ISSN: 0258-8013
Volume 45, Issue 07, August, 2025

CONTEMPORARY UNDERSTANDING OF THE CONDITION IN PATIENTS WITH CHRONIC HEART FAILURE

Alikulov I.T.[1], Solikhov M.U.[2], Khaytimbetov J.Sh.[3], Narziev N.M.[4], Abdullaev U.S.[5], Solikhov B.M.[6]

PhD, associate professor of Department of propaedeutics of internal diseases №1 of Tashkent State Medical University of Uzbekistan[1]
Senior lecturer of Department of propaedeutics of internal diseases №1 of Tashkent State Medical University of Uzbekistan[2,3,4]
PhD, assistant of Department of propaedeutics of internal diseases №1 of Tashkent State Medical University of Uzbekistan[5]
Assistant of Department of propaedeutics of internal diseases №1 of Tashkent State Medical University of Uzbekistan[6]

Keywords:
chronic heart failure, ejection fraction, dyspnea, muscle weakness.

DOI:
07.2200/Pcsee.22.10.2025.01

ABSTRACT

The article presents overview and statistical data on heart failure and cardiovascular diseases, data from world studies on different forms of heart failure in accordance with the modern classification, their clinical, anamnestic and prognostic differences, and different approaches to the treatment of heart failure. Over the past five years, the number of patients with chronic heart failure with preserved ejection fraction has increased from 38 to 54%. The increase in life expectancy, and, consequently, the number of patients with chronic heart failure, in particular with preserved ejection fraction, generates scientific interest in this problem. Pathophysiological changes in the body that determine the development of the symptom complex characteristic of this pathology are currently being actively studied. This review presents the main mechanisms responsible for the appearance of symptoms characteristic of patients with chronic heart failure: muscle weakness, decreased tolerance to physical activity, dyspnea. The pathophysiological and pathogenetic processes associated with muscle weakness and dyspnea in patients with chronic heart failure with both preserved and reduced ejection fraction are covered in detail.

1. INTRODUCTION

Some of the main manifesting symptoms of heart failure (HF) are dyspnea and weakness, limiting exercise tolerance (ET). With further unfavorable development of the disease, subsequent symptoms of HF may be wheezing in the lungs and dyspnea at rest associated with congestion in the pulmonary circulation, as well as edema of the lower extremities associated with congestion in the systemic circulation - a consequence of impaired liver and kidney function. The presented symptom complex may be a consequence of pathology of the valve apparatus, pericardium, large vessels, metabolic disorders; however, the most common cause of HF symptoms is pathology of the left ventricle (LV), associated with both impaired contractility and impaired filling. The classical concept of decreased exercise tolerance in patients with chronic heart failure (CHF), caused by impaired central hemodynamic mechanisms against the background of decreased cardiac output, has currently undergone significant changes. Modern concepts indicate complex disorders at various levels with a decrease in functional reserves in patients with CHF during exercise. Firstly, the involvement of mechanisms of decreasing ventilation parameters in the lungs is caused by the disturbance of respiratory mechanics and the decrease of gas diffusion. Secondly, the increased oxygen demand of muscle tissue during physical activity is not provided by the compensatory increase of cardiac output (CO) due to the decrease of chronotropic reflex, decrease of ventricular contractility, and development of concomitant anemia. Further, during physical activity, changes of diastolic function (DF) under conditions of tachycardia and increased venous return lead to the increase of LV filling pressure and the disturbance of cardiovascular coupling. In addition, during the exercise in patients with CHF, the disturbance of peripheral oxygen consumption is often limited by the decrease of capillary density and mitochondrial volume, selective loss of type I muscle fibers, and disturbance of afferent innervation of muscle tissue.

