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Relationship between electrical myocardial instability and postinfarction remodeling in patients with ST-segment elevation myocardial infarction

Aim	To study the clinical value of markers for myocardial electrical instability in combination with echocardiographic parameters for predicting the risk of cardiovascular complications (CVC) in the postinfarction period.
Material and methods	This study included 118 patients with ST segment elevation myocardial infarction (STEMI) and hemodynamically significant stenosis of one coronary artery. A percutaneous coronary intervention (PCI) with stenting of the infarct-related artery was performed for all patients. On day 7–9 and at 24 and 48 weeks after the treatment, ECG Holter monitoring was performed, which included analyses of ventricular late potentials, dispersion of QT interval duration, heart rate turbulence (HRT) and variability (HRV), and heart chronotropic load (HCL). At baseline and during postinfarction week 12, all patients underwent echocardiography with calculation of indexes of end-diastolic volume (iEDV) and end-systolic volume (iESV) to verify the signs of left ventricular (LV) myocardial remodeling. The criteria for LV pathological remodeling included increases in iEDV >20% and/or iESV >15% at 12 weeks after STEMI. The group without remodeling, R (-), consisted of 79 (67%) patients and the group with signs of LV pathological remodeling, R (+), consisted of 39 (33%) patients. Quality of life and achieved endpoints were evaluated during 144 weeks.
Results	By week 48 in group R (-), the stabilization of electrical processes in the myocardium was more pronounced as indicated by a decrease in HFLA by 12% (p=0.004) and by a fourfold increase in RMS (p=0.047). Only in this group, the baroreflex sensitivity restored; pathological TPC decreased from 20 to 5% (p=0.002) by the end of the active treatment. Stabilization of the repolarization phase duration in various parts of the myocardium was more active in patients without pathological remodeling as shown by decreases in disp QTa (p=0.009), disp QTe (p=0.03), sd QTa (p=0.006), and sd QTe (p=0.009). This was not observed in the group R (+). The recovery of vagosympathetic balance due to leveling the sympathetic component also was more effective in the group R (-), which was reflected in increased spectral and temporal HRV indexes (p<0.05). Both groups showed reduced HCL values at 24 weeks (p=0.047 and p=0.006); however, the HCL regression remained also at 48 weeks only in the group R (-) (p=0.006). Group R (-) patients reported higher quality of life (p=0.03) than group R (+) patients. Endpoints were achieved more frequently in the group R (+): 87.1% vs. 27.8% (odds ratio, 11.8; 95% confidence interval, 4.6–30.8; p=0.00001).
Conclusion	Pathological myocardial remodeling in early postinfarction period is associated with electrophysiological instability of the myocardium, which results in the development of CVC and low quality of life in patients with STEMI.

Keywords	Myocardial infarction; pathological left ventricular remodeling; electrical instability; heart rate turbulence; heart rate variability
For citation	Oleynikov V.E., Barmenkova Yu.A., Dushina E.V., Golubeva A.V. Relationship between electrical myocardial instability and postinfarction remodeling in patients with ST-segment elevation myocardial infarction. Kardiologiia. 2021;61(10):14–25. [Russian: Олейников В.Э., Барменкова Ю.А., Душина Е.В., Голубева А.В. Взаимосвязь электрической нестабильности миокарда и постинфарктного ремоделирования у больных инфарктом миокарда с подъемом сегмента ST. Кардиология. 2021;61(10):14–25]

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Introduction

The sequelae of ST-segment elevation myocardial infarction (STEMI) comprise a common cause of death in the Russian Federation [1]. Patients are known to face a significant risk of developing chronic heart failure (CHF) in the postinfarction period resulting from cardiac remodeling, including morphological and geometrical changes of the left ventricle (LV). Moreover, structural changes in the myocardium serve as a background for the reentry phenomenon; such violation of the stabilization of electrical processes in the myocardium can promote the activation of life-threatening trigger arrhythmias in patients with postinfarction remodeling [1].

ISSN 0022-9040. Kardiologiia. 2021;61(10). DOI: 10.18087/cardio.2021.10.n1626

The possibility of providing a timely assessment of the risk of developing severe life-threatening complications of STEMI is a relevant consideration. However, current diagnostic methods, which are mainly focused on collecting clinical and laboratory data or invasive interventions, do not adequately consider electrophysiological instability of the myocardium in the prognosis. This is despite its markers having been regarded as essential in this cohort of patients for decades [2].

Modern cardiology utilizes several non-invasive techniques that allow the complex study of electrophysiological and structural changes of the myocardium in the early postinfarction period. These include the analysis of additional techniques for electrocardiographic (ECG) Holter monitoring and echocardiography.

Objective

To study the clinical value of markers of electrical myocardial instability combined with echocardiographic indicators to predict the risk of developing cardiovascular events in the postinfarction period.

Material and methods

The single-center, open-label, controlled prospective study included 125 patients who were treated in the Emergency Cardiology Department of N. N. Burdenko Penza Regional Clinical Hospital. The study protocol and informed consent form was approved by the ethics committee of the University of Penza. All patients signed informed consent to participate in the study. The study is listed in the https://register.clinicaltrials.gov register under ID number NCT02590653.

The inclusion criteria were: age from 35 to 70 years; 12-lead ECG validated STEMI; high-sensitivity troponin I >99% percentile at least once; hemodynamically significant stenosis (>50%); atherothrombosis of infarct-related artery according to coronary angiography.

The exclusion criteria were: repeated and/or recurrent MI; hemodynamically significant stenosis (>50%) of two or more coronary arteries; >30% stenosis of the left coronary artery; CHF NYHA functional classes III–IV; non-sinus rhythm; pacemaker; sinoatrial and atrioventricular block grade II–III, bundle branch blocks; insulin-dependent diabetes mellitus (DM) type 2.

The duration of active treatment was 48 weeks, after which the following endpoints were monitored for 144 weeks: death, repeated MI, repeated revascularization surgery, life-threatening arrhythmias, hospitalizations for unstable angina and/or decompensated CHF.

A total of 118 patients completed the study: age 52 (from 45 to 58) years; 86.4% of patients were males. The mean body mass index was 27.3 (95% confidence interval (CI) 24–29.3) kg/m^2, i.e., patients of this cohort were overweight. Coronary artery disease debuted with STEMI in 97 (82.2%) patients. 63 (53.4%) patients had a history of arterial hypertension, 75 (63.6%) were smokers, 51 (43.2%) had a relevant family history, and 6 (5.1%) patients had DM type 2.

