DYNAMICS OF QT INTERVAL VARIANCE AND HEART RATE VARIABILITY AGAINST THE BACKGROUND OF SURGICAL MYOCARDIAL REVASCULARIZATION IN PATIENTS WHO HAVE SUFFERED A MYOCARDIAL INFARCTION WITH A MULTIVESSEL LESION OF THE CORONARY BED

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Abstract. *Predicting adverse outcomes in people who have suffered a myocardial infarction remains a serious and unresolved problem, which pushes researchers to search for new technologies. One of the relatively promising new noninvasive methods for predicting sudden coronary death in patients with coronary artery disease and ventricular arrhythmias may be a noninvasive assessment of myocardial electrical instability. Taking into account its important prognostic role, primarily in patients with ventricular arrhythmia who have suffered a myocardial infarction and have a multivessel character of coronary lesion, the purpose of this work was to study the characteristics of QT interval variance and heart rate variability in this category of patients.*

Keywords: *QT interval variance, heart rate variability, ventricular arrhythmia, myocardial infarction, sudden coronary death.*

Introduction. By the beginning of the 20th century, mortality from cardiovascular diseases was less than 10% of all diseases in the world. By the end of the 20th century, it accounts for almost half of all deaths in developed countries. In the structure of total mortality in the 90s of the 20th century, their share amounted to more than 14.3 million out of 50 million global deaths, or 28.5% annually. Of these, 6.3million deaths (44%) were due to coronary heart disease (CHD) [1]. At the same time, among the cardiovascular diseases that cause mortality, 80% is myocardial infarction (MI). According to Rosental M.E. et al., in the United States, about 500 thousand people are hospitalized annually for MI, of which 80% remain alive and are discharged. Within a year after discharge, 10 to 20% of patients die. Moreover, more than 50% of cases of death occur suddenly and only 5-4% of patients who died suddenly at autopsy reveal repeated acute focal changes in the myocardium. The risk of arrhythmic death in postinfarction patients reaches the highest values in the first 6 months and persists for the next 2 years [2].

The high medical and social significance of the phenomenon of sudden death (SCD) is due not only to its suddenness, but above all, to its mass character. In economically developed countries, about 2,500 people die every day, and only in 2-5% of cases death occurs in a medical facility. In Russia, according to estimates, the frequency of SCD corresponds to the level of 400-500 thousand annually, in the world – about 3 million annually with the possibility of survival of no more than 1%, and the probability of successful resuscitation even in developed countries does not exceed 5%. Since most of these events occur in a dream or without witnesses, it is not possible to provide assistance within 6-8 minutes. Therefore, it is necessary to take measures specifically to prevent life-threatening arrhythmias based on determining the risk of their development. Quite a lot of research has been devoted to the development of risk stratification schemes; to date, the factors affecting the risk of SCD, as well as prevention methods, have been studied [3]. The existing risk stratification schemes are not always applicable to our contingent of patients, since often the available algorithms use data from complex techniques that are impossible in our conditions, and do not take into account the specifics of first aid for MI. Many risk stratification schemes have been developed for patients who are admitted in the early stages of MI, and, consequently, they have undergone revascularization procedures. Whereas, unfortunately, in real conditions, our patients are admitted to hospitals a day or even several days after the onset of symptoms. All of the above points to the need to create your own risk stratification scheme based on your own research data. Assessing the combination of factors using standardized methods available in the conditions of medical institutions of the Republic, capable of predicting an unfavorable prognosis, will allow the doctor to recommend one of the types of treatment to the patient and thereby contribute to the prevention of SCD.

One of the important tasks in patients who have suffered a myocardial infarction (MI) is the earliest detection of life-threatening and potentially life-threatening ventricular arrhythmias (VDNRS) in them. To date, noninvasive indicators of myocardial electrical instability (ENM) have been proposed, determined using Holter ECG monitoring (HMECG), in particular, such as heart rate variability (HRV). [3-5]. Based on numerous data, their effectiveness in assessing the risk of cardiovascular mortality and sudden cardiac death (SCD) in patients with coronary heart disease and CHF has been demonstrated [1, 2].Currently existing models of stratification of patients by risk groups of NFRS provide, as a rule, an assessment of changes in the systolic function of the left ventricle (LV), and to a lesser extent, indicators characterizing ENM. At the same time, the study of HRV and the variance of the QT interval and to clarify the specific mechanisms of development and progression of HRV, especially in patients who have undergone MI, seems to be a promising direction [3-5].

