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HIGH PREVALENCE OF ARTERIAL HYPERTENSION AND THE AFFECTION OF TARGET ORGANS IN THE NATIVES OF YAKUTIA WITH VERIFIED CORONARY ATHEROSCLEROSIS - POSSIBLE LINKS WITH INSULIN RESISTANCE

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Summary

A comparison of the data of selective angiography, computed tomography and risk factors in patients with coronary atherosclerosis is carried out. Analysis of risk factors in patients revealed that among indigenous men at less severity of coronary artery atherosclerosis, low values of atherogenic lipids, less frequency of obesity (by BMI criterion) a high frequency of hypertension and myocardial hypertrophy was revealed.

Keywords: atherosclerosis of coronary arteries, risk factor, arterial hypertension, myocardial hypertrophy, indigenous and non-indigenous population of Yakutia.

According to population-based study conducted in Yakutia, hypertension in patients with coronary artery disease detected in 74,7% cases. However, effectively treated, only 14% of men and 28,8% of women - patients with hypertension. According to statistic (Yakutia) in the past 5 years has been an increase incidence of primary diseases of the circulatory system in 1,9 times, including hypertension - a 127%, angina - 75%, cerebrovascular disease - by 106%.

One should pay attention to the growth and death rate of the myocardial infarction and the stroke among indigenous population with the obvious tendency of "rejuvenation" of the given pathology.

It is known that hypertension is the main target of the myocardium, which develops hypertrophy of the left ventricular (HLV) and represents an important cardiovascular risk factor, along with hypertension, diabetes mellitus, hypercholesterolemia and smoking.

Objective: To study of risk factors and myocardial hypertrophy in patients with verified coronary atherosclerosis among indigenous **population** of Yakutia.

Materials and methods

The analysis of patients' clinical-tool indicators was done at cardiology and cardiosurgery republic hospital №1 - NCM, Yakutsk. Patients were made SCAG during the period 2004-2007 (n=1233). Patients arrived from the central regional hospitals from all 35 regions of Yakutia. We didn't analyze patients with atherosclerosis of coronary arteries in the combination of heart defect. SCAG was not done when the patient had unstable stenocardia presence, characteristic dynamics of cardiospecific enzymes in peripheral blood (Creatinine-kinase-MB, troponine) in the combination with typical electrocardiographic changes and status anginosus. Our work results present the analysis of 568 patients with the verified atherosclerosis of coronary arteries (CA). The examined patients have been divided into two groups for the comparative analysis:

1st – representatives of indigenous population (n=286), males – 266 (middle age $54,2 \pm 0,5$ years); females – 20 (middle age $55,0 \pm 1,6$ years);

2nd – representatives of non-indigenous population (n=282), males – 234 (middle age $52,6 \pm 0,6$ years); females – 48 (middle age $55,3 \pm 1,1$ years).

Indigenous population are Yakuts, Evenks, Chukchis and other minorities of Yakutia, non-indigenous – Russians, Ukrainians, Byelorussians and other nationalities constantly living in Yakutia.

Arterial hypertension (AH) was accepted at blood pressure $> 140/90$ mmHg level during several years, on the anamnesis base and its documentary increase and taking of hypertension drugs within several years.

Diabetes 2 type was diagnosed on documentary data at the endocrinology clinic. All patients with type 2 diabetes in the anamnesis received hypoglycemia therapy.

Anthropometrical examination provided measurement of patients' height and weight by a standard technique. The body weight was estimated on the basis of calculation of Kettle II index by formula: $\text{weight (kg)} / \text{growth (m}^2\text{)}$. For body's

overweight was accepted the MBI value ≥ 25 and < 30 kg/m², obesity was registered at MBI ≥ 30 kg/m².

The regular smoker was considered a man smoking at least 1 cigarette a day within 12 months. Family predisposition to cardiovascular disease (CVD) included the information about AH, MI and brain stroke presence the relatives' of the 1st line relationship.

Selective Coronary angiography (SCAG) was done by standard Judkins technique on the device «Axiom. Artis BA» (Siemens, Germany). Coronary ateriographic classification of atherosclerotic arteries defects was used for determining the stenosis degree: 1 – 50 % gleam area of stenosis, 2 – stenosis from 50 to 75 %, 3-stenosis from 75 to 90 %, 4 – stenosis over 90 % (subclusion or occlusion).

Multispiral Computer Tomography (MCT) was done on the tomograph Somaton Sensation-4 (Siemens), determining the total calcium index (TCI) which was calculated by the integrated computer system of the quantitative automatic analysis by standard Agatston A.S. technique according to which coronary calcification was defined as the site size with maximum density more than 130 Haunsphilds units (HU).

