



Pulmonary Hypertension: A Brief Guide for Clinicians

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Learning Objectives: On completion of this article, you should be able to (1) identify cases of suspected pulmonary hypertension (PH) and apply the appropriate diagnostic tests to confirm the diagnosis, (2) choose appropriate supportive and targeted therapies for patients with PH, and (3) recognize when referral to an expert center is necessary for further assessment and management of PH.

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Dr Mandras has received consulting fees and payment for lectures/service on speakers bureaus for Bayer AG, Berlin, Germany, and United Therapeutics Corporation. Dr Mehta has received speaker fees from Actelion Pharmaceuticals Ltd, Switzerland and Bayer AG, Berlin, Germany, consulting fees from Bayer AG, Berlin, Germany, and research support from Actelion Pharmaceuticals Ltd, Switzerland related to this work. Dr Vaidya has received speaker and consulting fees from Actelion Pharmaceuticals Ltd, Switzerland, Bayer AG Berlin, Germany, Liquidia Technologies, NC, USA, and United Therapeutics Corporation.

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Abstract

Pulmonary hypertension (PH) is classified into 5 clinical subgroups: pulmonary arterial hypertension (PAH), PH due to left-sided heart disease, PH due to chronic lung disease, chronic thromboembolic PH (CTEPH), and PH with an unclear and/or multifactorial mechanisms. A range of underlying conditions can lead to these disorders. Overall, PH affects approximately 1% of the global population, and over half of patients with heart failure may be affected. Cardiologists are therefore likely to encounter PH in their practice. Routine tests in patients with symptoms and physical findings suggestive of PH include electrocardiography, chest radiography, and pulmonary function tests. Transthoracic echocardiography is used to estimate the probability of PH. All patients with suspected or confirmed PH, without confirmed left-sided heart or lung diseases, should have a ventilation-perfusion scan to exclude CTEPH. Right-sided heart catheterization is essential for accurate diagnosis and classification. All patients with PAH or CTEPH must be referred to a specialist center. Surgical

pulmonary endarterectomy is the treatment of choice for eligible patients with CTEPH. Targeted treatments (phosphodiesterase type 5 inhibitors, soluble guanylate cyclase stimulators, endothelin receptor antagonists, prostacyclin analogues, and prostacyclin receptor agonists) are licensed for patients with PAH. The soluble guanylate cyclase stimulator riociguat is the only licensed targeted therapy for patients with inoperable or persistent/recurrent CTEPH. Management of PH resulting from left-sided heart disease primarily involves treatment of the underlying condition.

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Pulmonary hypertension (PH) is defined as a mean pulmonary arterial pressure (mPAP) of 20 mm Hg or greater at rest,¹ confirmed by right-sided heart catheterization. While there are many causes of PH, it is almost always associated with deteriorating symptoms and increased mortality, regardless of the underlying disease.² Pulmonary hypertension affects approximately 1% of the global population, up to 10% of individuals older than 65 years, and at least 50% of patients with heart failure (HF).² Cardiologists can therefore expect to encounter PH in their clinical practice. This article provides an overview of the diagnosis and management of PH.

CLASSIFICATION AND HEMODYNAMIC DEFINITIONS OF PH

The World Health Organization has classified PH into 5 clinical subgroups.^{1,3} Pulmonary arterial hypertension (PAH) (group 1) is characterized by loss and obstructive remodeling of the pulmonary vascular bed. Pulmonary arterial hypertension features precapillary PH, defined as an mPAP of 20 mm Hg or greater, pulmonary artery wedge pressure (PAWP) of 15 mm Hg or less, and pulmonary vascular resistance (PVR) of 3 Wood units (WU) or greater.¹ The chronic elevation of PVR can result in progressive right ventricular (RV) dysfunction and RV failure (RVF).⁴ In the presence of RVF, right atrial pressure may increase and cardiac index may decrease. Pulmonary arterial hypertension is divided into 7 subgroups: idiopathic PAH (group 1.1), heritable PAH (group 1.2), drug- and toxin-induced PAH (group 1.3), PAH associated with various conditions including

connective tissue diseases, HIV infection, portal hypertension, and congenital heart disease (group 1.4), PAH in long-term responders to calcium channel blockers (group 1.5), PAH with venous/capillary involvement (group 1.6), and persistent PH of the newborn (group 1.7).¹ Drugs definitely associated with PAH include aminorex, fenfluramine, dexfenfluramine, benfluorex, methamphetamines, dasatanib, and toxic rapeseed oil.^{1,3} Drugs possibly associated include cocaine, phenylpropranolamine, L-tryptophan, St John's wort, amphetamines, interferon- α and interferon- β , alkylating agents, bosutinib, direct-acting antiviral agents against hepatitis C, leflunomide, and indirubin.¹ There is an increased risk of persistent PH in newborns of mothers receiving selective serotonin reuptake inhibitors.³

