Factors of coronary artery disease unfavorable clinical course in Yakutia
(results of 7-year follow-up)

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In our research we have tried by means of complex clinical-functional and angiographic inspections to ascertain factors of unfavorable CAD (coronary artery disease) course in the remote 7-year period.

Keywords: CAD fatal outcomes, clinical-anamnestic risk factors of CAD, LV structural-functional indexes, degree of atherosclerotic lesion of coronary arteries, survival rate of CAD patients.

Background: Last decade among the population of Yakutia steady growth of CAD (coronary artery disease) morbidity is marked. Main causes of death rate of the population of Republic are illnesses of blood circulation system, more than half of them are coronary artery diseases [1]. Results of numerous epidemiological researches proved the significance of risk factors contribution to cardiovascular morbidity and mortality [2,3]. However, in the Yakut population, prognostic influence of risk factors on fatal outcome of CAD was not studied.

Research objective: To define connection of clinical-anamnestic data, functional and angiographic indexes of severity of CA atherosclerotic lesion with development of fatal cases of CAD course in patients of native and non-native nationality of Yakutia for the 7-year follow-up period.

Methods: 126 patients with CAD, verified angiographically since 2000 for 2001, have been included in research. For assessment of clinical state complaints, the anamnesis, the data of objective research of patients have been analyzed. The old myocardial infarction (MI), acute cerebral circulation impairment (ACCI), diabetes mellitus (DM), arterial hypertension (AH) and burdened heredity were taken into consideration. Data were received at poll, physical inspection of patients, and also on the basis of available medical documents, records in the clinical case record and out-patient card. The algorithm of research included: a biochemical laboratory blood test, electrocardiography (electrocardiogram), heart ultrasonic investigation (EchoCG), duplex ultrasonic investigation of carotids and vessels of the inferior extremities, Holter monitoring of electrocardiogram and selective coronary angiography (CAG) with ventriculography. CAG was performed in conditions of X-ray operation room on «Angioscop-33D with DCA Digitron Card» Siemens firm (Germany). Research was carried out under the practical standard by a puncture of a femoral artery according to Seldinger, by transfemoral access. For the characteristic of a state of coronal arteries the classification developed by J.S.Petrosyan and L.S. by Zingerman (1974) was used. On outcome of disease patients have been divided into 2 groups: the first- patients survived to the 7th year of follow-up - 110 (84 %), the second - the deceased - 16 (12,7 %). Among the deceased patients with CAD men - 87,5 %, women - 12,5 %.

Statistical processing was made with use of a package of statistical programs SPSS for Windows (version 17.0). Level $p < 0,05$ was considered as the test of significance.

Findings of investigation and discussion.

The patients who survived and not for the 7-year follow-up, were comparable on sex, body mass index, CAD risk factors, the experience of the ischemic and hypertensive anamnesis, CAD clinical manifestations: penetrating and non-penetrating myocardial infarction in the anamnesis, FC of stenocardia. However, CAD patients of the 2nd group in comparison with the

