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Prediction of Individual Risk Adverse Cardiovascular Events in for a Year after a Heart Attack Myocardium, Taken into Molecular Genetic Factors

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Annotation: Myocardial infarction is one of the clinical forms of coronary heart disease, which occurs with ischemic necrosis of an area of the myocardium as a result of occlusion of the coronary artery [1]. The most common cause is thrombosis, which develops when an unstable atherosclerotic plaque is damaged. Due to prolonged ischemia of the heart area, necrosis of cardiomycytes occurs, followed by the formation of a leukocyte shaft. The patient should be admitted to the cardiac intensive care unit as quickly as possible. In the first hours, it is necessary to perform thrombolysis, as well as angioplasty and stenting of the coronary arteries. [3] Myocardial infarction develops in patients aged 40 to 60 years and most often affects men, and is also the leading cause of disability throughout the world. Risk factors include: modifiable factors and non-modifiable factors. Modifiable factors include: smoking (which accompanies narrowing of the coronary arteries), frequent alcohol consumption, obesity BMI=more than 30, low primary physical activity (LPPA), imbalanced diet (the diet, as a rule, is dominated by fats and foods that contribute to increased in the blood LDL, HDL, cholesterol, triglycerides). Non-modifiable factors include: a family history of cardiovascular disease, gender, age (patients over 40 years old), as well as concomitant diseases: type II diabetes mellitus,

arterial hypertension, endocrinological disorders, myocardial infarctions suffered in the past. Myocardial infarction is the most common disease and the most common cause of death worldwide. Today, myocardial infarction occurs at a young age. Between the ages of 35 and 50, men get sick 10 times more than women. In 75% of patients who suffer from myocardial infarction, it does not develop suddenly, but a prodormal syndrome is noted, which occurs in three variants: 1) angina with a rapid course, 2) angina, which proceeds calmly, but can turn into unstable angina, 3) attacks of acute coronary insufficiency (ACS), 4) Prinzmetal's angina.

Keywords: myocardial infarction, hypersympathicotonia, ischemic heart disease, reperfusion technique.

Introduction. According to epidemiological studies, IHD and its most severe manifestation, myocardial infarction, still occupy leading positions in the structure of causes of mortality in the population, while the mortality rate from cardiovascular diseases in the Russian Federation remains one of the highest in the world [24, 84, 107, 198]. In addition, ischemic heart disease is one of the main causes of the development of CHF and is detected in 60-70% of patients with heart failure [21, 102, 109]. In the pathogenesis of acute MI, activation of the SAS plays an important role [63, 146, 163, 178]. Hyperactivation of the SAS not only makes a significant contribution to the development of MI, but also affects the course and prognosis of IHD in the post-infarction period [70, 167, 179, 239]. Currently, in our country there are few works devoted to the problem of studying the functional state of the SAS in MI by assessing the beta-adrenoreactivity of erythrocyte membranes. There are practically no prospective studies assessing the state of adrenoreactivity in the immediate and long-term post-infarction period, as well as data on the presence of a relationship with the characteristics of the course of CHF in patients who have suffered an MI. In addition, there is no clear data in the literature on the association of beta-adrenoreactivity with the genetic characteristics of the beta-adrenoreceptor apparatus of cells, in particular with polymorphisms of the beta-1-adrenoreceptor gene (ADRB1), which requires further study.

Purpose of the study. To evaluate the relationship between the level of beta-adrenoreactivity of erythrocyte membranes and the characteristics of the clinical course of acute MI.

Research methods. In accordance with the set goal and objectives, a research design was developed using the following methods:

1. Selection of patients, obtaining primary information about the features of the occurrence and course of acute MI, anamnesis data, laboratory and instrumental indicators and treatment were carried out using primary registration cards of the WHO epidemiological program "ROMI", as well as patient records and extracts from them.

2. At the time of hospitalization for index MI, patients underwent blood sampling to determine the beta-adrenoreactivity of erythrocyte membranes by changes in their osmoresistance and gene polymorphism ADRB1 (Ser49Gly, Arg389Gly), ACE (I/D), ITGB3 (T1565C), PON1 (Q192R) and APOE (Leu28Pro).