Pulmonary hypertension due to left-sided heart disease (LHD) (PH-LHD) (group 2) occurs in response to an increase in left atrial (LA) pressure and is usually a consequence of an underlying cardiac disorder such as HF (with preserved or reduced ejection fraction) or valvular heart disease.⁵ Patients with PH-LHD usually have isolated postcapillary PH (PAWP >15 mm Hg and PVR <3 WU [$\approx 240 \text{ dyn}\cdot\text{s}\cdot\text{cm}^{-5}$]), although some have combined postcapillary and precapillary PH (PAWP >15 mm Hg and PVR ≥ 3 WU).¹

Pulmonary hypertension due to chronic lung disease (CLD) (PH-CLD) and/or hypoxia (group 3) can occur in many lung diseases including chronic obstructive pulmonary disease (COPD), interstitial lung disease, and sleep-disordered breathing. Elevation of mPAP in COPD may result from loss of lung vasculature, vascular

distensibility, and reduced vessel recruitment.⁶ These patients have precapillary PH.¹

Chronic thromboembolic PH (CTEPH) (group 4) is characterized by obstruction of the pulmonary vasculature by organized thromboembolic material and vascular remodeling, resulting from prior pulmonary embolism.⁷ Chronic thromboembolic PH is likely underdiagnosed, and its incidence and prevalence have not recently been established.⁷ Estimates based on older data are probably too low, as awareness has increased in recent years.

Patients with unclear and/or multifactorial mechanisms are listed as group 5.¹ Group 5 is divided into PH associated with hematologic disorders (group 5.1: chronic hemolytic anemia, myeloproliferative disorders), systemic and metabolic disorders (group 5.2: glycogen storage disease, Gaucher disease, sarcoidosis, pulmonary Langerhans cell histiocytosis, lymphangioleiomyomatosis, and neurofibromatosis).¹ Pulmonary hypertension associated with fibrosing mediastinitis or chronic renal failure forms group 5.3, and PH associated with complex congenital heart disease is group 5.4.

PROGNOSIS OF PATIENTS WITH PH

Pulmonary hypertension is a life-threatening condition associated with increased mortality regardless of the classification and underlying etiology.² Pulmonary arterial hypertension registries report survival rates of between 68% and 93% at 1 year and 39% and 77% at 3 years.² Based on registry data, parameters that predict survival have been identified (Table).^{3,8-12} These parameters include exercise capacity, functional class, hemodynamic values, findings on imaging of the right side of the heart, and laboratory values. Because no single variable provides sufficient prognostic information, various clinical, functional, exercise, noninvasive, and invasive parameters have been combined to produce risk scores that predict survival and classify patients into low-, intermediate-, and high-risk groups (Table).^{3,8-12} These parameters include the REVEAL (Registry to Evaluate Early and Long-term PAH Disease Management) 2.0 risk score, based on data from

REVEAL, the largest US PH registry.¹² The survival rates of patients across the risk groups differ substantially between scores.¹¹

The 12-month mortality for patients with PH-LHD may be as high as 32%.¹³ Predictors of worse prognosis include renal dysfunction, anemia, older age, RV dysfunction, and the presence of combined postcapillary and precapillary PH rather than isolated postcapillary PH.^{13,14}

A cohort study in patients with PH-CLD reported 1-, 3-, and 5-year survival rates of 79%, 48%, and 31%, respectively.¹⁵ Patients with more severe lung disease and severe PH have a poor prognosis.⁶

In an international CTEPH registry, 3-year survival was 90% in patients who underwent pulmonary thromboendarterectomy (PTE) and 70% in those who did not.⁷ In patients with LHD (group 2) or CLD (group 3), the presence of PH greatly reduced survival.²

PATHOLOGY OF RV DYSFUNCTION IN PH

In patients with PH, particularly those with PAH, RV dilatation, RV dysfunction, and RVF can result from elevated PVR, which increases RV wall stress.¹⁶ When the pressure load increases slowly, the RV can adapt by increasing wall thickness and contractility. The RV thus remodels from a low-pressure to a high-pressure pump, maintaining RV output.¹⁶ The RV cannot remodel indefinitely, however, and when the elevated PVR persists, the RV will dilate in an attempt to maintain stroke volume.¹⁶ Ultimately, the RV becomes decoupled from the pressure load, and RVF develops.¹⁶ In other types of PH, cardiomyopathy, diastolic dysfunction, elevated right-sided filling pressures, myocardial fibrosis, and septal wall abnormalities can lead to RV dysfunction without elevated PVR.¹⁷⁻¹⁹

