

Joint Expert Consensus Report on the Diagnosis and Management of Pulmonary Arterial Hypertension in Türkiye

In collaboration with Turkish Society of Cardiology, Turkish Thoracic Society and Pulmonary Vascular Disease Research Association (ADHAD)

ABSTRACT

Pulmonary arterial hypertension (PAH) is a progressive and life-threatening disease characterized by increased pulmonary vascular resistance and right ventricular (RV) dysfunction, requiring early diagnosis and timely management. This joint expert consensus report, developed in collaboration with the Turkish Society of Cardiology, Turkish Thoracic Society, and Pulmonary Vascular Disease Research Association (ADHAD), provides a practical, real-world framework for the diagnosis and management of PAH in Türkiye. The document presents updated, practice-oriented diagnostic algorithms designed to facilitate early recognition and accurate classification of PAH. A key objective is the standardization of data collection across centers; therefore, recommended echocardiographic and hemodynamic parameters, along with their normal and pathological ranges, are clearly defined to improve consistency in clinical evaluation and reporting. Risk assessment remains a cornerstone of patient evaluation; however, current guideline-based models have important limitations. In a disease with high mortality such as PAH, greater emphasis should be placed on dynamic risk evaluation at follow-up, incorporating detailed RV assessment through imaging and hemodynamic parameters, and enabling more timely treatment escalation when needed. Accordingly, treatment algorithms have been updated to reflect contemporary therapeutic strategies, emphasizing early combination therapy, individualized management, and prompt escalation in patients who fail to achieve or maintain a low-risk profile with particular attention to RV performance. Overall, this consensus aims to harmonize clinical practice, enhance data quality, and support more proactive and standardized management of PAH across Türkiye.

Keywords: Clinical guidelines, consensus, diagnosis, pulmonary arterial hypertension, pulmonary hypertension, therapy

INTRODUCTION

Pulmonary arterial hypertension (PAH) is a life-threatening condition characterized by elevated pressure in the pulmonary circulation, driven by a complex interplay of vasoconstriction, vascular remodeling, inflammation, and thrombosis, which leads to progressive increases in pulmonary vascular resistance (PVR) and right ventricular (RV) pressure overload. It is associated with significant morbidity and mortality and therefore requires early recognition and appropriate management.

Because of its heterogeneous etiology and clinical presentation, the evaluation and management of PAH require a multidisciplinary approach involving cardiologists, pulmonologists, rheumatologists, radiologists, pediatric cardiologists, and other specialists.

This consensus report was developed by a multidisciplinary task force consisting of 7 cardiologists, 2 pulmonologists, and 2 rheumatologists, under the auspices

CONSENSUS REPORT

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of the Turkish Society of Cardiology, Pulmonary Vascular Disease Research Association (ADHAD), and Turkish Thoracic Society.

The aim of this document is to provide practical guidance for the early diagnosis and optimal multidisciplinary management of patients with PAH, while promoting the standardization of evaluation and treatment strategies across Türkiye. In addition, the committee encourages the use of standardized data collection and supports the development of a national PAH registry to improve data quality and clinical outcomes.

The target audience of this consensus report includes physicians, healthcare professionals involved in the management of PAH, physicians in training, patient organizations, reimbursement authorities, and other stakeholders.

Working groups were formed to develop individual sections of the report including definition and epidemiology, diagnostic strategies and risk evaluation in PAH, and management options and monitoring during follow-up. Draft texts were prepared by the respective groups and subsequently discussed during consensus meetings. After iterative revisions and discussions, the final document was approved by all members of the task force.

DEFINITION AND CLASSIFICATION OF PULMONARY HYPERTENSION

Pulmonary arterial hypertension should be clearly distinguished from the broader term pulmonary hypertension (PH). Pulmonary hypertension is a hemodynamic condition defined as a resting mean pulmonary arterial pressure (mPAP) >20 mm Hg, measured by heart catheterization, and may arise from a variety of underlying etiologies.^{1,2}

Based on differences in pathophysiology and clinical context, PH is classified into 5 groups (Table 1), each with distinct diagnostic and therapeutic implications. Among these, PAH represents a specific and relatively rare subgroup characterized by progressive pulmonary vascular remodeling and increased PVR.

Beyond clinical classification, PH can also be defined according to hemodynamic characteristics, which help distinguish the underlying mechanism of elevated pulmonary pressure. In this context, PH is broadly categorized into pre-capillary and post-capillary forms based on pulmonary arterial wedge pressure (PAWP) and PVR.

Pre-capillary PH is defined hemodynamically by a mPAP >20 mm Hg, a PAWP ≤ 15 mm Hg, and a PVR >2 Wood units (WU). This hemodynamic profile is observed in several clinical groups, including PAH, PH associated with lung diseases and/or hypoxia, PH due to pulmonary artery (PA) obstruction, and selected forms of PH with multifactorial mechanisms. Pulmonary arterial hypertension represents a distinct subtype of pre-capillary PH and is diagnosed only after exclusion of other causes of pre-capillary PH.

In contrast, post-capillary PH is defined by an mPAP >20 mm Hg and PAWP >15 mm Hg and is most commonly associated with left heart disease. Post-capillary PH can be further subdivided into isolated post-capillary PH (IpcPH) (PVR ≤ 2 WU) and combined pre- and post-capillary PH (CpcPH) (PVR >2 WU).

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HIGHLIGHTS

- This joint consensus of three Turkish societies provides practical guidance on the diagnosis and management of pulmonary arterial hypertension.
- Standardized diagnostic algorithms and reporting of echocardiographic and hemodynamic parameters aim to improve consistency across centers.
- During follow-up, risk assessment should integrate right ventricular imaging and/or hemodynamics alongside conventional risk scores.
- The treatment algorithm was adapted to therapeutic options available in Türkiye, with escalation guided by comprehensive risk assessment.
- Early referral for lung transplantation is recommended, and the expansion of transplant programs in Türkiye is strongly advocated.

Table 1. Clinical Classification of Pulmonary Hypertension (WHO Groups 1–5) and Corresponding Hemodynamic Characteristics¹

Pulmonary Hypertension mPAP > 20 mm Hg	Etiologies
Group 1 Pulmonary Arterial Hypertension <i>Primary pulmonary vascular disease</i> PAWP ≤ 15 mm Hg, PVR > 2 WU	<ul style="list-style-type: none"> – Idiopathic PAH <ul style="list-style-type: none"> * Long-term responders to CCB – Heritable PAH – Drug/toxin-associated PAH – Connective tissue disease-associated PAH – Congenital heart disease-associated PAH – HIV-associated PAH – Portal hypertension-associated PAH – Schistosomiasis-associated PAH – PAH with features of venous/capillary (PVOD/PCH) involvement – Persistent PH of the newborn
Group 2 PH Associated with Left Heart Disease <i>LV dysfunction or valvular disease: pressure overload to lungs</i> PAWP > 15 mm Hg, PVR normal or > 2 WU	<ul style="list-style-type: none"> – Heart failure <ul style="list-style-type: none"> * With preserved ejection fraction * With reduced or mildly reduced ejection fraction * Cardiomyopathies with specific etiologies (hypertrophic, amyloid, Fabry disease and Chagas disease). – Mitral/aortic/complex valvular disease – Congenital/acquired cardiovascular conditions leading to post-capillary PH
Group 3 PH Associated with Lung Disease or Hypoxia <i>Chronic lung disease + hypoxemia: remodeling</i> PAWP ≤ 15 mm Hg, PVR > 2 WU	<ul style="list-style-type: none"> – COPD and/or emphysema – Interstitial lung disease – Combined pulmonary fibrosis and emphysema – Other parenchymal lung diseases (not group 5) – Hypoventilation syndromes – Pneumonectomy – Hypoxia without lung disease (e.g., high altitude) – Developmental lung diseases
Group 4 PH Associated with Pulmonary Artery Obstructions <i>Persistent clotting or fibrotic lesions: flow obstruction</i> PAWP ≤ 15 mm Hg, PVR > 2 WU	<ul style="list-style-type: none"> – Chronic thromboembolic PH (CTEPH) – Other pulmonary artery obstructions: <ul style="list-style-type: none"> * Sarcomas (high- or intermediate-grade or angiosarcoma) * Other malignant tumors (e.g., renal carcinoma, uterine carcinoma, germ-cell tumors of the testis), * Nonmalignant tumors (e.g., uterine leiomyoma), * Arteritis without connective tissue disease * Congenital pulmonary arterial stenoses * Hydatidosis
Group 5 PH with Unclear/Multifactorial Mechanisms <i>Complex/multifactorial causes</i> PAWP ≤ 15 or > 15 mm Hg, PVR ≤ 2 WU or > 2 WU	<ul style="list-style-type: none"> – Hematological disorders (chronic hemolytic anemia, chronic myeloproliferative disorders) – Systemic disorders: sarcoidosis, pulmonary Langerhans cell histiocytosis and neurofibromatosis type 1 – Metabolic disorders (glycogen storage diseases and Gaucher disease) – Chronic renal failure with or without hemodialysis – Pulmonary tumor thrombotic microangiopathy – Fibrosing mediastinitis – Complex congenital heart disease

CCB, calcium channel blocker; COPD, chronic obstructive pulmonary disease; LV, left ventricle; PAH, pulmonary arterial hypertension; PAWP, pulmonary arterial wedge pressure; PVOD/PCH, pulmonary veno-occlusive disease/pulmonary capillary hemangiomatosis WHO, World Health Organization.

Patients who exhibit elevated mPAP values without increased PAWP or PVR are considered to have “unclassified PH.” It is frequently linked to high–cardiac output states that lead to increased pulmonary blood flow.

EPIDEMIOLOGY OF PULMONARY ARTERIAL HYPERTENSION

Pulmonary hypertension is estimated to affect approximately 1% of the general population, with prevalence increasing to nearly 10% among individuals older than 65 years.³ However, PAH accounts for only a small proportion

of PH cases, representing approximately 5% of the total burden. The estimated prevalence of PAH is approximately 48–55 cases per million, with an annual incidence of around 6 cases per million.⁴

Earlier international registries characterized PAH predominantly as a disease of younger individuals (30–45 years) with a female predominance. More recent data, however, demonstrate a gradual increase in the mean age at diagnosis, likely reflecting improved awareness and recognition of PAH in older populations.

Epidemiological data on PAH in Türkiye remain limited due to the absence of a unified national registry, heterogeneity in data collection across centers, and the inclusion of patients from different PH groups in available analyses. Nevertheless, existing registries provide important insights into patient characteristics and real-world clinical practice.^{5,6} Consistent with international data, both the SIMURG and TURKPAH registries demonstrate a clear female predominance, with women comprising approximately 69% of patients. The mean age at diagnosis has also increased over time, from 45 years in SIMURG to 52 years in the TURKPAH. However, it should be noted that available data are not restricted exclusively to PAH, as a proportion of patients from other PH groups were also included.

Within the PAH population, IPAH remains the most common etiology in the TURKPAH registry (47.4%).⁶ Congenital heart disease—associated PAH (CHD-PAH) represents a significant subgroup, accounting for approximately 47% of cases in the SIMURG registry and 32% in TURKPAH.^{5,6} Additional insights are provided by the nationwide THALES registry, which included 1034 patients and predominantly reflects a pediatric population.⁷ In this cohort, Eisenmenger syndrome and PAH associated with left-to-right shunts were the most common forms, observed in 49.2% and 42.7% of patients, respectively.

Overall, these findings highlight the increasing awareness of PAH in Türkiye, while emphasizing the urgent need for a contemporary multidisciplinary registry.

