

Pre-heart failure in young men with metabolic syndrome: clinical aspects, diagnosis and management strategies

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The relevance of the topic is underscored by the increasing prevalence of metabolic syndrome (MetS) among young men and its contribution to the early development of left ventricular diastolic dysfunction and pre-heart failure (pre-HF), which are the key predictors of cardiovascular complications and reduced quality of life. This necessitates the development of early diagnostic criteria and timely risk stratification systems.

The aim of this review is to summarize current data on the pathogenesis, clinical presentation, diagnostic criteria, disease course and management of pre-HF in young men with MetS, and to define the role of early identification of

diastolic dysfunction of as a marker of subclinical cardiac impairment in this population.

Methods. An analytical review of recent Russian and international scientific publications addressing pre-HF in the context of MetS was conducted, with a focus on its development, clinical course, and diagnosis in young men. The information search utilized the following databases: Russian Science Citation Index, Best Evidence, PubMed, Clinical Evidence, Cochrane Library.

Results. Pre-HF is an early stage of heart failure, where structural and functional cardiac alterations can be observed without any elicited clinical manifestations. In young

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men with MetS, pre-HF is developed due to the combination of arterial hypertension (AH), insulin resistance (IR), obesity, and dyslipidemia, leading to the chronic cardiac overload and cardiovascular disease progression. Identification of pre-HF in this population demands a combined approach, including echocardiography with diastolic function analysis, assessment of natriuretic peptides, inflammatory marker levels, and insulin resistance. Therapy for pre-HF against the background of MetS is aimed at modifying risk factors, normalizing the metabolic profile, and improving cardiovascular parameters. Early diagnosis and timely intervention for pre-HF in young men with MetS can significantly reduce the risk of disease progression and the development of cardiovascular complications.

Conclusion. Pre-HF in young men with MetS represents a subclinical stage of cardiovascular impairment, caused by the combined effects of IR, AH, obesity, and dyslipidemia. Its early identification with the use of echocardiog-

raphy, biomarkers, and metabolic parameters, as well as the timely correction of risk factors, allows the prevention of the development of clinical heart failure and decreases the long-term cardiovascular risk.

Keywords: arterial hypertension, insulin resistance, obesity, hyperlipidemia, dyslipidemia, heart failure.

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Introduction

Pre-heart failure (pre-HF) is a clinical condition characterized by impaired atrial function that can lead to a range of complications, including hemodynamic disturbances and the development of cardiovascular disease (CVD) [1]. Pre-HF is defined by the absence of current or prior symptoms and signs of chronic heart failure (CHF), combined with evidence of structural and/or functional cardiac abnormalities and/or elevated BNP levels. In recent years, there has been an increase in the incidence of pre-HF among young individuals, particularly men with metabolic syndrome (MetS) [1, 2]. MetS, which includes IR, hyperlipidemia, AH, and obesity, significantly elevates the risk of developing CVD, including pre-HF [2].

The concept of pre-HF, although formally defined only in the 21st century, has deep theoretical roots. In Russian cardiology, the foundations of a prenosological approach to CHF were laid as early as the mid-20th century. F.Z. Meerson, in his works from the 1960s–1980s, developed the concept of pathological myocardial adaptation, emphasizing that hypertrophy and neurohumoral activation in the context of metabolic disorders (obesity, IR) could transform from compensatory into damaging mechanisms, leading to impaired energetics, ionic homeostasis, and progression of fibrosis — long before the onset of clinical symptoms [3]. N.M. Mukharlyamov introduced into clinical practice the concept of “latent”

heart failure, linking it to diastolic dysfunction with preserved systolic function in patients with arterial hypertension and metabolic disorders [4]. Even then, the particular vulnerability of young men with abdominal obesity and hyperinsulinemia was highlighted. The work of E.I. Chazov and his school in the 1980s–1990s complemented this model by establishing the pathogenic link between hyperinsulinemia, endothelial dysfunction, and left ventricular (LV) remodeling—the precursor of a “metabolic” form of pre-HF [5]. On the international level, the concept was formalized within the ACCF/AHA classification (2005, 2013, 2022), where stages A (risk factors without structural changes) and B (structural-functional abnormalities without symptoms) correspond to the modern definition of pre-HF. The ESC guidelines (2016–2021) further refined the criteria: pre-HF is diagnosed by the combination of ≥ 1 risk factor (including MetS) and ≥ 1 objective sign of cardiac remodeling (LV hypertrophy, reduced GLS, fibrosis on MRI, elevated NT-proBNP or hs-cTn) in the absence of typical CHF symptoms [6, 7]. Alongside LV remodeling, a key role in the pathogenesis of pre-HF is played by atrial cardiomyopathy — a complex of structural, functional, and electrophysiological changes that develop in the atrial myocardium long before the clinical symptoms of CHF appear. In young men with MetS, this process is initiated by IR, visceral obesity, and systemic inflammation [8].

