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ABSTRACT

of the dissertation submitted for the degree of Doctor of Philosophy (PhD) on the topic:

"Assessment of the Post-Reperfusion State of the Myocardium in Patients with Overweight at Different Stages of Rehabilitation"

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Relevance of the Study

Cardiovascular diseases (CVDs) remain the leading cause of mortality and disability worldwide, including in the Republic of Kazakhstan [1,2,3]. According to the World Health Organization (WHO), CVDs accounted for approximately 19.8 million deaths in 2022, representing about 32% of all deaths worldwide [1]. If current trends persist, global CVD mortality may reach 23–24 million deaths annually by 2030, highlighting the magnitude of this problem and the importance of preventive and rehabilitation measures [1,4].

Metabolic syndrome, with overweight being one of its key components, plays an important role in cardiovascular risk. According to the WHO, in 2022, approximately 2.5 billion adults were overweight, including about 890 million living with obesity. Overweight and obesity are recognized as independent risk factors for coronary artery disease (CAD), arterial hypertension, stroke, and chronic heart failure [4–6].

Overweight adversely affects not only the development of CAD but also the recovery period following myocardial revascularization, including coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI). Current evidence emphasizes the clinical significance of overweight as a factor associated with a higher incidence of complications and increased residual risk in patients with chronic coronary syndromes and following coronary interventions. In clinical practice, this may manifest as more frequent progression of atherosclerosis, adverse myocardial remodeling, and complications associated with inflammation and thrombosis [7,8].

Epicardial adipose tissue (EAT) is a metabolically active endocrine fat depot capable of secreting a wide range of adipokines and proinflammatory cytokines. These mediators contribute to local and systemic inflammation, endothelial dysfunction, activation of myocardial remodeling processes, and progression of atherosclerosis [8,9]. Increased EAT thickness is associated with a more pronounced inflammatory state and an unfavorable postoperative course in patients undergoing CABG, making this parameter a promising marker for risk stratification [10,11].

Chronic inflammation and tissue hypoxia associated with overweight and increased EAT thickness contribute to disturbances in cellular energy homeostasis, accompanied by enhanced adenine nucleotide catabolism and activation of purine metabolism [12]. Under ischemic and reperfusion conditions, intensive degradation of adenosine triphosphate (ATP) and nucleic acids leads to the accumulation of purine bases and their catabolites, including adenine, guanine, hypoxanthine, xanthine, and uric acid. These metabolites reflect tissue hypoxia, energy deficiency, and oxidative stress [13–15].

Activation of purinergic signaling, in turn, contributes to the persistence of inflammatory responses, endothelial dysfunction, and a prothrombotic state. Extracellular nucleic acids (DNA and RNA), released during necrosis, apoptosis, and immune cell activation, represent an additional source of purine metabolites and markers of tissue injury. Increased concentrations of extracellular nucleic acids are considered indicators of tissue damage and innate immune activation, while their degradation contributes to the activation of purine metabolic pathways, potentially aggravating inflammation and oxidative stress [13,16,17].

Under conditions of systemic inflammation and innate immune activation, neutrophil extracellular traps (NETs) become increasingly important. NETs are web-like structures composed of DNA–histone complexes and proteolytic enzymes. They participate in immunothrombosis, exacerbate endothelial dysfunction, and impair microcirculation. Increased NET formation following cardiac surgery involving cardiopulmonary bypass has been associated with postoperative complications, including postoperative atrial fibrillation and increased mortality [16,17].

An important consequence of inflammatory activation, oxidative stress, and disturbances in purine metabolism is reduced synthesis and bioavailability of nitric oxide (NO), a key mediator of

endothelial function. Reduced NO availability promotes vasoconstriction, platelet activation, and progression of myocardial remodeling, which may be particularly relevant during long-term recovery after myocardial revascularization in patients with overweight.