Survival in Pulmonary Arterial Hypertension

Survival in PAH has improved substantially over the past decades. In the 1970s, data from the NIH registry reported a median survival of approximately 2.6 years whereas contemporary registries demonstrate median survival exceeding 6 years, reflecting advances in early diagnosis and targeted therapies.⁷⁻⁹ 1-, 3-, 5-, and 7-year survival rates were 85%, 68%, 57%, and 49%, respectively in PAH.¹⁰

Within PAH, patients with connective tissue disease-associated PAH (CTD-PAH) have historically exhibited worse survival compared with idiopathic PAH (IPAH). However, therapeutic advances over the past decade have been associated with improved outcomes, with patients treated after 2010 demonstrating better survival compared to those treated earlier (73% vs. 65%).¹¹

National data from Türkiye show comparable trends. In the SIMURG registry, the 3-year survival rate was reported as 69% in patients with IPAH and CTD-PAH, and higher, at approximately 80%, in patients with congenital heart disease-associated PAH (CHD-PAH).¹² In a more recent retrospective cohort of patients with systemic sclerosis-associated PAH (SSc-PAH), survival rates were 90.2%, 73.2%, and 56.6% at 1, 3, and 5 years, respectively.¹³

Overall, these findings suggest that medium-term survival rates in Turkish PAH cohorts are broadly consistent with those reported in contemporary international registries.

DIAGNOSIS OF PULMONARY ARTERIAL HYPERTENSION

Clinical Suspicion and Early Identification

Pulmonary arterial hypertension often develops insidiously, with exertional dyspnea being the earliest and most

common presenting symptom. Other manifestations include fatigue, reduced exercise capacity, exertional chest pressure, palpitations, lightheadedness, and exertional presyncope/syncope. As the disease progresses and RV dysfunction develops, symptoms of systemic venous congestion may emerge, including peripheral edema, abdominal fullness, ascites, hepatomegaly, early satiety, and eventually cardiac cachexia.

In some patients, aneurysmal enlargement of the pulmonary arteries may lead to compression of adjacent mediastinal structures, resulting in additional clinical manifestations. Extrinsic compression of the left main coronary artery (LMCA) may cause angina-like chest pain, whereas involvement of the left recurrent laryngeal nerve (Ortner's syndrome) may present with hoarseness. In addition, compression of the main bronchi may contribute to worsening dyspnea.

In patients with symptoms or clinical findings suggestive of PH, the diagnostic evaluation should begin with a comprehensive clinical assessment, including a detailed medical history and physical examination. The diagnostic algorithm recommended in this consensus report is summarized in Figure 1.

The medical history should focus on conditions associated with PH, including prior thromboembolic events, features suggestive of connective tissue disease, liver disease, family history of PAH, exposure to anorexigens, stimulants, or other drugs.

Physical examination findings may be subtle or absent in early stages. As the disease progresses, signs suggestive of PH and RV pressure overload may emerge, including a loud pulmonary component of the second heart sound (P2), RV heave, a systolic murmur due to tricuspid regurgitation (TR), and a diastolic murmur due to pulmonary regurgitation (PR). In more advanced stages, features of RV failure and systemic congestion may be present, such as jugular venous distension, hepatomegaly, peripheral edema, and cool extremities. The presence of digital clubbing or differential cyanosis should raise suspicion for Eisenmenger physiology.

Given the potential for delayed diagnosis, screening of high-risk populations should be emphasized. These include patients with systemic sclerosis (SSc) and other connective tissue diseases, uncorrected congenital heart disease, HIV infection, portal hypertension, and families with heritable PAH.

Initial Non-Invasive Evaluation

Initial non-invasive investigations typically include electrocardiography (ECG) and chest radiography. These modalities may provide indirect evidence of PH, with ECG findings such as RV hypertrophy and right atrial (RA) enlargement, and chest radiographic features including PA dilation and signs of right heart enlargement. In addition, both ECG and chest radiography may offer important clues for differential diagnosis; for example, findings such as left ventricular hypertrophy or left atrial enlargement may suggest left heart disease, while chest radiography may also reveal features of parenchymal lung disease.

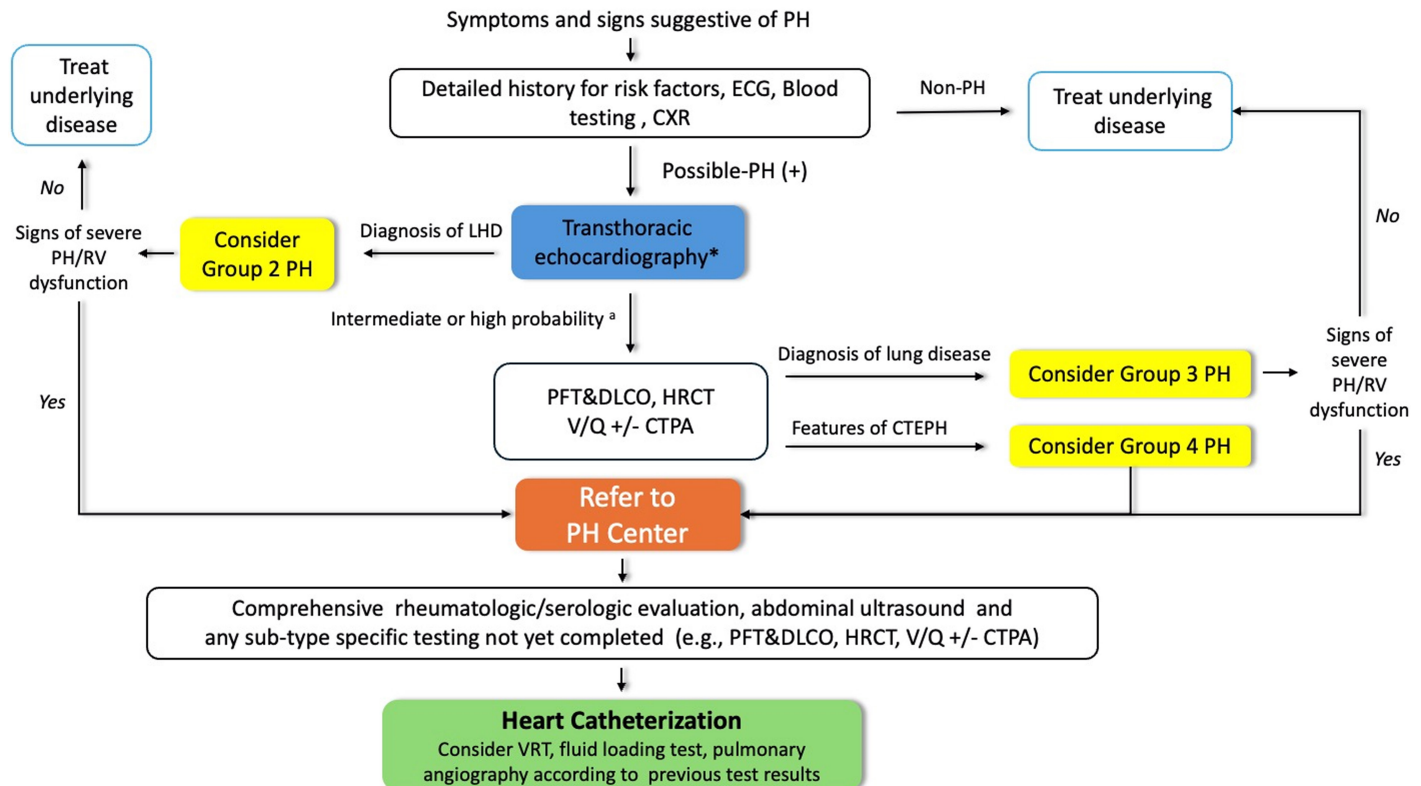


Figure 1. Proposed diagnostic algorithm for the evaluation of pulmonary hypertension.

CTEPH, chronic thromboembolic pulmonary hypertension; CTPA, computed tomography pulmonary angiography; CXR, chest X-ray; DLCO, diffusing capacity of the lung for carbon monoxide; ECG, electrocardiogram; HRCT, high-resolution computed tomography; PA, pulmonary artery; PAH, pulmonary arterial hypertension; PFT, pulmonary function tests; PH, pulmonary hypertension; PR, pulmonary regurgitation; RA, right atrium; RV, right ventricle; sPAP, systolic pulmonary artery pressure; TAPSE, tricuspid annular plane systolic excursion; TR, tricuspid regurgitation; TTE, transthoracic echocardiography; V/Q, ventilation/perfusion scan; VRT, vasoreactivity testing.

*Perform comprehensive echocardiography, including all parameters presented in Table 2. aEchocardiographic probability of PH (TTE-based): Intermediate probability is defined by a TR velocity of 2.9-3.4 m/s, or ≤ 2.8 m/s in the presence of ≥ 2 additional echocardiographic signs from different domains, including abnormalities in right heart size/function (e.g., RV/LV basal diameter >1.0 , abnormal LV eccentricity index, reduced TAPSE/sPAP), pulmonary artery findings (e.g., shortened acceleration time, mid-systolic notching, increased end-diastolic PR velocity, PA diameter >25 mm), and RA/IVC parameters (e.g., RA enlargement, IVC dilatation). High probability is defined by TR velocity >3.4 m/s, or 2.9-3.4 m/s with ≥ 2 additional PH echo signs. A TR velocity ≤ 2.8 m/s indicates low probability; however, in the presence of risk factors or conditions associated with PAH or CTEPH, further evaluation remains warranted. While high-probability findings generally support proceeding to right heart catheterization, decisions in other categories should be individualized and guided by the overall clinical context.

This initial assessment is complemented by measurement of oxygen saturation and laboratory testing, including blood counts, renal, hepatic, and thyroid function tests, as well as natriuretic peptides (BNP or NT-proBNP), which also provide important prognostic information. While none of these investigations is diagnostic, they provide important supportive information and may raise clinical suspicion of PH.

Further targeted investigations are required to confirm the diagnosis and to determine the underlying etiology, which is essential for appropriate classification and management, as treatment strategies differ significantly among PH groups.

Transthoracic echocardiography (TTE) plays a central role in the initial evaluation of patients with suspected PH. Echocardiography allows estimation of PA pressures and identification of structural and functional abnormalities suggestive of PH.

A resting TR velocity ≥ 2.9 m/s, or ≤ 2.8 m/s in the presence of at least 2 additional echocardiographic signs (including right

heart or PA dilatation, abnormal left ventricular eccentricity index, shortened pulmonary acceleration time, or inferior vena cava dilatation), is suggestive of PH and warrants further diagnostic evaluation (see Figure 1 legend for detail). In addition, echocardiography provides important information regarding potential underlying causes, particularly left heart disease, which remains the most common cause of PH.

Table 2 summarizes the key echocardiographic parameters and abnormal cut-off values recommended for reporting. Detailed methodologies for the measurement and interpretation of these parameters are described in the ESC/ERS guidelines and the recent American Society of Echocardiography (ASE) recommendations.¹⁴

Beyond its diagnostic role, TTE is essential for risk stratification and management decisions, both at baseline and during follow-up. It enables comprehensive assessment of RV size and function. Parameters such as RA area, the TAPSE/

sPAP ratio, and the presence of pericardial effusion provide important prognostic information and contribute to mortality risk assessment in patients with PAH.^{1,14}

When image quality or Doppler signals are suboptimal, contrast-enhanced echocardiography may improve delineation of endocardial borders and facilitate more accurate assessment of RV size and function, as well as estimation of TR velocity. It may also aid in the detection of intracardiac or intrapulmonary shunts and can be helpful in distinguishing portopulmonary hypertension (PoPH) from hepatopulmonary syndrome.