CLINICAL PRESENTATION

Common symptoms of PH include exertional dyspnea, fatigue, weakness, angina, presyncope, and syncope.³ Fluid retention leading to abdominal distention and ankle edema can develop with progressive RVF.³ Physical findings may include left parasternal lift or retraction, augmented second heart sound, an RV

TABLE. Parameters Associated With Worse Outcome in Registries of Patients with PAH^a

Variable	ERS/ESC guidelines ^{3,b}	French registry ^{8,c}	COMPERA registry ^{9,b}	Swedish registry ^{10,c}	REVEAL registry ^{12,d}
PAH diagnosis	NR	NR	NR	NR	CTD-PAH, PoPH, or heritable PAH
Demographic characteristics	NR	NR	NR	NR	Males >60 y
WHO FC	III-IV	III-IV	III-IV	III-IV	III-IV
6MWD (m)	≤440	<440	≤440	≤440	<165
Peak $\dot{V}O_2$ (mL/min/kg)	≤15	NR	NR	NR	NR
Peak $\dot{V}O_2$ % Predicted	≤65	NR	NR	NR	NR
$\dot{V}_E / \dot{V}CO_2$ slope	≥36	NR	NR	NR	NR
% Predicted DL_{CO}	NR	NR	NR	NR	<40
BNP (ng/L)	≥50	>50	≥50	NR	≥200
NT-proBNP (ng/L)	≥300	>300	≥300	≥300	≥1100
Right atrial area (cm ²)	≥18	NR	NR	≥18	NR
RAP (mm Hg)	≥8	≥8	≥8	≥8	>20 within 1 y
Cardiac index (L/min/m ²)	<2.5	<2.5	<2.5	<2.5	NR
SvO ₂ (%)	≤65	<65	≤65	≤65	NR
PVR (Wood units)	NR	NR	NR	NR	<5
Systolic blood pressure (mm Hg)	NR	NR	NR	NR	<100
Heart rate (beats/min)	NR	NR	NR	NR	>96
Pericardial effusion	NR	NR	NR	NR	Present
Renal function	NR	NR	NR	NR	eGFR ^e <60 mL/min/1.73 m ²
Hospitalization	NR	NR	NR	NR	All-cause hospitalization within 6 mo

^a6MWD = 6-minute walking distance; BNP = brain natriuretic peptide; COMPERA = Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension; CTD-PAH = pulmonary arterial hypertension associated with connective tissue disease; DL_{CO} = diffusion capacity of the lungs for carbon monoxide; eGFR = estimated glomerular filtration rate; ERS = European Respiratory Society; ESC = European Society of Cardiology; NR = not reported; NT-proBNP = N-terminal prohormone of BNP; PAH = pulmonary arterial hypertension; PoPH = portopulmonary hypertension; PVR = pulmonary vascular resistance; RAP = right atrial pressure; REVEAL = Registry to Evaluate Early and Long-term PAH Disease Management; SvO₂ = mixed venous oxygen saturation; $\dot{V}_E / \dot{V}CO_2$ = ventilatory equivalents for carbon dioxide; $\dot{V}O_2$ = oxygen consumption; WHO FC = World Health Organization functional class.

^bParameters associated with intermediate or high risk.

^cParameters used to define risk groups.

^dParameters associated with a higher risk score in the REVEAL 2.0 risk calculator.

^eOr renal insufficiency if eGFR not available.

third heart sound, elevated jugular venous pressure with abnormal waveform, low-volume arterial pulses, hepatomegaly, ascites, peripheral edema, and a tricuspid regurgitant murmur.³ History, physical examination, resting electrocardiography, and resting echocardiography in primary care can estimate the probability of PH.^{3,20} The H₂FPEF score, based on clinical and echocardiographic parameters, may help to identify HF with preserved

ejection fraction.²¹ Right-sided heart catheterization may be conducted in patients with PH-LHD or PH-CLD if referred to an expert PH center⁵ but may not be necessary if it will have no bearing on management.

If no LHD or lung disease is present, a ventilation-perfusion scan is mandatory to exclude CTEPH (discussed subsequently). In patients with PAH, further tests to establish the underlying cause may include chest

radiography, exercise echocardiography, pulmonary function tests, high-resolution computed tomography, contrast-enhanced tomography, pulmonary angiography, cardiac magnetic resonance imaging, laboratory tests (eg, thyrotropin, HIV, antinuclear antibodies, liver function tests, serum and urine protein electrophoresis), and sleep study or overnight oximetry.³ The European Society of Cardiology/European Respiratory Society diagnostic algorithm for diagnosis of PH is shown in [Figure 1](#).