3. In the process of prospective annual observation, prospective observation cards “ROMI”, outpatient cards of patients, medical histories and extracts from them were analyzed. Patients were also actively called for consultations with a cardiologist and telephone interviews were carried out. After collecting anamnesis, patients underwent a physical and laboratory-instrumental examination, which included repeated determination of beta-adrenoreactivity of erythrocyte membranes, a biochemical blood test and a detailed lipid spectrum, as well as echocardiography (EchoCG), and, if indicated, daily ECG monitoring.4. Statistical processing of the results was carried out using statistical programs STATISTICA 10.0 (StatSoft Inc.), as well as a demo version of the SPSS Statistics Desktop 20.0 program (IBM). The critical level of significance when testing statistical hypotheses was taken equal to 0.05 (p - achieved significance level).

Research results. In order to identify predictors of progression of IHD and CHF within a year after MI, a cohort of 62 patients was formed. Prospective 12-month follow-up data were obtained for 60 patients (96.8%) and information was unavailable for 2 patients (3.2%). The patients were divided into groups depending on the nature of the post-infarction period. The first group consisted of 33 patients with a favorable course of the post-infarction period. The second group included 27 patients with an unfavorable course of the post-infarction period. The criteria for an unfavorable course were (combined end point): death from CVD, non-fatal recurrent myocardial infarction, hospitalization for exacerbation of coronary artery disease with myocardial revascularization, worsening of the angina FC (by 1 or more FC), clinical significant violations rhythmhearts, progression / hospitalization due to progression of CHF (increase in NYHA FC by 1 or more) (Table 3.10).

Table 3.10 - Incidence of adverse cardiovascular events during 12-month prospective follow-up, n (%)

Index	Number of patients, n=60
Cardiovascular death (cause – acute repeated MI)	1 (1.7)
Nonfatal recurrent MI	2 (3.3)
Hospitalization due to exacerbation of coronary artery disease with myocardial revascularization	2 (3.3)
Worsening angina FC (by 1 or more FC)	6 (10.0)
Clinically significant NRS (VES III-IV according to Lown)	2 (3.3)

Continuation of Table 3.10

Progression of CHF (by 1 or more FC according to TSH data)	14 (23.3)
Note: VES - ventricular extrasystole, MI - myocardial infarction, CA - coronary artery, CABG - coronary artery bypass grafting, NRS - cardiac arrhythmias, TSH – 6-minute walk test, FC – functional class, CHF – chronic heart failure.	

In an intergroup comparative analysis, it was found that patients with an unfavorable course of the post-infarction period were on average 9 years older than patients with a favorable course of the post-infarction period (p = 0.023). Thus, among patients with an unfavorable course of the post-infarction period, people over the age of 65 were 5 times more likely (OR=5.2; 95% CI 1.54-17.52; p=0.006). In addition, patients in group 2 were characterized by a more frequent presence of coronary artery disease in combination with a history of hypertension before the development of index MI (p=0.002), and obesity was also 2 times more likely (p=0.026) (Table 3.11).

There were no statistically significant differences between the groups in the incidence of ALV development in the acute period of myocardial infarction. Thus, in group 1, ALV was observed in 18.2% of cases (n=6), in group 2 – in 37% of cases (n=10) (p=0.100). By the time patients were discharged from the hospital, the diagnosis of FC I CHF was made in 54.5% of cases (n=18) in

group 1 and in 48.1% of cases (n=13) in group 2; diagnosis of CHF II FC - in 39.4% of cases (n=13) in group 1 and in 37% of cases in group 2; CHF III FC – in 6.1% and 14.8% of cases, respectively.

When analyzing the results of coronary angiography (CAG) at the time of acute MI, it was found that among patients of group 2, there was more frequent damage to the anterior descending (AD) and circumflex artery (CA). LAD lesions were recorded in 21 patients (63.6%) of group 1 and in 25 patients (92.6%) 2 groups (p=0.043). OA lesions were recorded in 13 patients (39.4%) of group 1 and in 18 patients (66.7%) of group 2 (p=0.042).

With regard to the incidence of damage to the remaining coronary arteries, the study groups were comparable.