Given the relatively high prevalence of congenital heart disease (CHD) in Türkiye, transesophageal echocardiography (TEE) should be considered as part of the diagnostic evaluation in selected patients with suspected PAH, particularly in younger individuals. The TEE may help exclude left-to-right shunt lesions, such as atrial septal defects—including sinus venosus-type defects, which may occasionally be missed on TTE.

Further Diagnostic Work-up

Although TTE is essential for assessing PH probability, the final diagnosis should always be confirmed by heart catheterization, as echocardiography may over- or underestimate pulmonary pressures. Prior to heart catheterization, all relevant clinical information related to elevated pulmonary pressures should be carefully collected and evaluated to individualize both the indication and the procedural approach.

Additional investigations aimed at identifying the underlying etiology of PH are summarized below.

Respiratory and Pulmonary Vascular Investigations

Pulmonary function tests (PFT), including spirometry, lung volumes, and diffusion capacity for carbon monoxide (DLCO), arterial blood gas analysis, and chest computed tomography (CT) should be performed in all patients with suspected PH. These tests help distinguish PH groups, identify comorbidities, and assess the need for oxygen supplementation.

Arterial blood gas analysis typically shows normal or mildly reduced PaO₂ and normal or decreased PaCO₂ in patients with PAH. Markedly reduced PaO₂ is atypical for PAH and should prompt evaluation for alternative diagnosis or associated conditions such as parenchymal lung diseases, chronic thromboembolic PH (CTEPH), right-to-left shunting, or pulmonary veno-occlusive disease (PVOD) and may reflect coexisting comorbidities, particularly cigarette smoking.

Pulmonary function tests in PAH is typically normal or shows only mild restriction while DLCO is usually mildly reduced.^{1,2} A markedly reduced DLCO disproportionate to lung volumes may raise suspicion for PVOD, pulmonary capillary hemangiomas (PCH), SSc-associated PAH, or group 3 PH (e.g., interstitial lung disease or combined pulmonary fibrosis and emphysema) and is associated with poor prognosis.

Table 2. Essential echocardiographic parameters and abnormal cut-off values for the evaluation of pulmonary hypertension.

Parameters	Abnormal Values
Right heart hemodynamic assessment	
Tricuspid regurgitation velocity	TRV > 2.8 m/s
Systolic PA pressure*	sPAP > 35 mm Hg
Additional signs suggestive of PH	
Early-diastolic pulmonary regurgitation velocity	Peak early-diastolic PR velocity > 2.2 m/s
RVOT acceleration time	RVOT AccT < 105 ms
Right atrium diameter, area and/or volume	RA diameter ≥ 42 mm, RA area > 18 cm ² or RA volume index ≥ 30 ml/m ²
Right ventricle basal diameter	≥ 41 mm
LV eccentricity index	> 1 in end-systole and end-diastole
Pulmonary artery diameter	> 25 mm
Inferior vena cava diameter (> 21 mm) with inspiratory collapsibility (< 50%)	According to these parameters RA pressure values 3, 8, or 15 mmHg are assigned
RV systolic function	
Tricuspid Annular Plane Systolic Excursion	TAPSE < 17 mm
TDI peak systolic velocity of tricuspid annulus	S' < 9.5 cm/s
RV fractional area change	RV FAC ≤ 35%
TAPSE/sPAP ratio	< 0.32 mm/mm Hg is associated with RV/PA uncoupling
Valvular pathologies	Regurgitation or stenosis severity
Left-sided parameters	
LV E/E' ratio	8-14 (gray zone), > 14 elevated
LV Ejection fraction	Men < 52%, Women < 54%
LA volume index	> 34 mL/m ²
Presence/absence of pericardial effusion	If present describe the size, distribution and hemodynamic effect (evidence of tamponade yes/no)

LA, left atrium; LV, left ventricle; PA, pulmonary artery; RV, right ventricle; RVOT, right ventricular outflow tract.

*PASP equals RVSP in the absence of RVOT obstruction, pulmonary stenosis, or proximal pulmonary artery stenosis; otherwise, values should be reported as RVSP.

High-resolution computed tomography (HRCT) of the chest provides detailed anatomical assessment of the lung parenchyma and mediastinum, and contributes to the exclusion of secondary causes of PH, including interstitial lung disease, emphysema, and PVOD/PCH.

Computed tomography pulmonary angiography, especially ECG-gated thin section, gives valuable information related to CTEPH, congenital heart/vascular abnormalities (including intracardiac shunts, abnormal pulmonary venous return, patent ductus arteriosus, pulmonary arteriovenous malformations), enlarged PA diameter, enlarged right heart chambers, peripheral PA stenosis. Computed tomography pulmonary angiogram may overlook the CTEPH lesions, especially distal segmental lesions.

Ventilation–perfusion (V/Q) scintigraphy [Planar or Single Photon Emission Computed Tomography (SPECT)] remains the preferred screening test for CTEPH. A normal V/Q scan mostly excludes CTEPH, whereas segmental perfusion defects with normal ventilation or in the absence of parenchymal lung disease should prompt further evaluation with pulmonary angiographic imaging. V/Q abnormalities may be present in PAH, typically as mild, non-segmental defects; segmental mismatched defects should raise suspicion for CTEPH.

Overnight oximetry or polysomnography should be performed if there is suspicion of sleep-disordered breathing or hypoventilation.

Other Investigations

Abdominal ultrasound and portal Doppler should be used to evaluate portal hypertension and its causes, including cirrhosis, vascular malformations, and portal vein thrombosis or obstruction.

Detailed laboratory testing should include viral serology for hepatitis and HIV, as well as an immunological work-up including at minimum antinuclear antibodies (ANA), lupus anticoagulant, and other antiphospholipid syndrome antibodies for rheumatological diseases such as SSc, systemic lupus erythematosus (SLE), and mixed connective tissue disease.

Cardiac magnetic resonance (CMR) Imaging improves diagnostic accuracy and provides prognostic information by accurately quantifying right heart size, volumes, RV ejection fraction, mass, and stroke volume, and by enabling indirect, noninvasive assessment of RV–PA coupling. The presence of late gadolinium enhancement reflects myocardial fibrosis and is associated with worse outcomes. CMR can also detect congenital heart disease

Cardiopulmonary exercise testing (CPET) provides integrated assessment of cardiovascular and pulmonary responses to exercise and is useful in evaluating unexplained dyspnea and suspected PH. In patients with PAH, a characteristic pattern is observed, including reduced peak oxygen uptake (VO_2), low end-tidal CO_2 (PETCO_2), elevated ventilatory inefficiency (VE/VCO_2 slope), and decreased oxygen

pulse (VO_2/HR). While not diagnostic, CPET complements other tests and may guide further evaluation.

Heart Catheterization Although traditionally termed right heart catheterization, the committee adopts the broader term heart catheterization, acknowledging that comprehensive assessment may require both right- and left-sided chamber access for pressure measurements and oxygen saturation sampling in selected cases.

Heart catheterization remains the gold standard for confirming PH, enabling hemodynamic characterization, risk stratification, and evaluation of associated congenital heart disease. In newly diagnosed patients, a comprehensive approach including both right- and left-sided assessment may be considered when feasible, as this improves diagnostic accuracy and reduces misclassification between pre- and post-capillary PH.¹⁵ The catheterization report should include all key hemodynamic parameters (Table 3) and be adapted to the clinical context.

Accurate measurements require meticulous technique, including proper transducer leveling, zero calibration, and pressure recording at end-expiration. Hemodynamic values may be influenced by volume overload and uncontrolled systemic blood pressure; therefore, patients should be optimized to a euvolemic state with adequate blood pressure control prior to catheterization. Pulmonary arterial wedge pressure is the primary surrogate for left atrial pressure; when unreliable, left ventricular end-diastolic pressure may be used, and direct left atrial measurement may be considered in selected cases.

Measurement of mixed venous (SvO_2) and arterial (SaO_2) oxygen saturations is required at a minimum. Stepwise oxygen saturation assessment should be performed in the presence of clinical or imaging suspicion of a left-to-right shunt, or when PA oxygen saturation is unexpectedly elevated ($>75\%$). Cardiac output is commonly estimated using the indirect Fick method due to limited equipment availability. When feasible, the direct Fick method is preferred. In the absence of shunts, thermodilution methodology may be used, although it requires specialized catheters and software.

Diagnosis of PAH requires confirmation of pre-capillary PH and exclusion of alternative causes. Therefore, all investigations related to etiology should be taken into consideration when planning and performing heart catheterization. This is important to determine the need for further testing in precapillary PH; for example, in the presence of thromboembolic lesions on CT or perfusion defects on V/Q scanning, invasive pulmonary angiography or digital subtraction angiography (DSA) may be required. In patients with a primary diagnosis of PAH, acute vasoreactivity testing (VRT) should be performed, particularly in those patients with idiopathic, heritable, or drug/toxin associated PAH. In patients with clinical or imaging findings suggestive of left heart disease but PAWP ≤ 15 mmHg, fluid challenge or passive leg raise (PLR) during catheterization may be used to unmask heart

Table 3. Essential Parameters and Reference Values for Heart Catheterization Reports**Height (cm), Weight (kg), and Body Surface Area****WHO functional class****Current medications (dose and frequency)**

Measured variables	Normal value	Calculated parameters	Normal value
Mean RA pressure (mm Hg)	<8	Cardiac output (L/min)	4-8
Systolic PAP (mm Hg)	15-30	Cardiac index (L/min/m ²)	2.5-4.0
Diastolic PAP (mm Hg)	4-12	Stroke volume index (mL/m ²)	33-47
Mean PAP (mm Hg)	8-20	Pulmonary vascular resistance (WU)	0.3-2.0
PAWP / Left ventricular end-diastolic pressure	≤15	Systemic vascular resistance (WU)	10-15
PA oxygen saturation*	65%-80%	Acute vasoreactivity test	Performed/Not performed
Arterial oxygen saturation	95%-100%	VRT compound	Iloprost, NO, epoprostenol
Aortic or systemic blood pressure*	120/80 mm Hg	mPAP after VRT (mm Hg)	≥10 mm Hg decrease to ≤40 mm Hg
Heart rate	60-100 bpm	Cardiac output after VRT (L/min)	Stable or increased CO
		VRT result	Positive/negative

CO, cardiac output; PA, pulmonary artery; PAP, pulmonary arterial pressure; PAWP, pulmonary artery wedge pressure; RA, right atrium; VRT, vasoreactivity testing; WHO, World Health Organization.

* & PA oxygen saturation = Mixed venous oxygen saturation. If arterial access is not obtained, systemic blood pressure may be measured noninvasively from the appropriate extremity.

failure with preserved ejection fraction. However, results should be interpreted with caution and considered supportive rather than definitive.

The aim of VRT in PAH is to identify who may derive long-term benefit (above 1 year) from high-dose calcium channel blocker (CCB) therapy. Given the risks of inappropriate CCB therapy, VRT should be restricted to experienced centers. A positive VRT reflects an acute response; however, it does not necessarily guarantee sustained long-term clinical benefit, as approximately half of patients fail to respond durably to CCB therapy.¹⁶

The most commonly used agents for VRT are inhaled nitric oxide (NO) (10-20 ppm) and inhaled iloprost (5-10 µg). Intravenous epoprostenol (2-12 ng/kg/min) is an alternative; however, its use is more time-consuming and requires step-wise dose titration. A positive response in VRT is defined as a ≥10 mmHg reduction in mPAP to ≤40 mmHg, with stable or increased CO.¹⁶

An important practical question is how to interpret VRT in patients with a baseline mPAP between 21 and 40 mm Hg who fulfill the current hemodynamic definition of PAH. An absolute reduction in mPAP of ≥10 mm Hg may be considered a potential threshold for a positive vasoreactivity response; however, the supporting evidence remains limited, particularly in patients with only mildly elevated baseline mPAP. Alternative hemodynamic criteria previously proposed, such as a ≥20% reduction in PVR or combined reductions in mPAP and PVR, may indicate an acute vasodilatory response.^{17,18} However, these criteria have not been shown to reliably distinguish patients who derive sustained clinical benefit from those who do not respond to treatment.