All patients underwent pharmacoinvasive revascularization. The time from onset of pain to prehospital thrombolytic therapy (TLT) was 2 (95% CI 1.25–4.5) hours and 6.5 (95% CI 3.5–12.4) hours to percutaneous coronary intervention (PCI).

During active treatment, all patients received medication for secondary prevention as a part of the regional project entitled «Circulatory System Disease Control in the Penza Region», following the corresponding guidelines [3].

Patients completed the Seattle Angina Questionnaire (SAQ) and Minnesota Living with Heart Failure Questionnaire (MLHFQ) to assess the quality of life (QOL) on days 7–9, weeks 24, 48, 96, and 144.

24-hour ECG monitoring and analysis of additional techniques were performed on days 7–9, weeks 24 and 48, using the 12-lead Astrocard system. Rhythm and conduction disorders and ischemia events were examined [4]. Ventricular late potentials (VLPs), heart rate turbulence (HRT), heart rate variability (HRV), QT interval duration and dispersion, and chronotropic cardiac load were analyzed in a semiautomatic mode [4, 5].

HRT was determined in patients with ventricular beats (VBs). The baroreflex sensitivity was evaluated using two independent parameters: turbulence onset (TO) and turbulence slope (TS). Values TO >0 and TS <2.5 ms/RR were considered pathological. 24-hour HRV was assessed using temporal and spectral parameters following the measurement standards and guidelines [4].

The following parameters were considered to assess VLPs: filtered QRS width (QRSf), duration of the low-amplitude potentials appearing at the end part of the QRS complex (HFLA), mean square value of the last 40 ms of the QRS complex (RMS) [4, 5]. The QT interval was measured in an automatic mode: the 24-hour, daytime and nighttime QT interval duration was calculated on lead II: from the beginning of the Q wave to the peak of the T-QTa wave, and to its end

QTe, as well as the duration of the corrected QT against heart rate (HR) QTc [6, 7]. Simultaneously with the calculation of the QT interval duration, the software automatically analyzed the QT duration variance to the peak of the T wave (disp Qta) and its end (disp Qte) and the standard deviation of the variance of the QT duration to the peak of the T wave (sd Qta) and the intersection with the isoline (sd Qte) [5].

An original option implemented in the Astrocard system was used to determine chronotropic cardiac load, which occurs when the heart functions at increased threshold HR > 80% of the maximum possible HR for 24 hours, daytime, and nighttime periods according to the patient's diary. The chronotropic cardiac load was expressed by two indicators Ta and Sa. Ta (%) is the percentage of time during which the HR rate exceeded the threshold of the total ECG monitoring time; Sa is the parameter of the figure area, which is limited by the HR trend during the monitoring period and the threshold HR line [6].

All patients with STEMI underwent 2D echocardiography using a MyLab scanner at baseline and at week 12. The study included pulsed-wave and continuous Doppler and color flow mapping. During the study, standard indicators of systolic function were analyzed: biplane left ventricular ejection fraction (LVEF) using the Simpson method, left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), as well as their indices in two-dimensional mode (LVEDVI, LVESVI) [7]. LVEDVI > 20% and/or LVESVI > 15% versus the baseline values at the onset of STEMI were indicative of pathological LV remodeling [8].

The obtained data were analyzed with the Statistica 13.0 software suite. The quantitative variables are presented with 95% CI. Univariate analysis of variance was used to study changes in the indicators for related samples (more than two) adjusted for the Newman-Keuls test. Qualitative variables were compared using the chi-square test. The likelihood of developing endpoints was determined by calculating the odds ratio (OR) with 95% CI. The threshold of statistical significance was $p < 0.05$ [9].

Results

118 (94.4%) of 125 patients were followed up within 48 weeks. 7 (5.6%) patients dropped out of the study: 2 patients died (one patient due to LV rupture on day 16 and another one of acute heart failure (AHF) based on autopsy findings in month 10 of follow-up); two patients left for other cities; 3 patients were withdrawn from the study in months 3, 5, and 7, respectively, due to poor treatment compliance.

All patients were divided into two groups depending on the presence/absence of LV remodeling in week 12. The group without LV remodeling (R(–)) included 79 (67%) patients, while the group with signs of pathological LV remodeling (R(+)) included 39 (33%) patients. The groups did not differ in the main echocardiographic parameters at the baseline; however, in the intergroup comparison after 12 weeks of treatment, most of the indicators worsened in the R(+) group compared to those in the R(–) group (Table 1).

The groups were comparable in age, sex, anthropometric characteristics, cardiovascular risk factors, infarction location, and TLT and PCI timing. There were no differences at admission between the groups regarding the history of CAD, AH, DM type 2, AHF (Killip class). It should be noted that the treatment was carried out in both groups following the clinical guidelines [3, 10]; there were no differences in the treatment between the groups over the 48-week study duration (Table 2).

Table 1. Echocardiographic parameters in the study groups

Parameter	Group R(–)		Group R(+)		d_{1-3}	d_{2-4}
	Day 7–9	In 12 weeks	Day 7–9	In 12 weeks		
	1	2	3	4		
LVEDD, mm	53 (48–55)	53 (49–56)	53 (49–56)	56 (52–57)	0.67	0.02
LVESD, mm	34 (28–39)	34 (30–38)	32 (29–39)	34 (30–40)	0.45	0.072
LVEDV, mL	114 (99–136)	113 (94–134)	118 (92–130)	150 (121–168)	0.52	0.00001
LVESV, mL	59 (47–71)	53 (37–67)	56 (42–72)	74 (63–92)	0.42	0.00001
LVEDVI, mL/m^2	60 (50–67)	57 (48–66)	58 (47–68)	73 (63–87)	0.71	0.000004
LVESVI, mL/m^2	30 (24–37)	26 (19–34)	29 (21–34)	39 (31–46)	0.69	0.000003
LVEF, %	50 (43–56)	53 (45–58)	50 (45–54)	47 (44–52)	0.56	0.003

Data presented with 95% confidence interval.
LVEDD – left ventricular end-diastolic dimension; LVESD – left ventricular end-systolic dimension;
LVEDV – left ventricular end-diastolic volume; LVESV – left ventricular end-systolic volume;
LVEDVI – left ventricular end-diastolic volume index; LVESVI – left ventricular end-systolic volume index;
LVEF – left ventricular ejection fraction;
d_{1-3}, differences between the 1st and 3rd columns; d_{2-4}, differences between the 2nd and 4th columns.

