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Features of The Formation of An Unfavorable Functional Phenotype in Patients with Chronic Heart Failure and Obesity

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Abstract

Objective. To assess the functional manifestations of an unfavorable cardiometabolic phenotype in patients with chronic heart failure and obesity based on an analysis of exercise tolerance and quality-of-life indicators.

Materials and methods. A cross-sectional comparative study included patients with obesity and chronic heart failure, as well as individuals with obesity without clinical signs of heart failure. To assess the severity of cardiometabolic disorders, the examined patients were stratified by the presence of an unfavorable metabolic phenotype. Functional status was studied using a treadmill test with analysis of exercise duration, workload achieved, estimated oxygen consumption (VO_2), chronotropic index, heart rate increment, and features of the hemodynamic response to exercise. Quality of life was assessed with the Minnesota Living with Heart Failure Questionnaire (MLHFQ) and the SF-36.

Results. The formation of an unfavorable cardiometabolic phenotype was accompanied by a significant reduction in the functional reserve of the cardiovascular system. The examined patients showed lower treadmill test duration, workload achieved, oxygen consumption, chronotropic index, and heart rate increment, together with an enhanced pressor response to exercise. According to the MLHFQ, more pronounced limitations of physical activity, increased emotional

distress, and worse integral quality-of-life scores were found. According to the SF-36, physical functioning, vitality, and general health scores were reduced.

Conclusion. An unfavorable cardiometabolic phenotype in patients with chronic heart failure and obesity is associated with reduced aerobic working capacity, the development of chronotropic incompetence, impaired adaptive mechanisms of the cardiovascular system, and worse quality of life. The results obtained justify the introduction of cardiometabolic rehabilitation programs aimed at increasing functional reserve, optimizing the hemodynamic response to exercise, and improving the clinical status of patients.

Keywords: Chronic heart failure, obesity, cardiometabolic phenotype, exercise tolerance, quality of life, chronotropic incompetence, cardiometabolic rehabilitation.

1. Introduction

In recent years, chronic heart failure (CHF) has increasingly been viewed as a systemic cardiometabolic disease that goes far beyond isolated myocardial damage. Despite significant advances in modern pharmacotherapy, CHF remains one of the leading causes of disability, repeated hospitalizations, and premature mortality worldwide. This problem is especially relevant against the background of the global rise in the prevalence of obesity, which is now recognized as an independent factor in the progression of cardiovascular diseases and the formation of an unfavorable prognosis.

The combination of CHF and obesity forms a distinct cardiometabolic phenotype characterized by a complex interplay of hemodynamic, neurohumoral, and metabolic disturbances. This category of patients is characterized by chronic low-grade inflammation, insulin resistance, endothelial dysfunction, impaired autonomic regulation of the cardiovascular system, and a progressive decline in functional reserve. Together, these processes worsen the body's adaptation to physical exertion and limit daily activity.

In the modern concept of the cardiometabolic continuum, exercise tolerance is regarded as one of the most informative integral indicators of the state of the cardiovascular system. A reduction in peak oxygen consumption, impaired chronotropic response, decreased exercise tolerance, and worsening hemodynamic adaptation reflect not only the severity of heart failure but also the degree to which the patient is involved in the pathological cardiometabolic cascade. For this reason, exercise testing indicators are increasingly used for risk stratification and for assessing the effectiveness of therapeutic and rehabilitation interventions.

Patients' quality of life is of no less importance and has in recent years been regarded as an independent clinical endpoint alongside hospitalizations and mortality. In patients with combined CHF and obesity, limitation of physical functioning is often accompanied by emotional distress, reduced social activity, and a worse subjective perception of one's own health. In this regard, the use of validated quality-of-life questionnaires provides additional information on the impact of cardiometabolic dysfunction on the patient's daily functioning.

Despite the active study of the cardiometabolic mechanisms of CHF progression, the functional manifestations of an unfavorable cardiometabolic phenotype in patients with obesity remain insufficiently studied. Of particular interest is the comprehensive assessment of exercise tolerance and quality of life as interrelated components of functional status that reflect the depth of cardiometabolic dysfunction and the potential for its correction.

Aim of the study — to study the influence of cardiometabolic disorders on functional status and quality of life in patients with chronic heart failure and obesity using exercise tolerance indicators and validated quality-of-life scales.

2. Methods

A cross-sectional comparative study was conducted to examine the functional manifestations of an unfavorable cardiometabolic phenotype in patients with chronic heart failure and obesity. The study included patients with obesity and chronic heart failure, who formed the main group, and individuals with obesity without clinical and instrumental signs of heart failure, who formed the comparison group. To assess the influence of cardiometabolic disorders on functional status, the examined patients were additionally stratified according to the presence of metabolic syndrome.

