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Group 2 Pulmonary Hypertension: A Comprehensive Review of Diagnosis and Treatment in Left Heart Disease 2

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Abstract

The most prevalent type of pulmonary hypertension caused by left heart disease (PH-LHD), which considerably deteriorates outcomes for patients with valvular heart disease and heart failure. Elevations in pulmonary vascular resistance (PVR), right ventricular (RV) dysfunction, and decreased exercise capacity are the main factors influencing prognosis in PH-LHD. Mortality is independently predicted by a PVR >3 Wood units, with each additional Wood unit raising risk by roughly 20%. Reduced TAPSE, impaired RVEF, or aberrant RV strain are indicators of RV dysfunction, which strongly predicts clinical worsening and offers predictive information beyond left ventricular failure. Exercise intolerance replicates the combined effects of cardiac, pulmonary, and peripheral problems and further distinguishes high-risk patients as seen by decreased peak VO_2 and higher VE/VCO_2 slope. Because combined pre- and post-capillary PH (CpcPH) is characterized by fixed pulmonary vascular remodeling, higher PVR, and much lower survival, it is crucial to distinguish between isolated post-capillary PH (IpcPH) and CpcPH. This change signifies the development of intrinsic pulmonary vascular disease from passive venous congestion. Although pulmonary artery pressure can be lowered by valve correction, reversibility is mostly dependent on baseline PVR. After balloon valvotomy, patients with mitral stenosis and PVR <3 WU often return to normal pressure, while those with PVR >5 WU often have worse results and persistent PH. Guidelines emphasize optimizing left-sided illness instead of employing vasodilators, and clinical trials of PAH-specific treatments have failed to demonstrate efficacy. In general, pulmonary vascular remodeling, RV function, and exercise capacity determine the prognosis for PH-LHD, highlighting the importance of early identification and prompt intervention.

Keywords: PH-LHD (Pulmonary Hypertension due to Left Heart Disease); Right Ventricular Dysfunction; Hemodynamic Phenotyping; Heart failure; Echocardiography

Abbreviations: 6MWD: 6-Minute Walk Distance; ACE: Angiotensin-Converting Enzyme; ARB: Angiotensin Receptor Blocker; ARNI: Angiotensin Receptor-Neprilysin Inhibitor; BNP: Brain Natriuretic Peptide; CMR: Cardiac Magnetic Resonance; CO: Cardiac Output; CPAP: Continuous Positive Airway Pressure; CpcPH: Combined Post- and Pre-capillary Pulmonary Hypertension; CPET: Cardiopulmonary Exercise Testing; DLCO: Diffusion Capacity of the Lung for Carbon Monoxide; DPG: Diastolic Pressure Gradient; HFpEF: Heart Failure with Preserved Ejection Fraction; HFrEF: Heart Failure with Reduced Ejection Fraction; IpcPH: Isolated Post-capillary Pulmonary Hypertension; LHD: Left Heart Disease; LV: Left Ventricle / Left Ventricular; LVAD: Left Ventricular Assist Device; mPAP: Mean Pulmonary Arterial Pressure; MRA: Mineralocorticoid Receptor Antagonist; NT-proBNP: N-terminal pro-B-type Natriuretic Peptide; PAH: Pulmonary Arterial Hypertension; PAWP: Pulmonary Artery Wedge Pressure; PH: Pulmonary Hypertension; PH-LHD: Pulmonary Hypertension due to Left Heart Disease; PVR: Pulmonary Vascular Resistance; RA: Right Atrial; RV: Right Ventricle / Right Ventricular; SGLT2: Sodium-Glucose Cotransporter 2; TAPSE: Tricuspid Annular Plane Systolic Excursion; TRV: Tricuspid Regurgitation Velocity; WHO: World Health Organization; WU: Wood Units

Introduction

Pulmonary hypertension (PH) is a hemodynamic and pathophysiologic condition defined by elevated pulmonary arterial pressure, traditionally characterized by a mean pulmonary arterial pressure (mPAP) ≥25mmHg at rest, with updated guidelines recommending a threshold >20mmHg on right heart catheterization, along with pulmonary vascular resistance criteria to refine diagnosis. Clinically, PH is classified into five World Health Organization (WHO) groups based on underlying etiology and pathophysiology: Group 1 (pulmonary arterial hypertension), Group 2 (PH due to left heart disease), Group 3 (PH due to lung diseases or hypoxia), Group 4 (chronic thromboembolic PH), and Group 5 (PH with unclear or multifactorial mechanisms) [1]. Among these categories, Group 2 PH—also known as pulmonary hypertension due to left heart disease (PH-LHD)—is the most common form and arises from conditions such as left ventricular systolic or diastolic dysfunction, valvular heart disease, or congenital/acquired left-sided cardiac abnormalities that lead to chronically elevated left atrial pressure and subsequent pulmonary venous congestion [1,2].