ISSN 0022-9040. Kardiologiia. 2021;61(10). DOI: 10.18087/cardio.2021.10.n1626

Table 2. Treatment of patients in the study groups

Drug group	R (–) group (n=79)			R (+) group (n=39)			d_{1-4}	d_{2-5}	d_{3-6}
	Day 7–9	In 12 weeks	In 48 weeks	Day 7–9	In 12 weeks	In 48 weeks			
	1	2	3	4	5	6			
Beta-blockers	62 (78.5)	66 (83.5)	65 (82.3)	29 (74.4)	33 (84.6)	33 (84.6)	0.617	0.882	0.751
ACE inhibitors/ARBs	66 (83.5)	58 (73.4)	61 (77.2)	31 (79.5)	28 (71.8)	25 (64.1)	0.588	0.853	0.132
ASA + clopidogrel/ticagrelor	79 (100)	79 (100)	79 (100)	39 (100)	38 (97.4)	38 (97.4)	1	0.153	0.153
Statins	79 (100)	79 (100)	79 (100)	39 (100)	39 (100)	39 (100)	1	1	1
Amiodarone	3 (3.8)	1 (1.3)	2 (2.5)	3 (7.7)	2 (5.1)	2 (5.1)	0.365	0.21	0.464

ACE – angiotensin converting enzyme; ARB – angiotensin II receptor blocker; ASA – acetylsalicylic acid.
d_{1-4} – differences between the 1st and 4th columns; d_{2-5} – differences between the 2nd and 5th columns;
d_{3-6} – differences between the 3rd and 6th columns.

No significant changes occurred in the nature of life-threatening arrhythmias or conduction disorders in either group over the course of the study (48 weeks). However, an increase in the number of paired VBs from 5.1% at baseline to 25.6% by the end of active treatment (p=0.013) in patients with pathological LV remodeling was not observed in the P (–) group. Moreover, patients without pathological LV remodeling had no signs of myocardial ischemia by Week 48, although these signs were present in 11.4% at the baseline (p=0.003). In the P (+) group, myocardial ischemia was recorded twice as often (23.1%) on Day 7–9; by the end of treatment, the number of patients with ischemia decreased to 10.3%; however, the changes were not significant.

During the 48-week follow-up, the frequency of VLPs remained at the same level in both groups. However, positive changes in the parameters observed in the R (–) group by the end of the follow-up period were not observed in patients with pathological LV remodeling. In the R (-) group, HFLA decreased from 28.2 (95% CI 26.5–30) ms to 24.7 (95% CI 22.5–26.8) ms (p=0.004), while RMS increased from 43.6 (95% CI 38–49) μV to 187 (95% CI 52.9–321.1) μV from the baseline (p=0.047).

There were also positive changes in HRT in the R (–) group: the number of patients with pathological HRT decreased from 20% to 10% in 24 weeks (p=0.02) and to 5% in 48 weeks (p=0.002); this was indicative of the recovery of baroreflex sensitivity. HRT did not change significantly in the group with pathological remodeling. There were no clinically significant changes in TO and TS in both groups within the entire follow-up period.

The duration of the QT interval increased compared with the baseline values for 24-hour-, daytime-, and nighttime periods in both groups. The duration of QTa increased at every visit in the group without pathological LV remodeling (p=0.008) for all time intervals and QTe (p=0.03) for 24-hour- and nighttime periods. The duration of only QTa significantly increased (p=0.004) for 24-hour-, daytime- and nighttime periods in patients with pathological LV remodeling. A statistically significant increase in the duration of QTc observed in the R (–) group in 24 weeks (p=0.005) remained high in 48 weeks (p=0.007) for all time intervals; in the R (+) group, it increased only in 48 weeks (p=0.04) for 24-hour- and nighttime periods (Table 3, 4).

A more extended repolarization phase combined with the stabilization of its duration in different parts of the myocardium was evidenced by the regression of all QT dispersion indicators after 24 weeks in the R (–) group: decreased disp QTa (p=0.009); disp QTe (p=0, 03); sdQTa (p=0.006) for 24-hour-, daytime- and nighttime periods; sdQTe (p=0.009) for 24-hour- and daytime periods (Figure 1).

In the R (+) group, there was a regression only in disp QTa (p=0.04) and sdQTa (p=0.008) for 24-hour- and daytime periods at Week 48 (Figure 2).

After 48 weeks of treatment, there was an increase in the time indicators of HRV for 24 hours versus the baseline values in patients without pathological LV remodeling: SDNN by 23% (p=0.00002), SDNNi by 10% (p=0.01), SDANN by 28% (p=0.00002), RMSSD by 23% (p=0.002), NN50 by 62% (p=0.00003), pNN50 by 65% (p=0.00007) due to the leveling of the sympathetic component of the autonomic nervous system, which actively affects HR regulation during acute cardiac events. At the same time, only two indicators showed a similar trend for the 24-hour period in the R (+) group after 48 weeks of treatment: SDNN and SDANN increased by 28% and 36%, respectively (p=0.0001).

By the end of the treatment, there was an increase in the total power of the spectrum in both groups: by 49% in the R (–) group (p=0.0002), by 82% (p=0.0001) in the R (+) group compared to the baseline levels. Moreover, the 24-hour autonomic balance index L/H decreased by 20% in both groups after 48 weeks (p=0.03); however,

Table 3. Changes in the QT interval according to Holter monitoring data in the R (–) group (n = 79)