The study included 198 patients with obesity, of whom 112 were men (56.6%) and 86 were women (43.4%). The age of the examined patients ranged from 40 to 75 years, with a mean of 58.4±9.6 years.

In accordance with the study design, the following groups were formed:

• Main group (MG) — patients with chronic heart failure and obesity (n=102), including a subgroup with metabolic

syndrome (n=54) and a subgroup without metabolic syndrome (n=48).

• Comparison group (CG) — patients with obesity without signs of chronic heart failure (n=96), including a subgroup with metabolic syndrome (n=50) and a subgroup without metabolic syndrome (n=46).

The diagnosis of chronic heart failure was established on the basis of clinical symptoms, echocardiographic findings, and the current recommendations of the European Society of Cardiology (ESC, 2021). Metabolic syndrome was diagnosed according to the criteria of the International Diabetes Federation (IDF) and the National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III).

The study was carried out at the Republican Specialized Scientific and Practical Medical Center of Cardiology of the Ministry of Health of the Republic of Uzbekistan (Tashkent).

To assess functional status, all examined patients underwent a standardized treadmill test. The following were analyzed: exercise duration, maximum workload achieved, estimated oxygen consumption (VO_2), heart rate as a percentage of the predicted value, chronotropic index, heart rate increment, systolic blood pressure at peak exercise, and its increment relative to baseline values.

Quality of life was assessed using the validated Minnesota Living with Heart Failure Questionnaire (MLHFQ), which included analysis of physical activity limitation, emotional distress, and the total score, as well as the generic SF-36 questionnaire, which characterizes patients' physical and psychosocial functioning.

Statistical processing was performed using SPSS Statistics 26.0. Quantitative indicators are presented as the mean and standard deviation (M±SD). Student's t-test was used to assess intergroup differences. Differences were considered statistically significant at $p<0.05$.

3. Results

The results of exercise testing demonstrated pronounced differences in the functional status of the examined patients depending on the severity of cardiometabolic disorders (Table 1). The most unfavorable indicators were recorded in patients with chronic heart failure and obesity who had cardiometabolic dysfunction, which indicated a substantial reduction in the functional reserve of the cardiovascular system.

Table 1.

Characteristics of the functional cardiometabolic phenotype according to treadmill test data

Indicator	MG without MS	MG with MS	CG without MS	CG with MS
Treadmill test duration, min	8.2±1.6	6.4±1.1***	8.1±1.5	6.4±1.6***
Maximum workload achieved, MET	7.4±1.2	5.7±0.9***	7.4±0.8	5.6±0.9***
Estimated oxygen consumption (VO_2), mL/kg/min	27±3.8	20.1±3.1***	27.2±4.4	20.2±3.2***
Percent of predicted HR, %	90±10.3	84±13.4*	90.4±15.6	85.8±12.9
Chronotropic insufficiency index (CII), (dimensionless)	0.7±0.09	0.61±0.08***	0.7±0.09	0.6±0.09***
HR increment (peak – rest), bpm	65.1±11.1	54±8.1***	63.7±9.5	52.4±7.7***

SBP at peak exercise, mmHg	160.2±26.8	175.1±20.3*	162±21.1	176.8±34.9*
SBP increment during exercise (peak – rest), mmHg	42.2±6.8	50.9±8***	42±6.4	50.4±9.1***

Note: *p<0.05; **p<0.01; ***p<0.001 compared with the corresponding group without MS.

One of the most sensitive indicators of functional state proved to be treadmill test duration. In patients with an unfavorable cardiometabolic phenotype, exercise duration was significantly lower both in the main group (6.4±1.1 min versus 8.2±1.6 min; p<0.001) and in the comparison group (6.4±1.6 min versus 8.1±1.5 min; p<0.001). The data obtained indicate reduced overall exercise tolerance and diminished adaptive capacity of the body.

A similar pattern was observed in the analysis of maximum workload achieved. In patients with more pronounced cardiometabolic disorders, this indicator decreased to 5.7±0.9 MET in the main group and to 5.6±0.9 MET in the comparison group, whereas in those without signs of pronounced cardiometabolic dysfunction it was 7.4±1.2 and 7.4±0.8 MET, respectively (p<0.001). The reduction in workload achieved reflects decreased physical working capacity and a limitation of patients' functional potential.

The most pronounced differences were found in the estimated oxygen consumption (VO_2), which is one of the key integral indicators of aerobic performance. In patients with an unfavorable cardiometabolic phenotype, VO_2 decreased by almost a quarter and amounted to 20.1±3.1 mL/kg/min in the main group and 20.2±3.2 mL/kg/min in the comparison group, versus 27.0±3.8 and 27.2±4.4 mL/kg/min, respectively (p<0.001).