Main pathogenetic mechanisms of dyspnea in patients with CHF with reduced LV ejection fraction

Subjectively, dyspnea is the most common symptom-limiting complaint in most patients with CHF when performing LF. According to scientists, among 222 patients included in the study, dyspnea was the dominant complaint limiting the performance of the load in 160 patients [1]. Weakness in the lower limbs, limiting the performance of the load, is in second place in terms of frequency of occurrence [2]. A detailed analysis of the frequency of occurrence of these symptoms in patients with CHF during LF revealed that the type of load performed plays an important role. Among patients with a rapid increase in the degree of load, the test was more often stopped due to dyspnea, whereas in the case of a gradually increasing intensity, weakness in the lower limbs was a limitation of continuation [3]. The type of LF is also of no small importance: for example, patients performing a test on a bicycle ergometer most often stop the load due to weakness in the legs; on the contrary, when testing on a treadmill, the most common limiting cause is dyspnea [4]. Thus, one of the dominant symptoms in patients with CHF is the symptom of dyspnea during PE, leading to a significant limitation of motor activity and a decrease in the quality of life. When speaking about the pathogenetic cause of dyspnea in patients with CHF, logically, the factors leading to a violation of central hemodynamics should come to the fore: a decrease in CO and, consequently, the onset of tissue hypoperfusion. However, there is a fairly extensive series of studies indicating an insignificant contribution of the pumping function of the left and right ventricles to the development of dyspnea in patients with CHF. In 1992, and then in 2004, studies showed that the ejection fractions of the left and right ventricles do not have a relationship with the tolerance of PE [5]. When analyzing invasive hemodynamic parameters, no correlations were found between the cardiac index (CI), pulmonary artery pressure and peak oxygen consumption during PE [7]. In contrast, the velocity of the mitral valve annulus measured by tissue Doppler sonography is associated with both oxygen consumption and the level of exercise tolerance [8].

The two main reasons for the development of a feeling of shortness of breath during exercise in patients with CHF are a violation of the breathing pattern (decrease in the vital capacity of the lungs) and excessive hyperventilation [9]. In patients with CHF, a deliberately high ventilatory response is recorded during exercise, which consists of disproportionately high ventilation in response to an increase in the concentration/production of CO_2, which, in turn, leads to a violation of the ratio of the physiological dead volume of the lungs to their vital capacity (DLV/VC). In response to an increase in CO_2 concentration by 1 l/min1 in a healthy person, minute ventilation (MV) should be 20-25 l/min1, and in patients with CHF, a MV volume of about 30-50 l/min-1 is required to neutralize the same amount of carbon dioxide [10]. The increase in CO2 concentration in exhaled air in patients with CHF during low-intensity PE below the anaerobic threshold is explained by additional buffering of lactic acid [11]. Hyperventilation developing during PE in patients with CHF leads to an increase in lung volume at the end of exhalation, the formation of a “restrictive” limitation of vital capacity with a subsequent decrease in MV and the appearance of dyspnea symptoms [12]. Thus, in patients with CHF during PE, an increase in the UB/VT ratio occurs under hyperventilation conditions.

From the standpoint of gas exchange, an increase in the VP/VT ratio in the absence of an increase in hypoxemia or arteriovenous oxygen difference in patients with CHF indicates the absence of a pronounced perfusion/ventilation mismatch. However, from the standpoint of alveolar ventilation, impaired pulmonary tissue perfusion leads to an increase in venous pressure with an even greater decrease in pulmonary tissue perfusion. In addition, venous pressure is increased by vascular thrombosis against the background of chronic stasis in the lung tissue, a decrease in nitric oxide production, and an increase in endothelin-1 concentration. These vasoconstrictor mechanisms prevent the occurrence of transudation from the capillary bed and the development of pulmonary edema, but reduce pulmonary tissue perfusion, forming a vicious circle [13]. Violation of ventilation-perfusion relations at the alveolar level is also facilitated by prolonged remodeling of the alveolar-capillary membrane, which consists of increasing fibrosis of the pulmonary parenchyma, an increase in the proportion of connective tissue [14]. The central nervous system and the chemo- and ergoreflex system contribute to the violation of ventilation-perfusion relations during physical activity in patients with CHF, and, consequently, to the development of dyspnea. Studies conducted on animals have shown that in the presence of CHF, an increase in the activity of chemoreflexes is associated with hyperventilation characteristic of these patients [6]. It has been recorded that the sensitivity of chemoreceptors to hypoxia and hypercapnia in patients with CHF is significantly higher and is associated with an excessive ventilatory response to physical activity [7]. However, this theory has opponents, since in patients with CHF, acceptable levels of partial pressure of arterial oxygen and CO2 concentration are recorded during prolonged physical activity [8].

