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Biochemical markers of coronary atherosclerosis: building models and assessing their prognostic value regarding the lesion severity

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Aim. To assess the individual and complex prognostic value of various blood biochemical parameters (biomarkers) in the non-invasive diagnosis of coronary artery (CA) atherosclerosis.

Material and methods. The study included 216 patients (men, 115; women, 101) aged 24 to 87 years (mean age, 61,5±10,7 years), who underwent indicated coronary angiography. All patients underwent a biochemical blood tests to determine the parameters of lipid, carbohydrate and nitrogen metabolism, the hemostatic system, inflammatory markers, as well as the creatinine level as an indicator of renal function.

Results. Analysis revealed biomarkers, the deviations in the level of which contribute to the diagnosis and determination of the coronary involvement. These biomarkers include glucose, creatinine, C-reactive protein, and adiponectin. Using these biochemical parameters, a multivariate model (MVM) was constructed, which was significant for the diagnosis of coronary atherosclerosis and determination of its severity. With the help of ROC-analysis, the cutoff point of MVM of 2 was found. MVM >2 with a sensitivity of 72% indicate CA atherosclerosis of any severity, as well as with a specificity of 62,5%, it can be ruled out. Using MVM data and a cutoff point of 2, a binary logistic regression model was built, according to which, with a MVM >2, the odds for detecting CA atherosclerosis of any degree is 2,1 times higher (95% confidence interval (CI), 1,2-3,8; p=0,010), severe CA — 4,7 times (95% CI, 1,9-12,0; p=0,001) compared with individuals with MVM ≤2, who have 2,8 times (95% CI, 1,4-4,9; p=0,002) a higher chance of detecting intact CAs.

Conclusion. Thus, the total MVM score of 0-2 indicates the absence of coronary atherosclerosis, while 3-4 points –CA atherosclerosis of any severity.

Keywords: atherosclerosis, biochemical parameters, biochemical models, coronary arteries, risk factors.

Relationships and Activities: none.

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Coronary artery (CA) atherosclerosis is the pathological basis of ischemic heart disease, the prevalence and mortality from complications of which remain high both in Russia and throughout the world [1]. One of the reasons for this is the late disease establishment. Therefore, the search for early-stage markers of CA atherosclerosis remains an urgent area of modern cardiology.

Impaired function of some human body systems (lipid-transport, carbohydrate, hemostasis systems), chronic inflammation and related changes in blood parameters are a stimulus for an active search and study of early-stage biomarkers of atherogenesis. It has long been noted that the analysis of blood biochemical parameters as criteria reflecting various pathophysiological pathways of atherogenesis can improve the prediction of cardiovascular risk (CVR) [2].

Numerous studies considered various blood parameters, which make it possible to assess the relationship between changes in their blood content both with atherosclerosis in general and specifically with CA atherosclerosis [3, 4]. For a long time, lipid metabolism indicators were considered the main markers of atherosclerosis [5]. However, atherosclerotic cardiovascular events also develop with normal lipid profile [6]. Therefore, the researchers' attention is now attracted by other biochemical blood parameters, reflecting the relationship of their deviations from the norm. Moreover, due to the widespread use of statins and other lipid-lowering drug classes, the interpretation of lipid metabolism without an effect on lipid-transport system is difficult.

It should be noted that the contribution of most blood biomarkers to atherosclerosis prediction was studied separately for each indicator. At the same time, there is evidence that the use of their combination can increase the prognostic value and improve CVR stratification [7, 8]. The literature presents several studies combining imaging and circulating markers or involving the use of circulating, genetic and/or imaging markers (Framingham Heart Study, Malmö Diet and Cancer Study, MORGAN, Cardiovascular Health Study) [8-10]. Previously, we analyzed mathematical models including various combinations of blood biochemical parameters with each other, as well as with imaging plaque characteristics obtained by carotid duplex scanning and risk factors (RFs) of cardiovascular disease (CVD) [11]. Based on the study of a wide range of blood biochemical parameters and imaging markers, analysis of their various combinations, a novel indicator was developed, called an integrative biomarker (i-BIO), which reflects the total contribution of a complex of biochemical, clinical and instrumental markers to presence and severity of CA atherosclerosis. Following blood parameters were included in i-BIO: triglycerides (TG), glucose, fibrinogen (FG), high sensitivity C-reactive protein (hsCRP), and adiponectin. This set of biomarkers made it possible to diagnose severe CA atherosclerosis, however, the detection of subclinical atherosclerosis was less effective [11].