Table 3.11 - Clinical and anamnestic characteristics of patients at the time of index myocardial infarction, depending on the nature of the post-infarction period

Index	Group 1 Favorable course (n=33)	Group 2 Unfavorable course (n=27)	p-value
Men, n (%)	28 (84.8)	21 (77.8)	0.481
Women, n (%)	5 (15.2)	6 (22.2)	
Age at the time of index MI, Me (Q25;Q75), years	56.0 (47.8;61.0)	64.5 (52.8;76.5)	0.023
Persons over 65 years of age at the time development of index MI, n (%)	5 (15.2)	13 (48.1)	0.006
Index MI with Q wave, n (%)	27 (81.8)	21 (77.8)	0.697
OLZHN, n (%)	6 (18.2)	10 (37.0)	0.100
Single-vessel coronary artery disease (stenosis ≥50% in one coronary artery), n (%)	5 (15.2)	4 (14.8)	0.999
Multivessel coronary artery disease (stenosis ≥50% in two or more coronary arteries), n (%)	20 (60.6)	18 (66.7)	0.628
PCI, n (%)	28 (84.8)	24 (88.9)	0.719
AG, n (%)	26 (78.8)	25 (92.6)	0.166
History of coronary artery disease before development index MI, n (%)	9 (27.3)	18 (66.7)	0.002
Diabetes mellitus type 2, n (%)	3 (9.1)	4 (14.8)	0.690
Obesity, n (%)	5 (15.2)	11 (40.7)	0.026
Smoking, n (%)	7 (21.2)	5 (18.5)	0.795
Note - AH - arterial hypertension, IHD - coronary heart disease, MI - myocardial infarction, CA - coronary artery, AVF - acute left ventricular failure, PCI - percutaneous coronary intervention, Me (Q25;Q75) - median and interquartile range, p-value – achieved level of significance of differences.			

Analysis of therapy during the period of hospital stay with acute MI did not reveal statistically significant differences in the frequency of taking the main groups of medications in the groups of patients with a favorable and unfavorable course of the post-infarction period (Table 3.12). Beta blocker drugs, in accordance with existing recommendations, were prescribed to almost all patients with acute MI (in 87.9% of cases in group 1 and in 96.3% of cases in group 2). Moreover, in the

vast majority of cases, BAB were prescribed at doses below target. Thus, in group 1, only 1 patient (3.4%) received the target dose of beta blockers; in group 2 - 2 patients (7.7%) (p = 0.598)

(Table 3.12).

Statin drugs in the hospital were prescribed to 30 patients of group 1 (90.9%) and 27 patients of group 2 (100%) (p=0.245). At the same time, the most frequently prescribed drug in this group was atorvastatin, the dose of which by the time of discharge from the hospital in both groups was 20.0 (20.0; 40.0) mg (p = 0.624). The dose of rosuvastatin was comparable in both groups (p=0.874) (Table 3.12).

Table 3.12 - Results of a comparative analysis of therapy received in hospital in groups of patients with favorable and unfavorable course of the post-infarction period

Index		Group 1 Favorable course (n=33)	Group 2 Unfavorable course (n=27)	p-value
Taking beta blockers before index MI		11 (33.3)	11 (40.7)	0.554
BAB, appointedin hospital	Total	29 (87.9)	26 (96.3)	0.367
	BAB at target dose, n (%)	1 (3.4)	2 (7.7)	0.598
	Metoprolol succinate	2 (6.1)	1 (3.7)	0.669
	Metoprolol tartrate	4 (12.1)	6 (22.2)	0.322
	Bisoprolol	23 (69.7)	19 (70.4)	0.955
Antiplatelet agents		33 (100)	26 (96.3)	0.450
Dual antiplatelet therapy		30 (90.9)	24 (88.9)	0.999
ACEI		25 (75.8)	21 (77.8)	0.854
BRA		4 (12.1)	3 (11.1)	0.999
Statins	Total	30 (90.9)	27 (100)	0.245
	Atorvastatin	24 (80.0)	16 (59.3)	0.165
	Rosuvastatin	6 (20.0)	11 (40.7)	0.084
Diuretics		10 (30.3)	12 (44.4)	0.258
AMK		3 (9.1)	6 (22.2)	0.276

Continuation of Table 3.12

Calcium channel blockers	4 (12.1)	6 (22.2)	0.322
Anticoagulants	1 (3.0)	1 (3.7)	0.999
Note – MNA – mineralcorticoid receptor antagonists, BAB – beta-blockers, ARB – angiotensin II receptor blockers, ACEI – angiotensin-converting enzyme inhibitors, MI – myocardial infarction, p-value – achieved level of significance of differences.			