Another reason for the impaired ventilatory response to exercise in patients with CHF is the dysfunction of mechanoreceptors and metaboreceptors, which are ergoreceptors. Together, these receptors form a response to physical activity in the form of sympathetic tone, tachycardia, vasodilation in muscle tissue, and increased pulmonary ventilation, which together constitute an ergoreflex. The fibers of these receptors consist of myelinated or demyelinated afferent fibers originating in muscle tissue and following into the lateral spinothalamic tract [9]. Mechanoreceptors perceive mechanical stimuli from working muscles, and metaboreceptors are stimulated by increasing acidosis and increasing the concentration of prostaglandins and bradykinin. Among healthy people, activation of the ergoreflex underlies the adaptation of the cardiorespiratory system to exercise, and among patients with CHF, excessive activation of the ergoreflex leads to a disproportionate hyperventilation response to exercise [10].

Thus, respiratory failure in patients with CHF has a complex basis, characterized by dysfunction of the central and peripheral nervous systems, impaired perfusion-ventilation relationships in the lung tissue, and a decrease in central hemodynamic parameters.

The role of changes in skeletal muscles in the formation of a symptom complex in patients with CHF with a reduced LV ejection fraction

Skeletal muscle disorders play an important role in the development of weakness during physical activity in patients with CHF, and the idea of the primary role of these disorders forms the muscle theory of weakness in patients with CHF. The classical idea of the leading role of decreased blood flow in skeletal muscles due to a decrease in the pumping function of the heart as the main cause of weakness during physical activity is currently being questioned [11]. A number of authors indicate that structural changes in muscle tissue occur competitively with changes in tissue perfusion. This may explain the fact that 26% of patients with CHF and severe weakness during physical activity show no signs of muscle hypoperfusion. Nevertheless, during physical activity, these patients demonstrate a significant increase in lactic acid levels, which may indicate muscle disorders at the structural level [12]. The authors of the above study assessed blood flow in the lower extremities using direct measurements in the venous system. On the contrary, according to another group of scientists, in 1999, a reliable decrease in capillary density in muscle tissue was registered in patients with CHF, and this decrease is directly proportional to peak oxygen consumption [13]. Similar data were obtained in 2011: using infrared spectroscopy, it was shown that in patients with CHF, peripheral microcirculation is significantly reduced compared to healthy people and significantly correlates with the severity of CHF [14]. Nevertheless, today there is no convincing idea of whether changes in the muscles in patients with CHF are an independent process or they are a consequence of a decrease in systemic blood flow. However, the processes occurring in muscle tissue during the symptom complex of CHF are uniform and consist of a violation of vascular tone, a decrease in the response to endogenous vasodilator stimuli, an increased level of endothelin, and an increase in peripheral vascular resistance [5]. In patients with CHF, both peripheral muscles and respiratory muscle groups are subject to morphological, histological, enzymatic and metabolic disorders, which forms a symptom complex of myopathy. Histological changes in muscle tissue in patients with CHF consist of fiber atrophy, decreased isometric contraction force and impaired vascularization. A change in the proportion of muscle fibers (a decrease in type 2 and type 1 fibers) is also recorded, which occurs through insulin-like growth factor and calcineurin [6].

Some of the mechanisms that lead to muscle atrophy are apoptotic processes triggered by cytokinase and ubiquitin/proteasome reactions, as well as with the participation of tumor necrosis factor. The level of apoptotic activity in patients with CHF reliably correlates with the severity of symptoms and the degree of decreased tolerance to exercise necrosis [2]. Molecular disturbances are represented by a decrease in the oxidative activity of enzymes, as well as a decrease in the concentration of phosphocreatine. These changes, due to a decrease in the anaerobic threshold, lead to a more rapid development of acidosis during exercise necrosis. In addition, the early onset of the anaerobic threshold, and, consequently, the development of acidosis in muscle tissue, is facilitated by an increase in the proportion of type 2 muscle fibers, which are glycolytic and do not have the ability to contract for a long time [3]. Neuromuscular activity recorded by electromyography in patients with CHF was reduced both during maximum fiber contraction and during maximum isometric contraction [4]. These disorders have a pathogenetic basis, since in patients with CHF, a disorder of the excitation-contraction processes is recorded not only at the level of cardiomyocytes, but also at the level of skeletal muscles. Disruption of the first type of ryanodine receptors, recorded in an animal model, leads to an increase in the concentration of Ca^{2+}, which, in turn, leads to a disruption of the muscle fiber contraction process, and also has a number of toxic effects (impaired protein transcription, stimulation of apoptosis processes, disruption of energy balance) [1]. At the cellular level, patients with CHF experience a decrease in mitochondrial density and the activity of mitochondrial enzymes involved in the oxidative process. These disorders reliably correlate with a decrease in tolerance to exercise and peak oxygen consumption during spiroergometry [1]. However, understanding of the processes occurring at the cellular level remains incomplete and contradictory. Despite the proven reduced enzymatic mitochondrial activity in patients with CHF, the oxidative activity of mitochondria in patients with CHF and healthy people does not differ and is not limited by enzyme activity [2].