Chronotropic function indicators are of particular interest. In patients with pronounced cardiometabolic disorders, a significant decrease in the chronotropic index was found, to 0.61±0.08 and 0.60±0.09, respectively, whereas in the groups with a more favorable metabolic profile this indicator was 0.70±0.09 (p<0.001). At the same time, the heart rate increment during exercise was reduced, indicating the development of chronotropic incompetence and impairment of the adaptive response of the cardiovascular system to physical stress.

The hemodynamic response to exercise was characterized by changes in the opposite direction. Despite the decrease in aerobic performance and chronotropic reserve, patients with an unfavorable cardiometabolic phenotype showed a more pronounced pressor reaction. Systolic blood pressure at peak exercise reached 175.1±20.3 mmHg and 176.8±34.9 mmHg, which exceeded the values in the corresponding comparison groups (p<0.05). A similar tendency was found for the increment in systolic blood pressure, which rose to 50.9±8.0 and 50.4±9.1 mmHg, respectively (p<0.001).

Thus, the functional cardiometabolic phenotype of patients with chronic heart failure and obesity is characterized by a combination of reduced aerobic power, decreased exercise tolerance, the development of chronotropic incompetence, and an enhanced hemodynamic response to physical stress. Taken together, the identified changes indicate a substantial reduction in the functional reserve of the cardiovascular system and may be regarded as one of the clinical manifestations of cardiometabolic dysfunction.

Further analysis was aimed at assessing the subjective components of functional status using the specialized Minnesota Living with Heart Failure Questionnaire (MLHFQ), which makes it possible to characterize the impact of the disease on patients' physical and emotional functioning (Table 2).

Analysis of patients' quality of life on the MLHFQ revealed a negative impact of metabolic syndrome (MS) on physical and emotional state (Table 2).

Table 2.

Quality of life according to the MLHFQ in patients with CHF and obesity

Indicator	MG without MS	MG with MS	CG without MS	CG with MS
MLHFQ PAL, points (physical activity limitation)	16±2	16.7±2.7	16±2.3	16.9±2.8*
MLHFQ ED, points (emotional state)	12.3±1.5	12.8±1.9	12±2	13±2.2*
MLHFQ TS, points (total quality-of-life score)	46.7±6.9	50.3±8.6*	47.1±9.4	50.5±9

Note: *p<0.05; **p<0.01; ***p<0.001 compared with the corresponding group without MS.

The results obtained showed that the formation of an unfavorable cardiometabolic phenotype is accompanied by worse quality-of-life indicators, affecting both the physical and the psychoemotional aspects of daily functioning.

The most pronounced changes were noted in the domain reflecting limitation of physical activity. In patients with more pronounced cardiometabolic disorders, MLHFQ scores increased, indicating a greater impact of the disease on the ability to perform daily activities. In the main group, the physical activity limitation score was 16.7±2.7 points versus 16.0±2.0 points in patients with a more favorable metabolic profile. A similar tendency was observed in the comparison group, where the score reached 16.9±2.8 points versus 16.0±2.3 points, respectively (p<0.05).

Analysis of the emotional component of quality of life also revealed signs of an adverse influence of cardiometabolic dysfunction. Higher emotional distress scores were recorded in patients with pronounced metabolic disorders both in the main group (12.8±1.9 versus 12.3±1.5 points) and among those without signs of heart failure (13.0±2.2 versus 12.0±2.0 points; p<0.05). The data obtained indicate that cardiometabolic disorders affect not only patients' physical condition but also their emotional well-being.

The integral assessment of quality of life confirmed the identified patterns. The highest MLHFQ total scores, reflecting a more pronounced negative impact of the disease on daily functioning, were recorded in patients with chronic heart failure and an unfavorable cardiometabolic profile. In the main group, the total score reached 50.3±8.6 points compared with 46.7±6.9 points in patients without pronounced cardiometabolic dysfunction (p<0.05). In the comparison group, a similar tendency persisted but did not reach statistical significance.

Thus, an unfavorable cardiometabolic phenotype is associated not only with a decrease in objective indicators of physical working capacity but also with a worse subjective perception of one's own condition. The combination of physical activity limitation, emotional distress, and lower integral quality-of-life scores allows these changes to be regarded as an important component of functional cardiometabolic dysfunction in patients with chronic heart failure and obesity.