Currently, there is no universally accepted comprehensive algorithm for assessing the post-reperfusion state of the myocardium in patients with overweight at different stages of cardiac rehabilitation. The timing and mechanisms of atherosclerosis progression and myocardial remodeling, as well as the contributions of metabolic, inflammatory, and purinergic factors during long-term recovery, remain insufficiently investigated.

The third stage of cardiac rehabilitation, involving long-term follow-up, is of particular importance. Although clinical stabilization is generally expected during this period, persistent subclinical inflammation, endothelial dysfunction, and disturbances in purine metabolism may increase the risk of post-reperfusion complications and progression of myocardial remodeling [5,7–10,13–15].

In the present study, the term “post-reperfusion myocardial state” is used to comprehensively characterize structural, functional, and biochemical changes observed after restoration of coronary blood flow through CABG and assessed longitudinally during subsequent stages of cardiac rehabilitation. This term is not considered an independent diagnostic category and is not used to establish a clinical diagnosis.

Within the framework of this research, the scientific meaning of this concept is defined through a comprehensive assessment of cardiac structural and functional parameters, epicardial adipose tissue thickness, purine metabolism indicators, nitric oxide levels, and extracellular nucleic acids.

Thus, the term “post-reperfusion myocardial state” is used as a research-specific definition encompassing the instrumental and biochemical changes investigated following surgical myocardial revascularization.

Of particular scientific interest is the comprehensive assessment of structural, functional, and biochemical changes in patients with overweight after CABG at different stages of cardiac rehabilitation, identification of relationships among these changes, and determination of factors associated with their persistence during long-term recovery. The findings may contribute to improving approaches to longitudinal patient monitoring and individualizing rehabilitation strategies in this patient population.

Aim of the Study

To assess the characteristics of post-reperfusion changes in patients with overweight at different stages of cardiac rehabilitation following coronary artery bypass grafting and to identify factors associated with the persistence of these changes.

Research Hypothesis

In patients with overweight undergoing elective coronary artery bypass grafting, post-reperfusion myocardial changes are more pronounced and persist during subsequent stages of cardiac rehabilitation, as reflected by specific alterations in structural, functional, and metabolic parameters.

Research Objectives

1. To determine the characteristics of changes in transthoracic echocardiographic (TTE) parameters and biochemical indicators in patients with overweight following coronary artery bypass grafting.
2. To assess changes in transthoracic echocardiographic parameters and biochemical indicators in patients with overweight following coronary artery bypass grafting at different stages of cardiac rehabilitation.
3. To evaluate the relationships between transthoracic echocardiographic parameters and biochemical indicators in relation to the risk of developing post-reperfusion changes in patients

with overweight following coronary artery bypass grafting at different stages of cardiac rehabilitation.

4. To assess the prognostic significance of transthoracic echocardiographic parameters and biochemical indicators as factors associated with the development of post-reperfusion changes in patients with overweight following coronary artery bypass grafting.

5. To develop models for estimating the probability of post-reperfusion changes in patients with overweight following coronary artery bypass grafting.

Scientific Novelty

1. For the first time, the dynamics of cardiac structural and functional parameters, epicardial adipose tissue thickness, and biochemical markers were established in patients with overweight following coronary artery bypass grafting (CABG) at different stages of cardiac rehabilitation. Persistent signs of left ventricular remodeling and increased epicardial adipose tissue thickness were identified, accompanied by alterations in purine metabolism, nitric oxide levels, and extracellular nucleic acids, with the most pronounced changes observed in patients with overweight.

2. For the first time, statistically significant relationships were established between transthoracic echocardiographic (TTE) parameters and biochemical markers of post-reperfusion changes in patients with overweight following CABG at different stages of cardiac rehabilitation. These relationships demonstrate associations between cardiac structural and functional remodeling, epicardial adipose tissue thickness, and alterations in purine metabolism, nitric oxide levels, and extracellular nucleic acids.