Thus, the analysis showed that between the groups of patients with a favorable and unfavorable course of the post-infarction period there were no significant differences in therapy at the inpatient stage, while there were clinical and anamnestic differences. Thus, patients with adverse cardiovascular events were on average 9 years older than patients with a favorable course of the post-infarction period, more often had a history of a combination of coronary artery disease with hypertension, and were more likely to be obese. The results of CAG at the time of the index MI

showed that this category of patients was also characterized by more frequent lesions of the LAD and OA than the group of patients with a favorable course of the post-infarction period.

1. Characteristics of patients 6 months after myocardial infarction

6 months after the index MI, it was found that in 6 patients during this period of time there was a worsening of the clinical course of CHF, manifested by the occurrence of weakness, decreased exercise tolerance and increased shortness of breath. This condition was regarded as progression of CHF, the criterion of which was an increase in the NYHA FC of CHF by 1 or more. When analyzing cases of CHF progression within 6 months after the index MI, it was found that in 5 patients there was an increase in CHF FC from I to II, in 1 patient - from FC II to III (according to NYHA). Thus, 6 months after the index MI, 23 patients (69.7%) in group 1 and 8 patients (29.6%) in group 2 had class I CHF, 10 patients (30.3%) in group 1 and 14 patients (51.9%) of 2 groups had FC II CHF, 5 patients (18.5%) of 2 groups had FC III CHF.

All of the above is reflected in the functional characteristics. Thus, an intergroup comparative analysis showed that in group 2 of patients, 6 months after the index MI, the distance covered during the six-minute walk test (SMT) (380 (323;473) meters) was significantly inferior to the same indicator in group 1 (470 (388;500)) meters), which reflected lower physical performance in patients with an unfavorable long-term prognosis (p=0.048, Table 3.13).

Two patients suffered a repeated non-fatal large-focal MI in the first 6 months after the index MI: the first patient – 2 months later, the second patient – 4 months after the index MI.

When analyzing echocardiographic data, it was found that in group 1 there was an increase in left ventricular ejection fraction (LVEF) 6 months after the index MI from 51.5 (47.0;59.0)% to 58.0 (51.5; 63.5)% (p=0.003), while in group 2 there was no significant increase in this indicator (p=0.506). At the same time, in both groups this indicator was within the reference values (Table 3.13).

Table 3.13 – Clinical and functional characteristics of patient groups over time 6 months after the index myocardial infarction, depending on the nature of the post-infarction period, Me (Q25;Q75)

Index	Group 1 Favorable course (n=33)		p1	Group 2 Unfavorable course (n=27)		p2	*p**	*p***
	Originally	Through 6 months		Originally	Through 6 months			
SHOKS score, points	3.5 (1.0;4.0)	2.0 (2.0;4.2)	0.816	4.0 (1.0;4.0)	4.5 (2.0;6.0)	0.122	0.818	0.179
TSHH, meters	440 (385;493)	470 (388;500)	0.589	470 (378;518)	380 (323;473)	0.073	0.365	0.048
Echocardiography indicators								

Continuation of Table 3.13

IMM, g/m2	100.0 (87;114.5)	98.0 (89;115)	0.220	109.0 (97.5;129)	100.0 (97.115)	0.069	0.072	0.312
EDV, ml	108.5 (89.3;124, 3)	114.0 (91;126.5)	0.683	109.0 (91;131.5)	109.0 (98.3;136,0)	0.865	0.464	0.984
ESR, ml	50.0 (40.0;61.5)	45.0 (34.5;60.5)	0.073	49.0 (36.3;63.8)	47.5 (37.3;68.0)	0.468	0.983	0.582
PV, %	51.5 (47.0;59.0)	58.0 (51.5;63.5)	0.003	56.0 (49.3;60.8)	57.5 (45.3;63.0)	0.506	0.483	0.367

Peak E/A, c.u.	0.80 (0.70;1.5)	0.92 (0.72;1.2)	0.760	0.80 (0.70;1.0)	0.81 (0.73;1.2)	0.944	0.744	0.683
Note - IMI - myocardial mass index, EDV - end-diastolic volume, ESV - end-systolic volume, TSH - 6-minute walk test, EF - ejection fraction, ECS - clinical condition rating scale, E/A - early (E) phase ratio filling of the left ventricle to the atrial (A) component of diastolic filling of the left ventricle, Me (Q25;Q75) – median and interquartile range, p1 – significance of differences in group 1 between the initial value and after 6 months, p2 – significance of differences in group 2 between the initial value and the value at 6 months, p* – significance of differences between initial values in groups 1 and 2, p** – significance of differences between values after 6 months in groups 1 and 2.								