A fluid challenge is performed by infusing 500 mL of saline over 5–10 minutes during catheterization after the initial

evaluation is finished; an increase in PAWP to ≥18 mmHg is considered abnormal.¹

Passive leg raise during HC is a simple maneuver in which the patient's legs are elevated by staff at an angle off ≈50 degrees while the patient remains in a supine position, relaxed and breathing spontaneously. A PAWP_{PLR} ≥19 mmHg suggests occult heart failure. This maneuver requires appropriate venous access, typically via the internal jugular vein.¹⁹

Coronary Angiography

Coronary angiography should be considered in patients with PAH when there is clinical suspicion of concomitant coronary artery disease or in those with cardiovascular risk factors, particularly prior to advanced therapies or surgical interventions such as lung transplantation or pulmonary thromboendarterectomy. In addition, it is indicated when LMCA compression is suspected, especially in patients with severe PA dilation presenting with angina or ischemic symptoms.

EVALUATION FOLLOWING DIAGNOSIS OF PULMONARY ARTERIAL HYPERTENSION

Patients should be managed in, or in collaboration with, specialized PH centers for precise diagnosis and appropriate treatment.^{1,2} A multidisciplinary approach involving cardiology, pulmonology, radiology, rheumatology, and other relevant specialties is recommended. After confirmation of the diagnosis, patients should undergo comprehensive evaluation using clinical, laboratory, imaging, and heart catheterization parameters. Treatment strategy should be guided by risk stratification based on the estimated 1-year mortality.

Exercise Capacity Evaluation

Exercise capacity is a key component of risk assessment and follow-up in patients with PAH. It should be routinely evaluated using the World Health Organization (WHO) functional class and objective exercise testing.

The 6-minute walk test (6MWT) is the most widely used and practical method for assessing submaximal exercise capacity in PH and is recommended at baseline and during follow-up when clinically feasible.^{20,21} The test should be performed according to standardized protocols to ensure reproducibility and reliability. Patients are instructed to walk as far as possible along a flat, straight corridor for 6 minutes, with standardized encouragement. The total distance walked (6MWD) is recorded in meters.

In addition to distance, other parameters such as oxygen saturation, heart rate response, and symptom burden (e.g., dyspnea using the Borg scale) should be documented, as they provide important complementary information. A reduced 6MWD and/or significant oxygen desaturation during the test are associated with worse prognosis. Serial assessments are particularly valuable for monitoring disease progression and treatment response.

The test results may be influenced by age, sex, height, comorbidities, and patient motivation; therefore, consistent testing conditions and interpretation in clinical context are essential.

Cardiopulmonary exercise testing provides a comprehensive evaluation of exercise physiology and may offer additional prognostic and diagnostic information. However, its use is limited by the need for specialized equipment and expertise, and it is therefore not routinely required in all patients.

Initial Risk Stratification

A multidimensional approach is recommended for risk assessment in PAH, integrating clinical, functional, imaging, biomarker, and hemodynamic data. The ESC/ERS risk stratification algorithm is the most widely used model in Türkiye and is endorsed in this consensus as the preferred national standard to ensure uniform data collection and facilitate inter-center comparability.¹ Although alternative validated tools, such as REVEAL 2.0, may be used, a consistent risk assessment method should be applied at baseline and maintained during follow-up to accurately monitor disease progression.²²

At initial evaluation, the ESC/ERS 3-strata model should be applied to categorize patients as low, intermediate, or high risk based on parameters reflecting clinical status, exercise capacity, and right heart function, corresponding to estimated 1-year mortality risks of <5%, 5%-20%, and >20%, respectively (Table 4, modified from ESC/ERS Guidelines 2022).² Heart catheterization parameters play a central role in risk assessment, providing key prognostic information at diagnosis and during follow-up.

The primary therapeutic goal is to achieve and maintain a low-risk profile, which is associated with improved clinical outcomes. Risk status should be considered dynamic; therefore, any clinical deterioration or failure to achieve low-risk criteria should prompt timely treatment escalation or modification.

TREATMENT OF PULMONARY ARTERIAL HYPERTENSION

After diagnostic confirmation by heart catheterization, including VRT in appropriate patient groups, risk assessment

should be performed and both supportive (symptomatic) and PAH-specific therapies should be initiated accordingly. The treatment algorithm proposed in this document primarily applies to patients with IPAH, HPAH, CTD-PAH, and corrected CHD-PAH with a mPAP $\geq$ 25 mmHg and PVR > 3 WU (Figure 2).

Symptomatic Treatment

Optimization of fluid status represents a key component of supportive therapy in PAH, contributing to accurate clinical evaluation, appropriate risk stratification, and effective symptom control. Loop and thiazide diuretics are the most employed agents for volume management in this population. Mineralocorticoid receptor antagonists, such as spironolactone or eplerenone, are also frequently used to optimize volume status and may provide additional clinical benefits. The selection, dose, and frequency of diuretic therapy should be individualized based on the extent of volume overload and renal function. Supplemental oxygen therapy should be considered in patients with documented hypoxemia. In the presence of anemia, iron status should be assessed by measuring ferritin levels and transferrin saturation, and iron deficiency should be treated accordingly.^{23,24}

Appropriate management of the underlying condition, such as SSc, SLE, human immunodeficiency virus (HIV) infection, or portal hypertension, represents an essential component of standard care in PAH. In addition, optimal treatment of associated comorbidities is crucial.

Lifestyle counseling, including weight management and avoidance of tobacco use, should be emphasized. Preventive care should also include immunization against influenza and *Streptococcus pneumoniae*, and vaccination against respiratory syncytial virus should be considered where available and appropriate.

Treatment of Pulmonary Arterial Hypertension Patients with Positive Acute Vasoreactivity Test

Patients with IPAH, HPAH, or drug- and toxin-associated PAH who demonstrate a positive acute VRT should be treated with CCB.^{1,2} The choice of CCB should be guided by heart rate. In patients with a normal or low heart rate, a dihydropyridine agent such as amlodipine (initial dose 5 mg od, titrated to 15-30 mg od), nifedipine (initial dose 30 mg bid or tid, titrated to 60 mg bid or tid), or felodipine (initial dose 5 mg od, titrated to 15-30 mg od) may be preferred. In patients with tachycardia, a non-dihydropyridine agent such as diltiazem (initial dose 60 mg bid, titrated to 120-360 mg bid) is recommended. CCB therapy should be started at low doses and gradually up-titrated based on blood pressure, heart rate, and overall clinical response, including hemodynamic parameters. High doses may be required to achieve optimal therapeutic effect.

Treatment goals include attainment of a low-risk profile on non-invasive assessments and near normalization of hemodynamics. In cases where these treatment goals are not achieved, escalation of therapy with the addition of PAH-specific medications is recommended.

Table 4. ESC/ERS 3-strata Risk Algorithm for Initial Risk Assessment in PAH

Prognostic Factors Based on Estimated 1-Year Mortality		Low Risk (<5%)	Intermediate risk (5%-20%)	High Risk (>20%)
Signs and symptoms	• Signs of RHF	Absent	Absent	Present
	• Symptom progression	No	Slow	Rapid
	• Syncope	No	Occasional	Recurrent syncope
Exercise capacity	• WHO-Functional Class	I, II	III	IV
	• 6MWD (m)	>440	165-440	<165
	CPET			
	• Peak VO ₂ (mL/min/kg)	15	11 – 15	< 11
Right ventricular function	• VE/VCO ₂	<36	36 – 44	> 44
	Biomarkers			
	• BNP (ng/L)	<50	50-800	>800
	• NT-proBNP (ng/L)	<300	300-1100	>1100
	Echocardiography			
	• RA area (cm ²)	<18	18-26	26
	• TAPSE/sPAP (mm/mm Hg)	>0.32	0.19-0.32	<0.19
	• Pericardial effusion	No	Minimal	Moderate or large
	Cardiac MRI			
	• RV ejection fraction (%)	54	37-54	<37
	• Stroke volume index (mL/m ²)	>40	26-40	<26
	• RV ESVI (mL/m ²)	<42	42-54	>54
	Heart catheterization			
	• RA pressure (mm Hg)	<8	8-14	>14
	• Cardiac index (L/min/m ²)	≥2.5	2.0-2.4	<2.0
	• Stroke volume index (mL/m ²)	38	31-38	<31
	• SvO ₂	>65	60-65	<60

6MWD, 6-minute walk distance; CPET, cardiopulmonary exercise test; ESVI, end-systolic volume index; RA, right atrium; RV, right ventricle; sPAP, systolic pulmonary artery pressure; SvO₂, mixed venous oxygen saturation; TAPSE, tricuspid annular plane systolic excursion; WHO, World Health Organization.

Standard Pulmonary Arterial Hypertension Specific Therapy

For many years, main pharmacological treatments for PAH have targeted 3 major pathophysiological pathways: the endothelin, nitric oxide, and prostacyclin pathways (Table 5). These therapies modulate pulmonary vascular tone, induce vasodilation, and improve pulmonary hemodynamics, exercise capacity, and clinical outcomes. However, there remains a critical need for novel therapies that address mechanisms beyond these traditional pathways.

Recent advances have introduced therapies targeting the activin–transforming growth factor- β (TGF- β) signaling pathway, now recognized as a fourth therapeutic pathway in contemporary guidelines.^{1,25} Sotatercept, the first agent in this class, restores the balance between pro-proliferative activin and anti-proliferative bone morphogenetic protein (BMP) signaling.²⁶⁻³⁴ It has been associated with reductions in mPAP without significant changes in cardiac output, suggesting a potential role in pulmonary vascular remodeling rather than vasodilation. The addition of sotatercept to established background PAH therapy significantly improves exercise capacity, cardiac biomarkers, functional status, RV structure and function, pulmonary hemodynamics, and clinical outcomes. These improvements have largely been maintained at 1-2 years of follow-up.^{28,35} At the time of writing this consensus article, the authors agreed to include sotatercept in the treatment algorithm; however, it is not currently available in Türkiye.

Initial Treatment Strategy

Initial therapy following diagnosis should be based on an evaluation of risk status according to ESC/ERS 3-strata algorithm (Table 4). For patients not classified as high risk at diagnosis (i.e., low or intermediate risk patients), initial oral combination therapy with an endothelin receptor antagonist (ERA) and a phosphodiesterase type-5 inhibitor (PDE5i) is recommended as the preferred treatment strategy.^{1,25,36,37} As an alternative approach, combination therapy with an ERA and a soluble guanylate cyclase stimulator (sGCs) may be considered in selected patients.

In patients presenting with high-risk features, initial treatment should include parenteral prostacyclin therapy administered intravenously (epoprostenol) or subcutaneously (treprostinil) with an ERA and a PDE5i.

Follow-up

A comprehensive first follow-up assessment is recommended within 3 months after initiation of therapy. Earlier reassessment should be considered in patients with clinical instability or an inadequate response to treatment.

The frequency of subsequent visits should be individualized based on the patient's clinical status and treatment modality. For patients who are clinically stable, reassessment every 3 months is recommended.