PH-LHD carries a substantial global disease burden, reflecting its strong epidemiologic link to highly prevalent cardiovascular conditions such as heart failure with preserved or reduced ejection fraction. Studies demonstrate that PH-LHD is associated with worse functional capacity, increased morbidity, and a significantly poorer prognosis compared with patients with left heart disease alone. The presence of PH in this population predicts higher rates of hospitalization for heart failure and increased all-cause mortality, underscoring its clinical seriousness [3]. Hospitalizations related to PH-LHD pose a heavy demand on health systems, as repeated episodes of decompensation are common among patients with advanced heart failure and concomitant pulmonary vascular remodeling [3]. Distinguishing PH-LHD from other PH categories is crucial because management strategies differ dramatically. Unlike pulmonary arterial hypertension, which may respond to targeted vasodilator therapies, PH-LHD requires treatment of the underlying cardiac disorder, and inappropriate use of PAH-specific drugs may worsen pulmonary edema or lead to adverse outcomes [1,2].

Accurate differentiation ensures correct therapeutic decision-making, appropriate prognostic counseling, and optimization of outcomes, particularly because PH-LHD involves unique hemodynamic signatures—such as elevated pulmonary arterial wedge pressure—and heterogeneous phenotypes that can influence prognosis and treatment response [2]. The purpose of this comprehensive review is to synthesize current evidence on the diagnosis, pathophysiology, and management of PH-LHD to support clinicians in recognizing the condition, applying the correct diagnostic pathway, and implementing evidence-based treatment strategies. By integrating contemporary guidelines with recent clinical research, the review aims to clarify key diagnostic distinctions, highlight the burden of disease, and outline evolving therapeutic approaches to improve care for patients with PH-LHD.

Epidemiology and Clinical Classification

The most prevalent form of Pulmonary Hypertension is post-capillary pulmonary hypertension, which is caused by left heart disease (PH-LHD) and carries a very poor prognosis [4]. It is estimated to account for about 35-60% of all Pulmonary Hypertension cases [5]. In this category, the most predominant cases are due to heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF), accounting for about 40-80% of cases [4]. Other causes include valvular disease such as mitral stenosis, mitral regurgitation and aortic pathology. Symptomatic mitral valve stenosis has been strongly associated with Pulmonary Hypertension, as longstanding elevated left-atrial and pulmonary venous pressures may lead to pulmonary vascular remodeling [6]. The prognostic outcome of pulmonary hypertension in each scenario varies greatly depending on the causes, the level of severity of underlying disease and comorbidities associated with the cases. Patients who have left heart failure alongside pulmonary hypertension have been found to have a high mortality ratio [4].

A New York study of 307 patients with post-capillary pulmonary hypertension showed survival rates of 86.7%, 68.6%, and 55.6% in 1, 3 and 5 years of disease respectively [7]. This demonstrates the declining life expectancy seen as the disease progresses and the importance of early discovery and proper management. Another determinant of disease outcome is the development of right ventricular failure. In general, the presence of pulmonary hypertension greatly complicates the outcomes for patients with heart failure [8]. Although in the past, it was believed that the systolic function of the right ventricle was solely dependent on afterload, more studies are proving otherwise. PH has been seen to not just be a comorbidity in heart disease, but a strong prognostic marker for disease outcomes. Patients with PH-LHD have been noted with worse survival, higher morbidity, right heart dysfunction and poorer exercise capacity than patients without PH [9].