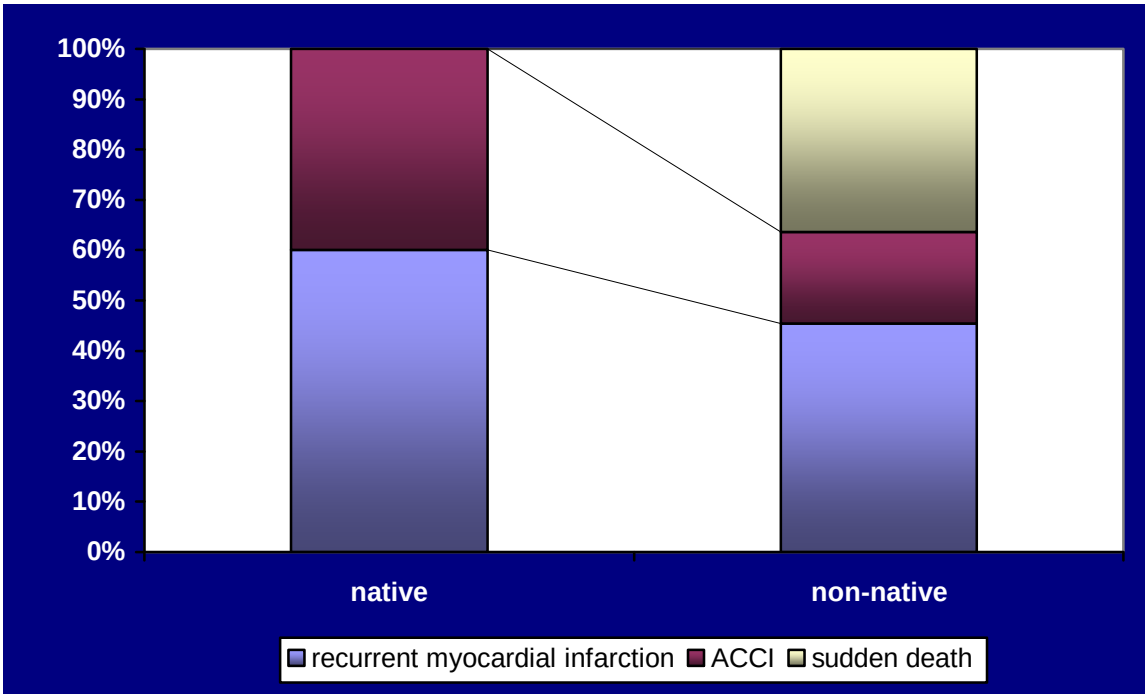
survived patients significantly more often initially have concomitant pathology - II type diabetes mellitus (p=0,023). It is possible to emphasise that in CAD patients presence of diabetes mellitus has affected on death rate for the 7-year follow-up (table 1).

Table 1

Relative initial clinical-anamnestic characteristic of groups of survived patients and the deceased for 7 –year follow-up

Index	I group patients-survivors (n=110)	II group died patients (n=16)	p
Age	56,75±0,64	51,38±1,61	0,328
Sex (m/f), person (%)	102 (92,7)/8 (7,3)	14 (87,5)/2 (12,5)	0,470
Body mass index, kg/м²	27,21±3,7	27,19±0,75	0,990
Body mass index above 25 kg/м², person (%)	79 (71,8)	12 (75)	0,791
CAD duration, years	4,60±0,31	5,13±0,68	0,544
Penetrating myocardial infarction (macrofocal), person (%)	73 (66,4)	12 (75)	0,449
Non-penetrating myocardial infarction (microfocal), person (%)	49 (44,5)	10 (62,5)	0,179
Stenocardia, person (%) FC-I FC-II FC-III	108 (98,2) 5 (4,5) 63 (57,3) 40 (36,4)	16 (100) 1 (6,3) 10 (62,5) 5 (31,3)	0,910
AH duration, years	6,96±0,72	10,44±2,53	0,104
Max. SAP, mm	169,95±2,72	165,94±7,87	0,605
Max. DAP, mm	100,50±1,35	97,50±3,10	0,424
Arterial hypertension, person (%) I d. II d. III d.	93 (84,5) 19 (17,3) 48 (43,6) 26 (23,6)	11 (68,8) 2 (12,5) 6 (37,5) 3 (18,8)	0,484
Hyperlipidemia, -“-	82 (74,5)	12 (75)	0,969
ACCI in anamnesis, -“-	4 (3,6)	2 (12,5)	0,120
Smoking, -“-	83 (87,3)	13 (81,3)	0,611
Diabetes mellitus, -“-	2 (1,8)	2 (12,5)	0,023
Burdened family anamnesis, -“- (in 2 and more relatives) Myocardial infarction Stroke Hypertension Diabetes mellitus	 81 (73,6) 27 (24,5) 30 (27,3) 72 (65,5) 6 (5,5)	 15 (93,8) 4 (25) 3 (18,8) 11 (68,8) 0 (0)	 0,078 0,969 0,469 0,795 0,338

The causes of CAD fatal cases within 7 years were: recurrent myocardial infarction in 8 (50 %) cases, ACCI - in 4 (25 %) and sudden death - in 4 (25 %) cases.



The causes of lethal outcomes in patients of native and non-native nationality for the 7-year follow-up (p=0,246)

From total number of non-survived patients 5 (31,3 %) - patients with CAD of native nationality (Yakuts), 11 (68,7 %) –of non-native (Russians). The recurrent myocardial infarction was a death cause for the 7-year-follow-up in 3 patients of native and 5 patients of non- native nationality. ACCI - in 2 patients of native and 2 patients of non-native nationality (figure). 4 patients suddenly died, all of them are representatives of non-native nationality of Yakutia. Statistically significant distinctions on frequency of the survived and deceased patients among native and non-native nationality are not revealed (p=0,246). For the 7-year follow-up 110 patients with CAD, including 51 (46,4 %) representatives of native nationality and 59 (53,6 %) - representatives of non-native nationality of Yakutia have survived.