Treatment-specific monitoring is essential. In patients receiving ERAs, liver function tests and hemoglobin levels

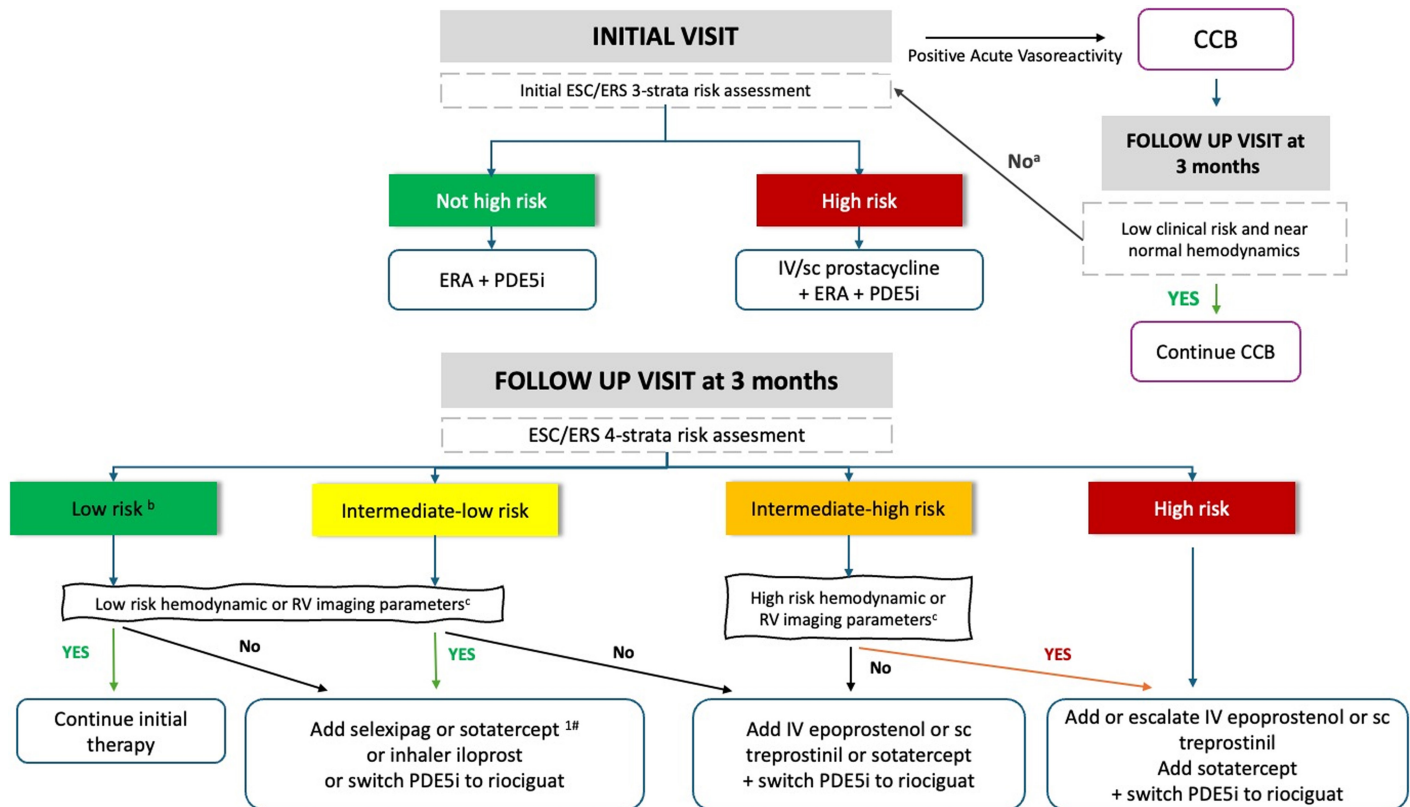


Figure 2. Proposed treatment algorithm for pulmonary arterial hypertension.

CCB, Calcium channel blocker, ERA, Endothelin Receptor Antagonist, PDE5i, Phosphodiesterase 5 inhibitor. ^{1#} first choice. ^aContinue CCB and add PAH specific therapy according to the patient's risk profile. ^bAdditional hemodynamic and imaging parameters may be required in selected situations, such as in younger patients or when one or more standard parameters included in the 4-strata risk model cannot be reliably obtained or adequately assessed. ^cLow or high risk hemodynamic or RV imaging parameters as defined in the ESC/ERS 3-strata risk model. ^d + Switching from PDE5i to riociguat may be considered as a salvage optimization strategy in patients who fail to achieve treatment goals despite maximally tolerated multidrug therapy. In high-risk patients, this approach is based on expert opinion. In both intermediate-high and high-risk patients, it should not delay referral for lung transplantation.

should be assessed during the first month of therapy. For patients treated with the sGCs riociguat, dose titration requires clinical evaluation at approximately 2-week intervals until the target dose is achieved. Patients receiving intravenous or subcutaneous prostacyclin therapy may require more frequent follow-up, often once or twice weekly,

during the titration period. Similarly, initiation of selexipag necessitates weekly dose titration with close monitoring of tolerability and adverse effects. For patients treated with subcutaneous sotatercept, hemoglobin, platelet count, and blood pressure should be assessed prior to each of the first 5 doses (administered every 3 weeks), followed by periodic

Table 5. Pharmacological Treatment Options in PAH According to Targeted Pathways

Pathway	Drug Class	Drug	Recommended Dose
Endothelin pathway	Endothelin receptor antagonists (ERAs)	Bosentan	62.5 mg bid → 125 mg bid
		Ambrisentan	5-10 mg once daily
		Macitentan	10 mg once daily
Nitric oxide (NO) pathway	Phosphodiesterase-5 inhibitors (PDE5i)	Sildenafil	20 mg tid
		Tadalafil	40 mg once daily
	Soluble guanylate cyclase stimulators (sGCs)	Riociguat	1 mg tid → up to 2.5 mg tid (titrated)
Prostacyclin pathway	Prostacyclin analogues	Epoprostenol (IV)	Continuous infusion, starting 2 ng/kg/min (titrated)
		Treprostinil (sc)	Starting 1.25 ng/kg/min (titrated)
		Iloprost (inhaled)	2.5-5 µg per inhalation, 6-9 times/day
	Prostacyclin receptor agonist	Selexipag	200 mcg bid → up to 1600 mcg bid (titrated)
BMP signaling pathway	Activin signaling inhibitor	Sotatercept	0.3 mg/kg SC → 0.7 mg/kg every 3 weeks

bid, twice daily; BMP, bone morphogenetic protein; iv, intravenous; sc, subcutaneous; tid, three times daily.

monitoring guided by clinical status; dose adjustment or temporary interruption may be required in cases of clinically significant abnormalities.

At each follow-up visit, a comprehensive clinical evaluation and risk assessment should be performed, including assessment of symptoms (e.g., dyspnea, angina, syncope), WHO-FC, and signs of right heart failure on physical examination, as well as oxygen saturation. Exercise capacity and biomarkers should be routinely evaluated, including 6MWD and BNP or NT-proBNP levels, to guide ongoing risk stratification and treatment optimization. Laboratory assessment should include hemoglobin and liver function tests. Echocardiography should be performed during follow-up, particularly after initiation or modification of therapy; in clinically stable patients, it may be repeated at approximately 6-month intervals.

Based on these findings, patient risk status should be reassessed using the ESC/ERS 4-strata risk stratification model (Table 6, modified from ESC/ERS guidelines 2022). As age and comorbidities may influence individual parameters, risk assessment should be interpreted in a comprehensive manner, incorporating additional variables as needed. In this context, right heart imaging and hemodynamic data provide important complementary information beyond simplified risk scores. Key echocardiographic (e.g., TAPSE/sPAP ratio, pericardial effusion, RA area) and hemodynamic parameters (e.g., SvO₂, cardiac index, stroke volume index, RA pressure), originally included in the 3-strata model, remain essential for accurate risk assessment and guiding therapeutic decisions during follow-up.

The optimal timing and frequency of hemodynamic reassessment may vary depending on institutional expertise and available resources. Nevertheless, given the robust prognostic and therapeutic information provided by heart catheterization, its incorporation into follow-up is encouraged. The committee recommends invasive hemodynamic evaluation in expert PAH centers in the setting of clinical deterioration, following treatment modification to assess response, and at approximately annual intervals in clinically stable patients.

Clinical Deterioration and Complications During Follow-up

Chest pain and syncope should raise suspicion for LMCA compression by a dilated PA, particularly when the PA diameter exceeds 40 mm.³⁸⁻⁴⁰ Coronary CT angiography should be performed to evaluate the PA–LMCA relationship and screen for possible coronary compression. It is important to clearly

inform the radiologist of the clinical suspicion and specifically request assessment for possible dilated PA–related LMCA compression. The PA–LMCA relationship may be categorized as normal (>1 mm separation), contiguity (≤1 mm without displacement or stenosis), dislocation (LMCA displacement by the enlarged PA, with or without luminal narrowing), or significant stenosis (≥50% narrowing due to external compression).³⁸

Invasive coronary angiography helps determine the degree of stenosis; however, multiple projections are required, as the lesion may not be apparent in all views.⁴⁰ The left cranial projection is generally the most informative. Given the potential for dynamic worsening of coronary compression during exercise, resting intravascular imaging with intravascular ultrasound or optical coherence tomography may underestimate the severity of stenosis.

In patients with hemodynamically significant LMCA compression, percutaneous coronary intervention with stent implantation represents an effective therapeutic option, providing rapid symptom relief and restoration of coronary flow. Given the extrinsic nature of the lesion, stent selection should prioritize high radial strength to resist ongoing external compression. However, treatment decisions should be individualized within a multidisciplinary framework. In selected cases, particularly in the presence of large or progressive PA aneurysms or complex anatomy, surgical options including PA repair and/or coronary artery bypass grafting should also be considered.

In addition to these structural complications, clinicians should be aware that even patients who appear clinically stable under optimal therapy may experience sudden clinical deterioration due to acute right heart failure.⁴¹ This life-threatening condition may be triggered by factors such as arrhythmias, infections, pulmonary embolism, progression of pulmonary vascular disease, treatment interruption, or volume imbalance. Timely recognition and diagnosis are crucial, and clinicians should actively search for reversible triggers of decompensation. Given the limited adaptive capacity of the RV to acute increases in afterload, early identification of warning signs—such as worsening dyspnea, hypotension, tachycardia, and signs of systemic congestion—is essential. Prompt referral to expert centers and timely escalation of therapy, including intravenous epoprostenol and inhaled nitric oxide, are critical to prevent further deterioration.⁴¹ In advanced cases, extracorporeal life support (e.g., ECMO) may be considered as a bridge to recovery in selected patients.

Table 6. ESC/ERS 4-Strata Risk Stratification Model for Follow-up

Prognostic Factors	Low risk (0%-3%)	Intermediate-low risk (2%-7%)	Intermediate-high risk (9%-19%)	High Risk (>20%)
WHO functional class	I, II		III	IV
6MWD (m)	>440	320-440	165-319	<165
BNP (ng/L)	<50	<50-199	200-800	>800
NT-proBNP (ng/L)	<300	300-649	650-1100	>1100
SCORE	1	2	3	4

An overall risk score is calculated by averaging the scores of the available parameters and rounding to the nearest integer, thereby assigning the patient to a final risk category.

6MWD, six-minute walk distance, WHO, World Health Organization.

Treatment Goals and Escalation Strategy

The primary goal of PAH treatment is to achieve and maintain a low-risk profile. Patients who meet low-risk criteria and do not exhibit high-risk features on echocardiography or heart catheterization at follow-up should continue their initial treatment strategy.