Another layer of prognostic importance is the distinction between isolated post-capillary pulmonary hypertension (IpcPH) and combined post- and pre-capillary pulmonary hypertension (CpcPH). This distinction is clinically important because the two conditions represent different stages of pulmonary vascular involvement. IpcPH results mainly from backward transmission of elevated left-sided filling pressures, while CpcPH reflects additional pulmonary vascular remodeling and increased pulmonary vascular resistance. This added vascular involvement places greater strain on the right ventricle and is associated with substantially worse outcomes. In a comprehensive review of pulmonary hypertension due to left-heart disease, Rosenkranz

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et al. emphasized that patients with CpcPH have more advanced disease and poorer hemodynamics than those with IpcPH [10]. Similarly, in a large cohort study, Gerges et al. demonstrated that CpcPH was linked to significantly higher mortality compared with both IpcPH and no PH, underscoring the prognostic importance of distinguishing these groups [11]. Together, these findings show that accurate hemodynamic assessment is essential for identifying patients at increased risk and for guiding appropriate management.

Pathophysiology

Pulmonary hypertension due to left heart disease (Group 2 PH) develops primarily from chronically elevated left-sided cardiac filling pressures. When the left ventricle becomes impaired, whether from systolic dysfunction, diastolic stiffness, or significant mitral or aortic valve disease, left atrial pressure increases persistently. That elevated pressure is transmitted backward into the pulmonary venous system, resulting in passive pulmonary venous hypertension [12]. This hemodynamic disturbance is characterized by a pulmonary artery wedge pressure (PAWP) greater than 15mmHg, the key measurement that differentiates Group 2 PH from pre-capillary forms [13]. Over time, sustained pressure overload induces structural and cellular changes within the pulmonary vasculature. Endothelial dysfunction, smooth muscle hypertrophy, and vascular wall remodeling contribute to an increase in pulmonary vascular resistance (PVR), indicating a transition from isolated post-capillary PH to combined post- and pre-capillary PH (CpcPH) [10,14]. In this advanced stage, pressure transmission alone no longer explains the disease process; rather, intrinsic pulmonary vascular pathology becomes a major contributor.

As PVR rises, the right ventricle (RV) faces a progressive increase in afterload. Early on, the RV compensates by increasing contractility and undergoing hypertrophy to preserve cardiac output and maintain RV–pulmonary artery coupling [15]. With prolonged overload, these adaptive mechanisms fail, leading to RV dilation, impaired myocardial oxygen delivery, metabolic dysregulation, and eventual RV systolic dysfunction and failure [16]. Right ventricular dysfunction is a major prognostic determinant in Group 2 PH and is strongly associated with exercise intolerance, more frequent heart failure hospitalizations, and increased mortality. Early recognition of RV impairment is therefore crucial for risk stratification and management decisions in this population [13].

Clinical Presentation

Pulmonary hypertension encompasses a broad spectrum of clinical signs and symptoms that arise secondary to elevated pulmonary arterial pressure [17]. In the early stages, manifestations typically emerge during states of increased oxygen demand, such as exercise; however, as the disease advances, symptoms may occur even at rest [18]. The hallmark symptom is progressive exertional dyspnea. Additional common manifestations include chest discomfort, palpitations, peripheral edema, and hemoptysis. Less frequently, cough and hoarseness may also be observed [19]. In patients who develop right-sided heart failure, a range of systemic findings may be present, including distended and pulsatile jugular veins, a positive hepatojugular reflux, hepatosplenomegaly, ascites, dizziness, and cool extremities [20]. The most prevalent clinical findings result from volume overload, which may give rise to an S3 gallop. Valvular abnormalities, particularly tricuspid and pulmonary regurgitation, are likewise frequently encountered in this population [21].

Although the symptoms of pulmonary hypertension may be nonspecific, a cornerstone of accurate diagnosis and effective management is a thorough clinical history. A detailed history can prompt early suspicion regarding the underlying etiology of pulmonary hypertension. Typical risk factors include a prior history of pulmonary embolism or venous thrombosis, underlying thrombophilic disorders particularly antiphospholipid syndrome and various comorbid conditions such as malignancy, chronic osteomyelitis, and myeloproliferative disorders. Additional predisposing factors include splenectomy, the presence of a ventriculoatrial shunt, connective tissue diseases, infectious etiologies such as HIV, specific congenital cardiac defects, and certain genetic mutations (notably BMPR2). Exposure to illicit drugs or toxins, including methamphetamines and appetite suppressants, also constitutes a well-recognized risk profile [22].

