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COMPREHENSIVE ANALYSIS OF CLINICAL, LABORATORY, AND INSTRUMENTAL DIAGNOSTICS OF PULMONARY HYPERTENSION IN SYSTEMIC SCLEROSIS

Ganieva N. A.
Djuraeva E. R.
Khare V.
Abdukahorov A. A.
Tashkent State Medical University

Abstract

Systemic sclerosis is a chronic, progressive autoimmune disease of connective tissue characterized by endothelial injury of microvessels, immune system dysregulation, and widespread fibrotic processes. This disease affects multiple organs and systems, particularly the lungs and cardiovascular system, significantly influencing patient prognosis. One of the most severe and life-threatening complications of systemic sclerosis is pulmonary hypertension.

This condition is characterized by a persistent increase in pulmonary circulation pressure, leading to increased right ventricular load, development of heart failure, and ultimately a higher risk of mortality. Recent clinical and epidemiological studies indicate that the development of pulmonary hypertension in patients with systemic sclerosis is an important prognostic marker of disease progression. Moreover, the asymptomatic or subclinical course of this complication in early stages complicates its timely diagnosis, emphasizing the need for early detection and effective treatment strategies.

This review article analyzes the main pathogenetic mechanisms of pulmonary hypertension associated with systemic sclerosis, including endothelial dysfunction, microvascular remodeling, and fibrosis, based on current scientific literature. In addition, the clinical manifestations of the disease—such as exertional dyspnea, fatigue, chest pain, and syncope - are discussed. The article also highlights the clinical significance of modern laboratory biomarkers, particularly NT-proBNP, immunological indicators, and inflammatory markers. Furthermore, the role and diagnostic value of instrumental methods, including

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echocardiography, diffusion capacity assessment (DLCO), computed tomography, and right heart catheterization, are evaluated.
In conclusion, early detection of pulmonary hypertension in patients with systemic sclerosis, a deeper understanding of its pathogenetic features, and the application of a comprehensive diagnostic approach significantly improve patient quality of life and prognosis.

Keywords: Systemic sclerosis, pulmonary hypertension, pulmonary arterial hypertension, endothelial dysfunction, microvascular damage, fibrosis, interstitial lung disease, clinical features, laboratory biomarkers, NT-proBNP, echocardiography, diffusion capacity (DLCO), right heart catheterization, hemodynamics, prognosis.

Introduction

Systemic sclerosis is a chronic autoimmune disease characterized by multisystem involvement [1,2,6]. Its pathogenesis involves endothelial dysfunction, immune system activation, and hyperactivation of fibroblasts [7]. As a result, structural changes occur in the vascular wall, leading to impaired microcirculation. These alterations are particularly significant in the pulmonary circulation, where they contribute to important pathophysiological changes.
Recent multicenter studies have shown that the prevalence of pulmonary hypertension in patients with systemic sclerosis ranges from 8% to 15% [5,12]. In some cases, subclinical forms of the disease are also detected, further emphasizing the importance of early diagnosis [18].

Pathogenesis. Several pathogenetic mechanisms are involved in the development of pulmonary hypertension. Endothelial cell damage leads to increased synthesis of vasoconstrictor mediators and decreased production of vasodilators [7,10]. This imbalance results in elevated pressure within the pulmonary arteries. In addition, proliferative changes in the vascular wall and fibrotic processes contribute to increased vascular resistance.

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Numerous studies have demonstrated that elevated levels of endothelin-1, reduced nitric oxide synthesis, and impaired prostacyclin metabolism enhance vasoconstriction in the pulmonary circulation [10,11]. When these changes persist over time, pulmonary arterial pressure progressively increases.