The aim of this study was to assess the individual and complex prognostic value of various blood biomarkers in the non-invasive diagnosis of CA atherosclerosis.

Material and methods

We analyzed a cohort of patients admitted to the National Medical Research Center for Therapy and Preventive Medicine in the period from 2016 to 2019, who, according to indications, underwent diagnostic coronary angiography (CAG). The study was carried out in accordance with the Declaration of Helsinki. The study protocol was approved by the Ethics Committee (№ 09-05/19). All patients signed informed consent for participation in the study, personal data processing, collection and biobanking of blood.

There were following inclusion criteria: patients aged >18 years who signed an informed consent for inclusion in the study, collection and biobanking of blood.

Exclusion criteria were as follows: acute clinical complication of atherosclerosis within prior 6 months; any acute inflammatory disease; stage ⩾III chronic kidney disease (glomerular filtration rate (GFR) <60 ml/min/1,73 m^2); decompensated type 1 and 2 diabetes (fasting blood glucose >11 mmol/l); left ventricular ejection fraction <40%; cancer; blood and immune system diseases, pregnancy or lactation.

All patients underwent CAG by the Judkins technique (1967) [12] using radial or transfemoral access on angiographic x-ray systems Philips Integris Allura and General Electric Innova 4100. For the quantitative assessment of stenosis, the computer program of General Electric Innova 4100 system was used.

The patients were admitted to the hospital for CAG for various indications, such as:

— Sternum or left-sided chest pain (presumably coronary origin); impossibility, contraindications or refusal of a patient to perform stress tests and CA multislice computed tomography (MSCT);

— Positive or questionable results of exercise stress tests (treadmill or stress echocardiography) or CA stenosis >50% according to MSCT;

— Abnormalities revealed by conventional electrocardiography (ECG) or 24-hour Holter monitoring (presumably ischemic origin) and the impossibility, contraindications or refusal of a patient to perform stress tests and CA MSCT;

— Patients who underwent inpatient treatment at the National Medical Research Center for Therapy and Preventive Medicine, who meet the inclusion criteria and agreed to participate in clinical testing, the protocol of which implies CAG;

— Professional activity peculiarities (professions with an increased risk for other people).

All patients underwent a biochemical blood tests. Determination of blood parameters was carried out in serum or plasma obtained by standard methods from venous blood taken after 12-hour fasting. The standardization and quality control was carried out in accordance with the requirements of the "Federal system for external quality control of clinical laboratory procedures".

The concentration of total cholesterol (TC), TG and high-density lipoprotein cholesterol (HDL-C) was determined by the enzymatic assay using Abbott reagents on an Architect C8000 Clinical Chemistry Analyzer (Abbot Diagnostics, USA). The concentration of low-density lipoprotein cholesterol (LDL-C) was estimated using the Friedewald equation at a TG level ⩽4,5 mmol/l: LDL-C = TC - (HDL-C+TG/2,2) mmol/l. The cholesterol concentration not included in HDL (non-HDL cholesterol) was calculated as the difference: TC - HDL-C. The level of lipoprotein(a) (Lp(a)) was determined on a Sapphire-400 analyzer (Japan) using enzyme kits. The concentration of the main proteins LDL and HDL (apolipoproteins (apo) B and apo AI) was determined on the same analyzer using DiaSys diagnostic kits. When assessing the lipid metabolism parameters, the normal ranges adopted in the 2019 ESC/EAS Guidelines for the management of dyslipidaemias were used [13].

The serum glucose concentration was determined by the glucose oxidase assay on an Architect C 8000 analyzer using Abbott reagents, and the insulin level was determined by Chemiluminescent immunoassay on an Architect i2000SR analyzer. An elevated glucose level was considered ⩾6,1 mmol/L, insulin — ⩾14,0 μU/ml [14].

The levels of adiponectin and leptin were determined using an enzyme-linked immunosorbent assay: adiponectin (BioVendor, Czech Republic), leptin (Diagnostic Biochem Canada Inc., Canada). Reduced adiponectin level was considered <8,0 μg/ml [11], which coincided with the data obtained in this study (ROC-analysis); an elevated leptin level was considered ⩾18 ng/ml, which corresponds to the median distribution of presented cohort for this indicator.

The CRP level was determined by a high-sensitivity turbidimetric immunoassay based on the interaction of test sample CRP with specific anti-CRP antibodies using an Architect C8000 analyzer. Levels of hsCRP ⩾1,0 mg/L were considered elevated [15].