Echocardiography was carried out by standard methods. All parameters were indexed to body surface area. The hypertrophy of the accepted value of LVMM ≥ 125 g/m² - for men, ≥ 110 g/m² - for women.

Statistical processing was done by standard package of SPSS program (version 13.0). Results were presented in the form of $M \pm m$, where M – a mean, m – a standard error of the mean. The basic studied indicators had abnormal character of distribution of studied indicators values that has allowed to check up distinctions reliability of average quantity indicators between two ethnic groups by nonparametric Mann-Whitney test. Quality indicators were checked by Student's t-test.

Results

Table 1. Frequency and degree of stenosis of coronary arteries among inhabitants of Yakutia, (%)

Degree of stenosis of coronary arteries	Frequency of defects with various degree of stenosis					
	Males		p _{I-NI}	Females		p _{I-NI}
	I (n=266)	NI (n=234)		I (n=20)	NI (n=48)	
Degree of stenosis <50 %	33 (12,5)	28 (12)	0,880	2 (10,0)	6 (12,5)	0,771
Degree of stenosis 50-75 %	48 (18,0)	27 (11,5)	0,042	7 (35,0)	8 (16,7)	0,101
Degree of stenosis 75 - 90 %	76 (28,6)	52 (22,2)	0,105	4 (20,0)	14 (29,2)	0,437
Degree of stenosis > 90 %	109 (40,9)	127 (54,3)	0,003	7 (35,0)	20 (41,6)	0,610

Note: p_{I-NI} – the comparison between native and non-native patients

The frequency and degree analysis (Table 1) of stenosis of CA has shown that indigenous males had stenosis - 50-75 % (18 % vs 12 % ; p=0,042), while non-indigenous – more often stenosis - 90 % (41 % vs 54 %; p=0,003). Significant distinctions have not been revealed among females. Among women, significant differences were detected. The quantity analysis of the affected arteries has shown, that one-vascular defects are met more among indigenous males (32 vs 12 %; p=0,001), three-vascular and more – in non-indigenous (55 vs 40 %; p=0,001). The average quantity of the affected arteries was $2,1 \pm 0,1$ and $2,4 \pm 0,1$ and was significantly less in natives (p=0,001). Significant distinctions has not been revealed among women, probably it was connected with the small quantity of the examined patients.

In the study of the total calcium level of the index according to its average level of MCT was significantly lower among indigenous males than non-indigenous and has made $349,1 \pm 129,8$ vs $621,8 \pm 115,2$ units. respectively (p = 0.011) among women significant differences were revealed - $179,0 \pm 48,1$ vs $255,2 \pm 98,6$ units, p = 0.465, respectively, and are consistent with studies that showed a high correlation index of calcium in the coronary arteries with the degree of atherosclerotic lesions [12].

Thus, the results SCAG and MCT for Indigenous more likely than non-indigenous ethnic groups are identified lighter coronary arteries and is consistent with conducted in Yakutia pathomorphological studies [2]. It is believed that a lesser degree of atherosclerosis in the indigenous population is the result of centuries of selection, which they have formed a special, optimal for local conditions, the genotype of the cardiovascular system, which has close links with historical traditions, lifestyle and food does not predispose to the development of atherosclerosis.

Table 2. Risk factors of cardiovascular diseases among patients with atherosclerosis of coronary arteries in Yakutia

Risk factor	Males			Females		
	I (n=266)	NI (n=234)	p _{I-NI}	I (n=20)	NI (n=48)	p _{I-NI}
Arterial hypertension, %	245 (92,1)	187 (79,9)	0,001	20(100,0)	48(100,0)	
Number of patients with blood pressure levels $\geq$ 140 mm Hg on admission,%	207(77,8)	174(74,4)	0,365	13(65,0)	30(62,5)	0,846
Type 2 diabetes, %	51 (19,2)	53 (22,6)	0,360	5 (25,0)	13 (27,1)	0,860
Overweight,%	123 (46,1)	102 (43,6)	0,552	14 (70,0)	10 (20,8)	0,000
Obesity,%	82 (30,8)	92 (39,3)	0,047	4 (20,0)	32 (66,7)	0,000
Smoking,%	109 (41,0)	98 (41,9)	0,777	10 (50,0)	18 (37,5)	0,412
Burdened by history of cardiovascular disease,%	94 (35,3)	92 (39,3)	0,333	18 (90,0)	26 (54,2)	0,005

Note: p_{I-NI} – the comparison between native and non-native patients

The analysis (Table. 2) of risk factors has shown that AH is more often met among indigenous males than non-indigenous ($p = 0,001$).