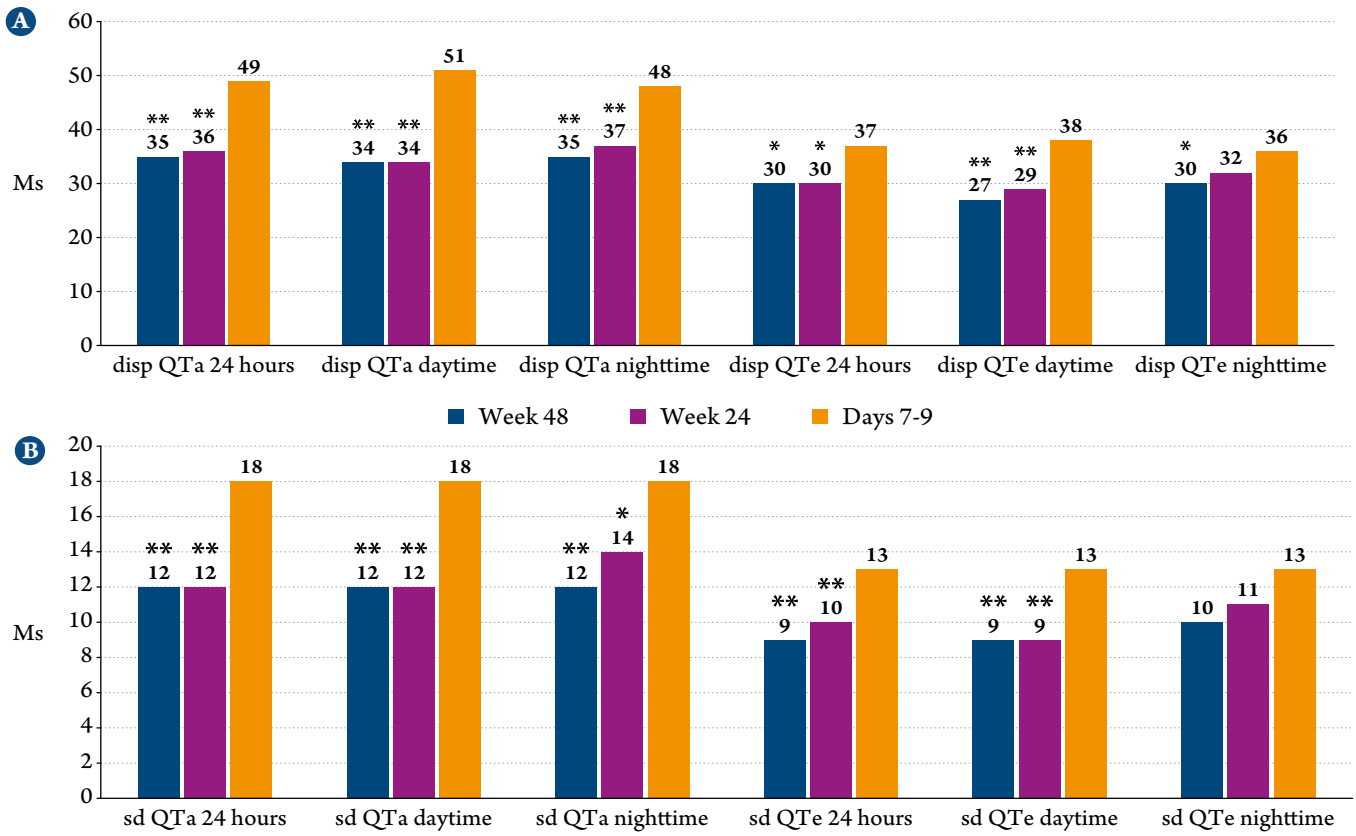
Parameter	Period	Day 7–9	In 24 weeks	In 48 weeks	d_{1-2}	d_{1-3}
		1	2	3		
QTa, ms	24 hours	279 (269–290)	315 (309–322)	317 (309–325)	0.001	0.001
	daytime	273 (262–282)	304 (297–310)	304 (297–311)	0.001	0.001
	nighttime	294 (283–305)	333 (325–342)	336 (329–344)	0.001	0.001
QTe, ms	24 hours	370 (362–377)	379 (373–384)	376 (370–383)	0.004	0.01
	daytime	357 (350–364)	363 (357–369)	362 (356–368)	0.37	0.41
	nighttime	392 (383–399)	400 (394–407)	399 (393–406)	0.003	0.003
QTc, ms	24 hours	395 (387–403)	406 (401–412)	406 (400–412)	0.001	0.001
	daytime	395 (387–403)	403 (392–414)	407 (401–413)	0.24	0.03
	nighttime	397 (390–405)	406 (400–411)	405 (398–411)	0.02	0.02

Data presented as the mean with 95% confidence interval. QTa – duration of the QT interval to the peak of the T wave; QTe – duration of the QT interval to the end of the T wave; QTc – corrected QT interval using the Bazett's formula.
d_{1-2} – differences between the 1st and 2nd columns; d_{1-3} – differences between the 1st and 3rd columns.

the trend was obtained in the R (–) group due to an increase in very low-frequency impulses VLfP (p=0.02) by 17%, while in the R (+) group, this occurred due to an increase in the ultra-low-frequency component UlfP, which is responsible for the predominance of sympathetic activity, by 97% (p=0.0001).

Analysis of chronotropic cardiac load revealed positive changes in 24-hour- and nighttime Ta and Sa in STEMI patients without LV remodeling. The proportion of time during which HR exceeded the threshold values decreased by 18% for the 24-hour period (p=0.006) and by 31% for the nighttime period

Figure 1. Changes in the QT interval duration variance according to Holter monitoring data in the R (–) group (n=79)



A – changes in the QT interval variance in the R (–) group; B – changes in the QT variance standard deviations in the R (–) group.
* p < 0.01, ** p < 0.001 – significant differences between the parameters on Day 7–9 and subsequent measurements.
Here and Figure 2: QTa disp – variance of the QT interval duration to the peak of the T wave; QTe disp – variance of the QT interval duration to the end of the T wave; sd QTa – standard deviation of the variance of the QT interval duration to the peak of the T wave; sd QTe – standard deviation of the variance of the QT interval duration to the end of the T wave.

ISSN 0022-9040. Kardiologiia. 2021;61(10). DOI: 10.18087/cardio.2021.10.n1626

Table 4. Changes in the QT interval according to Holter monitoring data in the R (+) group (n=39)

Parameter	Period	Day 7–9	24 weeks after STEMI	48 weeks after STEMI	d_{1-2}	d_{1-3}
		1	2	3		
QTa, ms	24 hours	267 (253–282)	311 (301–322)	310 (300–321)	0.001	0.001
	daytime	260 (245–274)	300 (289–311)	300 (290–309)	0.001	0.001
	nighttime	280 (263–297)	332 (319–346)	329 (316–343)	0.001	0.001
QTe, ms	24 hours	376 (365–386)	379 (371–388)	377 (365–388)	0.51	0.65
	daytime	363 (351–374)	364 (354–374)	361 (349–373)	0.72	0.43
	nighttime	394 (382–406)	405 (393–416)	399 (387–412)	0.27	0.33
QTc, ms	24 hours	400 (390–409)	406 (396–415)	413 (402–423)	0.38	0.29
	daytime	402 (392–412)	407 (397–417)	413 (403–424)	0.43	0.21
		395 (385–405)	410 (398–423)	414 (401–427)	0.02	0.009