Diagnostic Evaluation

Non-Invasive assessment

Echocardiography

Echocardiography is the first line and the most valuable noninvasive tool in the evaluation of patients with suspected pulmonary hypertension. It provides information on right and left heart function, valvular abnormalities, and hemodynamic rates [23]. The echocardiographic estimate for detecting pulmonary hypertension is a right ventricle systolic pressure of ≥4mmHg. The European Society of Cardiology and European Respiratory Society guidelines recommend categorizing the probability of detecting pulmonary hypertension in three ways based on tricuspid regurgitation velocity (TRV): low (<2.8m/s TRV), intermediate (2.9-3.4m/s TRV), and high (>3.4m/s TRV) [24]. Echocardiographic parameters in the assessment of pulmonary hypertension include: ventricles(right / left ventricle basal diameter ratio >1.0, flattening of the interventricular septum; decreased left ventricular eccentricity index), pulmonary artery: (right ventricular outflow Doppler acceleration time < 105msec, early diastolic pulmonary regurgitation velocity >2.2m/sec and pulmonary artery diameter >25mm.), Inferior cava diameter >21mm with decreased inspiratory collapse and right atrial area > 18cm^2 [25].

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Biomarkers

Many biomarkers have been investigated in pulmonary hypertension, but only brain natriuretic peptide (BNP) and N-terminal prohormone of BNP are widely used in routine practice and clinical trials. 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 [20]. In decompensated states, troponin elevation is a marker of myocardial injury and a predictor of poor prognosis in conditions like pulmonary hypertension. Elevated troponin in pulmonary hypertension, often due to right ventricular strain and ischemia, indicates ongoing myocyte damage and is associated with higher mortality [26].

Pulmonary function testing and imaging

Pulmonary function tests (PFTs) and analysis of arterial blood gas are necessary to distinguish between pulmonary hypertension groups, assess comorbidities and the need for supplementary oxygen, and determine disease severity. The lung diffusion capacity for carbon monoxide (DLCO) may be normal in patients with PAH, although it is usually mildly reduced. A severely reduced DLCO (45% of the predicted value) in the presence of otherwise normal PFTs can be found in PAH associated with systemic sclerosis, pulmonary veno-occlusive disease, in PH group 3. A low DLCO is associated with a poor prognosis in several forms of pulmonary hypertension [27]. The prevalence of nocturnal hypoxemia and central sleep apnea are high in PAH (70–80%). Overnight oximetry or polysomnography should be performed where obstructive sleep apnea syndrome or hypoventilation are considered [25].

Invasive assessment

Right heart catheterization

Right heart catheterization remains the gold standard for evaluating pulmonary hypertension. In general, circumstantial evidence for PH (echocardiographic PH) should ideally be confirmed by invasive assessment before considering PH-specific therapies. PH is considered to be due to left heart disease when left-heart filling pressures exceed normal reference ranges (PCWP >15mmHg), typically measured supine at rest. Right-sided heart catheterization performed at rest and during exercise allows distinction of exercise-induced PAH (PH due to pulmonary vascular disease) from PH due to LHD. Exercise PH is a hemodynamic condition describing a normal mPAP at rest with an abnormal increase of mPAP during exercise and is defined as a mPAP/cardiac output (CO) slope >3mmHg/L/min between rest and exercise [28].

Pulmonary Hypertension can be grouped phenotypically into precapillary, postcapillary, or combined pre and postcapillary pulmonary hypertension. Precapillary PH is defined by mPAP >20mmHg and the elevation of pulmonary vascular resistance (PVR) above the upper limit of normal, that is considered to be 2 Wood Units (WU), and by a pulmonary arterial wedge pressure (PAWP) ≤15mmHg. This form of PH is characteristic of hemodynamic conditions and diseases with pulmonary arterial involvement and no significant left heart disease. Post-capillary PH is defined by mPAP >20mmHg and PAWP >15mmHg and is strongly suggestive of left heart disease. The value of the PVR further distinguishes between isolated post-capillary PH (ipcPH, PVR ≤2 WU) and combined post- and pre-capillary PH (cpcPH, PVR >2 WU) [20].

Cardiopulmonary exercise testing

Cardiopulmonary exercise testing belongs to clinical examinations that explore the causes of exercise dyspnea. Patients with PAH show a typical pattern, with a low end-tidal partial pressure of carbon dioxide (PETCO2), high ventilatory equivalent for carbon dioxide (VE/VCO2), low oxygen pulse (VO2/HR), and low peak oxygen uptake (VO2). While not routinely required for the diagnosis of PH, it can be helpful in complex cases of dyspnea in which PH is a possible contributing factor [24].