Obesity was significantly less encountered among the indigenous than non-indigenous as among men ($p = 0,047$), and among women ($p = 0,001$). At the same time, indigenous women were significantly more frequently encountered overweight ($p = 0.000$), respectively. Indigenous females had more often the burdened CVD anamnesis, than non-indigenous ones (90 % vs 54,2 %; $p=0,005$). Both ethnic groups of males and females smoked equally often.

Table 3. Average levels of laboratory indicators at patients with atherosclerosis of coronary arteries in Yakutia

Indicator	Males, M±m			Females, M±m		
	I (n=266)	NI (n=234)	PI-NI	I (n=20)	NI (n=48)	PI-NI
TC, mmol/L	4,8±0,1	4,9±0,1	0,910	5,2±0,3	5,5±0,2	0,169
HDL, mmol/L	0,97±0,03	0,90±0,03	0,323	0,95±0,01	0,90±0,02	0,358
LDL, mmol/L	3,12±0,06	3,22±0,09	0,572	3,32±0,26	3,55±0,12	0,178
TG, mmol/L	1,45±0,03	1,56±0,04	0,030	1,53±0,08	1,64±0,06	0,106
Fasting glucose, mmol/L	5,82±0,14	5,81±0,13	0,198	5,6±0,4	6,4±0,5	0,575
Fibrinogen, g/L	3,45±0,09	3,56±0,11	0,214	4,02±0,52	3,9±0,29	0,770

Abbreviation: TC- total cholesterol; HDL- high-density lipoproteins; LDL- low-density lipoproteins; TG-triglycerides

Comparative analysis results of lipid profile indicators established (Table 3) that TC, LDL levels were lower among indigenous population, HDL – higher. However TG level was significantly lower, than among non-indigenous (1,45±0,03 mmol/L vs 1,56±0,04 mmol/L; p=0,030), respectively.

Both ethnic groups of males and females glucose and fibrinogen levels men and women did not differ.

Table 4. Average levels of structural-functional cardiac parameters at patients with atherosclerosis of coronary arteries in Yakutia, M±m

Parameters	Indigenous		Non-indigenous		PI-NI
	M±m	95% CI	M±m	95%CI	
Males					
	n=236		n=214		
LA index,sm/m ²	2,05±0,03	1,99-2,09	1,93±0,02	1,89-1,97	0,002
IST index, sm/m ²	0,62±0,01	0,59-0,64	0,57±0,01	0,56-0,59	0,002
PLVT index, sm/m ²	0,64±0,01	0,63-0,66	0,59±0,01	0,58-0,61	0,001
LVESD index, sm/m ²	2,03±0,03	1,97-2,09	1,88±0,29	1,82-1,94	0,001
LVEDD index, sm/m ²	3,01±0,03	2,95-3,07	2,79±0,29	2,73-2,85	0,001
LVMM index, g/m ²	141,0±2,4	136,2-145,8	132,6±2,8	127,1-138,0	0,003
LVESV index,ml/m ²	82,2±1,7	78,7-85,6	76,7±1,7	73,3-80,1	0,015
LVEDD index, ml/m ²	34,2±1,3	31,6-36,7	31,8±1,2	29,4-34,2	0,113
SV, ml/m ²	47,1±0,8	45,5-48,7	43,8±0,6	42,6-44,9	0,002
CO, l/min/m ²	3,0±0,1	2,9-3,2	3,0±0,1	2,9-3,2	0,147
EF, %	59,7±0,7	58,3-61,1	59,4±0,8	57,8-61,1	0,723
Females					
	n=20		n=48		PI-NI

LA index, sm/m ²	2,34±0,09	2,11-2,38	2,26±0,08	2,11-2,30	0,443
IST index, sm/m ²	0,65±0,21	0,62-0,72	0,59±0,28	0,61-0,69	0,360
PLVT index, sm/m ²	0,63±0,02	0,60-0,71	0,58±0,04	0,60-0,67	0,706
LVESD index, sm/m ²	2,09±0,10	1,97-2,36	2,09±0,09	1,88-2,29	0,178
LVEDD index, sm/m ²	3,05±0,11	2,93-3,32	3,05±0,08	2,81-3,06	0,106
LVMM index, g/m ²	130,6±7,5	113,8-145,8	110,3±8,7	113,1-140,7	0,459
LVESV index, ml/m ²	72,5±1,4	69,5-75,6	66,7±2,8	61,1-72,4	0,187
LVEDV index, ml/m ²	32,8±2,4	27,7-37,9	31,5±2,7	26,1-36,8	0,225
SV, ml/m ²	44,4±1,8	40,7-48,2	42,8±1,2	40,4-45,1	0,757
CO, l/min/m ²	2,7±0,1	2,5-2,9	2,6±0,1	2,4-2,9	0,240
EF, %	61,5±2,3	56,9-66,3	59,8±1,4	56,9-62,5	0,492

Abbreviation:

LA - left atrial

IST – the interventricular septum thickness

PLVT – the posterior septum thickness

LVESD – the left ventricular end-systolic diameter

LVEDD – the left ventricular end-diastolic diameter

LVMM - left ventricular myocardial mass

LVESV – the left ventricular end- systolic volume

LVEDV – the left ventricular end-diastolic volume

SV – the stroke volume

CO – cardiac volume

EF – the ejection fraction

CI – confidence interval

Indexed indicators were significantly higher among indigenous men than non-indigenous (Table 4). The mean value of EF did not differ. HLIV by echocardiographic criteria of LVMM found more commonly in indigenous than non-indigenous ($p = 0,001$).

