Original article

Skeletal muscle status, autonomic balance and short-term results of cardiac surgery

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Abstract: *Purpose* — To study the association between the status of lower extremities' skeletal muscles and autonomic balance with the short-term results of cardiac surgery patients.
Methods — 64 patients (57 men, median age 63 years) who underwent non-urgent cardiac surgery at the Research Institute for Complex Issues of Cardiovascular Diseases clinic from March 2015 to March 2016 were included in the study. Patients with exacerbation of underlying disease were excluded from the study. Additionally, muscle status of the patients was assessed using static-dynamic tests on a multifunctional training apparatus, and the autonomic nervous system (ANS) state was evaluated using the ORTOexpert program during an active orthostatic test. 9 patients developed complications in the postoperative period; groups with the postoperative complications present and absent were compared according to the studied preoperative indicators.
Results — The following indicators were revealed more often prior to the surgery in the group with the postoperative complications: cardiac arrhythmias (p=0.023), aortic valve regurgitation (p=0.002), left ventricle aneurysm (p=0.007), carotid stenosis (p=0.036), decreased muscle strength of the upper and lower extremities (p=0.047 and p=0.046), sympathetic activation (LF/HF ratio p=0.028), and ANS stress in response to the test.
Conclusion — Low status of skeletal muscles (upper and lower extremities) and ANS sympathetic activation and the overstrain of its adaptive mechanisms were associated with development of postoperative complications after cardiac surgery, along with severity of the underlying cardiac pathology, risk and duration of the surgery.

Keywords: cardiac surgery, postoperative complications, muscle status, autonomic status.

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Introduction

Risk assessment of cardiac surgery is an essential part of the "Heart team" work and affects the choice of optimal surgical tactics and the decision on the possibility of surgery [1]. Current trends in the standards for provision of high-quality, high-tech medical care are such that patients of older age constitute a large, increasing group due to increasing average patient's age [2, 3]. Age is considered one of the factors that significantly affect the outcome of the surgery in the existing scales for assessing the surgery risk (EuroSCORE II, STS, etc.) [1]. However, clinicians are well aware of the fact that biological age alone cannot characterize the degree of function loss by the patient; therefore, the term "frailty" was introduced to reflect this parameter [4, 5]. Experience of using "frailty assessment" in a surgical clinic showed that this indicator is able to successfully predict the results of a number of interventions, including heart [6, 7] and aorta [8] surgery, transcatheter aortic valve implantation, and malignant tumor surgery [9, 10]. Therefore, it seems appropriate to include frailty assessment in the preoperative risk assessment [2, 5] and, perhaps, even refine the evaluation criteria in the existing risk assessment scales. However, at present, there are a lot of criteria for frailty and it is not entirely clear which one is more appropriate to use for these purposes. For example, frailty index, Katz index, walking speed, handgrip strength and laboratory tests (plasma albumin and creatinine level) were used for such an assessment [5], and it has been proposed recently to evaluate the cross-sectional area of the psoas muscle in multispiral computed tomography [6-8]. Since the muscles of the lower extremities are most important for restoring physical activity after cardiac surgery, assessment of their functional status would be rational, which created the basis for the present study. Another option in assessing the patient's preoperative status is evaluation of their autonomic balance; in particular, heart rate variability indicators have been suggested as a complications prediction tool [11-12]. A comprehensive assessment of muscle and autonomic status in patients with cardiac surgery has not been carried out yet.

Accordingly, the aim of the study was to investigate the association of the lower extremities skeletal muscle state and autonomic status with the short-term results of the operations in the cardiac surgery patients.

Material and Methods

Study design

The present study included 64 patients (57 men and 7 women) aged 38 to 75 years (median age 63 years) who underwent cardiac surgery in the Research Institute for Complex Issues of Cardiovascular Diseases clinic from March 01, 2015 to March 01 2016. The study protocol was approved by the Local Ethics Committee of the Institution and was developed according to the World Medical Association's Declaration of Helsinki on Ethical Principles for Medical Research Involving Human Subjects, 2000 edition. Written informed consent was obtained from all patients prior to them entering the study.