Endocrine background in patients with a decrease in the LV ejection fraction and its role in the development of CHF symptoms.

According to the neurohormonal theory, patients with CHF have an anabolic/catabolic imbalance with a predominance of catabolism processes associated with hormonal activity disorders and playing a central role in the development of myopathy. This theory implies the primary role of pathological endocrine and neurohormonal disorders in response to changes in the functioning of the cardiovascular system with suppression of systemic circulation. Activation of the sympathetic and renin-angiotensin-aldosterone systems leads to a progressive deterioration in hemodynamic parameters under conditions of reduced cardiac output, and subsequently acquires features of a vicious circle [3]. In patients with CHF prone to cachexia, high levels of norepinephrine, epinephrine, cortisol, and tumor necrosis factor are recorded. In contrast, the concentration of hormones responsible for anabolism processes (dehydroepiandrosterone and testosterone) is reduced [4]. In patients with CHF, regardless of the cause of the disease (ischemic heart disease, idiopathic dilated cardiomyopathy), significantly lower concentrations of insulin-like growth factor, somatotropic hormone, and free testosterone were recorded compared to healthy individuals [5]. The described pathogenetic mechanisms are responsible for the development of exercise intolerance in patients with a decrease in the global LV ejection fraction, which implies a decrease in CI with the subsequent development of a pathological vicious circle. However, regardless of the type of CHF - with a decrease (HF-NFEF) or normal ejection fraction (HF-NEF) - the main symptoms of the disease are muscle weakness and dyspnea with exercise failure. However, if the pathogenetic mechanisms responsible for the development of symptoms in patients with a decrease in the ejection fraction have been widely studied and presented above, the causes of exercise intolerance among patients with HF-NEF are not covered so fully. Among the currently known mechanisms responsible for the development of the symptom complex in patients with HF-EF, several groups of disorders can be conventionally distinguished: central hemodynamic disturbances associated with a decrease in CO; peripheral circulatory disturbances; changes in skeletal muscles.

Pathogenetic mechanisms responsible for exercise intolerance in patients with CHF with a normal LV ejection fraction.

The first reports of a decrease in CO in patients with HF-EF appeared in 1991. It was found that in patients of this group, one of the reasons for the development of the HF symptom complex is a violation of the Frank-Starling mechanism with a subsequent decrease in CO [6]. In 2011, another group of scientists found that patients with HF-EF have a lower CO during exercise and, as a result, a decrease in the arteriovenous oxygen difference and peak oxygen consumption. Insufficient increase in CO during FE in patients with HFpEF, according to researchers, occurs due to insufficient chronotropic reserve and decreased LV myocardial contractility [7]. A series of new studies have shown that in patients with HFpEF, low CO plays a primary role in reducing tolerance to FE, while impaired chronotropic and inotropic reserves, as well as decreased vascular resistance, play a secondary role, since they, together with the arteriovenous oxygen difference, do not differ in healthy patients and patients with HFpEF [8]. It should be noted that in healthy patients, oxygen consumption increases more than 6 times during FE, since CO increases due to an increase in heart rate and left ventricular stroke volume (SV); improved oxygen extraction by peripheral tissues and, as a consequence, an increase in the arteriovenous oxygen difference [9]. In patients with HF-EF, there is no proper increase in CO during FE, which is the primary cause of decreased tolerance to FE due to both muscle weakness and dyspnea. For the necessary increase in LV end-diastolic volume during FE in patients with HF-EF, a more than threefold increase in LV filling pressure is required, which, in turn, leads to an increase in pressure in the pulmonary circulation and, consequently, to a decrease in the pumping function of the right ventricle with a decrease in CO. Thus, in patients with CHF with a reduced ejection fraction, only a 16% increase in LV stroke volume was recorded, which, together with a violation of the chronotropic reserve, also leads to an insufficient increase in CO during FE [10].