Discussion

We examined patients among the indigenous, particularly among men, with less severity of coronary artery atherosclerosis, low values of atherogenic lipids, lower incidence of obesity have a high incidence of hypertension.

Considering the given fact it is possible to speak about low adherence of native population treatment. Transport inaccessibility, far distances from the central regional hospitals, lack of highly qualified doctors, and social -cultural level of patients can be the cause. Low adherence to treatment is associated with poor prognosis. On the other - transportation inaccessibility, remoteness from the central district hospitals, shortages of qualified doctors, as well as social and cultural level of patients.

At the same time, it should be noted that hypertension - one of the most common diseases of adaptation [1], particularly, during which depend on many factors, including psychosocial [3] and heliophysical factors [8, 11]. Studies in recent years on human adaptation in the North have convincingly shown that biosocial fee for adaptation to the indigenous population in the North no less, and sometimes significantly greater than for non-indigenous population [6, 7, 10].

Last epidemiological researches in Yakutia show that the metabolic syndrome (MetS) is becoming the widespread phenomenon among indigenous population of Yakutia and the most frequent variant is a combination AO+AH+dislipidemia (48,8 %) and AO+AH+hyperglycemia/diabetes 2 types (37,9 %) and less often there is variant MetS without AH (4,5 %) [9].

Hypertrophy of the left atrium (HLA) and HLV have surveyed our patients demonstrated significantly more frequently among men in the indigenous as the ECG, and echocardiographic criteria. High AH prevalence among natives in Yakutia has been noted in other researches [13]. Initially, HLV and LLA of in

patients with hypertension is a compensatory reaction. Myocardial hypertrophy - is the first step in the development of congestive heart failure, cardiac arrhythmias, and coronary heart disease. In patients with atrial fibrillation, the main and sometimes only finding may be hypertrophy and dilatation of the atria.

Thus, the patients examined among men in the indigenous detected more frequently hypertensive and HLV, HLA with less severity of their coronary artery atherosclerosis, low values of atherogenic lipids and lower incidence of obesity. In the development of this phenomenon is a possible pathogenetic role played by insulin resistance (IR).

Insulin resistance (IR) - a deterioration of the hormone insulin in the cells to insulin-sensitive tissues (skeletal muscle, liver and adipose tissue), the severity of which may be different - from the slight decline in the effect of insulin on target cells to an almost complete lack thereof. IR is a common pathogenetic factor development of clinical and laboratory disorders such as impaired glucose tolerance, hyperinsulinemia, elevated levels of triglycerides and VLDL (very low density lipoprotein), reduced HDL cholesterol in the blood plasma, arterial hypertension.

State IR and compensatory hyperinsulinemia may occur for a very long period of time, while blood glucose levels remain normal. However, many persons who have insulin resistance, especially against the presence of certain genetic factors over time is the depletion of the function β -insular apparatus of the pancreas and developing so-called relative deficiency of insulin. Hyperinsulinemia, which performs a compensatory function and aims to maintain normoglycemia, while at the same time, and is damaging in nature. So, we have shown that elevated levels of insulin leads to increased concentrations of sodium in the blood and the activity of the sympathetic nervous system, which in turn predisposes to increased blood pressure and the development of hypertension. Indeed, the relationship between IR and high blood pressure found in many studies [4,5].

The obtained data testify the mechanism specificity development of coronary atherosclerosis complications among native nationalities of Yakutia. Of particular practical importance is his association with a large indigenous population with hypertension, hypertrophy

of the left atrium and left ventricle. Perhaps a pathogenic role in this matter a high prevalence of insulin resistance among the indigenous population of Yakutia.

Conclusions

1. Analysis of risk factors in patients with verified coronary atherosclerosis revealed that among indigenous men at lower severity of coronary artery atherosclerosis, low values of atherogenic lipids, a lower frequency of obesity (BMI criterion) a high prevalence of hypertension and associated hypertrophy of the left heart was revealed.
2. In the development of this phenomenon in the indigenous population of Yakutia the high prevalence of insulin resistance in them may be important.

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