3. A pathogenetic model of post-reperfusion changes in patients with overweight following CABG was developed, systematizing the relationships between excessive epicardial adipose tissue accumulation, cardiac structural and functional remodeling, and alterations in purine metabolism, nitric oxide levels, and extracellular nucleic acids during cardiac rehabilitation (Copyright Registration Certificate No. 70169 dated April 15, 2026, “Mechanism of Development of Post-Reperfusion Changes in Patients with Overweight Following Coronary Artery Bypass Grafting”), Appendix A.

4. An algorithm for predicting the probability of post-reperfusion changes in patients with overweight following CABG at different stages of cardiac rehabilitation was developed based on an integrated assessment of clinical, instrumental, and biochemical parameters (Copyright Registration Certificate No. 71498 dated May 5, 2026, “Integrative Model for Predicting the Risk of Post-Reperfusion Changes in Patients with Overweight Following Coronary Artery Bypass Grafting at Different Stages of Cardiac Rehabilitation”), Appendix A.

5. The prognostic significance of epicardial adipose tissue thickness, body mass index (BMI), and hypoxanthine levels for estimating the probability of post-reperfusion changes in patients with overweight following CABG was established. Epicardial adipose tissue thickness demonstrated the highest predictive performance at the second stage of cardiac rehabilitation (AUC=0.931), while BMI retained prognostic significance (AUC=0.812) across all stages. The inclusion of hypoxanthine in risk assessment provided additional information to the prognostic model (Copyright Registration Certificates No. 69728 dated April 8, 2026; No. 69926 dated April 10, 2026; and No. 69948 dated April 10, 2026), Appendix A.

Practical Significance of the Study

The prognostic significance of anthropometric, echocardiographic, and biochemical parameters in estimating the probability of post-reperfusion changes in patients with overweight following CABG at different stages of cardiac rehabilitation was established.

Prognostic models based on the comprehensive assessment of BMI, epicardial adipose tissue thickness, and hypoxanthine levels were developed to estimate the probability of persistent

post-reperfusion changes at different stages of cardiac rehabilitation. The findings support the inclusion of epicardial adipose tissue thickness assessment in comprehensive echocardiographic examinations of patients with overweight following CABG and may be used for longitudinal monitoring and risk stratification to identify patients requiring closer follow-up during cardiac rehabilitation.

Main Propositions Submitted for Defense

1. Statistically significant differences in cardiac structural and functional parameters and biochemical indicators were established between patients with overweight following CABG and those without overweight. These differences were characterized by increased left ventricular volumes, left ventricular myocardial mass, and epicardial adipose tissue thickness, reduced left ventricular ejection fraction (LVEF), and alterations in purine metabolism, extracellular nucleic acids, neutrophil extracellular traps (NETs), and nitric oxide ($p<0.05$).

2. At different stages of cardiac rehabilitation, patients with overweight following CABG exhibited more pronounced and persistent structural, functional, and metabolic changes compared with patients without overweight. These changes were characterized by higher left ventricular mass index (LVMI) and epicardial adipose tissue thickness, lower LVEF, and differences in purine metabolism, extracellular nucleic acids, NETs, and nitric oxide levels. At the third stage of rehabilitation, statistically significant between-group differences persisted in epicardial adipose tissue thickness, LVMI, LVEF, most investigated purine metabolites, selected extracellular nucleic acid parameters, NETs, and nitric oxide levels ($p<0.05$).

3. Statistically significant moderate to strong correlations were identified between purine metabolism indicators, extracellular nucleic acids, nitric oxide levels, and cardiac structural and functional parameters assessed by TTE in patients with overweight following CABG at different stages of cardiac rehabilitation ($p<0.05$).

4. Anthropometric, echocardiographic, and biochemical parameters were found to be associated with post-reperfusion changes in patients with overweight following CABG. BMI and epicardial adipose tissue thickness were identified as significant predictors. At the second stage of cardiac rehabilitation, an increase in BMI was associated with a 1.90-fold increase in the odds of post-reperfusion changes (OR=1.901; 95% CI: 1.153–3.133; p=0.012), while at the third stage, the odds increased 1.36-fold (OR=1.363; 95% CI: 1.014–1.832; p=0.040). Increased epicardial adipose tissue thickness at the third stage was associated with a 7.38-fold increase in the odds of post-reperfusion changes (OR=7.38; 95% CI: 2.15–25.37; $p<0.001$).