The criteria for inclusion in the study were planned coronary artery bypass grafting or valvular surgery. Patients with age less than 25 and more than 80 years; with exacerbation of underlying disease during the preoperative period (acute myocardial infarction, acute pulmonary embolism, unstable angina, etc.); unable to perform static-dynamic tests due to arthropathies or low pain threshold; with sarcopenia, rhabdomyolysis and other myopathies; with cognitive impairment were excluded from the study.

All patients underwent routine laboratory and instrumental examinations within the framework of inpatient examination standards before surgery, in the early postoperative period and upon discharge from the hospital. Additionally, all subjects before surgery performed a six-minute walk test (6MWT), in accordance with the "American Thoracic Society practical guidelines". The test was carried out indoors, in a direct closed 75 meters long corridor with distance markings. Before the test, patients were instructed. Subjective assessment of the patient's condition while walking was carried out verbally, with standardized phrases every minute, throughout the test. Initial and final control of blood pressure, heart rate, hemoglobin saturation (with digital pulse oximeter), and assessment of the perceived exertion scale were performed.

Static dynamic tests

Static-dynamic tests were carried out before surgery, on a multifunctional training device, which allows setting the load in the range of 5-100 kg. The measurement was performed in a sitting position, with a tightly fixed pelvis, with knees bent at a 90° angle. The patient performed knee extensions to the maximum range of motion. The load was increased gradually, in increments of 5 kg, to the maximum tolerated weight. Static tests for flexors and extensors of the lower extremities were carried out after the static-dynamic tests after resting for 5 minutes. Static endurance was measured in seconds holding weights of 50% of the maximum weight with knees extended until development of severe muscle fatigue.

Autonomic status assessment

Assessment of autonomic status was carried out using the ORTOexpert software package (NPP "Living Systems"), including a personal computer, and two cardiac sensors (transmitter and pickup sensor) with a radio interface placed on the front surface of the patient's chest.

Before examination the patient was placed in a horizontal position within 5 minutes. Under the control of the rhythmogram, cardiointervals (CI) were recorded to eliminate radiofrequency interference in the recording. The last two minutes were used to analyze the CI rhythmogram. Next, the patient took a vertical position (active orthostatic test – AOT), while continuing to stand motionless for three minutes. Throughout AOT, recording continued until a minimum of 200 CI was recorded.

During the analysis of the cardiac rhythmogram, the NN intervals (between successive QRS complexes) were estimated. The statistical characteristics of the CIs sequential series (SDNN, RMSSD), as well as the temporal characteristics of heart rate variability (HRV) – Mode (Mo), mode amplitude (AMo), Index of regulation strain (IS) were calculated for both horizontal (resting state) and orthostasis position (load).

Parasympathetic activity of autonomic regulation was assessed by RMSSD. RMSSD is a square root from the sum of squared differences of sequential NN pairs; the higher this indicator, the more active the component of parasympathetic regulation. HRV assessment also was carried out using the following geometric parameters: Mo — the number of the most frequently encountered RR intervals, which makes it possible to assess the state of the patient's regulatory systems; AMo is the fraction of intervals corresponding to the mode value; reflects the stabilizing effect of centralization of heart rhythm control; IS – index of regulatory systems, reflects the degree of the nervous system influence on the heart. IS is quite sensitive to increased tone of the sympathetic nervous system. Physical or emotional stress can increase IS by 50 to 100%, and a significant load elevates it by 5-10 times. In patients with constant voltage of regulatory systems, resting IS is 400-600 conventional units. In patients with progressive angina pectoris and myocardial infarction, resting IS reaches 1000-1500 units [13].

Parameters of the spectral analysis were estimated in the two-minute recording section at rest. The high-frequency (HF) range represents largely the parasympathetic influence on heart rate, while low-frequency (LF) range generally characterizes the sympathetic nervous activity, in particular, the system of vascular tone regulation. The LF/HF ratio is constant and reflects the sympatho-parasympathetic balance, or the index of vagosympathetic interaction. Very slow, low-frequency waves of the 2nd order (VLF – very low frequency), characterize the state of the neurohumoral, slow heart rate regulation system.

