p <0.05) and 22 .8% (p<0.01), respectively, compared with the control group; in individuals with high CVR, there was a significant increase in the level of total cholesterol, LDL, non-HDL cholesterol, TG by 12.5% (p<0.05), 27% (p<0.05), 25.5% (p<0.05) and 55.7% (p<0.001), respectively, compared with the control group; in persons with very high CVR without coronarogenic CVD, an increase in the level of TC, LDL, non-HDL cholesterol, TG and a decrease in HDL by 17.2% (p<0.01), 30.7% (p<0.001), 28% (p <0.001), 57% (p<0.001) and 11% (p>0.05), respectively, compared with the control group; in persons in very high CVR with coronary CVD, there was a significant increase in the level of TC, LDL, non-HDL cholesterol, TG and a decrease in HDL by 15.2% (p<0.01), 29.4% (p<0.001), 28% (p<0.001), 50% (p<0.001) and 23% (p<0.01), respectively, compared with the control group. All these disorders lead to the development of atherogenic dyslipidemia, which is characterized by: hypertriglyceridemia, a decrease in the concentration of HDL cholesterol, an increase in the content of atherogenic small dense LDL particles. The contribution of lipid metabolism disorders to the increased risk of developing CVD cannot be underestimated.
The results of our study showed an increase in the level of GC in the blood serum with significant values in patients with very high CVR in groups 3 and 4 with an increase of 71.2% (p<0.05) and 108% (p<0.05), respectively. compared with the indicators in the control group and in patients with CVD in group 4 was 15.2±6.2 µmol/l. The Framingham prospective study revealed a statistically significant increase in the frequency of stenosis in the carotid artery of more than 25% of its diameter with a GC of more than 14.4 µmol/L, while the concentration of folic acid and pyridoxine phosphate was simultaneously reduced [3,6]. Thus, HC may underlie the development of AH, coronary artery disease and thrombotic cerebrovascular diseases, especially at high homocysteine concentrations [5,7,8].

The hsCRP values in the very high CVR groups (groups 3 and 4) were significantly higher by 8 times (p<0.05) and 9 times (p<0.05), respectively, compared to the values in the control group. There is a high correlation between the level of CVR according to SCORE2 and non-HDL cholesterol, HC and hsCRP with a correlation coefficient of r=0.76, r=0.55 and r=0.44. The value of inflammatory markers in CVD risk assessment has been intensively studied over the past 20 years [2,4]. The largest number of studies are devoted to highly sensitive hsCRP. A large study of more than 28,000 healthy women assessed a panel of 12 vascular biomarkers, which included lipid and apolipoprotein fractions, homocysteine, lipoprotein(a), and 4 inflammatory biomarkers (hsCRP, soluble intercellular adhesion molecule 1,

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interleukin-6 and serum amyloid A) as potential determinants of future vascular events. Of the 12 markers evaluated, hsCRP was the strongest single-factor risk predictor, effective in predicting vascular events even at low LDL-C concentrations, and the only new biomarker that added prognostic information to traditional risk factors [1]. In the very high CVR group, a significant increase in homocysteine and hsCRP levels was detected in groups 3 and 4. High-sensitivity C-reactive protein (hsCRP) is recognized as an independent marker of cardiovascular disease risk, comparable in value to cholesterol or blood pressure. Kirichenko A.A. et al. It was found that an increase in hsCRP>2 mg/l was detected in 26.7% of the examined men. In the vast majority of cases (89.2%), the increase in CRP was from 2 to 5 mg/l, in 7.5% of cases - from 5 to 10 mg/l, and only in 3.2% exceeded 10 mg/l. All patients with elevated hsCRP levels showed no signs of an acute inflammatory response. A direct correlation was found between hsCRP levels and overweight and abdominal obesity, which increases with age. The high incidence of elevated basal levels of hsCRP in the group of relatively healthy working-age men of young and middle age, the tendency for this indicator to increase after a year in 45.3% of men make it advisable to include routine measurement of the basal concentration of hsCRP in men over 40 years of age in screening programs and standards for medical examinations. [4].

Conclusions. Thus, according to the results of our study, a pronounced decrease in GFR, an increase in glucose, and uric acid in the blood serum were noted in individuals with very high CVR and patients with CVD; There was a significant increase in total cholesterol, LDL, non-HDL cholesterol, TG with a decrease in HDL with a significant increase in individuals with high and very high CVR. The role of hyperhomocysteinemia, uric acid, hsCRP>3 mg/l, non-HDL cholesterol as potential biomarkers of increased CVR and atherosclerotic CVD has been demonstrated. A relationship between the level of hyperhomocysteinemia, hsCRP, and non-HDL cholesterol and the risk of developing CVD was revealed.

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