Comparison of clinical-anamnestic data among the survived patients with CAD has revealed significant distinctions between indigenous and non-indigenous on age and AH presence. Thus, the indigenous patients who have survived to the 7th year of follow-up were younger, than non-indigenous and more often suffered concomitant AH (p=0,010; p=0,003).

At comparison of clinical-anamnestic indexes in the survived and the deseased during follow-up among non-indigenous patients with CAD it was established that the 7-year survival rate in patients without ACCI in the anamnesis and the burdened heredity was better, than in the patients having such anamnestic indexes (p=0,001; p=0,041).

In group of indigenous CAD patients, the 7-year survival rate in patients without a diabetes was better, than in patients initially suffering CAD with a concomitant type II diabetes (p=0,0001).

By results of ultrasonic investigation of heart we had revealed that initial linear indices of LV dimensions of the survived statistically significantly differed with similar indexes of the deceased patients (table 2).

Table 2

Comparison of LV dimensions indexes in the survived and the deceased to the 7- year follow-up of CAD patients

Indices	I group (n=110)	II group (n=16)	p
LVBWThd, sm	1,05±0,02	1,05±0,04	0,934
LVBWThs, sm	1,44±0,02	1,31±0,04	**0,044**
IVSThd, sm	1,07±0,02	1,02±0,05	0,375
IVSThs, sm	1,44±0,02	1,32±0,04	0,065
LV EDD, sm	5,38±0,06	6,02±0,18	**0,0001**
LV ESD, sm	3,56±0,07	4,06±0,13	**0,007**
EF, %	60,93±0,96	52,31±1,70	**0,001**
LV Mass, g	222,66±6,26	263,06±18,46	**0,025**
LV Mass ind.	131,40±3,71	154,42±10,55	**0,031**

So, LVBWThS, EF average indexes were significantly higher, but EDD and ESD indexes were significantly lower in the survived patients with CAD in comparison with non-survived patients for the 7-year follow-up.

IVSThs index initially tended to decrease in group of the deceased patients (p=0,065) in comparison with an index in group of the survived patients. The LV mass was significantly larger, and an index of LV mass authentically was higher in group of the deceased patients in comparison with the survived group. Thus, for the patients who have not survived for the 7-year follow-up, initially maximum changes of LV geometry leading to decrease in a pumping ability and contractive myocardium function were characteristic.

At comparison of LV structurally functional state in patients of indigenous and non-indigenous nationality, survived and non-survived for years of follow-up, statistically significant distinctions are not found.

According to coronary angiography since 2000 for 2001, initial comparison of types of heart blood supply, weight of atherosclerotic lesion of coronary arteries between two groups of patients and in groups, between patients of indigenous and non-indigenous nationality is made.
In patients with CAD, survived and deceased for the 7-year follow-up, comparison has not revealed significant distinctions by heart blood supply type. The survived patients in 40 % of cases had the balanced type, in 33,6 % - the right type and in 26,4 % of cases - the left type of heart blood supply. Among the deceased patients initially in 50 % of cases the balanced type of blood supply, in 37,5 % - the right type and in 12,5 % - the left type of heart blood supply has been found.

Comparison of weight of atherosclerotic lesion of coronary arteries has shown that in deceased patients the multivascular atherosclerotic lesion of a coronary channel in comparison with the survived patients (p=0,031) significantly more often is marked (table 3).

Table 3

Comparison of degree of CA atherosclerotic lesion in the survived and non-survived CAD patients, prs. (%)

Weight of CA atherosclerotic lesion	Total (n=126)	I group (n=110)	II group (n=16)	p
No critical CA stenosis	34	32 (29,1%)	2 (12,5%)	0,165
1 CA critical stenosis (one-vascular)	51	46 (41,8%)	5 (31,3%)	0,423
2 CA critical stenosis (two-vascular)	31	26 (23,6%)	5 (31,3%)	0,510
3 CA critical stenosis (three-vascular)	10	6 (5,5%)	4 (25%)	**0,008**

Comparison of severity level of CA atherosclerotic lesion between the survived and non-survived patients of non-indigenous nationality for the 7-year follow-up has shown that in the survived non-indigenous patients at initial CAG three-vascularCA lesion was met significantly less often in comparison with non-survived patients (p=0,041). In group of the indigenous, survived and non-survived patients with CAD, statistically significant distinctions on weight of CA atherosclerotic lesion were not marked (Table 4).