Based on the performance of AOP, the parameters of the transient process (KFa, KFb, KFc, KFd) and autocorrelation indicators were estimated [13].

The ORTO expert software formed a conclusion about the functional state of the ANS regulatory systems of the body automatically, based on the assessment of vegetative tone, the degree of tension of regulatory systems, the parameters of the transition process, data on the activity of the autonomic nervous system at rest and during AOT.

Patients' basic characteristics

Presence of one or more perioperative complications was determined a criterion for sorting patients into groups, i.e. the combined endpoint (CEP) included development of stroke, myocardial infarction (MI), persistent arrhythmias and heart block, development of multiple organ dysfunction syndrome (MODS), death. Thus, 2 groups were formed – with CEP (n=9) and without CEP (n=55). The studied groups were compared according to the main anthropometric and demographic indicators, presence of risk factors for atherosclerosis, concomitant pathology, history of atherothrombotic events, laboratory and instrumental examination data and the immediate results of cardiac surgery.

No difference was found in gender-age characteristics of the two groups (*Table* 1). The groups were comparable in main clinical indicators as well; history of myocardial infarction was detected slightly more often in the group without CEP, but the differences were not statistically significant (p=0.067). In the same time, during the preoperative examination, arrhythmias were more often detected in the group with presence of CEP (p=0.023). The groups did not differ in prevalence of severe angina pectoris, percutaneous coronary interventions (PCI) and history of stroke, atrial fibrillation and diabetes.

While performing laboratory tests (*Table* 2), no significant differences between the groups were noted as well. According to instrumental examinations (*Table* 3), in the CEP group during the initial examination, severe aortic valve insufficiency (p=0.002) and aneurysm of the left ventricle (p=0.007) were significantly more often detected. Manifestations of peripheral atherosclerosis, such as hemodynamically insignificant ICA stenosis, were significantly more often observed in the group with CEP (p=0.036). At the same time, the groups did not differ in prevalence of the lower extremities arteries stenosis.

Statistical analysis

All statistical analyses were calculated with STATISTICA 10.0 (Dell Software, Inc., Round Rock, TX, USA). The Shapiro-Wilk test was used to test data for normal distribution. Since the distribution for all quantitative variables differed from normal, they are presented as median, lower and upper quartile – Me (LQ, UQ). Categorical data were reported as percentages. Differences in quantitative data between NMES groups and controls were evaluated using the Mann-Whitney test. Nominal and binary signs were compared using the χ2 criterion with Yates correction for small samples. The relationship of possible factors with likelihood of developing a combined endpoint was evaluated in a logistic regression model. The suggested predictors are: gender, age, LF/HF, indicators of muscle status, Amo at rest and in orthostasis, IS at rest and in orthostasis, cardiopulmonary bypass duration and glomerular filtration rate. The preliminary identification of possible correlations between the proposed predictors was carried out, then the regression models were formed taking into account the revealed correlations. Multivariate analysis included variables for which the criterion of statistical significance in univariate analysis was less than 0.05.