ECHOCARDIOGRAPHY TO ESTIMATE THE PROBABILITY OF PH

The probability of PH is estimated by transthoracic echocardiography.³ The unique geometry of the right ventricle makes it challenging to obtain RV ejection fraction from 2-dimensional echocardiography, and therefore surrogate measures of RV function are used. Firstly, peak tricuspid regurgitation velocity (TRV) is measured by continuous-wave Doppler echocardiography, and pulmonary artery systolic pressure is estimated using the simplified Bernoulli equation. Next, TRV is classified as 2.8 m/s or less or not measurable, 2.9 to 3.4 m/s, or greater than 3.4 m/s. Echocardiographic signs suggestive of PH include RV/left ventricular (LV) basal diameter ratio of greater than 1.0, flattening of the interventricular septum, and pulmonary artery RV outflow Doppler acceleration time of less than 105 ms ([Supplemental Table](#), available online at <http://www.mayoclinicproceedings.org>).³ According to the category of TRV and the presence or absence of echocardiographic signs, the patient can be assigned a low, intermediate, or high probability of PH.³ The presence of elevated pulmonary artery systolic pressure by this method, however, is neither specific to nor predictive of the hemodynamic subgroup or classification of PH, nor does it provide insight into the nature of changes in PVR, PAWP, or cardiac output. In addition, several other transthoracic echocardiographic parameters can indicate the probability of PH ([Supplemental Table](#)).²² Common abnormal measurements of the right side of the heart in PH include tricuspid annular plane systolic excursion of less than 17 mm, RV systolic tissue

Doppler velocity of less than 10 cm/s measured at the lateral tricuspid annulus, and RV ejection fraction of less than 45%. With cardiac magnetic resonance imaging and the presence of late gadolinium enhancement, reduced pulmonary arterial distensibility, and retrograde flow have a high predictive value for identification of PH, although no single measurement can exclude PH.³

OTHER ROLES OF ECHOCARDIOGRAPHY IN THE DIAGNOSIS AND ASSESSMENT OF PH

Echocardiography has several additional roles in the assessment of PH. For example, an echocardiogram can be used to predict the probability of elevated PVR with normal PAWP²³ or to detect occult postcapillary PH.²⁴ Signs suggesting PH-LHD include LV ejection fraction less than 50%, E/e' ratio (ratio between early mitral inflow velocity and mitral annular early diastolic velocity) greater than 15, LA volume index greater than 34 mL/m², LV mass index greater than 104 g/m² in males and greater than 90 g/m² in females, and evidence of valvular heart disease.²²⁻²⁴ Conversely, high pulmonary arterial pressures accompanied by a small LA volume are strongly suggestive of PAH.²³ An algorithm to estimate the probability of PH-LHD has been proposed ([Supplemental Table](#)).⁵

Echocardiographic parameters reported to predict survival in patients with PAH or CTEPH include TRV, tricuspid annular plane systolic excursion, pulmonary artery dilatation, moderate to severe tricuspid regurgitation, RV functional area change, pericardial effusion, and myocardial performance index.^{25,26}

FURTHER DIAGNOSIS AND ASSESSMENT OF PH

All patients with suspected or confirmed PH, without confirmed left-sided heart or lung diseases, should have a ventilation-perfusion scan to exclude CTEPH because of its high sensitivity (90% to 100%) and specificity (94% to 100%).³ Other imaging techniques may be indicated to confirm the diagnosis and characterize pulmonary vessel morphology.⁷ Right-sided heart catheterization is essential in all