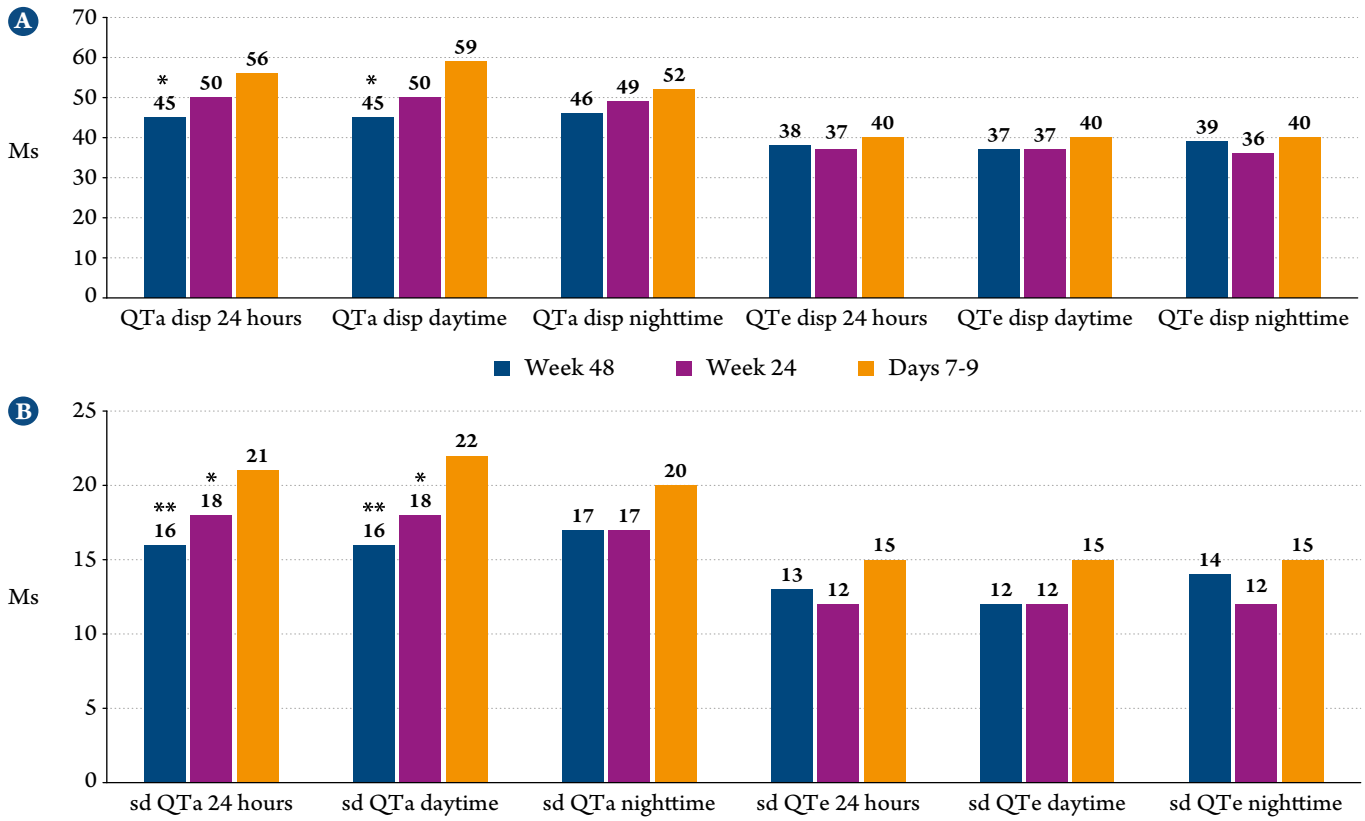
Data presented as the mean with 95% confidence interval. QTa – duration of the QT interval to the peak of the T wave; QTe – duration of the QT interval to the end of the T wave; QTc – corrected QT interval using the Bazett's formula.
d_{1-2} – differences between the 1st and 2nd columns; d_{1-3} – differences between the 1st and 3rd columns.

(p=0.0001) by Week 48. Sa also decreased by 33% for the 24-hour period (p=0.006), by 50% for the nighttime hours period (p=0.0002) compared to baseline values obtained on Day 7–9 of STEMI (Figure 3).

In pathological LV remodeling, there was a decrease in only Sa by 40% (p=0.047) for the 24-hour period and by 49% (p=0.03) for the nighttime period by Week 24. However, this indicator increased to the baseline values by Week 48 (Figure 4).

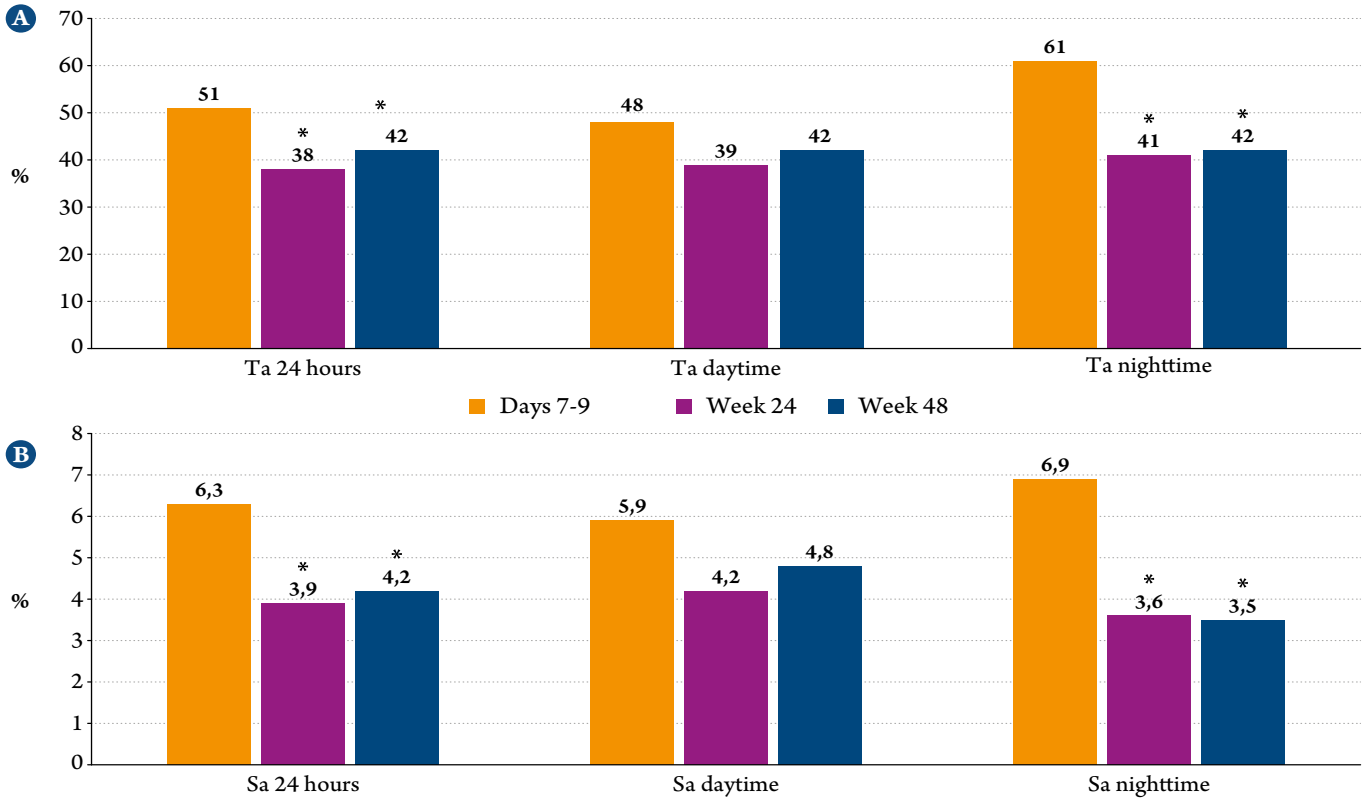
The intergroup analysis showed that the number of patients with rhythm and conduction disorders, as well as signs of myocardial ischemia, did not differ