Table 1. Baseline characteristics of patients

	Group 1 (with CEP) (n=9)	Group 2 (without CEP) (n=55)	P-level
Male	7 (77.78)	50 (90.91)	0.242
Female	2 (22.22)	5 (9.09)	0.242
Age, years	64.0 (60.0, 65.0)	61.0 (57.0, 65.0)	0.290
Body mass index, kg/m^2	25.67 (21.68, 27.44)	27.61 (24.90, 30.86)	0.135
FC angina pectoris ≥3	1 (11.11)	10 (18.18)	0.784
Old myocardial infarction	4 (44.44)	41 (74.54)	0.067
Creatinine, µmol / L	85.0 (75.0, 90.0)	78.0 (71.0, 86.0)	0.579
GFR, ml/min/1.73 m^2	80.78 (73.95, 90.43)	87.48 (78.04, 97.65)	0.496
AG duration ≥5 yeas	4 (44.44)	24 (43.64)	0.910
PCI history	3 (33.33)	14 (25.46)	0.620
Stroke history	1 (11.11)	4 (7.27)	0.691
CHF ≥2a	7 (77.78)	33 (60)	0.307
Rhythm disturbances	5 (55.56)	11 (20)	0.023
Atrial fibrillation	0 (0)	3 (5.45)	0.473
Diabetes mellitus	1 (11.11)	9 (16.36)	0.687
Peripheral arterial disease	1 (11.11)	5 (9.09)	0.847
	Operative procedure		
CABG	5 (55.56)	35 (63.64)	0.447
CABG + ventriculoplasty	1 (11.11)	6 (10.91)	0.958
CABG + valve replacement	2 (22.22)	3 (5.45)	0.074
CABG + radiofrequency ablation	0 (0)	4 (7.27)	0.412
Multivalve operations	1 (11.11)	3 (5.45)	0.494
Aortic valve replacement	0 (0)	2 (3.64)	0.568
Mitral valve replacement	0 (0)	2 (3.64)	0.568

Quantitative data are presented as median with lower and upper quartiles – Me (LQ, UQ), binary variables – as frequencies in absolute values and in percentage – n (%). CEP, combined endpoint; FC, functional class, GFR, glomerular filtration rates; AG, arterial hypertension; CHF, chronic heart failure; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting.

Table 2. Baseline characteristics of patients (laboratory tests)

	Group 1 (with CEP) (n=9)	Group 2 (without CEP) (n=55)	P-level
Glucose (mmol/L)	5.65 (5.35, 6.50)	5.95 (5.10, 6.50)	0.681
Urea (mmol/L)	6.3 (5.4, 7.8)	6.5 (5.2, 7.4)	0.856
Creatinine (µmol/L)	85.0 (75.0, 90.0)	78.0 (71.0, 86.0)	0.579
Total bilirubin (µmol/L)	16.2 (9.2, 21.8)	14.4 (10.7, 18.7)	0.946
Direct bilirubin (µmol/L)	5.05 (4.35, 6.15)	4.40 (3.70, 6.50)	0.836
Aspartate Aminotransferase (U/L)	21.0 (18.5, 24.0)	22.0 (19.0, 29.0)	0.672
Alanine Aminotransferase (U/L)	27.5 (17.0, 37.5)	26.0 (20.0, 37.0)	0.619
Cholesterol (mmol/L)	4.3 (3.8, 4.8)	4.4 (3.6, 5.2)	0.623
High density lipoproteins (mmol/L)	1.37 (0.78, 1.91)	0.97 (0.78, 1.27)	0.203
Low density lipoproteins (mmol/L)	2.25 (1.36, 2.33)	2.53 (1.98, 3.15)	0.138
Triglycerides (mmol/L)	1.34 (0.79, 1.39)	1.52 (1.11, 1.84)	0.143
Erythrocyte sedimentation rate (mm/h)	4.0 (4.0, 10.0)	7.0 (4.0, 10.0)	0.741

Data are presented as median with lower and upper quartiles – Me (LQ, UQ). CEP, combined endpoint.

Table 3 Baseline characteristics of patients (echocardiography and Doppler ultrasound of blood vessels)