In patients with intermediate–low risk at first follow-up, escalation of therapy is recommended. The addition of an oral prostacyclin receptor agonist, such as selexipag, or activin signaling inhibitor, such as sotatercept, represents a preferred treatment strategy supported by a high level of evidence.^{26–28,42} Inhaled prostacyclin therapy may also be considered as an alternative option. In selected patients, switching from PDE5i therapy to an sGC, such as riociguat, may also be considered, although the level of recommendation for this approach is lower.^{43–45}

Patients with an intermediate–high risk profile should be evaluated with caution. The presence of comorbidities may complicate clinical assessment, and in cases of potential confounding, repeat evaluation of diagnostic tests under optimal conditions should be considered to allow more accurate risk stratification and treatment decision-making. If the patient remains at intermediate–high risk despite reassessment, escalation of therapy with the addition of sotatercept or initiation of parenteral prostacyclin therapy (iv epoprostenol or sc treprostinil) should be considered following shared decision-making with the patient. Switching from PDE5i to riociguat may also be considered in selected patients who fail to achieve treatment goals despite treatment intensification.⁴⁵

In patients at high risk, or those at intermediate–high risk with adverse RV imaging findings or severely impaired hemodynamic parameters, the addition of both sc sotatercept and parenteral prostacyclin (intravenous or subcutaneous) should be considered. Data regarding switching from PDE5i to riociguat in high-risk patients remain limited. In this population, prostacyclin- and sotatercept-based aggressive treatment strategies should be prioritized. Nevertheless, given the substantial mortality risk associated with advanced PAH, individualized attempts at further therapeutic optimization may still be justified in selected patients.

Lung transplantation represents an important therapeutic option in the management of PAH. Although availability remains very limited in Türkiye, all patients classified as high risk at diagnosis, as well as those with intermediate–high or high risk at follow-up, should be referred to a lung transplantation center for evaluation. There is an urgent need to expand and strengthen transplant programs and to increase awareness of the importance of organ donation and transplantation.

Management of Patients in the Hemodynamic Gray Zone (Mean Pulmonary Artery Pressure 21–24 mmHg and/or Pulmonary Vascular Resistance 2–3)

Patients with a mPAP of 21–24 mmHg and/or a PVR of 2–3 WU represent a clinical gray zone. Currently, there is no evidence to support routine initiation of PAH-specific therapy

in this population. These patients should be evaluated in expert PH centers, undergo careful clinical and hemodynamic reassessment, and be followed closely for evidence of disease progression. Associated conditions, underlying diseases, and comorbidities should be identified and managed appropriately to minimize the risk of further pulmonary vascular disease progression. Follow-up should include clinical evaluation, WHO functional class, 6-minute walk distance, NT-proBNP, echocardiography, and repeat right heart catheterization when clinically indicated. Initiation of PAH-specific therapy should be considered only if progression to established PAH or other evidence-based indications develop.

PULMONARY ARTERIAL HYPERTENSION SUBGROUPS

Congenital Heart Disease–Associated Pulmonary Arterial Hypertension

Congenital heart disease–associated PAH is classified into 4 subgroups: 1) Eisenmenger syndrome, 2) PAH associated with persistent systemic-to-pulmonary shunts, 3) PAH with small or coincidental defects, and 4) PAH associated with repaired defects. Patients in the latter 2 groups are generally managed similarly to those with IPAH.

Patients with Eisenmenger syndrome and those with persistent systemic-to-pulmonary shunts should be evaluated in specialized centers by a multidisciplinary congenital heart disease team, given their complex pathophysiology and limited evidence base. A comprehensive evaluation, including assessment of operability/defect closure and PAH specific treatment strategy, should be performed. These patients often demonstrate longer survival than those with IPAH.⁴⁶

Defect closure is not indicated and is considered harmful in patients with Eisenmenger syndrome and in those with PAH and small defects. In patients with persistent systemic-to-pulmonary shunts, the indication for closure requires careful evaluation. Pulmonary vascular resistance is a key determinant: values ≥ 5 WU indicate that closure is harmful, whereas values < 3 WU are associated with a low-risk profile; values between 3 and 5 WU represent a gray zone requiring individualized assessment.⁴⁷ However, decisions should not rely solely on PVR and must incorporate a comprehensive evaluation of shunt physiology, RV function, left ventricular diastolic function, exercise-induced desaturation, and the anticipated long-term consequences of defect closure. In patients initially deemed inoperable, defect closure may become feasible following PAH-specific therapy if a significant reduction in PVR is achieved; however, evidence supporting the long-term benefit of this approach remains limited.

Pulmonary arterial hypertension–specific therapy should be initiated in a stepwise manner. In Eisenmenger syndrome, bosentan has the strongest evidence and a Class I, Level B recommendation for improving exercise capacity. Other agents from the main therapeutic classes (ERAs, phosphodiesterase type 5 inhibitors, sGCs, and prostacyclin analogues) may be used in both Eisenmenger syndrome and PAH associated with persistent systemic-to-pulmonary

shunts, based on individual patient characteristics and tolerability.

In patients who develop high-risk features, PAH therapy should be escalated with add-on treatment, including parenteral prostacyclins. Subcutaneous prostacyclins may be preferred in patients with Eisenmenger syndrome and systemic-to-pulmonary shunts, as they avoid the risk of catheter-related infective endocarditis associated with intravenous therapy.

Risk assessment in this population is challenging, particularly in Eisenmenger syndrome. Evaluation should include clinical (WHO functional class, 6-minute walk distance, resting SpO₂, signs of heart failure), laboratory (BNP), and imaging parameters (e.g., pericardial effusion). In cases of discordant findings, hemodynamic variables (right atrial pressure, cardiac index, PVR index, and response to VRT) provide additional prognostic information. High-risk features such as resting SpO₂ <85%, WHO functional class III-IV, recurrent hospitalizations, 6-minute walk distance <400 m, arrhythmias, rising BNP (>200 pg/mL), renal dysfunction, hypoalbuminemia, and adverse right heart findings (TAPSE < 15 mm, RA area > 25 cm², RA pressure > 8 mmHg, CI < 2.5 L/min/m², pericardial effusion) should prompt closer follow-up and early treatment escalation.⁴⁸

In patients with Eisenmenger syndrome, supplemental oxygen therapy may be considered after assessing its effect on arterial oxygen saturation; it should be used in patients in whom oxygen administration results in a consistent increase in saturation and improvement in symptoms.

Elevated hemoglobin levels due to secondary erythrocytosis are a common laboratory finding in patients with Eisenmenger syndrome. In the absence of moderate to severe hyperviscosity symptoms, phlebotomy should be avoided.

Connective Tissue Disease–Associated Pulmonary Arterial Hypertension

Pulmonary arterial hypertension is one of the most severe complications of CTDs and remains a major cause of morbidity and mortality. As early disease may be asymptomatic, routine screening is essential for timely diagnosis, particularly in SSc.

Echocardiography remains the cornerstone of screening in SSc. Multimodal screening algorithms such as ESC/ERS, DETECT, and Australian Scleroderma Interest Group (ASIG) combine clinical variables, PFTs, biomarkers, and echocardiographic parameters to improve early detection. However, when the updated 2022 ESC/ERS hemodynamic definitions are used, their sensitivity may be reduced, and none achieves perfect diagnostic accuracy.⁴⁹ In addition, their performance may be limited in patients with coexisting interstitial lung disease or left heart disease, which are common in SSc.⁵⁰

A recent multidisciplinary Turkish consensus statement recommends that screening strategies be tailored to patient characteristics and local resources, with annual echocardiographic evaluation prioritized in patients with SSc or SSc

overlap features.⁵¹ In line with these recommendations, the present consensus proposes a simplified algorithm for PAH screening in SSc (Figure 3). Evidence supporting routine screening of other CTD patients, such as SLE, mixed connective tissue disease remains limited, particularly in asymptomatic patients. For other CTD patients with symptoms, the proposed diagnostic algorithm in this document (Figure 1) should apply.

Connective tissue diseases are a multisystem disorder in which multiple mechanisms—including left heart disease, interstitial lung disease, chronic thromboembolic disease, and PVOD—may contribute to PH, either alone or in combination. Accurate identification of the underlying PH subtype is therefore essential, as treatment strategies differ substantially and PAH-specific therapies may be ineffective or potentially harmful in non-PAH forms of PH.

Regarding the management of patients with CTD-PAH, treatment recommendations are generally similar to those in IPAH.^{1,25,52} However, disease-specific features should be considered when selecting therapy. For example, in patients with SSc, the presence of digital ulcers may influence treatment choice, as PDE5i and bosentan are frequently used for both PAH and peripheral vascular manifestations.^{1,13,53,54}

In clinical practice, many patients with SSc-PAH are already receiving ERA and/or PDE5i therapy due to peripheral vascular manifestations at the time of diagnosis. Therefore, treatment strategies often involve sequential escalation, rather than upfront combination therapy, by adding additional PAH-targeted agents to existing treatment.

Altered immune responses and chronic inflammation contribute to the pathogenesis of PAH in CTDs. In patients with PAH associated with SLE or mixed connective tissue disease, immunosuppressive therapy—particularly cyclophosphamide-based regimens initiated early and combined with PAH-specific vasodilator therapy—may substantially improve or even reverse PAH and represents an important component of management in expert centers.⁵⁵⁻⁵⁸ In contrast, in patients with SSc-associated PAH, the evidence supporting immunosuppressive therapy is limited and inconsistent.^{13,59-61} Although some immunosuppressive regimens have shown potential benefit, current data do not support immunosuppression as a standard effective treatment for SSc-PAH. Standard care remains aggressive PAH-targeted therapy; immunosuppression should be considered on an individualized basis and preferably guided by a specialized PH/SSc team.

Drug and Toxin–Associated Pulmonary Arterial Hypertension

In patients with DT-PAH, exposure to the causative drug or toxin should be promptly discontinued and avoided. Clinical outcomes may vary depending on the specific agent responsible for PAH, and partial or complete reversal of PAH has been reported following discontinuation of certain drugs or toxins, such as dasatinib, interferon, carfilzomib.⁶²⁻⁶⁴

Accordingly, in patients exposed to these agents who present with low-risk features, withdrawal of the causative drug

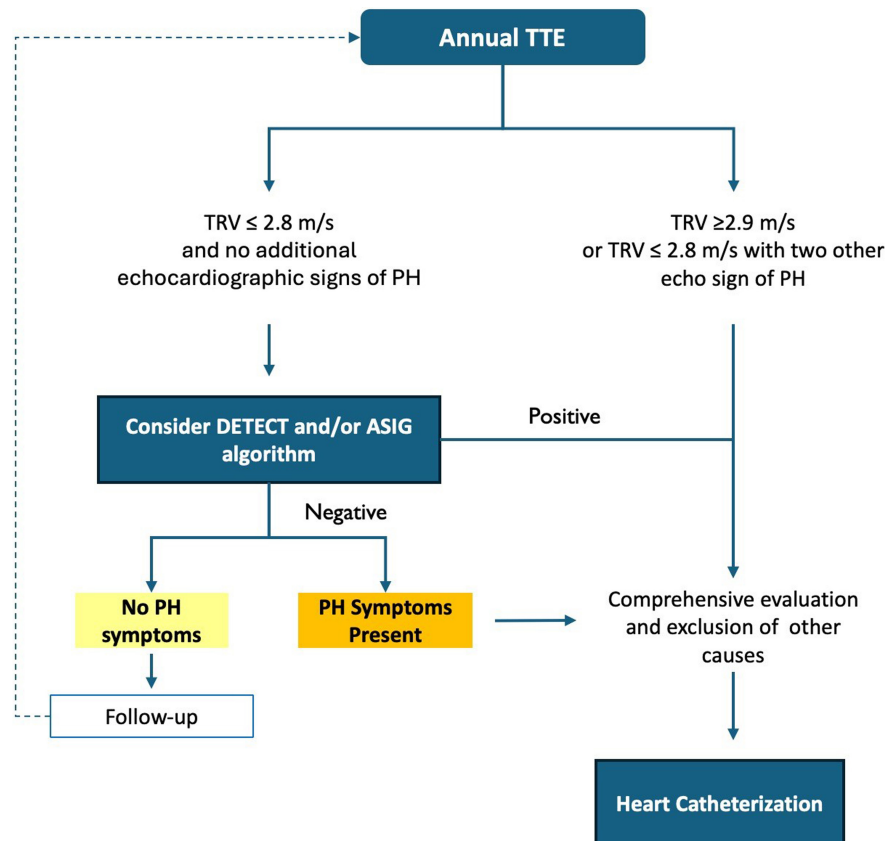


Figure 3. PAH screening algorithm in systemic sclerosis. PH, Pulmonary hypertension; TRV, Tricuspid regurgitation velocity; TTE, transthoracic echocardiography.

alone may be considered with close monitoring. If no appropriate clinical and hemodynamic improvement is observed, PAH-specific therapy should be started based on risk stratification. In patients with intermediate or high-risk presentation, the standard treatment algorithm should be followed. At follow-up, if sustained hemodynamic normalization is documented, cautious de-escalation or discontinuation of PAH therapy may be considered.