A study evaluating the arteriovenous oxygen difference in patients with HFpEF, HFrEF, and healthy subjects yielded the most opposite results. It was found that in patients with HFrEF, the arteriovenous oxygen difference was the most significant factor limiting PE, while CO was of lesser importance. Data were obtained showing that in 40% of patients with CHF with ejection fraction, the cause of impaired PE tolerance was impaired peripheral oxygen utilization, while in patients with HFrEF, this cause was primary in only 2% of cases. At the same time, the degree of peak oxygen consumption reduction between patients with HFrEF and HFrEF was approximately the same (13.9 ± 0.5 ml/kg/min and 12.1 ± 0.5 ml/kg/min, respectively) and had no reliable relationship with the LV SV value during PE. It is also noteworthy that the increase in LV SV during FE was heterogeneous among the studied groups. In the HF-EF group, the stroke volume during FE was recorded within 88 ± 3.6 ml, in patients of the HF-NFEF group 68 ± 2.8 ml and in healthy individuals 103 ± 4.3 ml, i.e. in patients with HF-EF and HF-NFEF, the stroke volume during FE was significantly lower than in healthy individuals. A decrease in chronotropic reserve was recorded in 75% of patients in the HF-NFEF group and 73% in the HF-EF group, which means that in patients with CHF, regardless of the EF value, an inadequate increase in CO was recorded. Having obtained these results, the authors believe that the impairment of peripheral oxygen utilization due to impaired passive diffusion of oxygen in the muscle microcirculatory bed is caused by impaired vascular capacity and is of primary importance in the development of muscle weakness in patients with HF-EF and, therefore, a decrease in CO in patients with HF-EF is not of primary importance [12]. This theory is not confirmed by the 2015 study, according to which in patients with HF-EF, it is the lack of the necessary increase in CO due to relatively low SV and inadequate increase in HR that plays a primary role in the development of the HF symptom complex. The authors also did not detect a decrease in the arteriovenous difference in oxygen, which indicates the absence of a significant impairment of peripheral oxygen utilization in patients with CHF-EF [13].

Thus, the research results point to two opposing points of view regarding the causes of decreased exercise tolerance: the lack of a proper increase in stroke volume during physical activity and peripheral impairment of oxygen utilization due to impaired microcirculation. There is an opinion that the results of the above studies represent links in the same chain. Thus, in healthy individuals, up to 50% of the stroke volume is distributed in the kidneys, liver and other parenchymatous organs, but during physical activity, due to vasoconstriction in the internal organs and vasodilation in muscle tissue, blood flow is redistributed with maximum intensity in the striated muscles. In patients with HF-EF, the sympatholytic expansion of the vascular bed accompanying physical activity may be impaired, and this, in turn, leads to impaired oxygen utilization and decreased tolerance to physical activity [14]. In the study [11], an increase in blood pressure was recorded in patients with HF, which also indicates a violation of the mechanism of peripheral blood flow redistribution. Thus, muscle weakness in patients with HFpEF is likely primarily due to the lack of an adequate increase in SV and reduced chronotropic reserve, and, consequently, a decrease in CO with subsequent impairment of peripheral blood flow. As presented above, patients with HFpEF, compared to healthy individuals, show a significant number of changes in muscle tissue, which ensures a decrease in tolerance to exercise. In contrast, the "peripheral" changes in muscle tissue inherent in patients with HFpEF have not been widely studied. Patients with HFpEF, compared to healthy individuals, show a decrease in the percentage of type 1 muscle fibers to type 2 muscle fibers, as well as a decrease in the ratio of capillary density to muscle fiber [5]. Data on the correlation between the degree of decrease in type 1 muscle fibers, the degree of decrease in capillary density, and peak oxygen consumption have also been obtained. Scientists have concluded that the changes found in the muscle fiber of patients with HFpEF and patients with HF-NEF are identical [6]. An increased ratio of intramuscular fat to muscle tissue volume is associated with peak oxygen consumption and, consequently, with exercise tolerance in patients with HFpEF [4]. Moreover, in older patients with signs of HFpEF, a decrease in pure muscle mass is recorded, which also correlates with peak oxygen consumption during exercise. Along with patients with a decrease in EF, patients with HFpEF have an impaired endothelial function, which is expressed in an insufficient decrease in peripheral arterial resistance during exercise and a decrease in blood flow [7]. Changes in cardiovascular coupling in patients with HFpEF also play an important role in reducing exercise tolerance. Normally, end-systolic elastance increases during FE, and this increase exceeds the change in effective arterial elastance, which is characterized by peripheral vasodilation, increased EF and SV. In patients with the HF-NFV pattern, there is no proper change in cardiovascular coupling, which is reflected in the absence of an increase in CO and peripheral vasoconstriction [8]. Conclusion. Thus, in patients with the CHF pattern, regardless of the ejection fraction value, pathogenetic changes are uniform. In patients with both low and preserved ejection fraction, a number of identical disorders are recorded that occur during FE (no increase in CO, decreased chronotropic response, impaired peripheral oxygen utilization), as well as a number of pathomorphological changes in muscle tissue and the endocrine system, which are associated with the course of this disease as a whole. However, despite the active study of this problem, there are a number of fundamental disagreements on the most important pathogenetic mechanisms for the development of the CHF symptom complex, and the influence of global LVEF on the pathogenesis of the development of this symptom complex in patients with CHF requires further study.