When analyzing therapy 6 months after the index MI, it was revealed that one patient of group 1 (3.4%) and two patients of group 2 (7.7%) independently stopped taking beta-blockers prescribed upon discharge from the hospital for acute THEM. The remaining patients continued taking this group of drugs in the doses recommended upon discharge from the hospital. All patients in group 1 and the majority of patients in group 2 (96.2%) continued taking antiplatelet agents. Two patients in group 1 (8%) and one patient in group 2 (4.8%) stopped taking angiotensin-converting enzyme inhibitors (ACEIs) during the first six months after the index MI. All patients in the group with a favorable course of the post-infarction period continued taking statins during the first 6 months after MI, the main one of which was atorvastatin (80% of cases). Two patients from the group of unfavorable course of the post-infarction period independently stopped taking statins in the first half of the year after the MI. The remaining patients continued taking this group of drugs in the doses recommended upon discharge from the hospital. Two patients 1 group (20% of cases) and two patients of group 2 (16.7% of cases) stopped taking diuretics prescribed upon discharge from the hospital. Patients took the remaining medications in the same volume in accordance with the recommendations upon discharge from the hospital. Patients with a favorable and unfavorable course of the post-infarction period 6 months after the index MI did not differ in the frequency of taking the main groups of medications (Table 3.14).

Table 3.14 - Results of a comparative analysis of the therapy taken in groups of patients with a favorable and unfavorable course of the post-infarction period 6 months after myocardial infarction

Index		Group 1 Favorable course (n=33)	Group 2 Unfavorable course (n=27)	p-value
Beta blockers	Total	28 (90.9)	24 (81.5)	0.325
	Metoprolol succinate	6 (21.4)	6 (27.3)	0.750
	Metoprolol tartrate	6 (21.4)	2 (9.1)	0.212
	Bisoprolol	16 (57.2)	14 (63.6)	0.735
Antiplatelet agents		33 (100)	25 (92.6)	0.198
ACEI		23 (69.7)	20 (74.1)	0.925
BRA		4 (12.1)	3 (11.1)	0.999
Statins	Total	30 (90.9)	25 (88.9)	0.725
	Atorvastatin	24 (80.0)	16 (64.0)	0.312
	Rosuvastatin	6 (20.0)	9 (36.0)	0.712
Diuretics		8 (24.2)	10 (37.0)	0.101
AMK		3 (9.1)	5 (18.5)	0.325

Calcium channel blockers	4 (12.1)	7 (25.9)	0.100
Anticoagulants	1 (3.0)	1 (3.7)	0.999
Note – AMK – mineralcorticoid receptor antagonists, ARB – blockers angiotensin II receptors, ACE inhibitors – angiotensin-converting enzyme inhibitors, p-value – achieved level of significance of differences.			

Thus, 6 months after the index MI, the groups of patients with and without adverse cardiovascular events in the post-infarction period did not have statistically significant differences in the frequency of taking and doses of the main groups of drugs. At the same time, differences in some clinical and functional characteristics were established between them. Thus, in the group of unfavorable course of the post-infarction period, the TSH distance was lower than in the group of favorable course of the post-infarction period.

2. Characteristics of patients 12 months after myocardial infarction

12 months after the index MI, it was found that in 5 of 6 patients who had progression of CHF in the first 6 months after MI, in the next 6 months there was again a deterioration in the clinical course of CHF, manifested by an increase in shortness of breath when walking shorter distances and a decrease in tolerance to physical activity, which was accompanied by the transition of patients from class II to class III CHF according to NYHA.

In 8 patients with a stable course of CHF in the first 6 months after the index MI, the clinical course of CHF worsened in the next 6 months. A criterion for the progression of CHF in them was also an increase in the FC of CHF. Thus, in 4 patients there was an increase in the FC of CHF from I to II and in 4 patients - from FC II to III.