The plasma FG level was determined by the Claus method. The measurements were carried out on an ACL Elite automatic coagulometer (USA) with Hemosil reagents (USA). An elevated level was considered the upper quartile for presented cohort >4,0 g/L.

To determine the serum content of stable nitric oxide metabolites (nitrates and nitrites (NO_X)), at the first stage, the blood serum was deproteinized by centrifugation. The NO_X concentration was determined spectrophotometrically using a Multiskan MCC/340 system (LabSystems, Finland) [16]. NO_X <36 μmol/L was considered reduced, which corresponds to the cut-off point found using the ROC analysis in our cohort of patients.

Creatinine levels were determined using enzyme-linked immunosorbent assay. The measurements were carried out on an Architect C 8000 analyzer. The range of values from 70 to 110 μmol/L is taken as a normal creatinine level according to international standards. In our study, according to the cut-off point found by ROC analysis, the creatinine level ⩾73 μmol/L was considered elevated.

Statistical analysis. Statistical analysis of results was carried out using the statistical software packages Statistica v.10 and SPSS v.20. Depending on the type of distribution of continuous variables, the arithmetic mean with standard deviation (total cholesterol, LDL-C, HDL-C, non-HDL cholesterol, apo AI, apo B, FG, glucose, creatinine) or the median and interquartile range, indicating maximum and minimum values (TG, Lp(a), NO_X, hsCRP, insulin, adiponectin, leptin) was estimated. To evaluate the cut-off points of continuous variables, ROC analysis was used with the creation of curves to determine the sensitivity and specificity of the test. The threshold level was determined by a combination of sensitivity and specificity values at curve intersection, giving 100% in total. A binary logistic regression was used to estimate odds ratios and 95% confidence interval (CI). Differences were considered significant at $p<0,05$.

Results

The study included 216 patients: 115 men and 101 women aged 24 to 87 years (mean age, 61,5±10,7 years), who were selected in accordance with the inclusion criteria in one of the following groups:

Group 1 (n=73) — asymptomatic patients without CA atherosclerosis (intact CA);

Group 2 (n=71) — asymptomatic patients with subclinical CA atherosclerosis (CA stenosis ⩽50%);

Group 3 (n=72) — symptomatic patients with severe CA atherosclerosis (stenosis in two or more CAs with hemodynamically relevant involvement of

Table 1

Biochemical blood parameters depending on CA involvement degree

Biochemical parameters	Group		
	Group 1 (intact CA) (n=73)	Group 2 (subclinical CA atherosclerosis) (n=71)	Group 3 (severe atherosclerosis of CA) (n=72)
Lipid metabolism parameters			
Total cholesterol, mmol/l	4,5±1,15	4,7±1,00	3,9±0,98[b,c]
LDL-C, mmol/l	2,6±0,98	2,8±0,91	2,2±0,84[b,c]
HDL-C, mmol/l: Men Women	 1,0±0,22 1,3±0,33	 1,2±0,33 1,3±0,28	 1,0±0,33[c] 1,1±0,21[b,c]
Non-HDL cholesterol, mmol/l	3,3±1,07	3,4±0,9	2,8±0,92[b,c]
TG, mmol/l	1,4 [1,00; 1,99]; (0,11-4,85)	1,3 [0,84; 1,74]; (0,38-3,62)	1,4 [1,1; 1,75]; (0,60-5,72)
Lp(a), mg/dl	15,9 [7,31; 36,8]; (0,9-229,5)	16,9 [6,82; 33,89]; (0,9-241,27)	15,2 [5,84; 54,21]; (1,46-169)
Apo AI, mg/dl	157±32,12	159±26,82	136±25,9[b,c]
Apo B, mg/dl	86±23,61	92±23,73	84±22,43
Hemostatic parameters			
Fg, g/l	4,6±1,42	4,5±0,87	5,2±1,42[b,c]
Inflammatory markers			
hsCRP, mg/l	2,3 [0,88; 5,37]; (0,14-186,2)	2,2 [1,38; 3,62]; (0,28-29,8)	4,5 [2,14; 10,05][b,c]; (0,52-136,69)
Carbohydrate metabolism markers			
Glucose, mmol/l	5,9±1,37	6,3±1,47	6,9±2,0[b,c]
Insulin, μU/L	8,9 [6,07; 12,45]; (1,30-73,80)	10,0 [6,9; 15,05]; (1,00- 81,00)	11,0 [8,20; 17,65]; (4,60-50,60)
Metabolism parameters of visceral adipose tissue			
Adiponectin, mg/ml	7,7 [5,97; 10,55]; (4,19-23,20)	8,8 [7,02; 11,65]; (1,10-56,30)	6,8 [4,73; 10,40][b,c]; (2,13-22,70)
Leptin, ng/ml	19,4 [5,8; 57,3]; (0,00-182,0)	27,2 [4,98; 73,2]; (0,33-225,0)	10,5 [4,0; 37,0]; (0,75-139,0)
End product of creatine phosphate reaction			
Creatinine, μmol/l	75,4±22,68	77,7±17,22	93,0±32,98[b,c]
NO metabolites			
NO_x, μmol/l	41,8 [42,04; 60,00]; (12,64-222,68)	30,0 [24,46; 42,06][a]; (13,91-132,12)	30,5 [25,18; 43,93][b,c]; (15,60-115,72)