5. Regression models were developed to estimate the probability of post-reperfusion changes in patients with overweight following CABG at different stages of cardiac rehabilitation. At the first stage, the model for estimating the probability of laboratory abnormalities included BMI and epicardial adipose tissue thickness. At the second stage, the model for estimating the probability of structural and functional changes based on TTE findings included BMI and epicardial adipose tissue thickness, whereas the model for the comprehensive assessment of biochemical and echocardiographic changes included BMI and hypoxanthine. According to receiver operating characteristic (ROC) analysis, the highest discriminative performance was demonstrated by epicardial adipose tissue thickness (AUC=0.931), BMI (AUC=0.812), and hypoxanthine (AUC=0.765).

Implementation in Clinical Practice

The developed models have been implemented in the clinical practice of the Tulpar Cardiac Rehabilitation Center LLP, Karaganda, and Polyclinic No. 8 LLP, Karaganda (Appendix B).

Presentation and Discussion of Research Findings

Conference Presentations

1. Oral presentation at the VI Scientific and Practical Forum “Karachinsky Readings 2022: Contemporary Aspects of Health Preservation: Approaches and Current Research in Prevention, Rehabilitation, and Health Resort Medicine,” January 19–20, 2023, Novosibirsk, Russia. Presentation entitled “Myocardial Status in Patients with Overweight at Different Stages of Rehabilitation Following Revascularization.”

2. Oral presentation entitled “Structural and Functional State of the Myocardium in Patients with Overweight at Different Stages of Rehabilitation Following Coronary Artery Bypass Grafting” at the Scientific and Practical Conference of Young Scientists, Master's Students, and Doctoral Candidates dedicated to Science Day, “The World of Science and Youth: Traditions and Innovations,” April 12, 2023, Karaganda, Kazakhstan.

3. Participation in the International Scientific and Practical Congress “Multidisciplinary Approaches in Medicine: Integration into Clinical Practice, Science, and Education,” April 16–17, 2026, Karaganda, Kazakhstan, with an oral presentation entitled “Epicardial Adipose Tissue Thickness and Inflammatory Biomarkers in Patients with Overweight Following Coronary Artery Bypass Grafting.”

Publications

Based on the dissertation research, three articles were published in journals indexed in the Scopus database, two articles in journals recommended by the Committee for Quality Assurance in Science and Higher Education of the Republic of Kazakhstan, and two articles in publications indexed in the Russian Science Citation Index (RSCI). The research findings were also presented at three scientific conferences, and two conference abstracts were published in the proceedings of international conferences.

Personal Contribution of the Author

The author personally collected anthropometric and laboratory data, performed clinical examinations of patients and transthoracic echocardiography, and determined the levels of purine metabolites, extracellular nucleic acids, neutrophil extracellular traps (NETs), and nitric oxide (NO).

The author independently performed statistical data analysis, interpreted the findings, developed models for assessing the risk of post-reperfusion changes, and designed a cardiac rehabilitation model (algorithm) accounting for metabolic and inflammatory disturbances in patients with overweight following CABG. All sections of the dissertation were written by the author.

Structure and Length of the Dissertation

The dissertation comprises 125 pages of typed text and consists of an introduction, a literature review, the main body (materials and methods, and research results), a conclusion, a list of references, and appendices.

The dissertation contains 23 tables and 25 figures. The reference list includes 102 sources, of which 10 are in Russian and 92 are in English. The dissertation includes seven appendices.

Study Design, Materials and Methods

The study was conducted in two phases. The first phase aimed to assess baseline differences between the study groups. The second phase aimed to evaluate changes in echocardiographic and biochemical parameters at different stages of cardiac rehabilitation following coronary artery bypass grafting (CABG).