Thus, pre-HF is a condition reflecting the transition from physiological compensation to pathological myocardial remodeling. It represents a reversible (with timely intervention) stage in the continuum of CHF, particularly relevant for young men with MetS, in whom hidden, metabolically-mediated impairments of diastolic function and cardiac output reserve predominate.

The aim of this review is to summarize current data on the pathogenesis, clinical presentation, diagnostic criteria, and disease course of pre-HF in young men with MetS, and to define the role of early detectable diastolic dysfunction as a marker of subclinical cardiac impairment in this population.

Methods

This work presents an analytical review of the scientific literature published over the past 10–15 years in Russian and international sources. A search for relevant publications was conducted in the following databases: Russian Science Citation Index (eLIBRARY.ru), PubMed, Cochrane Library, Best Evidence, and Clinical Evidence. Search terms and their combinations in Russian and English included: pre-heart failure, metabolic syndrome, diastolic dysfunction, young men, subclinical myocardial impairment. The analysis included clinical guidelines, systematic reviews, prospective and retrospective cohort studies, as well as original articles relevant to the review topic and possessing a high level of evidence.

Results

Metabolic syndrome and its association with pre-heart failure

Metabolic syndrome is a cluster of conditions that includes IR, hypertension, hyperlipidemia, and obesity. These risk factors significantly increase the likelihood of developing CVD, including pre-heart failure [9]. There is currently a trend of rising MetS incidence among young people, which is associated with lifestyle changes such as low physical activity, poor diet, and increased stress levels [10]. Chronic inflammation, elevated levels of C-reactive protein (CRP), and endothelial dysfunction — all components of MetS — play a key role in the pathogenesis of pre-HF [11]. Cardiac remodeling caused by excess weight and chronic inflammation leads to increased atrial pressure and impaired atrial function, which can subsequently result in heart failure (HF) [12].

In 2024, the Russian Society of Cardiology (RSC) continued to adopt and adapt international guidelines for the diagnosis and management of HF [13]. A significant step was the incorporation of concepts proposed in 2016 by the European Society of Cardiology and the American Heart Association [14]. One of the notable changes in the HF classification has been the identification of a pre-HF stage (Fig. 1). This conceptual innovation aims to facilitate earlier identification of patients at risk of developing HF before overt clinical symptoms appear.

Pre-HF includes patients with risk factors (RFs) such as AH, diabetes, obesity, and other metabolic disorders that could lead to HF, but who do not yet exhibit clear signs of heart disease. It is important to note that this state is not a disease per se, but rather a precursor to the development of more serious CVD.

For patients with MetS, which includes IR, hyperlipidemia, and abdominal obesity, identifying this stage is of particular importance as they are often at elevated risk. In this context, the timely recognition of pre-HF enables cardiologists to implement preventive measures and halt disease progression, thereby improving long-term patient outcomes. Special attention should be paid to young men with MetS. A recent trend shows increasing disease incidence in this group, associated with lifestyle changes, physical inactivity, and poor diet. Studies show that in such patients, pre-HF can develop against the background of chronic inflammation, hypertension, and metabolic disorders, which contributes to increased cardiac load [15–17]. Applying a classification that includes pre-HF allows for closer monitoring of at-risk young individuals and the introduction of preventive therapy before severe clinical symptoms appear.

Since 2024, the RSC has emphasized the importance of the timely diagnosis and correction of risk factors in patients with pre-HF and now recommends using a combined approach. This approach includes managing blood pressure, blood glucose levels, lipid profile, and body weight [2]. To prevent HF, medications that normalize these parameters may be prescribed, along with regular physical exercise and diet therapy. Furthermore, the use of “rapid diagnostics” involving inflammatory markers such as CRP, as well as conducting echocardiographic studies to detect early signs of myocardial dysfunction and other pathologies associated with the initial stage of HF, is recommended [18–20]. This