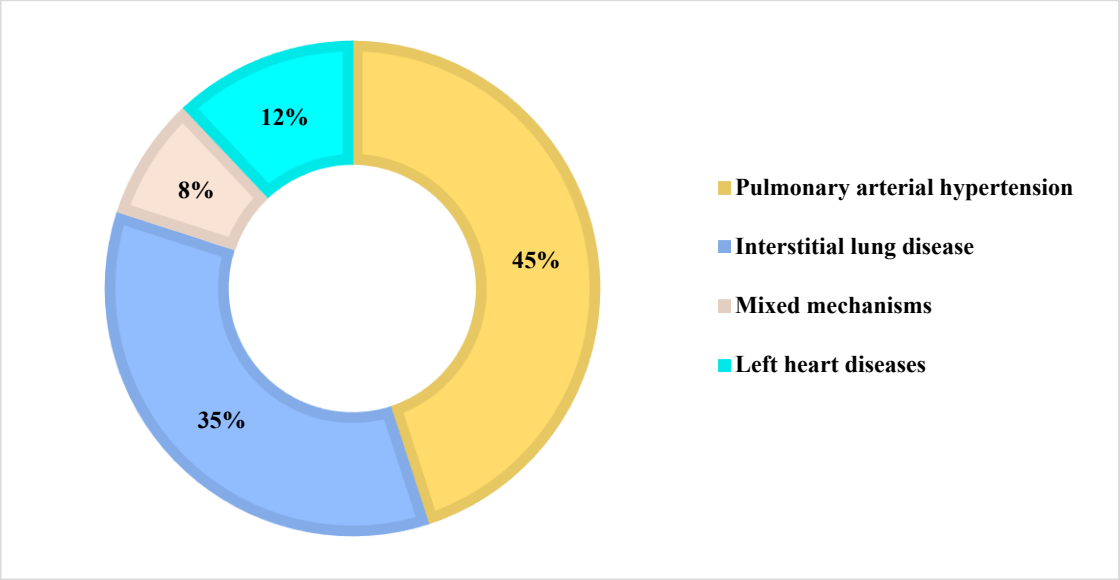

Figure 1. Mechanisms of Pulmonary Hypertension Development in Systemic Sclerosis

The first diagram illustrates the main pathogenetic variants of pulmonary hypertension development in patients with systemic sclerosis. Analysis of scientific literature indicates that pulmonary hypertension in this disease may develop through several mechanisms, the relative contribution of which is directly related to the clinical course of the disease and morphological changes in lung tissue.

As shown in the diagram, the majority of cases are represented by pulmonary arterial hypertension as an independent pathogenetic variant [9,16]. In this condition, progressive remodeling processes occur in the walls of pulmonary arteries. Endothelial dysfunction leads to increased synthesis of vasoconstrictor factors and a decrease in vasodilatory mediators. Elevated concentrations of biologically active substances such as endothelin-1, thromboxane, and serotonin result in persistent vasoconstriction of pulmonary arteries. At the same time, reduced levels of vasodilators such as nitric oxide and prostacyclin contribute to increased vascular tone. As a result, pulmonary vascular resistance increases, leading to a progressive rise in pulmonary arterial pressure.

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The diagram also shows that the second most common variant is pulmonary hypertension associated with interstitial lung disease [8,15]. In systemic sclerosis, fibrotic processes developing in the lung parenchyma disrupt the structure of the alveolar-capillary membrane and impair gas exchange. Prolonged hypoxia induces hypoxic vasoconstriction in pulmonary arteries, thereby increasing hemodynamic load. In such cases, pulmonary hypertension is associated not only with vascular pathology but also with structural damage to lung tissue.

Another important variant presented in the diagram is pulmonary hypertension associated with left heart disease [24]. In systemic sclerosis, myocardial fibrosis, diastolic dysfunction, and valvular abnormalities may develop. These changes lead to increased pressure in the left heart chambers, resulting in elevated pulmonary venous pressure and the development of secondary pulmonary hypertension.

In addition, the diagram indicates that mixed pathogenetic mechanisms also account for a certain proportion of cases. In clinical practice, pulmonary hypertension often develops due to the combined effect of several factors. For example, interstitial lung fibrosis may coexist with endothelial dysfunction and microvascular remodeling processes [12].

Overall, this diagram demonstrates the multifactorial and complex pathogenetic nature of pulmonary hypertension in systemic sclerosis. This underscores the need for a comprehensive approach to diagnosis and treatment.