The aim of the study was to evaluate the parameters of QT interval variance and heart rate variability in patients with ventricular arrhythmias who have suffered a myocardial infarction and have a multivessel character of coronary lesion, as well as their dynamics after surgical revascularization.

Materials and methods. 125 patients aged 35 to 84 years (average age 60.6±8.2 years) hospitalized at the Republican Specialized Scientific and Practical Medical Center of Cardiology for the preparation and conduct of coronary bypass surgery were examined.

The multivessel nature of the coronary lesion was established based on the results of diagnostic selective coronary angiography. The study did not include patients with a lack of stable sinus rhythm, impaired sinoauricular or atrioventricular conduction, lack of a history of MI, hyperthermia, the presence of diseases that significantly change the variability of heart rhythm (diabetes mellitus, hypo- or hyperthyroidism, alcoholism, severe respiratory, renal or hepatic insufficiency, oncological diseases, etc.).

Upon admission to the hospital, all patients underwent: comprehensive clinical and biochemical blood analysis, transthoracic echocardiography, selective coronary angioangio and ventriculography, as well as CMEG using the CardioSens+ system (KHAI-MEDIKA, Ukraine). Monitoring was carried out in conditions of free movement of patients, against the background of standard therapy, which included antiplatelet agents, beta-blockers, ace inhibitors or BAR, statins in individually selected doses, nitrates (if necessary), as well as amiodarone (if necessary in patients with NFRS).

Ventricular extrasystoles (VES) of III-V grades (Lown-Wolf), as well as 10 or more VES per hour (Bigger), were regarded as POFRS. The density of RE was determined as a percentage of the total number of RE to the total number of analyzed reductions during monitoring.

HRV analysis was performed using Time Domain Methods and Frequency Domain Methods.

The interpretation of HRV data was carried out according to the recommendations of the working group of the European Society of Cardiology and the North American Society of Stimulation and Electrophysiology (1999). The following temporal and spectral indicators were used to assess HRV:

RR cp (ms) — the average value of all R—R intervals per day;

SDNN (ms) is the standard deviation of all N—N intervals;

SDANN (ms) is the standard deviation of the average values of the N—N intervals calculated from 5-minute intervals throughout the recording;

SDNNi (ms) is the average value of the standard deviations of the N—N intervals calculated over 5-minute intervals throughout the recording;

RMSSD (ms) is the square root of the average sum of the squares of the differences between adjacent intervals N—N;

NN50 is the number of pairs of adjacent N—N intervals that differ by more than 50 ms during the entire recording;

pNN50 (%) is the value of NN50 divided by the total number of N—N intervals.

TR (In) (ms2) is the logarithm of the total power of all R—R intervals;

ULF (In) (ms2) is the logarithm of power in the ultra—low frequency range (<0.003 Hz);

VLF (In) (ms2) is the logarithm of power in the very low frequency range (0.003—0.04 Hz);

LF (In) (ms2) is the logarithm of power in the low frequency range (0.04—0.15 Hz);

HF (In) (ms2) is the logarithm of power in the high frequency range (0.15—0.4 Hz);

LF/HF is the ratio of the low—frequency to the high-frequency component of the spectrum.

To identify the electrophysiological heterogeneity of the ventricular myocardium, we determined in each of the 3-4 cardiac cycles following each other on the resting ECG: generalized QT interval durations and QT dispersion values (QTD) in the aVR, aVL, aVF, V1-V6 leads. The difference between the maximum and minimum values of the QT duration in these leads was taken as a measure of QT variance: QTD = QTmax -QTmin (no to all leads). According to various data, an increase in the dispersion of the QT interval above 40-80 ms with a sensitivity of 70-88% and a specificity of 60-80% is a predictor of life-threatening arrhythmias in patients with coronary heart disease [5].