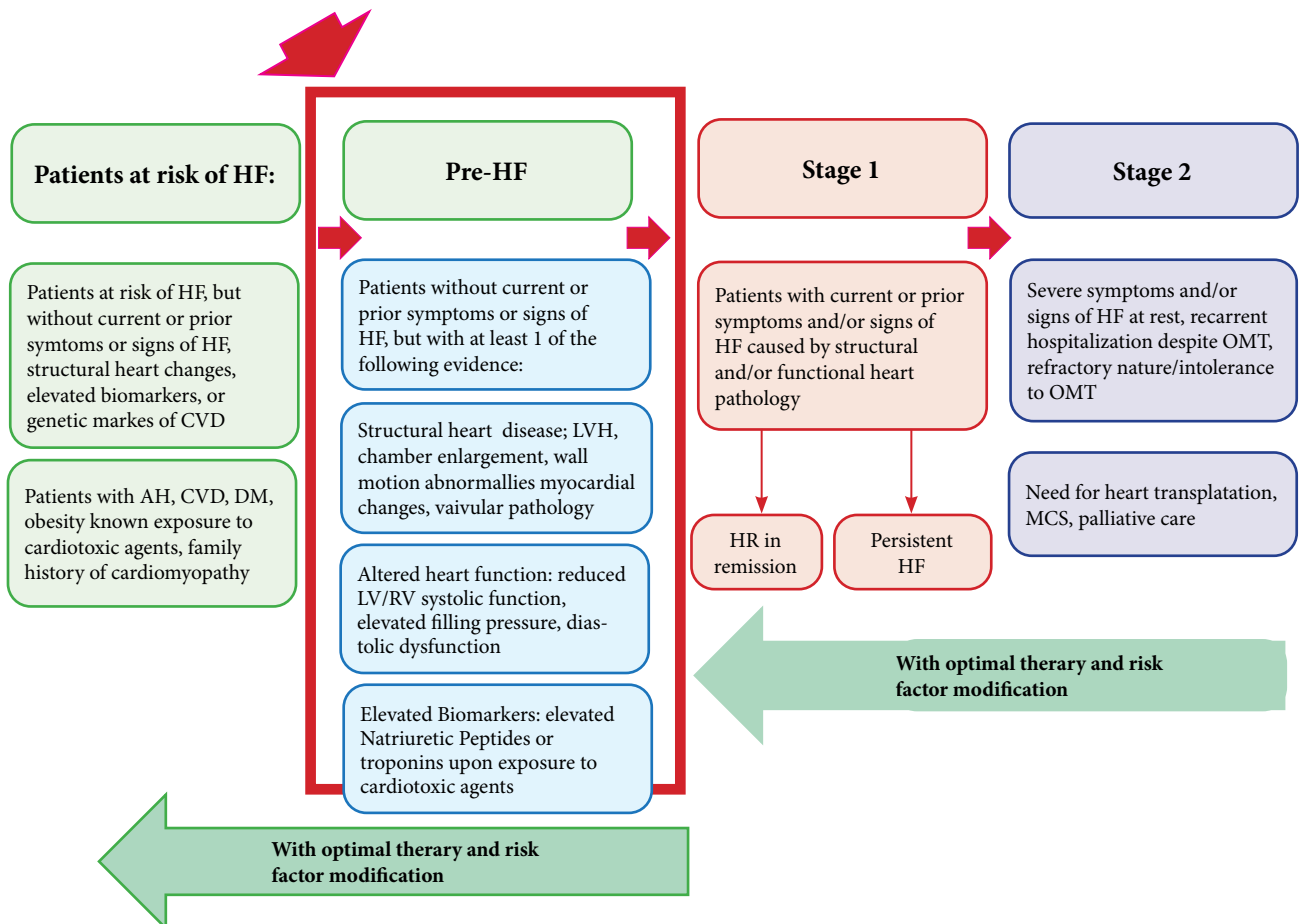


Fig. 1. Modification of the classification by Heidenreich PA, et al. and Bozkurt B [3].

is particularly important for young patients, as early intervention can prevent the development of more serious CVD in the future.

The HF classification that includes a pre-stage, as proposed by the European Society of Cardiology and the American Heart Association, has gained widespread acceptance and has been integrated into clinical practice, including within Russian guidelines [15, 21]. This concept enables more effective identification of individuals at high cardiovascular risk, such as young men with MetS, and facilitates the application of early preventive treatment. Consequently, the timely diagnosis and correction of risk factors can significantly reduce the prevalence of HF and improve long-term patient prognosis.

Pathophysiology of pre-heart failure

Pre-HF in young individuals with MetS develops in several stages [2]. The initial stage involves endothelial dysfunction, which reduces nitric oxide production, leading to vasoconstriction and elevated blood pressure. These vascular changes increase the load

on the heart, particularly the atria, which begin to hypertrophy and lose their efficiency [22].

Furthermore, IR, inherent to MetS, promotes the accumulation of adipose tissue. This, in turn, leads to obesity, increased circulating blood volume, and elevated atrial pressure [23]. These factors contribute to further cardiac remodeling, exacerbating atrial dysfunction and increasing the risk of pre-HF. Chronic inflammation, a hallmark of MetS, also plays a significant role in the development of pre-HF [24]. Elevated blood levels of CRP and interleukins activate immune cells, causing damage to blood vessels and the myocardium, thereby impairing its function [25].