Figure 2. Changes in the QT interval duration variance according to Holter monitoring data in the R (+) group (n=39)



A – changes in the QT interval variance in the R (+) group; B – changes in the QT variance standard deviations in the R (+) group.
* p < 0.01, ** p < 0.001 – significant differences between the parameters on Day 7–9 and the subsequent measurements.
QTa disp – variance of the QT interval duration to the peak of the T wave; QTe disp – variance of the QT interval duration to the end of the T wave; sd QTa – standard deviation of the variance of the QT interval duration to the peak of the T wave; sd QTe – standard deviation of the variance of the QT interval duration to the end of the T wave.

Figure 3. Changes in the parameters of chronotropic cardiac load duration variance according to Holter monitoring data in the R (–) group (n=79)



A – changes in Ta in the R (–) group; B – changes in Sa in the R (–) group.
* $p < 0.001$ – significant differences between the parameters on Day 7–9 and the subsequent measurements.
Ta – percentage of time when heart rate exceeds the threshold level of the total time of electrocardiographic monitoring;
Sa – area of the figure limited by the trend of the heart rate during the monitoring time and the heart rate threshold line.

at baseline; this was also true of electrical instability parameters. However, patients with pathological LV remodeling more frequently experienced paired VBs and myocardial ischemia by Week 48 (p=0.004). At the same time, a more pronounced regression of the variance parameters and standard deviation of the variance of the QT interval (p=0.02) was observed for all time intervals in the group R (–) by Week 24 and Week 48. Moreover, the more noticeable transformation of the time and frequency components of nighttime HRV observed after 48 weeks of treatment was indicative of the recovery of autonomic balance due to parasympathetic impulses in those patients.

According to the SAQ questionnaire, starting from Week 24 of follow-up, attitudes to the disease improved in both groups (p=0.0007); however, higher QoL was reported only by patients without pathological cardiac remodeling (p=0.03). In the group R (+), patients reported more pronounced restrictions on physical activity by Week 48 (p=0.047); this was not true of the R (–) group. According to the MLHFQ questionnaire, QoL improved in the R (–) group by Week 96 (p=0.045), but in the R (+) group, such an improvement was only reported by Week 144 of the follow-up (p=0.02).

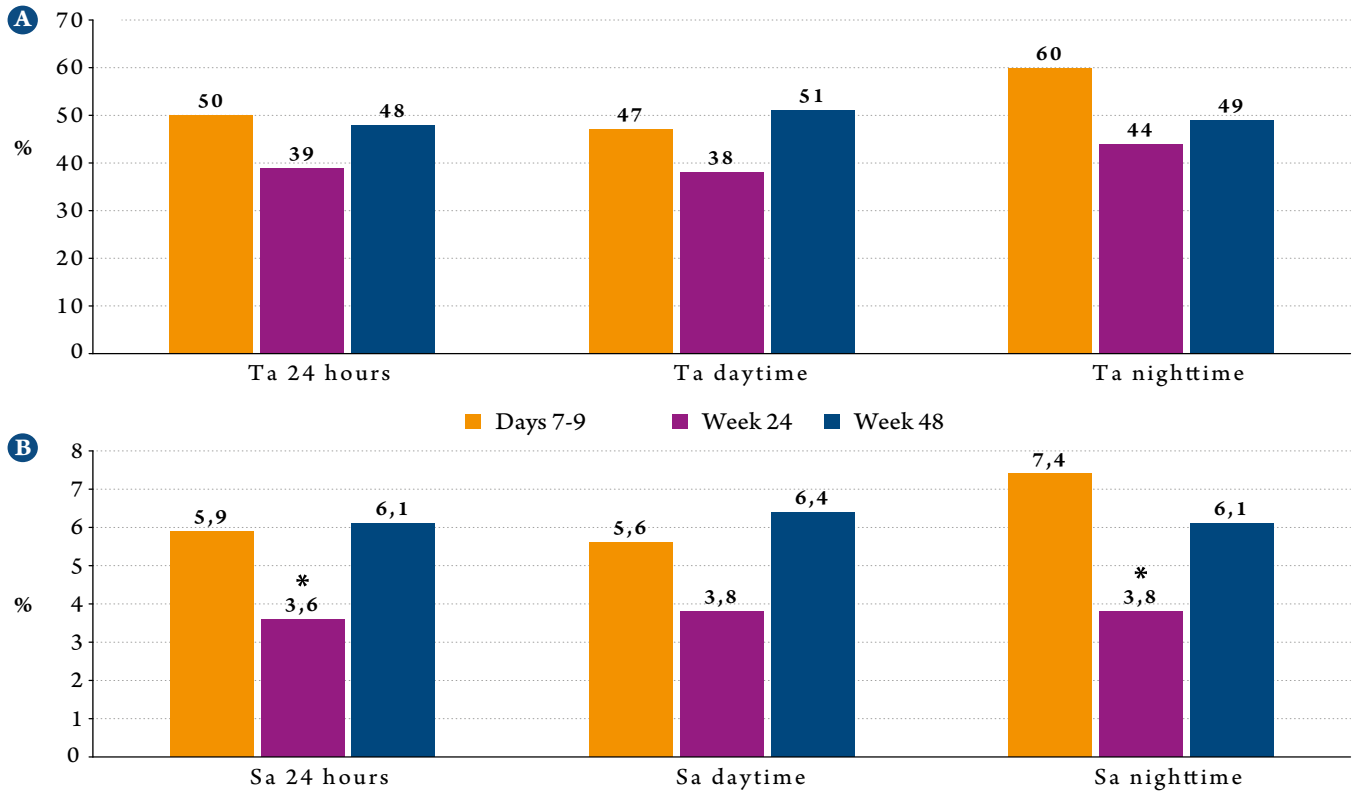
Intergroup comparative analysis of endpoint achievement in the R (–) and R (+) groups (Table 5) showed that this occurred more often in patients with pathological myocardial remodeling, which was mainly due to life-threatening rhythm disorders, cardiac surgeries, and hospitalizations for AHF and decompensated CHF: 82.1% vs. 27.8% (OR 11.8; 95% CI 4.6–30.8; p=0.00001).