The study included the following five groups (Figure 1):

Group 1 – Patients with coronary artery disease (CAD) and overweight who underwent coronary artery bypass grafting (CABG) (CAD + overweight + CABG +), n=85;

Group 2 – Comparison group comprising patients with CAD and normal body weight who underwent CABG (CAD + overweight − CABG +), n=70;

Group 3 – Comparison group comprising patients with CAD and overweight who did not undergo CABG (CAD + overweight + CABG −), n=19;

Group 4 – Comparison group comprising patients with CAD and normal body weight who did not undergo CABG (CAD + overweight − CABG −), n=18;

Group 5 – Control group (CG), comprising 30 participants without chronic diseases, n=30.

A total of 222 patients were included in the study, comprising 164 men (73.9%) and 58 women (26.1%). The participants were aged 35–65 years. No restrictions based on racial or ethnic background were applied during participant recruitment.

The study protocol was approved by the Local Bioethics Committee of the Non-Profit Joint-Stock Company “Karaganda Medical University” (Karaganda, Kazakhstan; Protocol No. 16 dated March 15, 2021), in accordance with the ethical principles for medical research involving human participants outlined in the Declaration of Helsinki of the World Medical Association.

Written informed consent was obtained from all participants prior to their inclusion in the study.

The research was designed as a prospective cohort study with longitudinal follow-up. Patient recruitment was conducted from February 2021 to October 2022, followed by longitudinal monitoring at different stages of cardiac rehabilitation after elective coronary artery bypass grafting (CABG). Patients undergoing elective CABG were enrolled at the Regional Cardiac Surgery Center, while subsequent follow-up was performed at the Tulpar Rehabilitation Center.

Assessments were conducted sequentially at stage 0 during hospitalization and at stages 1, 2, and 3 of cardiac rehabilitation. At each assessment point, clinical data, echocardiographic parameters, and the investigated laboratory indicators were evaluated.

In the present study, the term “post-reperfusion myocardial state” referred to a combination of structural, functional, and biochemical changes observed following the restoration of coronary blood flow through CABG and assessed longitudinally during cardiac rehabilitation. This term was used as a research-specific definition and was not considered an independent diagnostic category.

Post-reperfusion changes were assessed comprehensively using transthoracic echocardiographic (TTE) parameters and biochemical markers. The structural and functional state of the myocardium was evaluated using left ventricular end-diastolic diameter (LVEDD), left ventricular end-systolic diameter (LVESD), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), left ventricular ejection fraction (LVEF), left ventricular mass index (LVMI), and other echocardiographic parameters.

Epicardial adipose tissue thickness was additionally measured. Metabolic alterations were assessed by measuring purine metabolites in blood plasma and erythrocytes, endothelial

dysfunction was evaluated based on nitric oxide (NO) levels, and changes associated with cellular injury were assessed using extracellular nucleic acid concentrations.

The persistence of post-reperfusion changes was determined through longitudinal assessment of the investigated parameters at successive stages of cardiac rehabilitation. Structural, functional, and laboratory abnormalities that continued to demonstrate statistically significant differences compared with the corresponding comparison group during follow-up were classified as persistent changes.

The study was conducted at both inpatient and rehabilitation levels of care.

I. Inpatient Level

Main Study Group (Patients Following CABG)

The study was conducted at the Municipal State Enterprise "Multidisciplinary Hospital No. 2 of Karaganda" under the Healthcare Department of Karaganda Region.

The analysis included patients with stable coronary artery disease (CAD) and angiographically confirmed two-vessel or three-vessel coronary artery disease who were indicated for elective CABG based on comprehensive clinical and instrumental examinations and a multidisciplinary cardiac surgery team decision.

The study population included patients with both overweight and normal body weight, totaling 155 patients (n=155).

Following completion of cardiac surgical treatment, referral to subsequent stages of rehabilitation was coordinated with primary health care (PHC) professionals. General practitioners and cardiologists contacted patients at their registered primary care facilities and referred them for rehabilitation treatment. Subsequent admission to the cardiac rehabilitation center was arranged through the Hospitalization Bureau Portal.