Fluid challenge

Fluid challenge transiently increases systemic venous return and, in that way, tests the capacity of the afterload right ventricle (RV) to adapt to a sudden increase in preload. A fluid challenge for a failing RV in PH would be associated with increased right atrial pressure (RAP) with no or little increase in cardiac output, in contrast to a normal RV that would respond with an increase in CO to unchanged RAP. In Group 2 pulmonary hypertension, a fluid challenge will typically result in an increase in right atrial pressure with little or no increase in cardiac output (CO), indicating a failing right ventricle. A key finding is an increase in pulmonary artery wedge pressure (PAWP) greater than 18mmHg during the challenge, which supports the diagnosis of post-capillary PH [29].

Management Strategies

Treating the underlying left heart disease

The most effective way to manage pulmonary hypertension caused by left heart disease is actually to treat the underlying heart problem. In cases of heart failure, following the guidelines on how to treat it is key, and that usually involves using a combination of medications like ACE inhibitors or ARBs, ARNIs, beta-blockers, MRAs and SGLT2 inhibitors to ease the workload on the heart, make the ventricles work better, cut down on hospital stays and improve survival. Diuretics also come into play to deal with fluid buildup in the lungs and the rest of the body which in turn knocks down pulmonary venous pressures and relieves the symptoms that come with this, such as shortness of breath and swelling in the legs [13,30].

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In HFrEF, the activation of adrenergic and renin-angiotensin-aldosterone systems promotes sodium retention, renal vasoconstriction, LV dilatation, and fibrosis. These maladaptive responses contribute to fluid retention and increased left-heart filling pressures, triggering the development of PH. Interrupting this vicious circle by neurohormonal antagonism has been demonstrated to be effective in improving symptoms, cardiovascular biomarkers, hemodynamics, LV function, and eventually survival whether or not PH is present [30-33]. Targeting the mechanisms leading to HFpEF is much more challenging because of the multifactorial nature of this syndrome, incomplete understanding of its pathophysiology, and scarcity of recommended treatments. HFpEF has been associated with a peculiar neurohormonal setting, particularly in the setting of obesity: Aldosterone is overproduced by adipocytes, the renin-angiotensin system is directly activated, and neprilysin activity is increased. All these mechanisms could lead to decreased sensitivity to natriuretic peptides, inflammation, and eventually to sodium retention and congestion [30-33].

Despite this solid pathophysiologic rationale, no treatment has yet been shown to clearly reduce morbidity or mortality in HFpEF. In addition, several PAH-specific targets—including endothelin-receptor antagonists and drugs targeting the NO/cyclic guanosine monophosphate pathway—failed to demonstrate a benefit in this disease [31]. Therefore, the management of HFpEF focuses on managing comorbidities and decongestion with diuretics. However, the CHAMPION trial (Cardio MEMS Heart Sensor Allows Monitoring of Pressure to Improve Outcomes in NYHA Class III Heart Failure Patients), which evaluated the efficacy of an implantable device for continuously monitoring pulmonary pressure in HF, suggested that hemodynamic-guided management yielded a better outcome in terms of HF hospitalization, irrespective of LV ejection fraction or HF etiology. This highlights the importance of hemodynamic balance as a therapeutic target in HF [1,30-33].

Mitral valve repair or replacement can significantly lower left atrial pressure and improve pulmonary hemodynamics, while transcatheter aortic valve replacement (TAVR) or surgical aortic valve replacement (SAVR) is indicated in patients with hemodynamically significant aortic stenosis contributing to elevated left ventricular filling pressures [33]. Management of atrial fibrillation is another crucial component of treatment. Restoring or maintaining sinus rhythm, when feasible, may improve cardiac output and reduce left atrial pressures. When rhythm control is not achievable, rate control strategies are implemented to optimize ventricular response and limit worsening of heart failure. In addition, anticoagulation therapy is often necessary to reduce the risk of thromboembolic complications associated with atrial fibrillation [33].