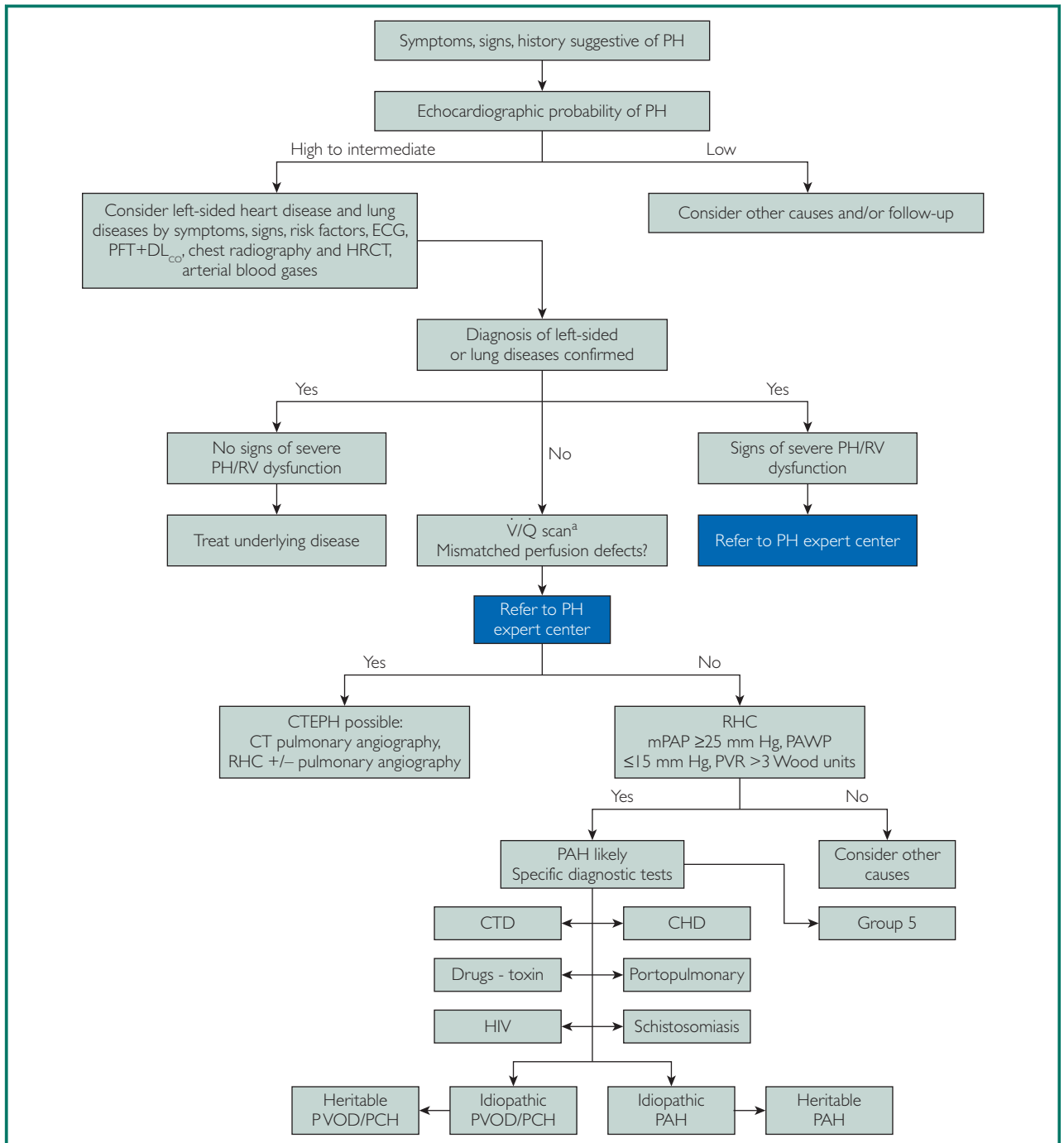


FIGURE 1. European Society of Cardiology/European Respiratory Society algorithm for diagnosis of pulmonary hypertension (PH). ^aComputed tomographic (CT) pulmonary angiography alone may miss a diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH). CHD = congenital heart diseases; CTD = connective tissue disease; DLCO = carbon monoxide diffusing capacity; ECG = electrocardiography; HRCT = high-resolution CT; mPAP = mean pulmonary arterial pressure; PAH = pulmonary arterial hypertension; PAWP = pulmonary artery wedge pressure; PFT = pulmonary function tests; PVOD/PCH = pulmonary veno-occlusive disease or pulmonary capillary hemangiomatosis; PVR = pulmonary vascular resistance; RHC = right-sided heart catheterization; RV = right ventricular; \dot{V}/\dot{Q} = ventilation-perfusion. From *Eur Respir J*,³ with permission from the European Respiratory Society. © ERS 2020.

patients with suspected PAH or CTEPH prior to starting therapy.³ It should be performed after other investigations so that it can answer specific questions that may arise from them and avoid an unnecessary procedure in which an alternative diagnosis is revealed.³ Considerations include zeroing of the external pressure transducer at the midthoracic line, determination of pressure assessments at end-expiration, and blood sampling with the balloon inflated at the wedge position to ensure that a true pulmonary capillary wedge pressure measurement has been taken.³