	Group 1 (with CEP) (n=9)	*Group 2 (without CEP) (n=55)*	*P-level*
Left Atrial Diameter, cm	4.6 (3.90, 4.70)	4.3 (4.0, 4.70)	0.882
Left Ventricle End-Diastolic Volume, ml	209.0 (160.0, 247.0)	180.0 (141.0, 201.0)	0.371
Left Ventricle End-Systolic Volume, ml	102.0 (88.0, 113.0)	76.5 (51.0, 132.50)	0.531
Interventricular Septal Thickness, mm	1.2 (1.0, 1.25)	1.2 (1.10, 1.20)	0.520
Posterior wall thickness, mm	1.2 (1.0, 1.25)	1.2 (1.0, 1.20)	0.394
Right ventricle mid-diameter, mm	1.8 (1.80, 1.90)	1.85 (1.80, 2.0)	0.564
Aorta, cm	3.6 (3.20, 3.80)	3.6 (3.50, 3.80)	0.545
Left ventricular ejection fraction, %	56.0 (50.0, 63.0)	58.0 (50.0, 64.0)	0.621
Pulmonary artery systolic pressure, mmHg	25.0 (22.0, 28.0)	28.0 (24.0, 34.0)	0.488
Mitral regurgitation ≥ grade 2	3 (33.33)	9 (16.36)	0.227
Aortic valve regurgitation ≥ grade 2	3 (33.33)	2 (3.64)	0.002
Left ventricular aneurysm	2 (22.22)	1 (1.82)	0.007
Left ventricular myocardial mass, g	293.8 (273.3, 349.0)	323.8 (256.0, 369.0)	0.455
Internal carotid artery stenosis ≥30%	6 (66.67)	19 (34.55)	0.036
Stenosis of lower limb arteries	2 (22.22)	13 (23.64)	0.656

Quantitative data in Tables 3, 4, 5, and 6 are presented as median with lower and upper quartiles – Me (LQ, UQ), binary variables – as frequencies in absolute values and in percentage – n (%). CEP, combined endpoint.

Table 4. Muscle strength of the lower and upper extremities and 6MWT results before surgery

	Group 1 (with CEP) (n=9)	*Group 2 (without CEP) (n=55)*	*p value*
Distance of 6MWT, m	320.0 (290.0, 355.0)	320.0 (300.0, 390.0)	0.690
Distance of 6MWT ≥300 m	6 (66.67)	42 (76.34)	0.785
Handgrip strength, kg	20.0 (15.0, 25.0)	25.0 (20.0, 30.0)	0.047
Knee extensors strength, kg	20.0 (15.0, 25.0)	25.0 (20.0, 30.0)	0.046
Knee extensors endurance, sec	63.0 (38.0, 113.0)	55.0 (40.0, 86.0)	0.690
Knee extensors work, kg*sec	950.0 (610.0, 2025.0)	1375.0 (810.0, 2370.0)	0.470

CEP, combined endpoint, 6MWT, 6-minute walk test.

Table 5. Autonomic status indicators before surgery in groups with and without CEP

	Group 1 (with CEP) (n=9)	*Group 2 (without CEP) (n=55)*	*P-level*
TF, ms^2	1955.0 (1087.0, 4137.0)	1158.5 (566.0, 2144.0)	0.779
VLF, ms^2	1275.0 (946.0, 2072.0)	693.5 (258.0, 1571.0)	0.901
LF, ms^2	504.0 (259.0, 1859.0)	248.5 (130.0, 455.0)	0.726
HF, ms^2	83.0 (36.0, 169.0)	84.0 (48.0, 229.0)	0.473
LF/HF	7.25 (3.85, 8.34)	2.71 (1.63, 5.33)	0.028
LF, %	88.0 (79.0, 89.0)	73.0 (62.0, 84.0)	0.013
HF, %	12.0 (11.0, 21.0)	27.0 (16.0, 38.0)	0.013
Kfa	2.0 (-235.0, 7.0)	-102.0 (-200.0, -6.0)	0.628
KFb	-29.0 (-94.0, 18.0)	1.5 (0.0, 47.0)	0.162
KFc	0.0 (-1.0, 8.0)	3.0 (0.0, 10.0)	0.818
KFd	0.0 (-13.0, 7.0)	-11.0 (-56.0, 0.0)	0.761
Amo supine, %	52.0 (44.0,61.0)	68,0 (50.0,84.0)	0.026
IS supine	150.9 (95.0, 61.0)	265.85 (118.8, 488.0)	0.094
Amo upright, %	60.0 (55.0, 72.0)	60.5 (49.0, 84.0)	0.593
IS upright	393.0 (155.50, 523.80)	258.45 (138.20, 632.40)	0.390
Amo supine-upright, %	-15.0 (-20.0, -9.0)	-1.5 (-13.0, 13.0)	0.145
IS supine-upright	-211.0 (-368.50, -42.30)	-28.4 (-291.20, 105.80)	0.783