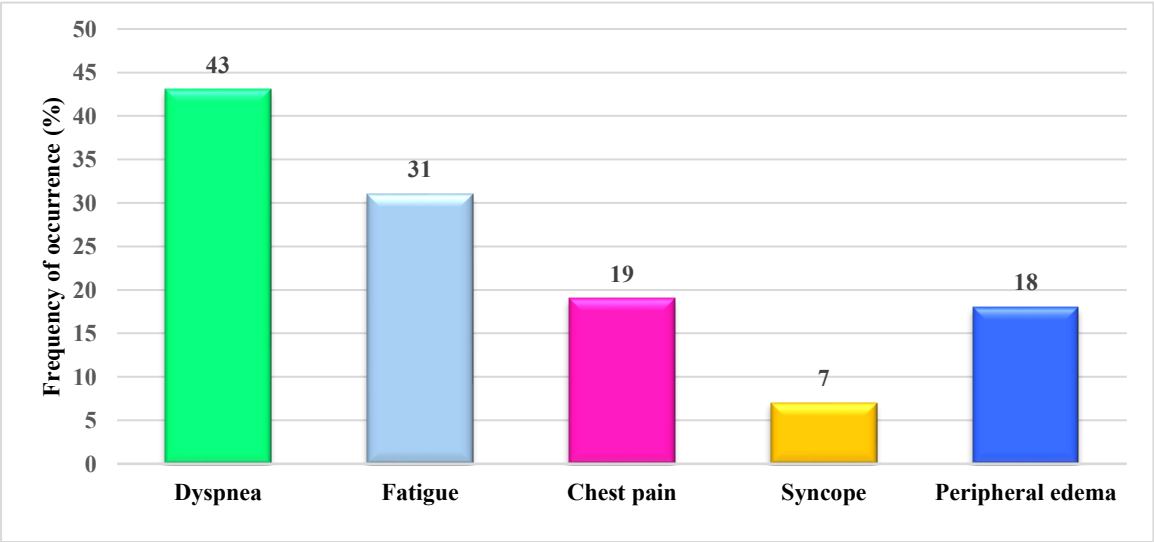

Figure 2. Main Clinical Symptoms in Systemic Sclerosis and Pulmonary Hypertension

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The second diagram presents the prevalence of the main clinical symptoms observed in patients with systemic sclerosis and pulmonary hypertension. In clinical practice, the analysis of these symptoms plays a crucial role in the early detection of the disease [18].

According to the diagram, the most common symptom is dyspnea during physical exertion. This condition is associated with hemodynamic changes in the pulmonary circulation and functional impairment of the pulmonary capillary network. As pulmonary arterial pressure increases, blood flow through the lungs becomes more difficult, and the efficiency of gas exchange decreases [12,17,19]. As a result, patients experience a sensation of breathlessness even during minimal physical activity.

The diagram shows that the second most frequent symptom is fatigue. This is related to reduced oxygen delivery to body tissues. As pulmonary hypertension progresses, the load on the right heart chambers increases. This leads to a decrease in cardiac output and disruption of overall hemodynamics [23].

Chest pain is also one of the clinically significant symptoms. It is mainly associated with right ventricular hypertrophy and ischemic changes in the myocardium. In some cases, this symptom may also be explained by mechanical stress on the pulmonary artery wall.

The diagram also indicates that syncope is a less common but clinically important symptom. Syncope usually occurs in advanced stages of pulmonary hypertension and is associated with a sharp decrease in cardiac output. It is considered an unfavorable prognostic sign [13,21].

The development of peripheral edema is typically observed in the later stages of the disease. This condition is associated with right ventricular failure and results from increased venous pressure in the systemic circulation.

Overall, this diagram demonstrates the varying degrees of clinical symptom manifestation and their relationship with disease severity. This serves as an important diagnostic criterion for clinicians in the assessment of patients [14,22].

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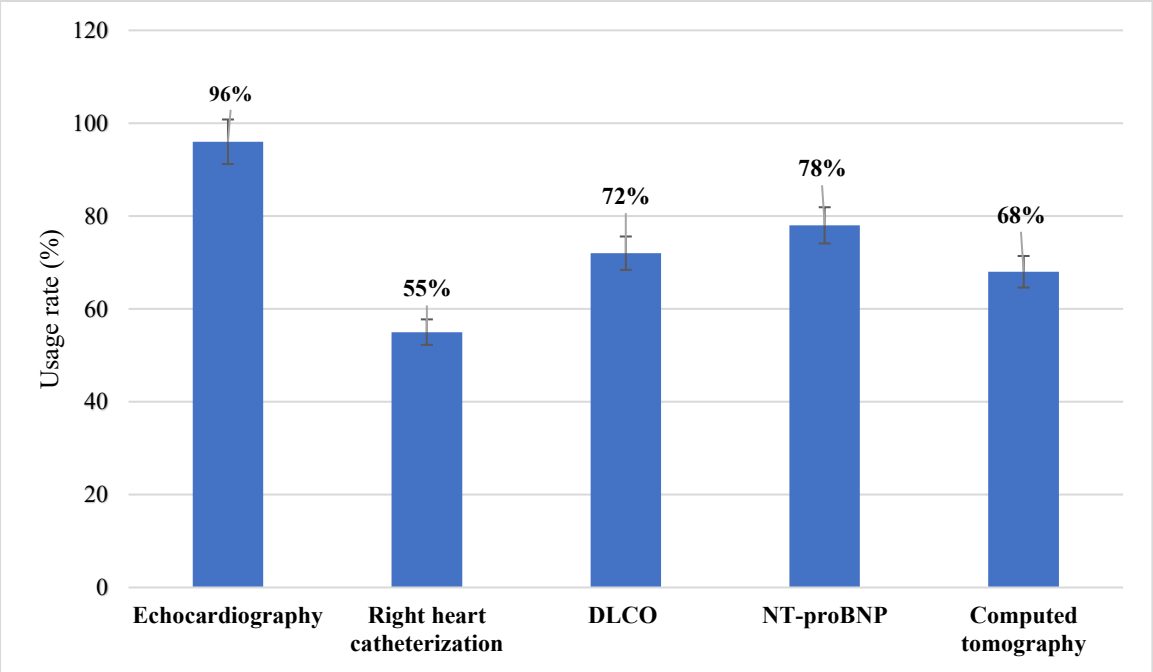

Figure 3. Importance of Diagnostic Methods in the Detection of Pulmonary Hypertension

The third diagram illustrates the clinical significance of the main diagnostic methods used to detect pulmonary hypertension in systemic sclerosis. In modern rheumatology and cardiology practice, a comprehensive diagnostic approach is applied to ensure early detection of this condition.

