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Level of FABP3, FABP4, Nt-proBNP and Total Cardiovascular Risk in the Population of Central Kazakhstan

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Abstract

AIM: The study analyzed the level of cytokines playing the significant role in the diagnosis of circulatory system diseases and total cardiovascular risk.

MATERIAL AND METHODS: The study involved 1,244 residents of Karaganda region. We had studied baseline participant characteristics, in addition to calculating the total cardiovascular risk and assessment of Fatty Acid Binding Proteins 3 (FABP3), Fatty Acid Binding Proteins 4 (FABP4) and N-Terminal Prohormone of Brain Natriuretic Peptide (NT-proBNP) level.

RESULTS: The results showed the combination of high cardiovascular risk (CVR) with increased titers of cardiac markers, reflecting common pathogenic mechanisms in its development, among residents of Karaganda region.

CONCLUSION: The combination of high CVR with the increased titers of cardiac markers showed common pathogenic mechanisms in its development, and support the diagnostic and prognostic value of these parameters among residents of Karaganda region, and also reflects the possibility to include these cardiac markers in the program of screening survey of population for early prevention of cardiovascular disease and its complications.

Introduction

Currently, according to the data of many epidemiological studies cardiovascular disease remains the leading cause of death in our country and abroad [1-7]. Scientists interested the problem of predicting of complications of cardiovascular disease (CVD) for a long time. One of its decisions was the conducting of the large study by the experts of the European Society of Cardiology. Prospective studies with the participation of more than 205 thousand patients were conducted in 12 European countries, including Russia (State Research Center for Preventive Medicine) [8].

The result of this 27-years study was the formation of the European model SCORE (Systemic Coronary Risk Evaluation). Blood cardiac markers found the wide use, reflecting the most of section of pathophysiological process and playing the definite prognostic role, in addition to determining of total cardiovascular risk for early diagnosis of CVD [9-15]. The value of each of the selected cardiac markers studied in detail in the pathogenesis and diagnostics of arterial hypertension, congestive heart failure, atherosclerosis, myocardial infarction and stroke. However, there is insufficient data on the combination of the levels of FABP3, FABP4 and NT-proBNP with a total risk of cardiovascular disease.

The aim of our work was to analyse the role of FABP3, FABP4 and NT-proBNP in the diagnosis of total cardiovascular risk (CVR).

Material and Methods

In addition to determining the levels of FABP3, FABP4 and NT-proBNP, the following work with the population was conducted: survey, anthropometry, blood pressure measurement, determination of blood glucose and total cholesterol. It was conducted the immunological multiplex study of the blood of 1,244 people aged 18-65, including 872 women and 372 men. Pregnant women, people with decompensated cardiac, endocrinology, nephrology pathologies, as well as persons with severe mental illness and oncological diseases were excluded from the study. The index of total cardiovascular risk SCORE was calculated for all examined people [8].

Determination of cardiac markers was carried out by immunofluorescence method using XMap technology on the Bioplex 3D with Human CVD Magnetic Bead Panel 1. We determined the levels of FABP3, NT-proBNP, FABP-4. FABP3 is heart form of protein, binding the fatty acid, and it is detected in patients with acute myocardial infarction, heart failure. It evidences of permanent myocardium damage and is associated with worsening prognosis and high mortality [16, 17]. N-terminal fragment of brain natriuretic peptide (NT-proBNP) is evaluated as a predictor of cardiac events and lethal outcomes in acute and chronic heart failure [18], and also plays a significant role in the formation of atherosclerosis [9, 19]. Increased level of FABP-4, is associated with obesity, insulin resistance, hypertension, atherosclerosis [12, 20-21].

Statistical analysis

For statistical analysis, we used IBM SPSS Statistics, Version 24. Data analysis was performed with the significance level $\alpha = 0.05$. Check on the normal distribution of quantitative data was performed using the Kolmogorov-Smirnov test. Description of the quantitative data was carried out bofy median and quartiles. For qualitative data, it was calculated the proportion of individuals with traits of interest and 95% confidence interval of the proportion calculated by Klopper-Pearson method. We used U criterion of Mann-Whitney to compare the independent samples.