BIOMARKERS OF PH

Many biomarkers have been investigated in PH, but only brain natriuretic peptide (BNP) and *N*-terminal prohormone of BNP are widely used in routine practice and clinical trials.³ Both markers correlate with myocardial dysfunction, provide prognostic information at diagnosis and during follow-up, and have been incorporated into risk scores, but *N*-terminal prohormone of BNP seems to be a stronger predictor of prognosis than BNP.³

TREATMENT OF PH

Patients with known or suspected PAH or suspected CTEPH should be referred to an expert PH center. Referral to a PH center of excellence is especially important in PAH because high-volume centers achieve better results in this rare disease.³ These centers can also expedite a diagnostic work-up for CTEPH, assess for operability, and perform PTE or balloon pulmonary angioplasty (BPA).^{3,7}

Management of comorbidities (eg, sleep apnea and COPD) is essential in all patients with PH, and patients in any group may require supportive therapies such as diuretics, oxygen, and management of HF, including treatment of aggravating factors, optimization of fluid status, reduction of RV afterload, and cardiac inotropes if indicated.^{3,27} Oral anticoagulation is indicated in all patients with CTEPH even if they do not have a known history of pulmonary embolism and may be appropriate in other types of PH. Iron deficiency is common in PAH, and monitoring of iron levels, with iron substitution when necessary, is indicated.

Specific treatment of PH depends on the disease group. Insights into the pathophysiology of PAH²⁸ led to the development of targeted treatments, which improve exercise capacity, hemodynamics, and outcomes compared with untreated patients.^{3,12} The first agents introduced were the prostacyclin analogues, potent vasodilators that act on the prostacyclin receptor.³ Available prostacyclin analogues include oral beraprost, intravenous epoprostenol, intravenous and subcutaneous treprostinil, and iloprost, available in intravenous, oral, and nasal aerosol formulations. Selexipag is a selective oral nonprostanoid prostacyclin receptor agonist. Endothelin receptor antagonists, including bosentan, macitentan, and ambrisentan, prevent the vasoconstrictive and mitogenic effects of endothelin 1.²⁹ The nitric oxide (NO)—soluble guanylate cyclase (sGC)—cyclic guanosine monophosphate (cGMP) pathway is also involved in the pathogenesis of PAH.²⁸ Production of cGMP triggers vasodilation and inhibits cell proliferation, but in PAH, the NO-sGC-cGMP pathway is suppressed and phosphodiesterase type 5, which hydrolyzes cGMP, is induced, leading to vasoconstriction and cell proliferation. Phosphodiesterase type 5 inhibitors prevent breakdown of cGMP, while the sGC stimulator riociguat stabilizes NO-sGC binding, sensitizing sGC to NO, and also stimulates sGC directly, resulting in increased cGMP synthesis.

The European Society of Cardiology/European Respiratory Society³ and the American College of Chest Physicians (Figure 2)³⁰ have published recommendations for the use of targeted therapies in PAH. Patients should receive initial combination therapy, while high-risk patients should be considered for early escalation to triple therapy.^{3,12,30} In high-risk patients (eg, RV dysfunction and/or severe hemodynamic impairment), initial combination therapy should include parenteral prostanoids, with epoprostenol having the highest recommendation because of mortality reduction in a high-risk cohort of patients.¹² The combination of riociguat with phosphodiesterase type 5 inhibitor is contraindicated.^{3,12} Lung transplant is an option