Note: p<0,05: [a] — between 1 and 2 groups.; [b] — between 1 and 3 groups.; [c] — between 2 and 3 groups. The interquartile range and minimum and maximum values are indicated in square brackets and parentheses, respectively.

Abbreviations: apo — apolipoproteins, hsCRP — high-sensitivity C-reactive protein, CA — coronary arteries, Lp(a) — lipoprotein(a), LDL — low density lipoproteins, HDL — high density lipoproteins, TG — triglycerides, FG — fibrinogen, NO_x — nitric oxide metabolites.

one and/or several vessels). Hemodynamically relevant stenoses were considered as follows [17]:

- stenosis >50% in any CA with imaging data confirming myocardial ischemia in the area of corresponded affected vessel;
- stenosis >90% in any CA even without ischemia confirmation by imaging methods.

Table 1 shows the serum biochemical parameters in groups with different CA involvement.

Analysis presented in Table 1 showed that in the group with severe CA atherosclerosis (group 3), the lipid profile was less atherogenic compared to patients with intact CA (group 1) and subclinical coronary artery disease (group 2), which, most likely, is due to statin therapy. Indeed, 93% of group 3 patients took statins, 50,7% — group 2, and 26% — group 1. At the same time, HDL-C cholesterol and apo AI levels in women with severe CA atherosclerosis were lower than in other patients, and in men — lower than in patients with subclinical CA involvement. The levels of FG and hsCRP, as inflammation indicators, were higher in patients with severe coronary atherosclerosis in comparison with patients without hemodynamically significant CA atherosclerosis (group 1 and 2).

Glucose and insulin values, reflecting the carbohydrate metabolism activity, was higher in patients with any CA atherosclerosis (group 2 and 3), compared with those without coronary atherosclerosis (group 1). Among visceral adipose tissue

Table 2

Univariate and multivariate logistic regression models for determining coronary atherosclerosis of any severity (groups 2 and 3)

Biochemical parameters	Univariate analysis		Multivariate analysis	
	OR (95%; CI)	p	OR (95%; CI)	p
Glucose, mmol/l	2,44 (1,34-4,47)	0,004	2,17 (1,15-4,11)	0,017
Creatinine, μmol/l	2,37 (1,33-4,22)	0,003	2,45 (1,35-4,52)	0,004
hsCRP, mg/l	2,80 (1,36-5,76)	0,005	2,83 (1,37-6,41)	0,008
Adiponectin, μg/ml	0,71 (0,40-1,25)	0,232	0,51 (0,27-0,96)	0,037

Note: glucose, mmol/L ⩾6,1 (1), <6,1 (0); creatinine, μmol/l ⩾73 (1), <73 (0); hsCRP, mg/l ⩾1 (1), <1 (0); adiponectin, μg/ml <8 (1), ⩾8 (0).
Abbreviations: CI — confidence interval, hsCRP — high-sensitivity C-reactive protein, OR — odds ratio.