Discussion

Pathological myocardial remodeling after STEMI is accompanied by significant changes in LV geometry, which clearly affects the destabilization of electrophysiological processes and autonomic regulation of sinus rhythm. To study such changes and assess the unfavorable long-term prognosis in postinfarction LV remodeling, our study divided patients into two groups: a group without LV remodeling (R (–) n=79 (67%) patients) and a group

ISSN 0022-9040. Kardiologiia. 2021;61(10). DOI: 10.18087/cardio.2021.10.n1626

Figure 4. Changes in the parameters of chronotropic cardiac load duration variance according to Holter monitoring data in the R (+) group (n=39)



A – changes in Ta in the R (+) group; B – changes in Sa in the R (+) group.
* $p < 0.01$ – significant differences between the parameters on Day 7–9 and the subsequent measurements.
Ta – percentage of time when heart rate exceeds the threshold level of the total time of electrocardiographic monitoring;
Sa – area of the figure limited by the trend of the heart rate during the monitoring time and the heart rate threshold line.

with pathological LV remodeling (R (+) n=39 (33%) patients). LVEDVI > 20% and/or LVESVI > 15% were used in this study as the criteria of postinfarction LV remodeling [8].

Fixation of post-depolarization myocardial activity and increased QT dispersion are markers of electrophysiological instability. According to the literature, the role of VLPs in the postinfarction period remains controversial. In some studies (CARISMA, REFINE), the registration of late post-depolarizations had no prognostic value [11]. However, according to other authors, VLPs are predictors of repeated adverse cardiovascular events, including death [12]. In our study, there were no differences in the number of patients with fragmented myocardial activity depending on the presence of postinfarction LV remodeling. However, positive changes in HfLA and RMS were exhibited by patients of the R (–) group (p=0.04 and p=0.047, respectively), which was indicative of the stabilization of electrophysiological processes in the myocardium.

The QT dispersion is known to reflect the heterogeneity of the myocardial repolarization process, and its increase is regarded as a higher risk of developing life-threatening arrhythmias and sudden cardiac death in post-infarction patients [5, 13]. The absence of pathological myocardial remodeling in patients with a history of STEMI was accompanied by stabilization of the repolarization phase duration in different parts of the myocardium, which was evidenced by reduced disp QTa and disp QTe (p=0.009 and p=0.03, respectively), and the standard deviation of the sdQTa variance (p=0.006) for all time intervals, and sdQTe (p=0.09) for 24-hour and daytime periods.

The unique data obtained in this study showed the relationship between morphological and electrophysiological destruction of the myocardium in pathological remodeling following primary STEMI.

Hypersympathicotonia is an obligate concomitant of gross morphological changes occurring in the myocardium: autonomic dysfunction affects the development of postinfarction remodeling, while structural changes in the myocardium result in a sympathovagal imbalance. On the one hand, a shift in the autonomic balance towards the prevalence of sympathetic impulses

Table 5. Endpoints achieved in the study groups

Endpoint	R (–) group (n=79)	R (+) group (n=39)	p
Life-threatening heart arrhythmias	8 (10,1%)	12 (30,7%)	0,005
Unstable angina	6 (7,6%)	6 (15,4%)	0,188
Recurrent myocardial infarction	–	1 (2,6%)	0,718
PCI for coronary artery restenosis	3 (3,8%)	2 (5,1%)	0,736
PCI for newly onset coronary artery stenosis	2 (2,5%)	1 (2,6%)	0,992
Hospitalizations for AHF and decompensated CHF	1 (1,3%)	4 (10,3%)	0,023
Cardiac surgery (CABG, mammary artery bypass, valve repair, LV aneurysm)	2 (2,5%)	6 (15,4%)	0,009
Total	**22 (27,8%)**	**32 (82,1%)**	**0,00001**

PCI – percutaneous coronary intervention; AHF – acute heart failure;
CHF – chronic heart failure; CABG – coronary artery bypass grafting; LV – left ventricle.

can directly trigger the development of a cardiovascular catastrophe, i.e., MI [14]. On the other hand, structural changes in the geometry of the damaged myocardium can lead to increased afferent stimulation of the sympathetic autonomic nervous system, which can cause a reflex decrease in the parasympathetic tone [15]. Moreover, postinfarction LV remodeling depends on HR and the state of the autonomic nervous system [16]: sympathicotonia promotes higher HR, which accelerates the progression of pathological cardiac remodeling [7], while structural remodeling of the myocardium reduces HRV, which is reflected by changes in temporal and spectral parameters [16, 17]. Tachycardia increases the oxygen demand of the myocardial and causes progressive depletion of energy reserves. The resulting overload of Ca^{2}+ mitochondria contributes to a decrease in adenosine diphosphate rephosphorylation, along with reduced levels of creatine phosphate and adenosine triphosphate, which results in reduced myocardial contractility. Activation of phospholipases and proteases in a lack of energy reserves causes the death of cardiomyocytes, followed by fibrosis and electrophysiological destruction of the myocardium [18]. The concomitant activation of the renin-angiotensin-aldosterone system contributes to electrolyte disturbances and myocardial hypertrophy, while increased aldosterone-dependent collagenase activity causes fibrosis and aggravates the progression of cardiac remodeling [18, 19], resulting in a so-called vicious circle.

Many studies have shown that temporal and spectral parameters of HRV decrease within 24 hours from the onset of MI [20]. According to our data, patients without postinfarction LV remodeling showed a favorable trend in the recovery of sympathovagal balance within 48 weeks of follow-up evidenced by temporal parameters: SDNN (p=0.00002), SDNNi (p=0.01), SDANN (p=0.00002), RMSSD (p=0.002), NN50 (p=0.00003), pNN50 (p=0.00007). In patients with postinfarction LV remodeling, several temporal indicators increased by week 24: SDNN and SDANN (p=0.0001). However, unfavorable changes (i.e., a decrease) in these parameters were observed by the end of active treatment. As for the frequency indicators, an increase in the total spectrum power and regression of the autonomic balance index was noted in both groups by the end of treatment. However, L/H decreased in pathological postinfarction remodeling due to the ultra-low-frequency impulses responsible for the sympathetic autonomic nervous system.