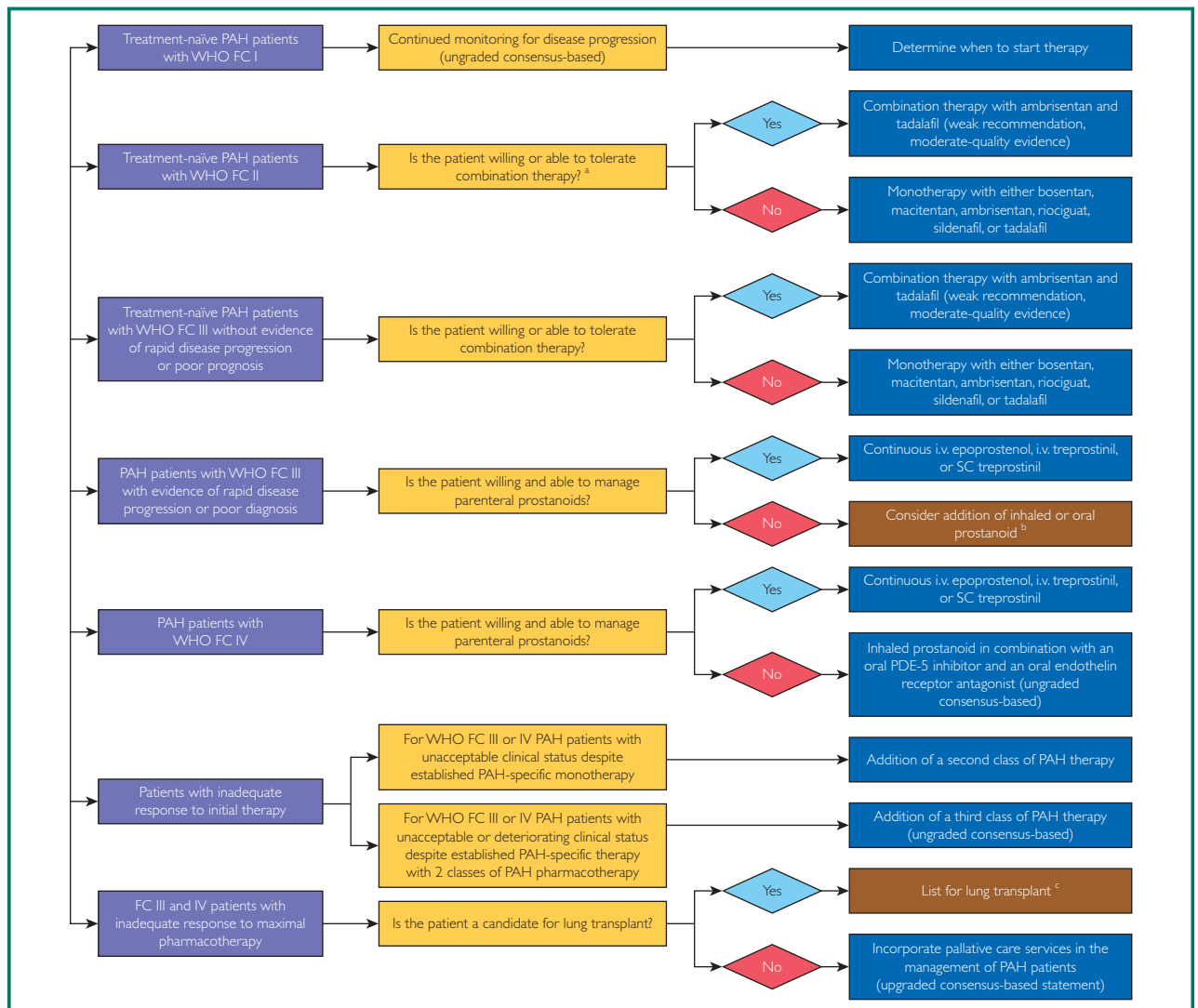


FIGURE 2. United States recommendations for the use of pulmonary arterial hypertension (PAH)—approved therapies. ^aCombination therapy carries with it costs as well as multiple medications, including the potential for increased adverse events that may be undesirable for some patients. In these situations patients are unwilling or unable to tolerate combination therapy and the US panel suggests monotherapy. ^bNo data available for the use of oral or inhaled prostanoids in patients in whom parenteral prostanoids are indicated, but patient is unable to comply. Thus, the US panel does not have a specific recommendation for this population. ^cLung transplant is outside the scope of this guideline, which focuses on pharmacotherapy for patients with PAH. Thus, the evidence based for lung transplants in patients with PAH has not been evaluated by this panel. Please consult the guidelines publication for further details.³⁰ FC = functional class; IV = intravenous; PDE-5 = phosphodiesterase type 5; SC = subcutaneous; WHO = World Health Organization. From *Chest*,³⁰ with permission from Elsevier.

for selected patients with severe PAH that does not respond to maximal medical therapy. However, with the increase in PAH treatment options and the progressive approach with combination therapy, lung transplant should be used only as a last resort.³

The cornerstone of PH-LHD therapy is management of the underlying heart disease.³

Examples include repair of valvular heart disease and aggressive treatment of HF with reduced systolic function.³ Nonspecific vasodilators may be beneficial, although the evidence is limited.³ In severe HF, it is essential to optimize volume status, potentially through invasive monitoring. Patients with PH-LHD have a poor prognosis and should be referred

to expert PH centers for individual assessment and management, including consideration for clinical trials. There is no evidence for benefit from PH-approved therapies in PH-LHD, and some have shown potential safety signals.⁵ Guidelines recommend against PH-approved therapies in this group.⁵