2. References

[1] Mirzaeva, G. P., Zhabbarov, O. O., Alikulov, I. T., Buvamukhamedova, N. T., & Rakhmatov, A. M. (2022). Features of the course of gouty kidney disease in patients with obesity.

[2] Kamilova, U. K., & Alikulov, I. T. (2014). Evaluation of renal dysfunction indicators in patients with chronic heart failure. Cardiovascular Therapy and Prevention, 13(2), 51-54.

[3] Alikulov, I. T., Yusupova, M. Sh., Sultanova, F. T., & Narziev, N. M. (2025). Study of the features of the clinical course of the disease in patients with chronic heart failure with renal dysfunction. World Scientific Research Journal, 36(1), 61-65.

[4] Alikulov, I. T., Khaitimbetov, Zh. Sh., & Narziev, N. M. (2023). Myocardial infarction: patogenesis, signs and symptoms, diagnosis.

[5] Alikulov, I. T., Khaitimbetov, Zh. Sh., Narziev, N. M., & Botirova, N. (2023). Clinical course of the disease in patients with chronic heart failure with impaired renal function. Doctor's Herald, 11.

[6] Alikulov, I. T., Khaitimbetov, Zh. Sh., & Abdakimova, B. I. (2024). Cardiac remodeling in patients with chronic heart failure and chronic kidney disease.

[7] Mirakhmedova, H. T., Nigina, B., Narziev, N. M., & Alikulov, I. T. (2023). General Examination of the Patient (General Condition of the Patient, Consciousness, Position, Physique). Examination by Parts of the Body: Head, Face, Neck, Limbs, Skin Integuments.

[8] Zhuraev, B., Guliev, H. T., & Alikulov, I. T. (2019). Study of risk factors for cardiovascular diseases in patients with hypertension and cerebrovascular disorders. Eurasian Journal of Cardiology, (S1), 105.

[9] Alikulov, I. T., Khaitimbetov, Zh. Sh., Narziev, N. M., & Botirova, N. (2023). The study of cardiac remodeling processes in patients with chronic heart failure and renal dysfunction. Cardiovascular Therapy and Prevention, 13(S2), 8-8a.

[10] Khudayberganova, N. K., & Alikulov, I. T. (2023). Helicobacter pylorosis in children: Features of diagnosis and treatment. European Science Methodical Journal, 1(9), 23-28.

[11] Khudayberganova, N. K., Rakhmatullaeva, G. K., & Alikulov, I. T. (2023). Helicobacter pylori infection and principles of therapy in children. Best Intellectual Research, 9(3), 272-277.

[12] Khudayberganova, N. K., Azadaeva, K. E., & Alikulov, I. T. (2023). Determination of Nutrition-Dependent Micronutrient Deficiencies Among School-Age Children.

[13] Kamilova, U. K., & Alikulov, I. T. (2014). Kidney dysfunction evaluation in chronic heart failure patients. Cardiovascular Therapy and Prevention, 13(2), 51-54.