This approach ensured continuity of care across different levels of the healthcare system and enabled longitudinal follow-up of the same patient cohort throughout the successive stages of cardiac rehabilitation.

II. Rehabilitation Level

The study was continued at the Tulpar Cardiac Rehabilitation Center (Karaganda, Kazakhstan), where the same cohort of patients underwent repeated examinations following their initial inpatient assessment.

The standard cardiac rehabilitation program after coronary artery bypass grafting (CABG) was implemented in accordance with Orders No. 116 and No. 65 of the Ministry of Healthcare of the Republic of Kazakhstan and comprised three stages. The program included therapeutic exercise, massage, breathing exercises, and physiotherapy procedures, taking into account individual contraindications, alongside standard pharmacological treatment, including antiplatelet therapy (Trombopol, Quorex), cardioprotective therapy (Preductal), antianginal therapy (nitroglycerin), antihypertensive therapy (Fosinopril-Teva, bisoprolol), and lipid-lowering therapy (rosuvastatin).

Comparison Group (Negative Control)

The comparison group comprised patients from the Medical University Clinic in Karaganda (n=37) with documented coronary artery disease (CAD), with either overweight or normal body weight, who had not undergone coronary interventional procedures.

Patient Selection Criteria

Inclusion Criteria

Patients aged 35–65 years of either sex, with overweight or normal body weight, stable coronary artery disease, and angiographically confirmed two-vessel or three-vessel coronary artery disease, who had undergone elective coronary artery bypass grafting.

Exclusion Criteria

- Class I–III obesity.
- A history of acute or decompensated cardiac disease, previous acute myocardial infarction, or stroke, with diagnoses confirmed by coronary angiography and computed tomography, as applicable.
- Diagnosed type 1 or type 2 diabetes mellitus.
- Uncontrolled arterial hypertension (blood pressure above 190/100 mmHg).
- Chronic kidney disease or renal dysfunction, defined by an estimated glomerular filtration rate (eGFR, CKD-EPI) ≤90 mL/min/1.73 m² or serum creatinine above 179 μmol/L.
- Hepatic dysfunction characterized by transaminase levels more than twice the upper limit of normal.
- Severe psychiatric disorders, including alcohol or drug dependence, and oncological diseases.
- Pregnancy.
- Confirmed chronic infectious diseases or exacerbations of chronic diseases.
- Previous use of lipid-lowering medications, immunosuppressants, or hormone replacement therapy.
- Inflammatory joint diseases or systemic lupus erythematosus.

Study Procedures and Methods

The study included collection of medical history, general clinical examination, anthropometric measurements with calculation of body mass index (BMI), transthoracic echocardiography (TTE) to assess cardiac structural and functional parameters and epicardial adipose tissue thickness, and specialized biochemical investigations.

Biochemical assessments included measurement of purine metabolism indicators, nitric oxide (NO) metabolites, extracellular nucleic acids, and neutrophil extracellular traps (NETs).

Comprehensive patient examinations were performed within the first 24 hours after CABG (stage 0), as well as at the first, second, and third stages of cardiac rehabilitation. This approach enabled assessment of the dynamics of structural, functional, and biochemical changes during different periods of recovery.

Statistical Analysis

Statistical analysis was performed using SPSS version 27.0 and MedCalc version 22. Graphical presentation of the results was carried out using GraphPad Prism version 7.

The normality of quantitative data distributions was assessed using the Kolmogorov–Smirnov test. As most quantitative variables were not normally distributed, they were presented as medians (Me) and interquartile ranges (Q25–Q75), while categorical variables were expressed as absolute frequencies and percentages.

The Mann–Whitney U test and Kruskal–Wallis test were used to compare quantitative variables between independent groups, while Pearson's chi-square (χ^2) test was applied to categorical variables. Changes in quantitative parameters across follow-up stages were assessed using the Friedman test.