Results

Table 1 and 2 show the baseline characteristics of the examined people depending on gender. The median of age women included in the study was more than median of male (56.00, Q_{25} – 51.00; Q_{75} – 61.00 and 52.00, Q_{25} – 45.00; Q_{75} – 59.00, $p < 0.001$). Assessing the BMI noted that both populations are overweight, and women BMI was significantly greater (29.38, Q_{25} – 25.96; Q_{75} – 33.67 and 27.22, Q_{25} – 24.00; Q_{75} – 30.49, $p < 0.001$).

Table 1: Qualitative baseline participant characteristics

	Men				Women				p-value
	N	Median	Q_{25}	Q_{75}	N	Median	Q_{25}	Q_{75}	
Age, years	372	52.00	45.00	59.00	872	56.00	51.00	61.00	0.000
BMI, kg/m^2	370	27.22	24.00	30.49	867	29.38	25.96	33.67	0.000
Systolic BP, mm Hg	369	130.0	120.0	140.0	869	130.0	120.0	145.0	0.072
Cholesterol, mmol/L	366	4.975	3.870	5.900	866	5.140	3.870	6.120	0.056

The proportion of women with hypertension was much higher than men – 59.08% and 37.20%, respectively ($p < 0.001$), though the median of systolic arterial pressure had no differences. Total cholesterol levels were increased in both groups, but higher rates were observed in women (5.140, Q_{25} – 3.87; Q_{75} – 6.12 and 4.97, Q_{25} – 3.87; Q_{75} – 5.90, $p = 0.005$). Also, the higher percentage of smokers was observed in male population (45.78% and 10.76% respectively, $p < 0.001$).

Table 2: Quantitative baseline participant characteristics

	Men			Women			
	N	%	95% CI	N	%	95% CI	p-value
Arterial hypertension	138	37.20	32.26;42.34	514	59.08	55.73;62.37	0.000
Smoking	168	45.78	40.60;51.03	93	10.76	8.78;13.02	0.000

The results of immunological studies of blood for cardiac markers are described in tables 3-5. The results of the general population (Table 3) show that the median of values of all three cardiac markers was significantly higher in the group of high CVR ($p < 0.05$).

Table 3: Comparison of cardiac markers indicators (pg/ml) in the groups with high and low total cardiovascular risk in the general population

	SCORE, high risk				SCORE, low risk				p-value
	N	Median	Q_{25}	Q_{75}	N	Median	Q_{25}	Q_{75}	
FABP 3	942	2099.06	1449.08	3088.71	302	1686.71	1153.73	2432.48	0.000
NT-proBNP	942	78.63	49.29	109.25	302	67.91	44.25	94.05	0.002
FABP 4	942	15417.30	9148.77	24441.47	302	14587.26	8855.39	20493.94	0.019

Table 4 shows the results of comparing of cardiac markers level in men – only the NT-proBNP level was significantly higher in the group of high CVR (78.49, Q_{25} – 50.58; Q_{75} – 110.28 and 65.91, Q_{25} – 43.99; Q_{75} – 90.10, $p < 0.05$). The differences were not observed in FABP 3 and FABP 4.

Table 4: Comparison of cardiac markers indicators (pg/ml) in the groups with high and low total cardiovascular risk in men

	SCORE, high risk				SCORE, low risk				p-value
	N	Median	Q_{25}	Q_{75}	N	Median	Q_{25}	Q_{75}	
FABP 3	304	1952.23	1396.90	2936.02	68	1676.68	1336.16	2290.45	0.065
NT-proBNP	304	78.49	50.58	110.28	68	65.91	43.99	90.10	0.039
FABP 4	304	14085.63	7711.29	19704.68	68	14685.49	9903.65	21687.69	0.552

In the female population (Table 5), with high probability, the median of titers FABP 3 (2204.09, Q_{25} – 1492.74; Q_{75} – 3277.31 and 1693.39, Q_{25} – 1101.83; Q_{75} – 2442.27, $p < 0.001$), NT-proBNP (78.66, Q_{25} – 49.00; Q_{75} – 108.39 and 68.25, Q_{25} – 44.25; Q_{75} – 98.13, $p < 0.05$) and FABP 4 (16791.89, Q_{25} – 9961.06; Q_{75} – 26256.08 and 14544.90, Q_{25} – 8823.34; Q_{75} – 20112.41, $p < 0.001$) was higher in the group with high total cardiovascular risk.