Pulmonary vasodilator therapy

Although pulmonary vasodilators are the mainstay of treatment in pulmonary arterial hypertension (PAH), they are generally not recommended for patients with pulmonary hypertension due to left heart disease. These medications can worsen pulmonary congestion by increasing blood flow to a left ventricle that is already unable to handle the increased volume, potentially leading to pulmonary edema and clinical deterioration. Several clinical trials have failed to demonstrate clear benefit of PAH-specific therapies in this patient population [32].

For example, studies evaluating the use of sildenafil, a phosphodiesterase-5 inhibitor, in patients with HFpEF have shown neutral or even harmful outcomes, with no improvement in exercise capacity or clinical status. Similarly, endothelin receptor antagonists such as bosentan and macitentan have not provided clinical benefit in PH-LHD and are associated with significant side effects, including fluid retention and worsening heart failure symptoms. Prostacyclin analogues, which are effective in PAH by reducing pulmonary vascular resistance, have also shown no improvement in outcomes for patients with left heart disease-related pulmonary hypertension and may increase the risk of pulmonary edema due to increased pulmonary blood flow [31-34].

In rare and highly selected cases, pulmonary vasodilators may be considered within the setting of controlled clinical trials, particularly in patients with combined post- and pre-capillary pulmonary hypertension (CpcPH), where pulmonary vascular remodeling contributes more significantly to elevated pulmonary resistance. However, outside of research settings, the use of these agents remains discouraged due to the lack of proven benefit and risk of harm [30-33].

Advanced and supportive therapies

Supportive and advanced treatment strategies play a vital role in improving quality of life and slowing disease progression in patients with PH-LHD. Oxygen therapy may be indicated for patients with hypoxemia, as adequate oxygenation reduces pulmonary vasoconstriction and alleviates symptoms such as dyspnea and fatigue. Pulmonary rehabilitation programs, which incorporate supervised exercise training, education, and breathing techniques, can enhance functional capacity and overall well-being, even in patients with advanced disease [32-34]. It is also essential to identify and manage contributing comorbidities. Obstructive sleep apnea (OSA), for example, can worsen pulmonary hypertension if untreated and should be managed with continuous positive airway pressure (CPAP) therapy when indicated. Obesity contributes to increased cardiac workload and impaired ventilation, making weight management an important part of long-term care. Chronic kidney disease must be carefully monitored due to its impact on fluid balance and medication clearance [32-34].

In severe, refractory cases where medical therapy fails to control symptoms or prevent disease progression, mechanical circulatory support such as a left ventricular assist device (LVAD) may be considered in select patients with advanced HFrEF. This

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intervention can offload the failing left ventricle and reduce pulmonary pressures over time. For eligible individuals with end-stage heart failure and pulmonary hypertension refractory to conventional therapies, heart transplantation remains a definitive treatment option, although careful patient selection and extensive evaluation are necessary to ensure optimal outcomes [32-34].

Prognosis

Pulmonary hypertension owing to left heart disease (PH-LHD) includes a heterogeneous population with significantly different clinical trajectories. Although its presence often implies more advanced cardiac disease and confers worse outcomes than left heart disease without pulmonary hypertension, substantial variation exists within PH-LHD itself [10]. Accurate identification of mortality predictors enables doctors to stratify risk, guide treatment decision-making, establish scheduling for advanced therapies such as transplantation, and provide educated prognostic counseling. Three prognostic categories regularly indicate good predictive value: pulmonary vascular resistance (PVR), right ventricular (RV) function, and exercise capacity [14,35]. These metrics reflect diverse but linked components of PH-LHD pathophysiology and offer supplementary prognostic information.

Pulmonary vascular resistance (PVR)

In PH-LHD, PVR is a critical metric of pulmonary vascular remodeling and disease development [36]. Chronic venous congestion causes vasoconstriction, vascular remodeling, and endothelial dysfunction, which eventually results in persistently elevated PVR typical of combined pre- and post-capillary PH, even though PVR is normal or only slightly elevated in early PH-LHD [8,37]. In populations with heart failure and valvular illness, higher PVR is also a potent predictor of death; thresholds exceeding 2-3 Wood units identify high-risk patients [38-41]. Because of increased right ventricular afterload, reduced cardiac output reserve, and advanced endothelial dysfunction [14,42], each 1-WU increase in PVR is linked to a roughly 20% increase in mortality [35].