Correlations were analyzed using Spearman's rank correlation coefficient.

Logistic regression analysis was performed to identify factors associated with post-reperfusion changes at different stages of cardiac rehabilitation. The dependent variable was the presence or absence of post-reperfusion changes. Regression results were expressed as odds ratios (ORs) with 95% confidence intervals (95% CIs).

Regression models were adjusted for sex, age, arterial hypertension, and impaired glucose tolerance as potential confounding factors.

The predictive performance of the investigated parameters was evaluated using receiver operating characteristic (ROC) curve analysis, including determination of the area under the curve

(AUC), sensitivity, and specificity. Optimal cut-off values were determined using the Youden index.

A p-value <0.05 was considered statistically significant.

Given the multiple between-group and within-group comparisons, the potential increase in the risk of type I error was taken into account when interpreting the findings. Results were evaluated considering the level of statistical significance, the direction and consistency of changes over time, and their agreement with correlation, regression, and ROC analyses.

Research Results

Patients with overweight following CABG demonstrated more pronounced structural, functional, and biochemical changes compared with patients with normal body weight.

On the first postoperative day, patients with overweight had higher epicardial adipose tissue thickness (4.23 vs. 2.43 mm; $p<0.0001$), left ventricular mass index (110.0 vs. 82.0; $p<0.0001$), hypoxanthine levels (206 vs. 151; $p<0.0001$), and NETs levels (14.0 vs. 7.5; $p<0.0001$), along with lower left ventricular ejection fraction (47% vs. 53%; $p<0.0001$) and nitric oxide levels (3.30 vs. 4.21; $p<0.0001$).

At the third stage of cardiac rehabilitation, statistically significant between-group differences persisted in epicardial adipose tissue thickness (4.66 vs. 1.79 mm), left ventricular mass index (111.0 vs. 78.0), left ventricular ejection fraction (47% vs. 58%), NETs levels (15.0 vs. 1.0), and nitric oxide levels (2.85 vs. 4.30) ($p<0.0001$ for all listed parameters). Differences in purine metabolism indicators and extracellular nucleic acids also persisted ($p<0.05$).

Correlation analysis at the third stage revealed statistically significant positive correlations between hypoxanthine and left ventricular end-systolic volume ($r=0.986$; $p<0.001$) and left ventricular end-diastolic volume ($r=0.982$; $p<0.001$). Nitric oxide levels were negatively correlated with left ventricular end-diastolic volume ($r=-0.986$; $p<0.001$) and left ventricular mass index ($r=-0.947$; $p<0.001$), while a positive correlation was observed with left ventricular ejection fraction ($r=0.908$; $p<0.001$).

Regression models were developed to estimate the probability of post-reperfusion changes at different stages of cardiac rehabilitation. At the first stage, the model for assessing laboratory abnormalities included BMI and epicardial adipose tissue thickness. At the second stage, the model for assessing structural and functional changes based on TTE findings included BMI and epicardial adipose tissue thickness, while the combined model for biochemical and echocardiographic changes included BMI and hypoxanthine ($B=-0.006$; $p=0.005$).

A statistically significant association was established between BMI and post-reperfusion changes at the first (OR=1.52; $p=0.008$), second (OR=1.90; $p=0.012$), and third (OR=1.36; $p=0.040$) stages of cardiac rehabilitation, as well as between epicardial adipose tissue thickness and post-reperfusion changes at the third stage (OR=7.38; $p<0.001$).

According to ROC analysis, the highest discriminative performance was demonstrated by epicardial adipose tissue thickness (AUC=0.931), BMI (AUC=0.812), and hypoxanthine (AUC=0.765).

Conclusions

1. Patients in Group 1 with overweight following CABG demonstrated more pronounced structural, functional, and biochemical changes compared with patients in Group 2 without overweight following CABG.

These changes were characterized by higher epicardial adipose tissue thickness (4.23 vs. 2.43 mm; $p<0.0001$), left ventricular mass index (110.0 vs. 82.0 g; $p<0.0001$), and lower left ventricular ejection fraction (47% vs. 53%; $p<0.0001$).