Thus, 12 months after the index MI, 25 patients (75.8%) in group 1 and 4 patients (14.8%) in group 2 had class I CHF, 8 patients (24.2%) of group 1 and 9 patients (33.3%) of group 2 had CHF II FC, 14 patients (51.9%) of 2 groups had CHF III FC.

All of the above is reflected in the clinical and functional indicators in such a way that a year after the index MI, according to the SCS data, the number of points in the unfavorable course group post-infarction period (6.0 (1.0;9.0) points) was 6 times higher than the same indicator in the group of favorable course of the post-infarction period (1.0 (1.0;4.0) points) ($p=0.004$, Table 3.15). In addition, in patients of group 1 during the 12-month observation period, an increase in values according to the results of TSH was recorded, which was not observed among patients in group 2 ($p<0.001$). Moreover, the TSH distance after a year in group 2 was 315 (173;478) meters, which was significantly inferior to the same indicator in group 1 - 500 (408;520) meters ($p<0.001$).

In the second half of the year after the index MI, 2 patients (3.3%) were hospitalized for exacerbation of coronary artery disease with endovascular myocardial revascularization. In 6 patients (10.0%) 12 months after the index MI, a worsening of the angina FC was observed (by 1 more FC), in 2 patients (3.3%) clinically significant cardiac arrhythmias were recorded (VES grades III-IV according to Lown) .

One patient suffered a repeat large-focal MI with a fatal outcome 8 months after the index MI.

When analyzing the main echocardiographic parameters, it was revealed that in group 1 there was a decrease in end-systolic volume (ESV) within a year after MI ($p = 0.03$), which was not typical for group 2 (Table 3.15). In addition, in group 1 there was an increase in LVEF values during the year after the index MI ($p<0.01$), which was also not typical for patients in group 2. One year after the index MI, patients in group 2 had a lower LVEF according to echocardiography than patients in group 1, however, this indicator corresponded to the reference values. Thus, LVEF one year after MI in patients of group 1 was 60.0 (53.5;64.5)%, while in patients of group 2 it was 56.0 (45.3;60.0)% ($p=0.028$; Table 3.15). At the same time, LVEF <40% was recorded in 2 patients of group 2 one year after the index MI.

Table 3.15 – Clinical and functional characteristics of patient groups over a 12-month observation period depending on the nature of the post-infarction period, Me (Q25;Q75)

Index	Group 1 Favorable course (n=33)			p1	Group 2 Unfavorable course (n=27)			p2	*p**	*p***	*p#*
	Originally	Through 6 months	After 12 months		Originally	Through 6 months	In 12 months				
SHOKS, points	3.5 (1.0;4.0)	2.0 (2.0;4.2)	1.0 (1.0;4.0)	< 0.01	4.0 (1.0;4.0)	4.5 (2.0;6.0)	6.0 (1.0;9.0)	0.47	0.81	0.18	0.00
TШХ, meters	440 (385;493)	470 (388;500)	500 (408;520)	< 0.01	470 (378;518)	380 (323;473)	315 (173;478)	0.23	0.37	0.05	0.00
Echocardiography indicators											
IMM, g/m2	100.0 (87;114.5)	98.0 (89;115)	99.5 (89.3;115)	0.16	109.0 (97.5;129)	100.0 (97.115)	102.0 (97.0;115)	0.32	0.07	0.31	0.26
KDO, ml	108.5 (89.3;124)	114.0 (91;126.5)	114.0 (91;134)	0.98	109.0 (91;131.5)	109.0 (98.3;136)	109.5 (102;141)	0.38	0.46	0.98	0.60
CSR, ml	50.0 (40.0;61.5)	45.0 (34.5;60.5)	42.0 (34.5;58.0)	0.03	49.0 (36.3;63.8)	47.5 (37.3;68.0)	51.0 (38.5;81.0)	0.50	0.98	0.58	0.25
PV, %	51.5 (47.0;59.0)	58.0 (51.5;63.5)	60.0 (53.5;64.5)	< 0.01	56.0 (49.3;60.8)	57.5 (45.3;63.0)	56.0 (45.3;60.0)	0.48	0.48	0.36	0.03
Peak E/A, a.u.	0.80 (0.70;1.5)	0.92 (0.72;1.2)	0.99 (0.73,1,2)	0.85	0.80 (0.70;1.0)	0.81 (0.73;1.2)	0.81 (0.73;1.34)	0.51	0.74	0.68	0.56