Clinical presentation of pre-heart failure

Young men with MetS may not experience overt symptoms during the pre-HF stage. However, as the condition progresses, symptoms such as shortness of breath, fatigue, swelling in the legs and ankles, and chest heaviness may appear. These manifestations can be nonspecific and similar to other conditions, complicating early diagnosis.

Diagnosing pre-HF in patients with MetS primarily involves echocardiography and analysis of remodeling markers (BNP and NT-proBNP) and inflammatory markers such as CRP (standard CRP, sCRP, and high-sensitivity CRP, hsCRP) and fibrinogen [26]. Echocardiography allows for the assessment of atrial size and function, as well as the detection of signs of hypertrophy and remodeling. Monitoring blood lipid and insulin levels is also crucial, as changes in these parameters indicate the presence of MetS and a predisposition to CVD [27].

Management strategies for pre-heart failure

Pre-HF is characterized by the absence of HF symptoms and signs, yet the patient has risk factors such as AH, diabetes mellitus, obesity, or a history of CVD. According to the updated clinical guidelines of the RSC, approved in 2024 and effective from 2025, treatment at this stage is focused on modifying risk factors and preventing disease progression [3].

Main therapeutic approaches for pre-HF

1. Blood pressure control: Maintaining target blood pressure levels (<130/80 mm Hg) through lifestyle modifications and, if necessary, pharmacotherapy (renin-angiotensin-aldosterone system inhibitors or calcium channel blockers — particularly in the presence of left ventricular remodeling signs; β -blockers should be prescribed with caution and only when clearly indicated, as they may worsen insulin resistance).

2. Lipid profile management: Prescribing lipid-lowering agents in cases of atherogenic dyslipidemia or high cardiovascular risk (statins, ezetimibe, omega-3-acid ethyl esters, bempedoic acid; PCSK9 inhibitors, inclisiran, or pelacarsen may be used if required).

3. Glucose level monitoring and control: Ensuring adequate glycemic control in patients with diabetes mellitus (metformin, empagliflozin, dapagliflozin)

4. Limiting cardiotoxic exposure: Restricting the use of cardiotoxic agents (non-steroidal and steroidal anti-inflammatory drugs — only for strict indications).

5. Avoiding harmful habits: Providing recommendations for smoking cessation and limiting alcohol consumption.

6. Physical activity: Encouraging regular physical exercise tailored to the patient's condition.

7. Dietary recommendations: Reducing intake of salt and saturated fats, increasing consumption of fruits, vegetables, and whole grains, and weight management.

Thus, the modern approach to managing pre-HF in young men with MetS is based on early and aggressive modification of risk factors, the use of organ-protective medications, and regular monitoring of subclinical cardiac impairment markers. This strategy aims to prevent progression to overt clinical HF. It is important to note the typically low treatment adherence in this patient group. Therefore, motivational support and digital tools (software, telemedicine) are necessary.

Prognosis and long-term perspectives

The prognosis for young men with MetS-related pre-HF depends on the timeliness of diagnosis and the effectiveness of treatment [3, 9]. With adequate intervention focused on controlling risk factors and improving cardiac function, many patients can achieve significant improvements in quality of life and avoid disease progression. However, without proper treatment, pre-HF can lead to the development of more serious conditions, including chronic heart failure and atherosclerosis [28, 29].

Conclusion

Pre-HF in young men with MetS is a medical problem, requiring a combined approach for diagnosis and management. Introducing the concept of pre-HF into clinical practice allows the identification of patients at early stages of risk of disease development and its effective prevention. Contemporary treatment strategies, including pharmacologic therapy, lifestyle modification and risk factors control, might significantly improve the prognosis and decrease the prevalence of CVDs in this population.

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Review article

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Effectiveness of sodium-glucose cotransporter 2 inhibitors in the treatment of chronic heart failure

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Chronic heart failure (CHF) is one of the outcomes of cardiovascular diseases (CVDs) that significantly worsens patient prognosis. For this reason, research has been ongoing for decades to find effective drugs that can improve the prognosis for patients with CHF.

Methods. The article was prepared based on a review of literature published in peer-reviewed journals available on PubMed, eLIBRARY.RU, CyberLeninka, and other research platforms over the last 10 years.

Results. Despite significant progress in understanding the pathogenesis and treatment of CHF, the search for effective therapies continues. One of the discoveries of recent years has been drugs from the class of sodium-glucose cotransporter 2 inhibitors (SGLT2i), the efficacy of which in CHF has been demonstrated in a number of major clinical trials.

Conclusion. SGLT2i are antidiabetic drugs that hold an important place in the management of type 2 diabetes mellitus. They have been shown to favorably influence the

course of CHF, thereby reducing cardiovascular risks and mortality from CHF.

Keywords: sodium-glucose cotransporter 2 inhibitors, chronic heart failure, diabetes mellitus, left ventricular ejection fraction, blood volume, cardiovascular diseases.

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