In the present study, it was found that baroreflex sensitivity was restored after STEMI only in patients without postinfarction myocardial remodeling: the number of patients with pathological HRT decreased from 20% to 5% by the end of active treatment (p=0.002) but remained at the same level within 48 weeks of follow-up in the R (+) group.

When chronotropic cardiac load was assessed using the original method [6], it was found that postinfarction remodeling prevented a decrease in the frequency load on the myocardium despite heartrate lowering therapy. This is due to the increased activity of the sympathetic-adrenal system. Thus, pathological remodeling after STEMI prevents the normalization of autonomic regulation of sinus rhythm due to hypersympathicotonia, which is manifested by increased chronotropic cardiac load, decreased spectral and temporal parameters of HRV, and impaired HRT.

It is evident that a persistent impairment of the normal myocardial morphology in pathological remodeling contributes to the development of a series of adverse events in the postinfarction period, as well as significantly reducing QoL. In this regard, early detection of the signs of postinfarction myocardial remodeling by assessing an increase in volumetric indices is clearly of practical utility. According to the

ISSN 0022-9040. Kardiologiia. 2021;61(10). DOI: 10.18087/cardio.2021.10.n1626

ATTR

ЗАПОДОЗРИТЬ *и* ВЫЯВИТЬ

НАЙТИ КЛЮЧ К ВЕРНОМУ ДИАГНОЗУ

КАК РАСПОЗНАТЬ СИМПТОМЫ ТРАНСТИРЕТИНОВОЙ АМИЛОИДНОЙ КАРДИОМИОПАТИИ (ATTR-КМП) У ВАШЕГО ПАЦИЕНТА?

ATTR-КМП — это зачастую недооцененная причина сердечной недостаточности, в частности сердечной недостаточности с сохраненной фракцией выброса (СНсФВ). Это тяжелое жизнеугрожающее заболевание с медианой выживаемости 2-3,5 года.

ATTR-КМП встречается у 17% пациентов с СНсФВ.[1-5]

ATTR-КМП часто пропускают или диагностируют поздно. Стандартные методы диагностики сердечной недостаточности, эхокардиография (ЭхоКГ) и электрокардиография (ЭКГ) совместно с методами лучевой диагностики могут помочь в поиске правильного диагноза.

ОЗНАКОМЬТЕСЬ С КЛИНИЧЕСКИМИ ПРИЗНАКАМИ, КОТОРЫЕ ПОМОГУТ ОПРЕДЕЛИТЬ ВЕРОЯТНОСТЬ НАЛИЧИЯ ATTR-КМП У ПАЦИЕНТА И НЕОБХОДИМОСТЬ ДАЛЬНЕЙШЕЙ ДИАГНОСТИКИ.

СЕРДЕЧНАЯ НЕДОСТАТОЧНОСТЬ С СОХРАНЕННОЙ ФРАКЦИЕЙ ВЫБРОСА обычно у пациентов старше 60 лет[5]

НЕПЕРЕНОСИМОСТЬ стандартной лекарственной терапии для лечения СН: ингибиторов ангиотензин-превращающего фермента, блокаторов рецепторов ангиотензина и бета-блокаторов[6]

РАСХОЖДЕНИЕ между амплитудой зубцов комплекса QRS и ЭКГ и толщиной стенки левого желудочка при ЭхоКГ[7,8]

КАРПАЛЬНЫЙ ТУННЕЛЬНЫЙ СИНДРОМ или **СТЕНОЗ ПОЗВОНОЧНОГО КАНАЛА**[9,10]

Эхокардиография показывает **УВЕЛИЧЕНИЕ ТОЛЩИНЫ СТЕНКИ ЛЖ**[7]

Дисфункция **ВЕГЕТАТИВНОЙ НЕРВНОЙ СИСТЕМЫ,** включая нарушения со стороны желудочно-кишечного тракта или необъяснимое снижение массы тела[11]

ОТСКАНИРУЙТЕ QR-КОД, ЧТОБЫ ОЗНАКОМИТЬСЯ С КЛИНИЧЕСКИМИ ПОДСКАЗКАМИ, КОТОРЫЕ МОГУТ ПОМОЧЬ РАСКРЫТЬ ПРИЧИНУ СЕРДЕЧНОЙ НЕДОСТАТОЧНОСТИ[12-16]

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PP-VDM-RUS-0098, 16.02.2022

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SAQ and MLHFQ questionnaires, patients without pathological LV remodeling reported better QoL (p=0.03 and p=0.04, respectively); moreover, they had less frequent adverse events: life-threatening heart rhythm disturbances, repeated cardiac events, decompensated CHF, hospitalizations for repeated PCI, cardiac surgeries: 27.8% vs. 82.1% (OR 11.8; 95% CI 4.6–30.8; p=0.00001).

The findings of this study confirm the relevance of early diagnosis of postinfarction myocardial remodeling. This is demonstrated by persistent structural changes in the myocardium after the index event that prevent the recovery of autonomic regulation of sinus rhythm and impair the harmonization of electrophysiological processes in the myocardium, thus affecting the frequency of recurrent cardiac events in STEMI patients.

Conclusion

Pathological remodeling developed within 12 weeks after MI contributes to the development of severe changes in the electrical properties of the myocardium and concomitant impairment of autonomic regulation of the heart rhythm, which causes electrical instability leading to unfavorable cardiac events. Early detection of the signs of pathological remodeling by left ventricular end-diastolic and end-systolic volume indices allows the prediction of life-threatening arrhythmias and poor quality of life indicators, as well as recurrent cardiovascular events in patients with ST-segment elevation myocardial infarction.

Funding

The study was supported by the Russian Foundation for Basic Research (grants 19-315-90024 and 19-315-90031) and the Scholarship of the President of the Russian Federation to young scientists, PhD and DSc, (project title: «Interrelation of essential mechanisms of arrhythmogenesis with myocardial contractility and major markers for development and progression of heart failure in patients after ST segment elevation myocardial infarction», MK-553.2020.7).

No conflict of interest is reported.

The article was received on 25/03/2021

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ISSN 0022-9040. Kardiologiia. 2021;61(10). DOI: 10.18087/cardio.2021.10.n1626

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