According to the diagram, echocardiography is the most widely used diagnostic method. This non-invasive technique allows assessment of the anatomical and functional state of the cardiac chambers. During echocardiographic examination, parameters such as tricuspid regurgitation velocity, right ventricular size, and estimated pulmonary arterial pressure are evaluated [4,20]. Therefore, echocardiography is commonly used as a screening tool.

The diagram also highlights NT-proBNP as an important diagnostic biomarker. The concentration of this biomarker increases in response to elevated load on the right heart chambers. Thus, an increased NT-proBNP level is considered one of the early laboratory indicators of pulmonary hypertension.

Assessment of diffusing capacity also has significant diagnostic value [9]. A decrease in DLCO reflects functional alterations in the pulmonary capillary network. In patients with systemic sclerosis, an early decline in this parameter is

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regarded as a prognostic marker for the development of pulmonary hypertension [15].

Computed tomography plays an important role in identifying morphological changes in lung tissue. This method allows detection of interstitial fibrosis, bronchiolar abnormalities, and other structural alterations [3,8].

Right heart catheterization is considered the "gold standard" for confirming pulmonary hypertension. This invasive method enables direct measurement of pulmonary arterial pressure. In addition, it provides accurate evaluation of hemodynamic parameters in the pulmonary circulation [16,22].

Thus, the diagram demonstrates the complementary value of various diagnostic methods and highlights the necessity of a comprehensive approach in the detection of the disease.

Figure 4. Relationship Between Pulmonary Arterial Pressure and Disease Outcomes

The fourth diagram illustrates the relationship between increasing pulmonary arterial pressure and worsening clinical prognosis. Research findings indicate that the severity of pulmonary hypertension is directly associated with patient survival and the development of complications [13,19].

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As pulmonary arterial pressure rises above normal values, hemodynamic resistance in the pulmonary circulation progressively increases. This leads to an elevated functional load on the right heart chambers. Prolonged overload results in right ventricular hypertrophy, followed by dilation. As shown in the diagram, higher pressure levels are proportionally associated with an increased risk of clinical complications [22]. This is linked to reduced cardiac output, worsening hypoxia, and impaired systemic hemodynamics.

Patients with elevated pulmonary arterial pressure have a higher likelihood of developing heart failure, arrhythmias, and thromboembolic complications. In addition, severe pulmonary hypertension may lead to conditions requiring lung transplantation or intensive care management [24].

This diagram emphasizes the importance of regular monitoring of pulmonary arterial pressure in clinical practice. Early diagnosis and effective therapeutic interventions can slow disease progression and improve patients' quality of life.

Conclusion

Pulmonary hypertension in systemic sclerosis is one of the most severe and prognostically significant complications of the disease. Its pathogenesis is multifactorial, with endothelial dysfunction, microvascular remodeling, and fibrotic processes playing key roles [1,6]. These pathophysiological changes lead to increased pulmonary vascular resistance and a persistent elevation of pulmonary arterial pressure.

Clinically, pulmonary hypertension often presents with nonspecific symptoms. Dyspnea on exertion and fatigue are typically the earliest manifestations. As the disease progresses, chest pain, syncope, and signs of right ventricular failure may develop. This highlights the importance of comprehensive evaluation of symptom dynamics in clinical assessment.

In laboratory diagnostics, biomarkers such as NT-proBNP are important indicators reflecting the load on the right heart chambers. In addition, immunological and inflammatory markers help assess disease activity [16,20]. Among instrumental methods, echocardiography plays a leading role at the screening stage, while right heart catheterization is considered the most reliable "gold standard" for confirming pulmonary hypertension [7]. Assessment of lung

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diffusing capacity and computed tomography provide deeper insights into the morphological and functional characteristics of the disease.

Analysis of studies shows a direct relationship between increased pulmonary arterial pressure and worsening disease outcomes. Elevated pressure increases the load on the right ventricle, thereby raising the risk of heart failure and other severe complications [18,22]. Therefore, early detection and continuous monitoring of pulmonary hypertension remain key priorities in clinical practice.

In general, the integrated use of clinical, laboratory, and instrumental diagnostic methods in systemic sclerosis allows for early detection, accurate prognostic evaluation, and selection of effective treatment strategies. This ultimately contributes to improved quality of life and increased survival of patients.

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