A re-examination of the QT interval variance and heart rate variability was performed 1 year after surgical revascularization in an outpatient setting. The mathematical processing of the material was carried out using Microsoft Office Excel 2013, Statistica for Windows v10 programs. The materials are presented in the form of an average value and a standard deviation. The changes at $p<0.05$ were considered significant.

Results: According to the results of the initial examination, the clinical characteristics of patients were compiled (Table 1). The main group of patients were men (n=110; 88.0%) of older age (59.7±8.1 years).

Table 1. Clinical characteristics of the examined patients.

Parametres		M±SD	Me [Q1; Q3]
Age, years		59,7±8,1	61 [55; 65]
Sex	Male Female	110 (88,0%) 15 (12,0%)	
BMI, kg/m2		28,8±4,1	29,4 [25,3; 31,6]
Normal body weight, n (%)		27 (21,6%)	
Overweight, n (%)		49 (39,2%)	
Obesity of the	1st degree 2st degree 3st degree	46 (36,8%) 2 (1,6%) 1 (0,8%)	
LV aneurysm		13 (10,4%)	
Creatinine mmol/l,		115±22	
EF %		50,9±9,1	

In the initial analysis of the heart rate (HR), as well as the frequency, density and categories of VHF using HMECG (Table 2), attention is drawn to the relative rigidity of the basic sinus rhythm, which is expressed in a slight difference between the average daily and night heart rate and, accordingly, in a decrease in the circadian index (CI).

Ventricular arrhythmias (VHF), initially noted in all subjects, were generally relatively favorable. However, 55.2% of patients (n=69) had potentially dangerous ventricular arrhythmias (VDNRS). When assessing the frequency of RE, according to the Bigger classification, frequent extrasystole >10 RE/hour was detected in 50.4% of cases (n=63). When analyzing the structure of the NFRS registered in patients, grade II of the FE, as the maximum class, was not noted in any of the examined patients, grade III was detected in 19 patients (15.2%), IVA – in 32 (25.6%), and IVB – in 12 (9.6%).

HRV, estimated per day by both time and frequency methods, was characterized by a significant decrease in the values of the indicators of the total HRV. In particular, the value of SDNN ≤100 ms, indicating a decrease in total HRV, was observed in all 125 (100%) patients included in the study, and a decrease in SDNN ≤70 ms was observed in 116 (92.8%), indicating a pronounced decrease in total HRV. Attention is also drawn to the predominance of the low-frequency component (LF) of HRV with an increase in the LF/HF ratio >3, which indicates increased sympathetic activity (Table 3).

When re-evaluating the studied parameters 1 year after surgical revascularization, reliable dynamics of heart rate indicators with an increase in the value of the circadian index was revealed, which may indirectly indicate an improvement in the autonomic regulation of cardiac activity.

Table 2. Heart rate and circadian index

Parameter	Original value (M±SD)	After 1 year (M±SD)	p
Average heart rate, beats/min	67±8,6	73,4±9,3	0,000
Maximum heart rate, beats/min	97,3±13,9	114,3±22,1	0,001
Minimum heart rate, beats/min	52,7±6,8	54,4±6,8	0,009
Heart rate avg. day, beats/min	69,5±9,1	77,5±9,9	0,000
Heart rate avg at night, beats/min	63,8±8,5	66,9±8,9	0,022
Circadian index	1,09±0,07	1,16±0,08	0,004

Heart rate variability indicators showed some improvement, but the overall HRV, estimated by the SDNN indicator, remained as low as before surgical revascularization. At the same time, the value of the triangular index (HR V TI), which also reflects the overall heart rate variability, significantly decreased (Table 3).

Table 3. Dynamics of heart rate variability indicators.