Portopulmonary Hypertension

Although patients with PoPH are underrepresented in major PAH clinical trials, treatment strategies are generally similar to those for IPAH. Macitentan and riociguat have been studied in POPH in prospective registries and showed benefit. In patients with advanced liver disease, caution is required because of impaired drug metabolism. Liver transplantation can improve or sometimes normalize PoPH; however, many patients are not eligible for transplantation. Recommended hemodynamic targets prior to consideration of transplantation include a mPAP < 35 mmHg and a PVR < 5 WU, or a mPAP 35–45 mmHg with a PVR < 3 WU.^{65,66} Following liver transplantation, hemodynamics should be carefully reassessed, and PAH-specific therapy should be continued or adjusted as clinically indicated.

HIV-Associated PAH

The HIV-PAH is very rare in Türkiye. The treatment algorithm is similar to that for IPAH. However, careful attention to potential drug–drug interactions between antiretroviral

therapy and PAH-specific medications is essential, particularly with PDE5i, and such interactions should be carefully reviewed before and during treatment.

Schistosomiasis–Associated Pulmonary Arterial Hypertension

Schistosomiasis-associated PAH has not been systematically reported in Türkiye. However, treatment principles for PAH are similar in these patients. In addition to PAH-specific therapy, antihelminthic treatment should also be considered.

Pulmonary Veno-Occlusive Disease and Pulmonary Capillary Hemangiomatosis

The PVOD and PCH are rare forms of PAH within the same disease spectrum, characterized by predominant involvement of small pulmonary veins and capillaries. Early recognition is essential, as management differs from other PAH subtypes and inappropriate therapy may lead to clinical deterioration; moreover, prognosis is worse compared with other forms of PAH in the absence of lung transplantation.⁶⁷

The PVOD/PCH should be suspected in patients with PH presenting with severe hypoxemia, markedly reduced DLCO, and characteristic imaging findings. A history of exposure to organic solvents or chemotherapeutic agents, particularly alkylating agents such as mitomycin, should raise suspicion.⁶⁸ High-resolution CT typically demonstrates a triad of centrilobular ground-glass opacities, interlobular septal thickening, and mediastinal lymphadenopathy. Although

these findings are not specific and may be seen in conditions such as pulmonary edema or infection, their presence especially in combination supports the diagnosis. Parenchymal changes can be present even before the development of PH. The development of pulmonary edema following the initiation of any PAH-targeted therapy is strongly suggestive.

Diagnosis should be based on clinical, radiological, and hemodynamic findings. Right heart catheterization typically shows a precapillary PH profile and is not distinguishable from other forms of PAH. Genetic testing (e.g., *EIF2AK4* mutations) may support the diagnosis. Lung biopsy is not recommended due to the high risk of complications.

Management should be undertaken in expert centers. PAH-specific therapies should be used with caution, preferably initiated at low doses with close monitoring due to the risk of pulmonary edema. Supportive therapy, including oxygen supplementation in hypoxemic patients and diuretics to manage RV overload and prevent fluid retention, is recommended. Early referral for lung transplantation evaluation should be considered, as this remains the only definitive treatment.

CONCLUSION

Pulmonary arterial hypertension remains a life-threatening and complex disease that requires early recognition and coordinated multidisciplinary care. This consensus, developed in the context of real-world clinical practice in Türkiye, provides a pragmatic framework by integrating evidence-based recommendations with local experience and resource considerations. The proposed diagnostic and treatment algorithms, together with standardized echocardiographic and hemodynamic parameters, aim to harmonize clinical practice, support consistent decision-making, and improve data quality across centers. Timely diagnosis, regular risk-based follow-up, and appropriate treatment escalation—ideally within expert PH centers—are essential to improving outcomes. This effort represents an important step toward more standardized, accessible, and data-driven PAH care in Türkiye.

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REFERENCES

- Humbert M, Kovacs G, Hoeper MM, et al. 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Heart J*. 2022;43(38):3618-3731. [\[CrossRef\]](#)
- Kovacs G, Bartolome S, Denton CP, et al. Definition, classification and diagnosis of pulmonary hypertension. *Eur Respir J*. 2024;64(4):2401324. [\[CrossRef\]](#)
- Hoeper MM, Humbert M, Souza R, et al. A global view of pulmonary hypertension. *Lancet Respir Med*. 2016;4(4):306-322. [\[CrossRef\]](#)
- Leber L, Beaudet A, Muller A. Epidemiology of pulmonary arterial hypertension and chronic thromboembolic pulmonary hypertension: identification of the most accurate estimates from a systematic literature review. *Pulm Circ*. 2021;11(1):2045894020977300. [\[CrossRef\]](#)
- Kaymaz C, Mutlu B, Küçüköğlu MS, et al. Preliminary results from a nationwide adult cardiology perspective for pulmonary hypertension: RegiStry on clinical outcome and survival in pulmonary hypertension Groups (SIMURG). *Anatol J Cardiol*. Published online 2017;18(4):242-250. [\[CrossRef\]](#)
- Akbulut M, Akdeniz B, Kaplan M, et al. Pulmonary hypertension registry in Turkey (TURKPAH). In: *Anatol J Cardiol*. 2025:S49-S50. [\[CrossRef\]](#)
- Küçüköğlu SM, Kaymaz C, Alehan D, et al. Pulmonary arterial hypertension associated with congenital heart disease: lessons learnt from the large Turkish Nationwide Registry (Thales). *Pulm Circ*. 2021;11(3):20458940211024206. [\[CrossRef\]](#)
- Condliffe R, Kiely DG, Peacock AJ, et al. Connective tissue disease-associated pulmonary arterial hypertension in the modern treatment era. *Am J Respir Crit Care Med*. 2009;179(2):151-157. [\[CrossRef\]](#)
- Hendriks PM, Staal DP, van de Groep LD, et al. The evolution of survival of pulmonary arterial hypertension over 15 years. *Pulm Circ*. 2022;12(4):e12137. [\[CrossRef\]](#)
- Benza RL, Miller DP, Barst RJ, Badesch DB, Frost AE, McGoon MD. An evaluation of long-term survival from time of diagnosis in pulmonary arterial hypertension from the REVEAL registry. *Chest*. 2012;142(2):448-456. [\[CrossRef\]](#)
- Khanna D, Zhao C, Saggart R, et al. Long-term outcomes in patients with connective tissue disease-associated pulmonary