Treatment of PH-CLD primarily involves management of the underlying lung disease, and the only potentially curative treatment is lung transplant. Pulmonary hypertension—CLD is associated with increased mortality, and patients should be referred to expert PH centers and considered for clinical trials.^{3,6} There is no established medical therapy for PH-CLD and no evidence that PH-approved therapies are beneficial.⁶ Ambrisentan is contraindicated in idiopathic pulmonary fibrosis and riociguat is contraindicated in PH associated with idiopathic interstitial pneumonias.⁶

Pulmonary thromboendarterectomy is the treatment of choice for CTEPH as it is potentially curative, achieving substantial symptom relief and improvement of hemodynamics and RVF in most patients.^{3,31} Surgery should therefore not be delayed in favor of medical therapy in patients who are candidates for PTE. However, up to 40% of patients are ineligible for PTE, and in up to 51%, persistent/recurrent PH develops after PTE.⁷ These patients are candidates for targeted medical therapy and should be considered for BPA at an expert CTEPH center.^{3,7,32} Riociguat, the only approved medical therapy for CTEPH, is indicated for adults with inoperable or persistent/recurrent CTEPH based on efficacy and safety data from the CHEST-1 (Chronic Thromboembolic Pulmonary Hypertension Soluble Guanylate Cyclase—Stimulator Trial 1) study.^{3,7} Several other PAH-approved agents have been evaluated in patients with CTEPH, most notably macitentan, which showed benefits on PVR in patients with inoperable CTEPH in the MERIT-1 (Macitentan for the Treatment of Inoperable Chronic Thromboembolic Pulmonary Hypertension) study and in preliminary results from its long-term extension, MERIT-2.^{33,34} In selected patients with

CTEPH, BPA can improve hemodynamics, symptoms, exercise capacity, and RV function.⁷

CONCLUSION

Pulmonary hypertension features progressive loss and obstruction of the pulmonary vascular bed, leading to elevated mPAP and PVR, which can ultimately produce RV dysfunction and RVF. Pulmonary hypertension is subdivided in 5 groups: PAH (group 1), PH-LHD (group 2), PH-CLD (group 3), CTEPH (group 4), and unclear and/or multifactorial mechanisms (group 5). Careful assessment of medical history, physical condition, echocardiograms, and hemodynamic parameters (obtained via right-sided heart catheterization) is essential to diagnose and characterize the different forms of PH effectively. Management of PH-LHD and PH-CLD concentrates on treatment of the underlying disorder, with referral to expert PH programs for individual assessment and tailored therapy. Targeted pharmacological and surgical treatments are available for patients with PAH or CTEPH, for whom early referral to a specialist PH center is recommended.

SUPPLEMENTAL ONLINE MATERIAL

Supplemental material can be found online at <http://www.mayoclinicproceedings.org>. Supplemental material attached to journal articles has not been edited, and the authors take responsibility for the accuracy of all data.

Abbreviations and Acronyms: BNP = brain natriuretic peptide; BPA = balloon pulmonary angioplasty; cGMP = cyclic guanosine monophosphate; CLD = chronic lung disease; COPD = chronic obstructive pulmonary disease; CTEPH = chronic thromboembolic pulmonary hypertension; HF = heart failure; LA = left atrial; LHD = left-sided heart disease; LV = left ventricular; mPAP = mean pulmonary arterial pressure; NO = nitric oxide; PAH = pulmonary arterial hypertension; PAWP = pulmonary artery wedge pressure; PH = pulmonary hypertension; PH-CLD = pulmonary hypertension due to chronic lung disease; PH-LHD = pulmonary hypertension due to left-sided heart disease; PTE = pulmonary thromboendarterectomy; PVR = pulmonary vascular resistance; RV = right ventricular; RVF = RV failure; sGC = soluble guanylate cyclase; TRV = tricuspid regurgitation velocity; WU = Wood units

Grant Support: Medical writing services provided by Richard Murphy, PhD, of Adelphi Communications Ltd, Bellingham, Macclesfield, UK, were funded by Bayer AG in accordance with Good Publication Practice (GPP3) guidelines.

Potential Competing Interests: Dr Mandras has received consulting fees and payment for lectures/service on speakers bureaus for Bayer AG, Berlin, Germany, and United Therapeutics Corporation. Dr Mehta has received speaker fees from Actelion Pharmaceuticals Ltd, Switzerland and Bayer AG, Berlin, Germany, consulting fees from Bayer AG, Berlin, Germany, and research support from Actelion Pharmaceuticals Ltd, Switzerland related to this work. Dr Vaidya has received speaker and consulting fees from Actelion Pharmaceuticals Ltd, Switzerland, Bayer AG Berlin, Germany, Liquidia Technologies, NC, USA, and United Therapeutics Corporation.

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