Parameter	Original value (M±SD)	After 1 year (M±SD)	p
SDNN, ms	40,9±13,7	40,6±12,6	0,126
SDANN, ms	80,3±24,4	101,5±30,7	0,478
rMSSD, ms	22,0±12,0	18,8±7,6	0,296
pNN50, %	4,8±6,8	3,0±3,5	0,156
HRV TI	9,2±2,6	8,6±2,0	0,002
TP, ms^2	2255,0±1725,2	2422,8±1485,4	0,664
ULF, ms^2	81,3±266,7	128,0±205,7	0,067
VLF, ms^2	1492,8±1122,0	1517,2±933,5	0,289
LF, ms^2	454,5±381,1	560,6±426,2	0,654
LF norm, %	68,2±11,7	73,0±9,4	0,881
HF, ms^2	226,3±255,1	217,0±182,1	0,204
HF norm, %	31,8±11,7	27,0±9,4	0,881
LF/HF	3,4±1,8	4,4±3,0	0,970

The duration of both the QT interval and its corrected QTc index, calculated using the Bazett formula, did not undergo significant changes in dynamics in both studied groups. There was only a significant positive trend in the duration of the QT interval in the group of patients who underwent CABG after 1 year (Table 4)

Table 4 QT interval duration and variance

Parametres	CABG				p
	Original value		After 1 year		
	M±SD	Me [Q1; Q3]	M±SD	Me [Q1; Q3]	
QT, ms	403,1±39,2	402 [376; 428]	379,0±26,8	376 [360; 396]	0,002
QTc (Bazett), ms	420,1±33,1	418 [396; 440]	415,3±23,1	417 [401; 431]	0,820
dQT, ms	92,3±42,4	84 [64; 108]	98,1±43,6	86 [68; 112]	0,584
dQTc, ms	73,0±41,9	60 [44; 87,5]	79,8±43,5	61 [44; 116]	0,689

Conclusion.

The development and widespread introduction of modern technologies in the treatment of coronary heart disease, such as coronary artery bypass grafting, are changing the clinical and functional picture of the disease and its course. To assess the rehabilitation process of the patient and his cardiovascular system after reconstructive interventions, a dynamic assessment of hemodynamic parameters, clinical and functional characteristics, biochemical parameters, as well as a study of non-invasive indicators of myocardial electrical instability, such as heart rate variability, is used. A decrease in the main HRV parameters during the course of coronary heart disease, for example, with the development of acute myocardial infarction, angina pectoris, the development of chronic heart failure, and other diseases and pathological conditions is a fairly universal reaction and is not specific, but, apparently, has a general adaptive character.

At the same time, it is known that during surgical revascularization in conditions of artificial circulation, damage to sympathetic and parasympathetic nerve endings occurs. At the same time, partial vegetative denervation of the heart develops with the formation of dysfunction, manifested in changes in the parameters of frequency and variability of the heart rhythm. There is a significant decrease in HRV indicators, in particular, parasympathetic tone is significantly reduced, which, as is known, is a prognostically unfavorable factor. HRV indicators show a sharp decrease in SDNN, a violation of the LF/HF ratio.

For the purpose of early diagnosis of autonomic dysfunction in patients who have undergone CABG, it is recommended to include an assessment of heart rate variability in a comprehensive analysis for full-fledged rehabilitation and prevention of the development of early and late complications in the postoperative period. Also, in our opinion, the introduction of minimally invasive surgical revascularization techniques in recent years will, among other things, reduce the number of complications associated with impaired autonomic innervation of the heart.

Findings:

1. In patients who have suffered a myocardial infarction and have a multivessel lesion of the coronary bed, during CMECG, LVRS of various gradations were detected in 100% of cases

2. In patients with ventricular arrhythmia who have suffered a myocardial infarction and have a multivessel lesion of the coronary artery, HRV is characterized by a significant decrease in both the total HRV and its components, as well as the predominance of the low-frequency component (LF) HRV with an increase in the ratio LF/HF >3, which indicates high sympathetic activity.

3. Heart rate variability indicators, 1 year after surgical myocardial revascularization, did not demonstrate significant dynamics, which may indicate the presence of partial cardiac denervation, preventing a decrease in the severity of autonomic dysfunction.

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