CEP, combined endpoint; TF, Total Frequency; VLF, Very Low Frequency; LF, Low Frequency; HF, High Frequency; Kfa, first phase of the calculated transient parameter coefficients during AOT; Kfb, second phase of the calculated transient parameter coefficients during AOT; Kfc, third phase of the calculated transient parameter coefficients during AOT; Kfd, fourth phase of the calculated transient parameter coefficients during AOT; Amo, mode amplitude; IS, Index of regulation strain.

Table 6. Perioperative characteristics of surgery in groups with and without CEP

	Group 1 (with CEP) (n=9)	*Group 2 (without CEP) (n=55)*	*P-level*
EuroSCORE, %	2.32 (2.57, 5.46)	1.89 (1.33, 2.37)	0.005
EuroSCORE, units	4.5 (4.0, 5.50)	3.0 (2.0, 4.0)	0.005
Cardiopulmonary bypass duration, min	128.0 (86.0, 185.0)	81.0 (61.0, 98.0)	0.002
Aortic cross-clamp time, min	104.0 (49.0, 147.0)	53,0 (38.0, 68.0)	0.007
Congestive heart failure	4 (44.44)	0 (0)	<0.001
Atrial fibrillation	2 (22.22)	0 (0)	<0.001
Atrial flutter	1 (3.70)	0 (0)	0.013
MODS	1 (3.70)	0 (0)	0.013
Extracorporeal hemocorrection	1 (3.70)	0 (0)	0.013
Hydrothorax	4 (44.44)	31 (56.36)	0.505
Pneumonia	2 (22.22)	0 (0)	<0.001
Stroke	1 (3.70)	0 (0)	0.013
Death	1 (3.70)	0 (0)	0.013

CEP, combined endpoint; MODS, multiple organ dysfunction syndrome.

Table 7. Associations between basal characteristics and risk of CEP development

Characteristics	*Odds ratio (-95% CI; +95% CI)*	*p*
Univariate logistic regression analysis		
Old myocardial infarction	0.035 (0.082; 1.502)	0.151
Rhythm disturbances	1.769 (0.377; 8.292)	0.461
Aortic valve regurgitation ≥ grade 2	1.687 (0.160; 18.828)	0.658
Left ventricular aneurysm	3.563 (0.276; 46.029)	0.321
Internal carotid artery stenosis ≥ 30%	9.545 (1.030; 88.467)	0.043
Handgrip strength	0.893 (0.786; 1.001)	0.048
Knee extensors strength	1.012 (0.997; 1.029)	0.098
LF/HF	1.104 (0.944; 1.292)	0.207
HF, %	0.999 (0.997; 1.000)	0.628
Amo supine	0.958 (0.920; 0.998)	0.037
IS supine	0.996 (0.990; 1.000)	0.096
Amo upright	0.991 (0.957; 1.025)	0.587
IS upright	0.999 (0.997; 1.000)	0.398
EuroSCORE, %	1.249 (0.834; 1.868)	0.270
EuroSCORE, units	1.643 (1.003; 2.694)	0.043
Cardiopulmonary bypass duration	1.010 (1.001; 1.022)	0.068
Aortic cross-clamp time	1.009 (0.998; 1.023)	0.138
CABG + valve replacement	5.142 (0.701; 37.713)	0.112
Multivariable logistic models; p=0.001		
LF/HF	1.175 [0.972; 1.420]	0.088
Amo supine	0.950 [0.905; 0.997]	0.034
Handgrip strength	0.863 [0.750; 0.993]	0.036

CEP, combined endpoint; CI, confidence interval; HF, High Frequency; LF, Low Frequency; Amo, mode amplitude; IS, Index of regulation strain; CABG, coronary artery bypass grafting.