Table 3

Univariate and multivariate logistic regression models for determining severe coronary atherosclerosis (group 3)

Biochemical parameters	Univariate analysis		Multivariate analysis	
	OR (95%; CI)	p	OR (95%; CI)	p
Glucose, mmol/l	2,87 (1,60-5,15)	0,000	2,41 (1,31-4,43)	0,005
Creatinine, μmol/l	3,03 (1,63-5,62)	0,000	2,79 (1,47-5,33)	0,002
hsCRP, mg/l	3,83 (1,42-10,39)	0,008	3,48 (1,24-9,77)	0,018
Adiponectin, μg/ml	1,61 (0,91-2,85)	0,103	1,33 (0,72-2,45)	0,368

Note: glucose, mmol/L ⩾6,1 (1), <6,1 (0); creatinine, μmol/l ⩾73 (1), <73 (0); hsCRP, mg/l ⩾1 (1), <1 (0); adiponectin, μg/ml <8 (1), ⩾8 (0).
Abbreviations: CI — confidence interval, hsCRP — high-sensitivity C-reactive protein, OR — odds ratio.

metabolism parameters, adiponectin and leptin were considered. The highest leptin values were obtained in group 2, and the lowest — in group 3. Creatinine levels increased from group 1 to 3. Lower NO_X values were obtained in patients with subclinical CA atherosclerosis, and higher values — in those without CA atherosclerosis compared with the group of severe CA atherosclerosis.

To determine the contribution of blood parameters to the likelihood of CA atherosclerosis and its severity, logistic regression was used; at the same time, significant differences between the groups in the analyzed blood parameters were taken into account in univariate and multivariate models (Table 1).

Univariate analysis with the inclusion of above biochemical parameters revealed that an independent contribution to the diagnosis of severe coronary atherosclerosis (group 3) is made by an increased levels of HDL-C >1 mmol/L in men (p=0,006) and >1,2 mmol/L in women (p=0,002), non-HDL cholesterol >2,2 mmol/L (p<0,001), glucose ⩾6,1 mmol/L (p=0,000), hsCRP ⩾1 mg/L (p=0,008) and creatinine ⩾73 μmol/L (p<0,001). When diagnosing CA atherosclerosis of any severity, the following parameters maintain its value in univariate models: glucose ⩾6,1 mmol/L (p=0,004), hsCRP ⩾1 mg/L (p=0,005), creatinine ⩾73 μmol/L (p=0,003), and NO_X <36 μmol/L (p=0,001). However, multivariate models that take into account various combinations of lipid metabolism parameters, as well as their combinations with other biochemical indicators, turned out to be insignificant neither for detecting CA atherosclerosis, nor for determining its severity (p>0,05).

At the same time, models including glucose, creatinine, hsCRP, and adiponectin turned out to be significant. According to univariate analysis (Table 2), which determines the independent contribution of each parameter to the assessment of presence and severity of CA atherosclerosis, all included indicators, except for adiponectin, were significant.

The multivariate model, including the above parameters (Table 3), turned out to be significant both for the detection of atherosclerosis of any severity (group 1 and 2) (p<0,001), and the detection of severe coronary involvement (group 3) ($p=10^{-4}$).

Given the multifactorial etiology of atherosclerosis, the close conjugation of biomarkers with each other and their mutually potentiating effect, as well as the results of univariate and multivariate analysis, we have formed a multivariate biochemical model (MVM) that allows non-invasive diagnosis of CA atherosclerosis. The following biomarkers were included in the MVM: glucose, creatinine, hsCRP,

Table 4
MVM scoring of biochemical deviations

Biochemical parameters	Score
Glucose, mmol/l	⩾6,1 mmol/l — 1 <6,1 mmol/l — 0
Creatinine, μmol/l	⩾73 μmol/l — 1 <73 μmol/l — 0
hsCRP, mg/l	⩾1 mg/l — 1 <73 mg/l — 0
Adiponectin, μg/ml	<8 μg/ml — 1 ⩾8 μg/ml — 0

Abbreviation: hsCRP — high-sensitivity C-reactive protein.

Table 5
Determination of CA atherosclerosis severity according to MVM

MVM, total score	Group
0-2	Intact coronary arteries (no CA atherosclerosis)
3-4	CA atherosclerosis of any severity (plaques in CA ⩾20%)

Abbreviation: CA — coronary arteries.

adiponectin. The deviation from the norm of one biochemical parameter was estimated at 1 point. Thus, the total MVM can range from 0 to 4 points (Table 4).

The ROC analysis was used to assess the MVM significance for diagnosis of CA atherosclerosis; a cut-off point of 2 was found. MVM >2 points with a sensitivity of 72% indicated the CA atherosclerosis of any severity, and with a specificity of 62,5%, it was ruled out. Using the MVM data and a cutoff point of 2, a binary logistic regression model was built, according to which, with a MVM >2, the likelihood of detecting any CA atherosclerosis increases by 2,1 times (95% CI, 1,2-3,8; p=0,010), severe atherosclerosis — by 4,7 times (95% CI, 1,9-12,0; p=0,001). MVM ⩽2 points increased the likelihood of detecting intact CAs by 2,8 times (95% CI, 1,4-4,9; p=0,002). The interpretation of the results depending on total MVM score is presented in Table 5.