Table 5: Comparison of cardiac markers (pg/ml) in the groups with high and low total cardiovascular risk in women

	SCORE, high risk				SCORE, low risk				p-value
	N	Median	Q_{25}	Q_{75}	N	Median	Q_{25}	Q_{75}	
FABP 3	638	2204.09	1492.74	3277.31	234	1693.39	1101.83	2442.27	0.000
NT-proBNP	638	78.66	49.00	108.39	234	68.25	44.25	98.13	0.021
FABP 4	638	16791.89	9961.06	26265.08	234	14544.90	8823.34	20112.41	0.000

Discussion

We investigated the level of cardiac form of protein, binding the fatty acids 3 (FABP3), N-terminal prohormone of natriuretic peptide (NT-pro-BNP) and protein, binding fatty acids 4 (FABP 4) in people with low and high total cardiovascular risk. The main results of this study showed that the median of all three cardiac markers was higher in the group with high CVR. Differences were observed only in the male population, where the rate of only one substance (NT-proBNP) had the significantly greater median in the group of persons with high CVR.

We chose FABP3 as one of the cardiac markers localised in cardiac myocytes. It provides the transport of fatty acids, as one of the most important energy resources of heart, to mitochondria. Also, it protects against free radicals accumulated as a result of myocardial ischemia [13, 22-24]. Thus, the higher titers of this protein in the peripheral blood are one of the earliest and specific indicators of myocardial damage of various origins, whether ischemia, cardiomyopathy, heart failure [17, 20, 25-26].

The results of our study showed that in the group women with high total CVR the median of titers of FABP3 significantly higher than in the low-risk group, in a case of the male population it was no differences. This indicates about damaged myocardium in the group with high CVR and reflects the diagnostic and prognostic value of this indicator in patients with cardiovascular disease. This can also be explained by the high number of women in the study and by the results of the comparison of general characteristics, in which more percentage of persons were women with hypertension and the highest median of total cholesterol.

The second cardiac marker, used in this study, was NT-pro-BNP. The peptide is released in response to tension and hypoxia of cardiomyocytes and is used as a diagnostic and prognostic indicator of chronic heart failure, the risk of fatal complications (myocardial infarction, stroke) [18], and also has an effect on the vascular wall, which allows us to estimate the risk of development of atherosclerosis and hypertension [9, 11, 19, 27]. The analysis of the level of titles of NT-pro-BNP shows that the median value in the male and female populations has differences. This may indicate damaged myocardium in the studied group with high CVR and reflects the diagnostic and prognostic value of this indicator in patients with cardiovascular disease.

The last cardiac marker, which was used in the study, was FABP 4. This substance is adipokine, secreted by adipose tissue (adipocytes), and is involved in the regulation of energy metabolism and inflammation process [12]. According to the results of several large studies, the increased titers of this marker associated with obesity, metabolic syndrome, and the risk of developing of the resistance to insulin, diabetes mellitus of type 2 and as a consequence increasing cardiovascular risk [12-14, 22]. In our study, the median titers of the protein are higher in women with high CVR. In the male population, the differences between these values and the level of CVR are not revealed. These results correlate with the presence of large BMI values in the female population.

As a result, the combination of high CVR with the increased titers of cardiac markers showed common pathogenic mechanisms in its development, and support the diagnostic and prognostic value of these parameters among residents of Karaganda region, and also reflects the possibility to include these cardiac markers in the program of screening survey of population for early prevention of cardiovascular disease and its complications.

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