Biochemical changes included higher plasma hypoxanthine levels (206 vs. 151; $p<0.0001$), NETs levels (14.0 vs. 7.5; $p<0.0001$), plasma extracellular DNA (0.51 vs. 0.29; $p<0.0001$), and plasma acid-soluble fraction (1.52 vs. 0.70; $p<0.0001$), together with lower nitric oxide levels (3.30 vs. 4.21; $p<0.0001$).

Compared with Group 3 patients with CAD and overweight who had not undergone CABG, Group 1 patients demonstrated higher epicardial adipose tissue thickness, left ventricular mass index, plasma hypoxanthine, NETs, and selected extracellular nucleic acid indicators. More pronounced structural, functional, and biochemical differences were also observed compared with the control group.

2. Throughout cardiac rehabilitation, patients with overweight following CABG exhibited more pronounced and persistent structural, functional, and biochemical changes compared with patients without overweight.

At the third stage, epicardial adipose tissue thickness was 4.66 mm versus 1.79 mm, left ventricular mass index was 111 g versus 78.0 g, left ventricular end-diastolic diameter was 57.0 mm versus 39 mm, and left ventricular end-systolic diameter was 38.5 mm versus 25 mm. Left ventricular ejection fraction was lower, at 47% versus 58% ($p<0.0001$).

Statistically significant between-group differences in purine metabolism indicators, extracellular nucleic acids, NETs, and nitric oxide levels also persisted.

At the third stage, NETs levels in Group 1 were 15 times higher than those in Group 2 (15.0 vs. 1.0, respectively; $p<0.0001$), whereas nitric oxide levels were 33.7% lower (2.85 vs. 4.30, respectively; $p<0.0001$).

3. At the third stage of cardiac rehabilitation, patients with overweight following CABG demonstrated strong, statistically significant relationships between biochemical indicators and cardiac structural and functional parameters.

Plasma hypoxanthine levels were positively correlated with left ventricular end-systolic volume ($r=0.986$; $p<0.001$) and left ventricular end-diastolic volume ($r=0.982$; $p<0.001$).

Nitric oxide levels were negatively correlated with left ventricular end-diastolic volume ($r=-0.986$; $p<0.001$) and left ventricular mass index ($r=-0.947$; $p<0.001$), and positively correlated with left ventricular ejection fraction ($r=0.908$; $p<0.001$).

Epicardial adipose tissue thickness demonstrated statistically significant correlations with purine metabolism indicators, extracellular nucleic acids, and nitric oxide levels ($p<0.05$).

4. In patients with overweight following CABG, BMI and epicardial adipose tissue thickness were statistically significant factors associated with post-reperfusion changes at different stages of cardiac rehabilitation.

An increase in BMI was associated with a 1.52-fold increase in the odds of post-reperfusion changes at the first stage ($p=0.008$), a 1.90-fold increase at the second stage ($p=0.012$), and a 1.36-fold increase at the third stage ($p=0.040$).

Increased epicardial adipose tissue thickness at the third stage was associated with a 7.38-fold increase in the odds of post-reperfusion changes ($p<0.001$).

In the combined regression model for the second stage, hypoxanthine was also a statistically significant factor ($B=-0.006$; $p=0.005$).

5. Regression models were developed to estimate the probability of post-reperfusion changes in patients with overweight following CABG.

The first-stage model for assessing the probability of laboratory abnormalities included BMI and epicardial adipose tissue thickness.

The second-stage model for assessing the probability of structural and functional changes based on TTE findings also included BMI and epicardial adipose tissue thickness.

The combined model for assessing biochemical and echocardiographic changes at the second stage included BMI and hypoxanthine.

According to ROC analysis, epicardial adipose tissue thickness demonstrated the highest discriminative performance (AUC=0.931), followed by BMI (AUC=0.812) and hypoxanthine (AUC=0.765).

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