Right ventricular function

The RV initially compensates for increased afterload with enhanced contractility and mild hypertrophy, but sustained pressure overload leads to maladaptive remodeling, dilation, functional decline, and right heart failure [37,42]. RV function is evaluated using echocardiographic indices such as TAPSE, RV fractional area change, S′ velocity, and RV free-wall strain [43], with CMR providing precise measurements of RVEF and volumes. Hemodynamic markers—particularly RA pressure and cardiac index—also reflect RV performance [43,44]. RV dysfunction is a strong predictor of mortality: TAPSE <14mm, RVEF <35-45%, impaired RV strain, RA pressure >10mmHg, and cardiac index <2.0 L/min/m^2 each signal high risk [8, 17-20]. Metrics of RV–pulmonary artery coupling, such as reduced Ees/Ea or TAPSE/PASP <0.35mm/mmHg, offer additional prognostic value [38,43].

Exercise capacity

Exercise intolerance in PH-LHD results from diminished cardiopulmonary reserve, poor cardiac output augmentation, ventilatory inefficiency, and aberrant peripheral oxygen extraction [32]. CPET gives extensive evaluation through peak VO_2, percent predicted VO_2, VE/VCO_2 slope, OUES, and oscillatory breathing, whereas the 6MWD provides a straightforward measure of submaximal capacity [14,42]. Peak VO_2 <14mL/kg/min identifies high-risk patients and remains prognostic across heart failure phenotypes, including HFpEF [27-29]. The VE/VCO_2 slope (>34-36) is an equally strong predictor and correlates closely with pulmonary vascular and RV dysfunction [30]. A 6MWD < 300m also predicts increased mortality [31]. Changes in VO_2 or 6MWD over time further enhance risk assessment, with gains suggesting a better prognosis and decreases signifying increased risk [24].

Integrative risk stratification

The integration of PVR, RV function, and exercise capacity improves risk prediction due to their complementary value. Multivariable tools, such as the REVEAL and ESC/ERS PH-LHD frameworks, use clinical, haemodynamic, echocardiographic, biomarker, and functional parameters to classify patients into low-, intermediate-, or high-risk categories, thereby informing treatment escalation [32]. Integrated models demonstrate superior prognostic performance; for example, the combination of elevated PVR, reduced TAPSE, and abnormal peak VO_2 yields markedly poor survival [14,39].

Prognostic differences between IpcPH and CpcPH

PVR, diastolic pressure gradient, and pulmonary vascular remodeling are used to differentiate between isolated post-capillary PH (IpcPH) and CpcPH [6]. IpcPH indicates passive left atrial pressure transmission, whereas CpcPH entails additional pulmonary vascular disease with increased PVR and DPG [33]. Reduced exercise ability, decreased RV function, structural vascular alterations, and significantly lower survival are all linked to CpcPH [14,43].

Impact of valvular correction on PH progression

Valvular heart disease is a significant driver of PH-LHD. Hemodynamic response to valve intervention depends on lesion severity, prolonged left-sided pressure increase, and pulmonary vascular remodeling [35,36]. Correction often lowers pulmonary artery pressures (PAP), with PVR <3 WU predicting substantial improvement and PVR >5 WU indicating limited reversibility [37]. Persistent PH following intervention suggests irreversible pulmonary vascular and RV changes and predicts unfavorable

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outcomes. There is currently insufficient data to justify the routine use of PAH-specific vasodilators; instead, therapy should only be administered to a small number of patients under close hemodynamic monitoring [38].

Conclusion

Pulmonary hypertension due to left heart disease (PH-LHD) represents the most frequent form of pulmonary hypertension and carries a significant burden of morbidity and mortality. Its pathophysiology is rooted in chronically elevated left-sided filling pressures, which may eventually lead to intrinsic pulmonary vascular remodeling (CpcPH) and right ventricular failure. Distinguishing between IpcPH and CpcPH through accurate hemodynamic assessment—primarily right heart catheterization—is essential for risk stratification and the prevention of inappropriate vasodilator therapy. Prognosis in this population is dictated by the interplay of pulmonary vascular resistance, right ventricular function, and exercise capacity. Management remains centered on the aggressive optimization of the underlying left heart condition, as PAH-specific therapies have largely failed to demonstrate clinical benefit in this group. Early identification, prompt valvular intervention when indicated, and meticulous management of comorbidities are the cornerstones of improving long-term outcomes for patients with PH-LHD.

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