Results

The physical tests found no difference in endurance of the lower extremities skeletal muscles or the distance covered by the results of 6MWT between the groups. At the same time, the group with CEP was characterized by lower strength of the skeletal muscles of the upper and lower extremities (p=0.047 and p=0.046, respectively; *Table* 4).

When assessing the vegetative status (*Table* 5) at the preoperative stage, an initially more pronounced sympathetic activation can be noted in the CEP group based on the percentage of the low and high frequency ranges (88 to 12% in the CEP group, 73 to 27% in the no CEP group, p=0.013), which reflects the degree of the sympathetic component activity in the regulation of the autonomic nervous system (ANS). Also, larger values of the total power of the HRV frequency spectrum (TF) in the CEP group were revealed as compared to the non-CEP group, although these differences were not statistically significant (1955.0 and 1158.5, p=0.779).

It is also worth paying attention to the mode amplitude parameter (Amo), which illustrates distribution of the most frequently recorded cardiointervals (CI), and the stress index (IS) calculated on its basis for characterizing the stress adaptation of regulatory systems. Initially, at rest, IS was lower in the CEP group (150.9 and 265.85, p=0.094), but after transitioning to the orthostatic position it increased more than twice and surpassed the number in the group without CEP (393.0 and 258.45, p=0.390). Values of the transition process parameters also had no significantly significant differences between groups (Kfa p=0.628; KFb p=0.162; KFc p=0.818; KFd p=0.761).

The risk of surgery was initially higher in the CEP group when assessed according to the EuroSCORE II scale (p=0.005), so, expectedly, the cardiopulmonary bypass duration and aortic clamping time were longer (p=0.002 and p=0.007, respectively). The spectrum of complications is presented in *Table* 6; their presence is explained primarily by the severity of the underlying disease and the duration of the operation.

According to the data obtained with the univariate logistic regression analysis, the most likely factors associated with the development of CEP in this study are poor functional state of skeletal muscles (particularly upper limbs), internal carotid artery stenosis stenosis of 30 percent or more; higher EuroSCORE surgery risk, cardiopulmonary bypass duration and HRV indices characterizing the overstrain of the mechanisms of regulation of the ANS and the tendency to sympathicotonia (*Table* 7).

Given the strong correlation between the strength indicators of the upper and lower extremities muscles, only the upper extremities strength, that demonstrated significance in the univariate analysis, was included in the multivariate model. Multivariate regression analysis allowed us to establish the relationship of poor skeletal muscle status, pronounced sympathicotonia, overstrain of adaptogenic ANS mechanisms and a high incidence of significant, life-threatening postoperative complications (*Table* 7).

Discussion

Our study shows that, in addition to generally accepted indicators (risk and duration of surgery), such parameters as muscle strength of the upper and lower extremities and autonomic imbalance are associated with immediate results of cardiac surgery. It is not much of a surprise, if we consider the reduced functional state of these muscle groups as one of the manifestations of patients' fragility. It was shown in a study by Foldyna et al. that patients with the smallest cross-sectional area of the psoas muscle according to computed tomography had the highest mortality within 1-2 years after transcatheter aortic valve implantation [14]. In a mixed group of patients (open-heart aortic valve surgery and transcatheter implantation of the aortic valve), sarcopenia was also evaluated by the total psoas area during computed tomography. Independent predictors of a 30-day outcome (death, stroke, acute renal failure, prolonged mechanical ventilation, deep wound infection) were STS scale risk (OR 91.1; p=0.02) and total psoas area (OR 0.5; p=0.024). The two-year survival rate was 85.7% in patients with sarcopenia compared to 93.8% in patients without sarcopenia (p=0.02); accordingly, the total psoas area was an independent predictor of long-term survival (OR 0.47; p=0.02) [15]. During aortic valve replacement surgery, patients with sarcopenia (psoas index values within the lower quartile) had a large annual mortality rate (31.9% versus 16.9% p=0.03), with the psoas index having an independent prognostic effect on the annual (OR 0.84; p=0.02) and long-term (OR 0.92; p=0.04) mortality [7]. As we can see, all these methods are able to predict the risk of complications. According to our data, knee extensor muscle strength can also be used to assess the likelihood of developing complications after cardiac surgery and, in our opinion, may be preferable in this group of patients. There are studies that have shown that the electric skeletal muscle stimulation (EMS) in patients after cardiac surgery are safe [16] and can improve skeletal muscle metabolism [17]. Therefore, assessing the muscles' status before and after EMS allows to evaluate its effectiveness. This will help to answer another clinically important question – is it possible to improve the results of surgical treatment by preoperative training of skeletal muscles? The data available so far is mainly focused on the postoperative period and refers to patients with complicated postoperative period, while the use of EMS in rehabilitation is extremely limited and refers to non-cardiac surgery [18].