4. Discussion

The results obtained indicate that the decline in functional status in patients with chronic heart failure and obesity is closely related to the severity of cardiometabolic disorders. The study showed that, as the unfavorable cardiometabolic phenotype develops, there is a consistent deterioration in physical working capacity, chronotropic function, and quality of life. The identified changes make it possible to regard functional maladaptation as one of the key clinical manifestations of cardiometabolic dysfunction.

Of particular importance is the identified decrease in exercise tolerance. A reduction in treadmill test duration, workload achieved, and estimated oxygen consumption reflects decreased aerobic performance and a smaller functional reserve of the cardiovascular system. In the modern literature, a decrease in VO_2 is regarded as one of the most informative integral indicators of the severity of heart failure and of an unfavorable prognosis. The data obtained indicate that cardiometabolic disorders can exert an additional negative effect on exercise tolerance independently of cardiac dysfunction per se.

No less important appears to be the identified impairment of the chronotropic response. A decrease in the chronotropic index and a smaller heart rate increment during exercise point to the development of chronotropic incompetence, which is currently regarded as a manifestation of autonomic dysregulation and neurohumoral imbalance. It is known that the combination of obesity, insulin resistance, and chronic inflammation is accompanied by changes in the autonomic regulation of the cardiovascular system, which limits the body's adaptive capacity during physical stress. As a result, even moderate exertion may be accompanied by premature fatigue and reduced tolerance of physical effort.

An interesting feature of the identified functional phenotype is the combination of a reduced chronotropic reserve with an enhanced pressor response to exercise. Higher systolic blood pressure values at peak testing and a greater increment in this indicator suggest the presence of impaired vascular adaptation. Such a hemodynamic profile may reflect the combined influence of endothelial dysfunction, increased arterial stiffness, and chronic sympathetic activation, which are regarded as important components of the cardiometabolic continuum.

The results of the quality-of-life assessment complement the data of objective exercise testing. Higher physical activity limitation and emotional distress scores on the MLHFQ indicate that an unfavorable cardiometabolic phenotype affects not only the physiological mechanisms of adaptation but also the patient's subjective perception of his or her own condition. The worsening of integral quality-of-life indicators reflects the combined impact of functional limitations, the symptom burden of the disease, and psychoemotional factors.

Particular attention should be paid to the fact that the changes in quality of life developed in parallel with the decline in physical working capacity. This confirms the existence of a close relationship between the objective characteristics of functional reserve and the subjective perception of health. Consequently, quality-of-life assessment can be regarded as an important additional tool for patient phenotyping alongside traditional exercise tests.

From the standpoint of modern cardiometabolic medicine, the results obtained make it possible to regard the combination of reduced aerobic performance, chronotropic incompetence, an enhanced pressor response, and worse quality of life as a single functional cardiometabolic phenotype. The formation of this phenotype reflects the integration of hemodynamic, metabolic, inflammatory, and neurovegetative disturbances and may be regarded as one of the manifestations of progression of the cardiometabolic continuum in patients with chronic heart failure and obesity.

The strengths of the study include the comprehensive assessment of both objective indicators of functional state (treadmill test, VO_2, chronotropic index, hemodynamic response to exercise) and subjective characteristics of quality of life using validated questionnaires. This approach provided a holistic picture of the functional manifestations of an unfavorable cardiometabolic phenotype in patients with chronic heart failure and obesity.

5. Conclusion

The study showed that in patients with chronic heart failure and obesity, the severity of cardiometabolic disorders is associated with the formation of an unfavorable functional phenotype characterized by reduced aerobic performance, limited exercise tolerance, and impaired adaptive capacity of the cardiovascular system. The most significant manifestations of this phenotype are a shorter treadmill test duration, lower estimated oxygen consumption, a smaller maximum workload achieved, and signs of chronotropic incompetence.

At the same time, a combination of reduced chronotropic reserve with a more pronounced pressor response to exercise was found, which indicates impaired neurovegetative and hemodynamic adaptation. The data obtained make it possible to regard the features of the response to exercise as an important component of the functional cardiometabolic phenotype in patients with chronic heart failure and obesity.

The decline in physical working capacity was accompanied by worse quality of life according to the MLHFQ and SF-36 questionnaires, which confirms the close relationship between the objective characteristics of functional status and the subjective perception of health. The most pronounced changes affected physical functioning, vitality, and integral quality-of-life indicators.

Thus, the combination of reduced exercise tolerance, chronotropic incompetence, impaired hemodynamic response, and worse quality of life forms a single functional cardiometabolic phenotype that reflects the depth of systemic cardiometabolic dysfunction in patients with chronic heart failure and obesity. The results obtained underscore the importance of a comprehensive assessment of exercise tolerance and quality of life for more accurate patient phenotyping and for improving personalized approaches to their management.

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