Discussion

The study of biomarkers of key pathophysiological mechanisms of atherogenesis is a promising direction, since their action is carried out at the molecular-cellular level and covers all stages of atherosclerosis development.

We considered markers of lipid and carbohydrate metabolism, hemostasis system, inflammatory mediators, metabolic products of visceral adipose tissue, and the end product of creatine-phosphate reaction.

The search for atherosclerosis markers, lipid metabolism parameters are traditionally studied. Despite the fact that about half of cardiovascular events occur in patients with normal lipid profile, dyslipidemia continues to occupy the leading place among CVD RFs, and its correction is the primary task of treating patients with high and very high CVR [13]. In this regard, we analyzed the main lipid profile parameters. It turned out that in the examined cohort of patients, a less atherogenic lipid profile was observed in patients with severe CA atherosclerosis (group 3), which is probably due to statin therapy. The created univariate and multivariate regression models, including various lipid metabolism indicators, as well as their combination with other biomarkers, was insignificant (p>0,05).

The analysis of relationship between disorders of insulin-dependent glucose uptake by cells showed that glucose >6,1 mmol/L and adiponectin <8 μg/ml reliably indicate CA atherosclerosis in patients. Our results are consistent with the literature data, which show that patients with atherosclerosis are significantly more likely to have metabolic disorders [18-20].

Taking into account the pathogenetic aspects of atherosclerosis associated with chronic inflammation, we examined such indicators as FG and hsCRP. These biomarkers were not chosen due to evidence-based medicine and practical significance [21-23]. According to research data, an increased FG level is significant diagnostic and prognostic marker of atherosclerosis, in which a number of pronounced hemostatic disorders are associated with complications and higher cardiovascular mortality [24, 25]. According to literature data, the level of hsCRP is independently associated with atherosclerosis severity and stenosis area. However, the rationale of using hsCRP to detect subclinical atherosclerosis is not fully clear [23]. A meta-analysis of 22 studies showed that hsCRP concentration ⩾3,0 mg/L was associated with a 60% probability with coronary artery disease development. At the same time, for cardiovascular risk stratification, hsCRP ⩾1,0 mg/l is considered as high [24]. The study results showed a significant relationship between FG and hsCRP not only with the presence, but also with the severity of CA atherosclerosis.

Chronic kidney disease is also associated with an increased CVD risk independently of other RFs. Decreased GFR increases the cardiovascular death risk. According to the European clinical guidelines on cardiovascular disease prevention in clinical practice [25], in the presence of chronic kidney disease with

GFR <30 ml/min, a patient is classified with very high risk, <60 ml/min — a high risk. Since the creatinine level is used in calculating GFR, we analyzed its possible associations with CA atherosclerosis and its severity, both in isolation and in combination with other biomarkers. It turned out that the level of creatinine is positively associated not only with the presence, but also with CA atherosclerosis severity.

The feasibility of assessing NO_X level to assess the endothelial NO-producing activity has been confirmed in studies both in laboratory animals and in humans [26, 27]. Literature data show that NO_X is associated not only with cardiovascular mortality, but also with all-cause mortality [28]. There is evidence that NO_X is associated with atherosclerosis [29]. In our study, when analyzing the blood concentration of NO_X, we found a cut-off point of 36 μM/L and revealed a negative correlation of this biomarker with the presence and severity of CA atherosclerosis. However, given the small sample and the complexity of NO_X determination, this indicator was not included in multivariate regression models. This result requires further study in a larger cohort.

Based on this analysis of blood biomarkers, an MVM was developed, which makes it possible to verify coronary atherosclerosis. However, the potential of this model for verifying the atherosclerosis severity are limited. This is most likely due to the fact that detected deviations are associated with the atherosclerosis initiation, and during its progression they do not change significantly.

Conclusion

Thus, blood biochemical parameters were selected for diagnostic scale, which makes it possible to verify patients with and without CA atherosclerosis. The quantitative determination of glucose, creatinine, hsCRP and adiponectin levels included in MVM is quite accessible, which allows it to be widely used in practical health care. According to the obtained MVM score, patients can be reclassified according to CA atherosclerosis likelihood and, if necessary, send them to additional studies to confirm the diagnosis and determine atherosclerosis severity.

Relationships and Activities: none.

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