Data on the possibility of using HRV indicators in predicting the outcome of cardiac surgery is limited, despite a fairly large number of studies evaluating HRV in these patients. The fact is that they mainly investigate the peri- and postoperative period. It was previously shown that cardiac surgery itself leads to a decrease in HRV indices, which are later restored to the initial level [19]. Failure of the HRV indices to recover may be an adverse surgery outcome factor [19] (although this opinion is debated [20]). Preoperative HRV scores have been shown to be significant in a study by de Godoy MF et al. [21], who showed that nonlinear domains of HRV indices can help to identify a group of patients with a high risk of perioperative complications of CABG.

In our study, when directly comparing the prognostic significance of muscle status indicators and HRV data, the possibility of using these indicators in combination is convincingly shown. It should be noted that the great prognostic significance of HRV indicators was noted. Perhaps this should not be surprising, since sympathetic activation can develop not only with a decrease in the pumping function of the heart, but also with skeletal muscle dysfunction [22]. Therefore, autonomic dysfunction can be expected to be more pronounced (due to a combination of central and peripheral influences) than the degree of muscle maladaptation. Ultimately, when assessing the parameters of the transition process, both groups go through the stage of adaptive activation of the ANS, but for the group with initial pronounced sympathicotonia, activation occurs with a high tension of regulatory systems, with a slower, probably not clinically significant, speed of fast adaptive reactions. Given the dynamic changes in the mode amplitude indicators (Amo) and IS, we can talk about decreased adaptive ability of the ANS to adequately respond to loads of any type in the group having complications after surgery. So the role of the ANS regulation maladaptation in the formation of early postoperative complications requires further study.

Study Limitations. The main limitations of the study are the short duration of observation and the small sample size of patients, which to some extent affects the prognostic value of the results obtained on the dynamics of muscle and autonomic parameters. Only 64 patients who underwent open coronary revascularization or correction of valvular heart disease were included in this study. The presented comparison groups are rather small; therefore, the use of multiple regression analysis to study the dynamics of indicators of muscle and vegetative status is complicated. The groups included in the study are quite heterogeneous, which suggests the possible impact of surgical procedures on the contribution of muscle status and autonomic balance to immediate results. However, the study of Shvartz V.A. et al. [12] with assessment of the pre and postoperative cardiovascular autonomic parameters showed no differences in the groups of patients undergoing CABG and valve prosthetics. Autonomic balance indices did not depend on the type and volume of surgical intervention and clinical characteristics of the patients. A more accurate study of this issue will be necessary in more homogeneous groups of patients in subsequent studies. Also, another limitation is the lack of studying the daily variability of autonomic indicators and the use of only short data on HRV during AOT.

Conclusion

Perioperative complications (development of acute cerebrovascular accident, myocardial infarction, persistent arrhythmias and conduction disorders, multiple organ failure syndrome, death) occurred in 9 out of 64 cases after cardiac surgery. Not only the severity of the underlying cardiac pathology, the risk and duration of the operation, but also muscle strength of the upper and lower extremities, as well as sympathetic activation of the autonomic nervous system and its adaptive reserve were associated with development of CEP. The possibility of improving the postoperative outcomes by improving the functional status of skeletal muscles in the preoperative period, and the effect of muscle status on the autonomic balance requires further analysis.

Conflict of interest

All authors declare no conflict of interest.

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