Note - IMI - myocardial mass index, EDV - end-diastolic volume, ESV - end-systolic volume, TSH - 6-minute walk test, EF - ejection fraction, ECS - clinical condition rating scale, E/A - early (E) phase ratio filling of the left ventricle to the atrial (A) component of diastolic filling of the left ventricle, Me (Q25;Q75) – median and interquartile range, p1 – significance of differences in group 1 between the initial value and the value after 6 months. and 12 months, p2 – significance of differences in group 2 between the initial value and the value after 6 months. and 12 months, p* – significance of differences between initial values in groups 1 and 2, p** – reliability of differences between values after 6 months in groups 1 and 2, p# – reliability of differences between values after 12 months. in groups 1 and 2.

When analyzing therapy 12 months after the index MI, it was found that two patients of group 1 (6.9% of cases) and 5 patients of group 2 (19.2% of cases) stopped taking beta blockers during the second half of the post-infarction period. In the vast majority of cases, the drugs were stopped spontaneously. Ultimately, during the year, 3 patients of group 1 (10.3%) and 7 patients of group 2 (26.9%) independently stopped taking the beta blockers prescribed upon discharge from the hospital, while the differences between the groups did not reach statistical significance (p= 0.164).

Three patients of group 1 (12% of cases) and three patients of group 2 (14.3% of cases) also stopped taking ACE inhibitors in the second half of the year after myocardial infarction. Two patients of group 1 (6.7% of cases) and one patient of group 2 (3.7% of cases) stopped taking statins in the second half of the year after MI. Five patients in the group with a favorable course of the post-infarction period (50% of cases), in whom diuretics were prescribed as part of combination antihypertensive therapy, stopped taking them in the second half of the year after the index MI. Thus, in group 2, a year after MI, a larger number of patients than in the first group took diuretics (p = 0.002), as well as mineralocorticoid receptor antagonists (p = 0.008), the reason for which was the presence of progression of CHF in patients in this group during years after myocardial infarction and less often achieving target blood pressure values (Table 3.16).

Table 3.16 - Results of a comparative analysis of the therapy taken in groups of patients with a favorable and unfavorable course of the post-infarction period 12 months after myocardial infarction

Index		Group 1 Favorable course (n=33)	Group 2 Unfavorable course (n=27)	p-value
Beta blockers	Total	26 (78.8)	19 (70.4)	0.554
	Metoprolol succinate	7 (26.9)	6 (31.6)	0.925

Continuation of Table 3.16

	Metoprolol tartrate	6 (23.1)	2 (10.5)	0.276
	Bisoprolol	13 (50)	11 (57.9)	0.916
Antiplatelet agents		33 (100)	25 (92.6)	0.198
ACEI		20 (60.6)	17 (63.0)	0.852
BRA		4 (12.1)	4 (14.8)	0.999
Statins	Total	28 (84.8)	24 (88.9)	0.719
	Atorvastatin	21 (75.0)	18 (75.0)	0.999
	Rosuvastatin	7 (25.0)	6 (25.0)	0.999
Diuretics		3 (9.1)	12 (44.4)	0.002
AMK		1 (3.0)	8 (29.6)	0.008
Calcium channel blockers		1 (3.0)	1 (3.7)	0.999
Anticoagulants		-	1 (3.7)	0.999
Note – MNA – mineralcorticoid receptor antagonists, β-ARM – indicator of beta-adrenoreactivity, ARB – angiotensin II receptor blockers, ACEI – angiotensin-converting enzyme inhibitors, MI – myocardial infarction, Me (Q25; Q75) – median and interquartile range, p-value – achieved level of significance of differences.				

Thus, one year after the index MI, the groups of patients with the absence and presence of adverse cardiovascular events in the post-infarction period differed significantly in clinical and functional characteristics. Thus, patients from the group of unfavorable course of the post-infarction period one year after MI were characterized by higher scores on the SCS scale and low TSH scores, in comparison with patients from the group of favorable course of the post-infarction period. Due to the presence of progression of CHF in some patients within a year after the index MI, in the group of unfavorable course of the post-infarction period, the need for diuretic therapy more often arose.