Table 4

Comparison of weight of CA atherosclerotic lesion in the CAD indigenous and non-indigenous patients, prs. (%)

Weight of CA atherosclerotic lesion	Survived patients (n=110)		p 1-2	Deceased patients (n=16)		p 3-4	p 1-3	p 2-4
	Indigenous pts (n=51)	Non-indigenous pts (n=59)		Indigenous pts (n=5)	Non-indigenous pts (n=11)			
	1	2		3	4			
No CA critical stenosis	13 (25,5)	19 (32,2)	0,794	1 (20)	1 (9,1)	0,157	0,788	0,124
1 CA critical stenosis (one-vascular)	25 (49)	21 (35,6)	0,145	1 (20)	4 (36,3)	0,361	0,220	0,961
2 CA critical stenosis (two-vascular	11 (21,6)	15 (25,4)	0,924	2 (40)	3 (27,3)	0,659	0,356	0,898
3 CA critical stenosis (three-vascular)	2 (3,9)	4 (6,8)	0,778	1 (20)	3 (27,3)	0,505	0,133	0,041

At comparison of ventriculography results between patients of I and II groups significant distinctions are revealed. In patients of the II group LV aneurysms initially have been revealed in 7 (63,6 %), and I - only in 23 (23,7 %) patients (p=0,005). Thus, in CAD patients the

unfavorable forecast has connected with presence of postinfarction LV aneurysms and, on the contrary, at the patients who do not have LV aneurysms, the 7-year-old survival rate was significantly the best.

At studying of death causes in the patients of indigenous and non-indigenous nationality having various weight of a lesion of coronary arteries, the following is revealed: among the patients who do not have critical stenoses in CA, 2 patients have died. The causes of a lethal outcome were ACCI - in the native patient and sudden death – in the non-native patient. In case of CA 1-vascular lesion 5 patients have died, including 4 non-native (2 - recurrent MI, 2 - sudden death) and 1 native- recurrent MI. Among the patients having CA 2- vascular lesion, 5 patients have died, including 3 non-natives (1- recurrent MI, 1 - ACCI, 1-sudden death) and 2 natives (1- recurrent MI, 1- ACCI). Among the deceased patients having 3-vascular lesion (n=4), 3 - representatives of non-native and 1 - native nationality. In the non-native patients a cause of death in 2 cases were recurrent MI and in 1 case - ACCI, in the native - recurrent MI.

46 (36.5 %) CAD patients were operated (CABG and MBG), the rest 80 (63.5 %) patients had only standard medicamentous treatment. From total number of CAD patients with surgical revascularization of myocardium, 41 (89.1 %) patient has survived, including 18 indigenous and 23 non-indigenous. After operative treatment within 7 years 5 (10.9 %) patients have not survived, all of non-indigenous nationality. From them, to 4 patients at operative treatment 2 autovenous shunts have been appllied, to 1 patient - 3 shunts. Analyzing outcomes of operative and only medicamentous treatment influence of a choice of treatment method on 7-year-old survival rate of CAD patients is not revealed.

Medicamentous treatment was received by all patients included in our research. At studying of influence of drugs on 7-year-old survival rate of patients with CAD significant communication with development of CAD fatal course at a choice of ACE inhibitors, β-blocators, Ca antagonists, vasodilators is not revealed. At comparison of duration of statins reception (probucol, lipostat, vasilip) significant distinctions in groups of the survived and non-survived patients by 7 year of follow-up have been revealed. Patients with fatal CAD course in comparison with the survived more often did not take statins and, on the contrary, patients with CAD which have survived for the 7-year-follow-up, constantly, within a year received hypolipidemic therapy. Thus, the 7-year-old survival rate in the patients who were constantly taking statins was the best in comparison with the patients who were not.