- arterial hypertension in the modern treatment era: meta-analyses of randomized, controlled trials and observational registries. *Arthritis Rheumatol*. 2021;73(5):837-847. [CrossRef]
12. Basarici I, Kaymaz C, Akbulut M, et al. Multiparametric risk predictions for morbidity and mortality in patients with pulmonary arterial hypertension: insights from a nation-wide registry. *Eur Heart J*. 2024;45(suppl 1). [CrossRef]
 13. Sarı A, Satış H, Ayan G, et al. Survival in systemic sclerosis associated pulmonary arterial hypertension in the current treatment era-results from a nationwide study. *Clin Rheumatol*. 2024;43(6):1919-1925. [CrossRef]
 14. Mukherjee M, Rudski LG, Addetia K, et al. Guidelines for the echocardiographic assessment of the right heart in adults and special considerations in pulmonary hypertension: recommendations from the American Society of Echocardiography. *J Am Soc Echocardiogr*. 2025;38(3):141-186. [CrossRef]
 15. Kovacs G, Avian A, Olschewski A, Olschewski H. Zero reference level for right heart catheterisation. *Eur Respir J*. 2013;42(6):1586-1594. [CrossRef]
 16. Sitbon O, Humbert M, Jaïs X, et al. Long-term response to calcium channel blockers in idiopathic pulmonary arterial hypertension. *Circulation*. 2005;111(23):3105-3111. [CrossRef]
 17. Rich S, Brundage BH, Levy PS. The effect of vasodilator therapy on the clinical outcome of patients with primary pulmonary hypertension. *Circulation*. 1985;71(6):1191-1196. [CrossRef]
 18. Rich S, Kaufmann E, Levy PS. The effect of high doses of calcium-channel blockers on survival in primary pulmonary hypertension. *N Engl J Med*. 1992;327(2):76-81. [CrossRef]
 19. van de Bovenkamp AA, Wijkstra N, Oosterveer FPT, et al. The value of passive leg raise during right heart catheterization in diagnosing heart failure with preserved ejection fraction. *Circ Heart Fail*. 2022;15(4):e008935. [CrossRef]
 20. Meriç M, Çağlıyan ÇE, Eker Akıllı R, et al. Altı dakika yürüme testi: Pulmoner Hipertansiyonlu Hastalarda güvenilir bir testi nasıl yapalım, Yorumlayalım ve Prognoz Tayininde kullanalım? *Türk Kardiyol Dern Ars*. 2023;51(7):516-520. [CrossRef]
 21. Demir R, Küçüköğlu MS. Six-minute walk test in pulmonary arterial hypertension. *Anatol J Cardiol*. 2015;15(3):249-254. [CrossRef]
 22. Benza RL, Gomberg-Maitland M, Elliott CG, et al. Predicting survival in patients with pulmonary arterial hypertension: the REVEAL risk score Calculator 2.0 and comparison with ESC/ERS-based risk assessment strategies. *Chest*. 2019;156(2):323-337. [CrossRef]
 23. Howard LS, GE, He J, Watson GMJ, et al. Supplementation with iron in pulmonary arterial hypertension. Two randomized crossover trials. *Ann Am Thorac Soc*. 2021;18(6):981-988. [CrossRef]
 24. Quatredeniens M, Mendes-Ferreira P, Santos-Ribeiro D, et al. Iron deficiency in pulmonary arterial hypertension: a deep dive into the mechanisms. *Cells*. 2021;10(2):477. [CrossRef]
 25. Chin KM, Gaine SP, Gerges C, et al. Treatment algorithm for pulmonary arterial hypertension. *Eur Respir J*. 2024;64(4):2401325. [CrossRef]
 26. Hoeper MM, Badesch DB, Ghofrani HA, et al. Phase 3 trial of sotatercept for treatment of pulmonary arterial hypertension. *N Engl J Med*. 2023;388(16):1478-1490. [CrossRef]
 27. Humbert M, McLaughlin V, Gibbs JSR, et al. Sotatercept for the treatment of pulmonary arterial hypertension. *N Engl J Med*. 2021;384(13):1204-1215. [CrossRef]
 28. Humbert M, McLaughlin V, Gibbs JSR, et al. Sotatercept for the treatment of pulmonary arterial hypertension: Pulsar open-label extension. *Eur Respir J*. 2023;61(1):2201347. [CrossRef]
 29. Souza R, Badesch DB, Ghofrani HA, et al. Effects of sotatercept on haemodynamics and right heart function: analysis of the STELLAR trial. *Eur Respir J*. 2023;62(3):2301107. [CrossRef]
 30. Hoeper MM, Gomberg-Maitland M, Badesch DB, et al. Efficacy and safety of the activin signalling inhibitor, sotatercept, in a pooled analysis of Pulsar and STELLAR studies. *Eur Respir J*. 2025;65(5):2401424. [CrossRef]
 31. Humbert M, McLaughlin VV, Badesch DB, et al. Sotatercept in patients with pulmonary arterial hypertension at high risk for death. *N Engl J Med*. 2025;392(20):1987-2000. [CrossRef]
 32. Shalabi L, Tabassum S, Al Zoubi BM, Taha HI, Gowaily I, Abuelazm M. Efficacy and safety of sotatercept in pulmonary arterial hypertension: a systematic review and meta-analysis of randomized controlled trials with trial sequential analysis. *Nauyn Schmiedebergs Arch Pharmacol*. 2025;398(12):16767-16778. [CrossRef]
 33. Manasrah A, Shehada W, Saad Rakab M, et al. Sotatercept for pulmonary arterial hypertension on background therapy: a systematic review and meta-analysis of randomized controlled trials. *Proc (Bayl Univ Med Cent)*. 2025;38(6):893-906. [CrossRef]
 34. Ershed M, da Silva ABN, Felix de Farias dos Santos AC, Heo D, Cavalcante DVS, Aljazeera J. Efficacy and safety of sotatercept in pulmonary arterial hypertension: a meta-analysis of randomized controlled trials. *Expert Rev Respir Med*. 2025;19(12):1273-1281. [CrossRef]
 35. Preston IR, Badesch D, Ghofrani HA, et al. A long-term follow-up study of sotatercept for treatment of pulmonary arterial hypertension: interim results of SOTERIA. *Eur Respir J*. 2025;66(1):2401435. [CrossRef]
 36. Galiè N, Barberà JA, Frost AE, et al. Initial use of ambrisentan plus tadalafil in pulmonary arterial hypertension. *N Engl J Med*. 2015;373(9):834-844. [CrossRef]
 37. Grünig E, Jansa P, Fan F, et al. Randomized trial of Macitentan/Tadalafil single-tablet combination therapy for pulmonary arterial hypertension. *J Am Coll Cardiol*. 2024;83(4):473-484. [CrossRef]
 38. Galiè N, Saia F, Palazzini M, et al. Left main coronary artery compression in patients with pulmonary arterial hypertension and angina. *J Am Coll Cardiol*. 2017;69(23):2808-2817. [CrossRef]
 39. Badea R, Dorobantu DM, Sharabiani MTA, Predescu LM, Coman IM, Ginghina C. Left main coronary artery compression by dilated pulmonary artery in pulmonary arterial hypertension: a systematic review and meta-analysis. *Clin Res Cardiol*. 2022;111(7):816-826. [CrossRef]
 40. Gülhan D, Çimci M, Durmaz EŞ, Kılıçkiran Avcı B. Heart of the matter: From hemoptysis and left arm pain to diagnosis, importance of imaging. *Cerrahpaşa Medical Journal. Heart of the Matter*. 2024;48(3):309-310. [CrossRef]
 41. Giannakoulas G, Farmakis IT, Hobohm L, Verbrugge FH, Tedford RJ, Sanz J. Acute right ventricular failure: pathophysiology, aetiology, assessment, and management. *Eur Heart J*. 2025;46(26):2520-2535. [CrossRef]
 42. Sitbon O, Channick R, Chin KM, et al. Selexipag for the treatment of pulmonary arterial hypertension. *N Engl J Med*. 2015;373(26):2522-2533. [CrossRef]
 43. Hoeper MM, Al-Hiti H, Benza RL, et al. Switching to Riociguat versus maintenance therapy with phosphodiesterase-5 inhibitors in patients with pulmonary arterial hypertension (REPLACE): a multicentre, open-label, randomised controlled trial. *Lancet Respir Med*. 2021;9(6):573-584. [CrossRef]
 44. Hoeper MM, Simonneau G, Corris PA, et al. RESPITE: switching to Riociguat in pulmonary arterial hypertension patients with inadequate response to phosphodiesterase-5 inhibitors. *Eur Respir J*. 2017;50(3):1602425. [CrossRef]
 45. Benza RL, Simonneau G, Ghofrani HA, et al. Application of REVEAL Lite 2 and COMPERA 2.0 risk scores to patients with

- pulmonary arterial hypertension switching to Riociguat in the REPLACE study. *J Heart Lung Transplant*. 2024;43(10):1756-1760. [\[CrossRef\]](#)
46. Diller GP, Körten MA, Bauer UMM, et al. Current therapy and outcome of Eisenmenger syndrome: data of the German National Register for congenital heart defects. *Eur Heart J*. 2016;37(18):1449-1455. [\[CrossRef\]](#)
 47. Baumgartner H, De Backer J, Babu-Narayan SV, et al. 2020 ESC Guidelines for the management of adult congenital heart disease. *Eur Heart J*. 2021;42(6):563-645. [\[CrossRef\]](#)
 48. D'Alto M, Giannakoulas G, Aboulhosn J, et al. Risk stratification for adult patients with pulmonary arterial hypertension associated with congenital heart disease. A scientific statement of the ESC Working Group on Pulmonary Circulation & Right Ventricular Function, the ESC Working Group on Adult Congenital Heart Disease, and the Association of Cardiovascular Nursing & Allied Professions of the ESC. *Eur J Heart Fail*. Published online March 9, 2026:xuag059. [\[CrossRef\]](#)
 49. Erdogan M, Kilickiran Avcı B, Ebrén C, et al. Screening for pulmonary arterial hypertension in patients with systemic sclerosis in the era of new pulmonary arterial hypertension definitions. *Clin Exp Rheumatol*. Published online 2024;42(8):1590-1597. [\[CrossRef\]](#)
 50. Erdoğan MHG. Screening methods for pulmonary hypertension in systemic sclerosis [Pulmoner hipertansiyonun bağ dokusu hastalıklarında taranması]. *PAH Bulteni*. Published online 2023.
 51. Sarı A, Temiz Karadağ D, Erdoğan M, et al. Screening for pulmonary hypertension in connective tissue diseases: literature review and multidisciplinary consensus statement. *Anatol J Cardiol*. Published online 2025;29(11):599-607. [\[CrossRef\]](#)
 52. Erdogan M, Esatoglu SN, Kilickiran Avcı B, Hatemi G. Treatment of pulmonary arterial hypertension in patients with connective tissue diseases: a systematic review and meta-analysis. *Intern Emerg Med*. 2024;19(3):731-743. [\[CrossRef\]](#)
 53. Del Galdo F, Lescoat A, Conaghan PG, et al. EULAR recommendations for the treatment of systemic sclerosis: 2023 update. *Ann Rheum Dis*. 2025;84(1):29-40. [\[CrossRef\]](#)
 54. Temiz Karadağ D, Yalcinkaya Y, Akdoğan A, et al. Treatment of systemic sclerosis-associated digital ulcers: recommendations of the Turkish Society for Rheumatology. *Clin Exp Rheumatol*. Published online February 21, 2023;41(8):1679-1687. [\[CrossRef\]](#)
 55. Sanchez O, Sitbon O, Jaïs X, Simonneau G, Humbert M. Immunosuppressive therapy in connective tissue diseases-associated pulmonary arterial hypertension. *Chest*. 2006;130(1):182-189. [\[CrossRef\]](#)
 56. Ding Y, Qian J, Zhang S, et al. Immunosuppressive therapy in patients with connective tissue disease-associated pulmonary arterial hypertension: a systematic review. *Int J Rheum Dis*. 2022;25(9):982-990. [\[CrossRef\]](#)
 57. Luppino-Assad AP, Alves Junior JL, Figueiredo Neves Yuki E, et al. Reversibility of pulmonary hypertension in systemic lupus erythematosus after induction immunosuppressive therapy: an inflammatory manifestation? *Lupus*. 2025;34(1):18-27. [\[CrossRef\]](#)
 58. Tamura Y, Tamura Y, Takemura R, et al. Immunosuppressive therapy for pulmonary arterial hypertension associated with connective tissue diseases: insights from Japanese registry. *Adv Ther*. 2025;42(12):6103-6117. [\[CrossRef\]](#)
 59. Zamanian RT, Badesch D, Chung L, et al. Safety and efficacy of B-cell depletion with rituximab for the treatment of systemic sclerosis-associated pulmonary arterial hypertension: a multicenter, double-blind, randomized, placebo-controlled trial. *Am J Respir Crit Care Med*. 2021;204(2):209-221. [\[CrossRef\]](#)
 60. Rodolfi S, Ng CCM, Ruiz Bejerano AM, Kanitkar M, Ong VH, Denton CP. Impact of immunosuppression on development and outcome of systemic sclerosis-associated pulmonary arterial hypertension. *Clin Exp Rheumatol*. Published online August 1, 2025;43(8):1492-1498. [\[CrossRef\]](#)
 61. Rodolfi S, Ong VH, Denton CP. OA42 Impact of immunosuppression on development and outcome of systemic sclerosis-associated pulmonary arterial hypertension. *Rheumatology*. 2025;64(suppl 3). [\[CrossRef\]](#)
 62. Weatherald J, Chaumais MC, Savale L, et al. Long-term outcomes of dasatinib-induced pulmonary arterial hypertension: a population-based study. *Eur Respir J*. 2017;50(1):1700217. [\[CrossRef\]](#)
 63. Savale L, Chaumais MC, O'Connell C, Humbert M, Sitbon O. Interferon-induced pulmonary hypertension: an update. *Curr Opin Pulm Med*. 2016;22(5):415-420. [\[CrossRef\]](#)
 64. Yang JZ, Buckstaff T, Narezkina A, Fernandes TM. Carfilzomib-associated pulmonary arterial hypertension in multiple myeloma. *Pulm Circ*. 2021;11(4):20458940211049300. [\[CrossRef\]](#)
 65. Jose A, Koprass EJ, Shah SA, Elwing JM. Portopulmonary hypertension practice patterns after liver transplantation. *Liver Transpl*. 2023;29(4):365-376. [\[CrossRef\]](#)
 66. Tamura Y, Tamura Y, Taniguchi Y, et al. Clinical management and outcomes of patients with portopulmonary hypertension enrolled in the Japanese multicenter registry. *Circ Rep*. 2022;4(11):542-549. [\[CrossRef\]](#)
 67. Montani D, Achouh L, Dorfmueller P, et al. Pulmonary veno-occlusive disease: clinical, functional, radiologic, and hemodynamic characteristics and outcome of 24 cases confirmed by histology. *Medicine*. 2008;87(4):220-233. [\[CrossRef\]](#)
 68. Lechartier B, Boucly A, Solinas S, et al. Pulmonary veno-occlusive disease: illustrative cases and literature review. *Eur Respir Rev*. 2024;33(171):230156. [\[CrossRef\]](#)