3. Beta-adrenoreactivity of erythrocyte membranes in predicting adverse cardiovascular events within a year after previous myocardial infarction

Analysis of the dynamics of changes in the levels of beta-adrenoreactivity of erythrocyte membranes during the year after the index MI showed that in group 1, β-ARM values initially (6 hours after the onset of MI) were lower than in patients in group 2 (31.8 (18.3;38.9) conventional units and 37.2 (29.0;48.3) conventional units, respectively, p=0.044) (Figure 3.2).

6 months after the index MI, both in group 1 and group 2, β-ARM values became higher than the initial ones (p=0.040 and p<0.001, respectively). At the same time, 6 months after the index MI, the level of β-ARM in group 2 (59.8 (50.1;78.4) conventional units) was significantly higher than the same indicator in group 1 (43.1 (29.5) ;55.6) conventional units) (p=0.001).

12 months after the index MI, patients with an unfavorable course of the post-infarction period still maintained significantly higher levels of β-ARM (62.6 (43.4; 69.7) conventional units) than in patients with a favorable course of the post-infarction period. period (42.1 (26.4;52.5) conventional units) (p=0.020). (Figure 3.2).

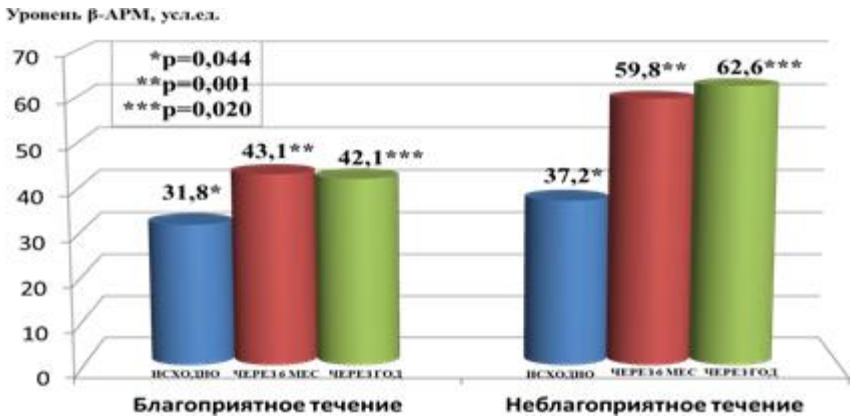

Figure 3.2 – Dynamics of changes in β-ARM in groups of patients with favorable and unfavorable course of the post-infarction period over a 12-month observation period

Thus, it was found that patients with adverse cardiovascular events within 12 months after MI are characterized by higher initial values of β-ARM than patients with a favorable course of the post-MI period (Figure 3.2). Taking these differences into account, a logistic regression analysis was carried out, and it was found that an initially higher level of β-ARM in the acute period of MI was associated with the development of adverse cardiovascular events within a year after MI (OR 1.037; 95% CI 1.003-1.073 ; p=0.035).

In order to assess the possibility of using the β-ARM value to predict the development of adverse cardiovascular events within a year after MI, a ROC analysis was performed. According to the results of the ROC analysis, the area under the AUC curve was 0.69 with p=0.015 (95% CI 0.55-0.82). When analyzing the characteristics of the ROC curve, a "cut-off point" of the β-ARM indicator was established ≥ 35.4 conventional units, which allows predicting the development of adverse cardiovascular events within a year after MI with sensitivity - 70.4% and specificity - 66.7%. (Figure 3.3).

Figure 3.3 - Sensitivity and specificity of the β-ARM indicator in predicting adverse cardiovascular events within 12 months after myocardial infarction (ROC analysis)

Conclusions:

1. In the acute period of MI, an excess of the established norm for beta-adrenoreactivity of erythrocyte membranes (more than 20 conventional units) is associated with the development of acute left ventricular failure, as well as a larger volume of damage to the heart muscle according to echocardiography and higher concentrations of biomarkers of myocardial necrosis in the blood (CPK, CPK-MB and high-sensitivity troponin I), compared with patients with normal β-ARM levels.
2. The 1165CC genotype of the Arg389Gly polymorphism of the ADRB1 gene is associated with an increased value of beta-adrenoreactivity of erythrocyte membranes in the acute period of MI, while carriage of the 1165G allele of this polymorphism is typical for patients with normal values of beta-ARM.

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