Table 5

Duration of statins reception in groups of the survived and non-survived patients to the 7-year - follow-up, pts %

Statins reception	Total (n=126)	I group (n=110)	II group (n=16)	p
Constantly, within a year	36 (30.2)	37 (33.6)	1 (6.3)	0.028
Less than 6 months in a year	79 (62.7)	68 (61.8)	11 (68.6)	0.590
Did not	9 (7.1)	5 (4.5)	4 (25)	0.004

Prognostic value of clinico-anamnestic indexes remains rather significant, despite introduction of new hi-tech methods of CAD diagnostics. According to the majority of researches, age of patients, AH in anamnesis, old myocardial infarction, diabetes, disturbances of cardiac rhythm, quantity of lead on an ECG with lifting of ST segment play an important role in CAD prognosis [5-7]. In our research it is revealed that clinico-anamnestic factors affecting on CAD forecast during the 7-year-follow-up in patients of indigenous and non-indigenous nationality, differ. In group of non-indigenous patients with CAD it is an ACCI in anamnesis and

the burdened heredity. In group of indigenous patients with CAD - presence of concomitant disease - type II diabetes mellitus.

In group of the survived CAD patients significant distinctions also have been found: the indigenous patients, who have survived to the 7 year of supervision, were younger, than non-indigenous and more often suffered from concomitant AH.

According to some authors, mild augmentation of EDV and ESV in LV in patients after a myocardial infarction in 4-5 times increases risk of death. At observing patients with CAD within 3 years, Udelson J.E. [et al.] have positioned that on CAD prognosis the maximum influence render increase of EDD, EDV, ESV and decrease in LV EF [4, 6].

Studying of influence of structurally functional LV status on CAD prognosis in our research has shown that for the patients who have not survived for the 7-year-follow-up, initially maximum changes of LV geometry are characteristic, indicating decrease of pumping and contractile functions of myocardium. So, average indexes of LVBWThS, EF were significantly lower, and indexes EDD, ESD, LV mass, LV mass index significantly higher in the non-survived for the 7-year-follow-up of CAD patients in comparison with the survived patients.

Comparison of LV structural-functional state between patients of indigenous and non-indigenous nationality among the survived and the non-survived during follow-up has not revealed statistically significant distinctions.

At forecast studying at CAD in a number of researches the association of CA multivascular lesion with unfavorable outcome has been revealed [7]. Thus, in patients, died during the 7-year-follow-up, by results of initial CAG the multivascular atherosclerotic lesion of a coronary channel in comparison with the survived patients significantly more often was marked. In group of non-indigenous patients with CAD in the survived patients three-vascular CA lesion was met significantly less often in comparison with non-survived patients, and in group of indigenous patients distinctions on weight of atherosclerotic CA lesion in survived and non-survived CAD patients were not marked. Thus, it is possible to assume that in the aboriginals of Yakutia suffering from CAD, the disease unfavorable outcome was not associated with multivascular CA lesion unlike non-indigenous CAD patients.

At present, agree to the data of the majority of researches, the forecast for patients with CAD is not defined by a choice of various methods of treatment - invasive (CABG) or optimal medicamentous therapy [10,12]. We also have not revealed influence of a choice of a treatment method on 7-year-survival rate of patients with CAD. However, at low adherence to application of statins in CAD medicamentous therapy, the forecast was worse, than in patients, receiving hypolipidemic drugs for a long time.

There are convincing numerous evidences of necessity of application of hypolipidemic therapy in patients with CAD [9, 13]. In 1994 the Scandinavian research 4S in which 4444 CAD patients received simvastatin, has shown decrease on 34 % of frequency of heavy coronary complications, on 42 % - coronary death and on 30 % - the general death [11]. Our research also has shown that duration of statins reception has positively affected on 7-year-survival rate of CAD patients.

In conclusion, it would be desirable to notice that in CAD patients the prognosis substantially is defined by initial clinico-anamnestic factors, LV structural- functional state, weight of CA atherosclerotic lesion and adherence to hypolipidemic therapy. In our research for the first time the distinctions in the significance of prognostic factors on the 7-year survival rate of CAD patients in group of indigenous and non-indigenous Far North residents are revealed, that is most probably explained by genetical features and hereditary aggravation of populations of Yakutia and demands the further studying of major risk factors for each ethnic group of patients, for the purpose of initiating of individual programs of CAD secondary prevention.

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