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BRN Rev. 2025;11(3):211-222

BRN Reviews

REVIEW ARTICLE

When interstitial lung diseases associates pulmonary hypertension, what to do?

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ABSTRACT

Pulmonary hypertension (PH) is one of the major comorbidities of interstitial lung diseases (ILD) and negatively impacts on patients' symptoms and prognosis. PH-ILD diagnosis is made following a three-step strategy. In a first step, suspicion of PH-ILD should be raised if a combination of symptoms, signs, functional impairments, radiological features, and biomarkers is present. In a second step, patients in whom PH-ILD is suspected should undergo transthoracic echocardiography (TTE) for PH screening. In a third step, depending on TTE findings and clinical suspicion, right heart catheterization should be performed to diagnose or rule out PH. Once PH-ILD is diagnosed, a holistic approach is needed, considering optimization of the underlying ILD, assessment of comorbidities, pulmonary rehabilitation, oxygen supplementation, symptom control, evaluation for lung transplantation, and PH therapy. The decision about PH-targeted therapies should be made using a multimodal approach in a multidisciplinary PH-ILD committee.

Keywords: Pulmonary hypertension. Interstitial lung diseases. Pulmonary fibrosis.

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Received: 06-07-2025
Accepted: 11-08-2025
DOI: 10.23866/BRNRev:2025-M0136
www.brnreviews.com

INTRODUCTION

Interstitial lung diseases (ILDs) are a heterogeneous group of over 200 different conditions characterized by inflammation and/or fibrosis of the lung interstitium. They may involve different compartments of the lung parenchyma, including the distal airways, alveoli, and endothelium, and have a wide range of etiologies, clinical courses, functional impairments, and radiological features.

Pulmonary hypertension (PH) is one of the major comorbidities of ILDs and impacts very negatively on symptoms, exercise tolerance, quality of life, and survival[1-3]. It is especially relevant in fibrosing ILDs due to its prevalence and great clinical impact[2].

PH is defined by an elevation of mean pulmonary artery pressure (mPAP) > 20 mmHg measured at rest, according to the latest 2022 European Society of Cardiology/European Respiratory Society (ESC/ERS) guidelines. Pre-capillary PH is defined by mPAP > 20 mmHg, pulmonary artery wedge pressure (PAWP) ≤ 15 mmHg, and pulmonary vascular resistance (PVR) > 2 Wood Units (WU), whereas post-capillary PH is defined by mPAP > 20 mmHg, PAWP > 15 mmHg, and PVR ≤ 2 WU[4]. The diagnosis of PH-ILD is based on a "suspect, detect, and confirm" strategy[2]. Early diagnosis is challenging as symptoms of both conditions frequently overlap until advanced stages of vascular remodeling[3]. Transthoracic echocardiography (TTE) is the main non-invasive tool for PH screening, despite some limitations. PH diagnosis requires hemodynamic assessment through right heart catheterization (RHC), which should be reserved for prognostic assessment, treatment decisions, lung transplant evaluation, or clinical trial eligibility[2].

Until recently, no pharmacological treatment had demonstrated efficacy in PH-ILD. However, the publication of the INCREASE trial in late 2021, showing the benefit of inhaled treprostinil for this population[5], has renewed interest in the detection and treatment of this condition.

This review will deep into PH-ILD detection and management, highlighting not only pharmacological treatment but also emphasizing a holistic perspective in the care of patients with PH-ILD.

WHY ASSESSING PH IN ILD MATTERS

Group 3 PH due to lung diseases and/or hypoxia is the second most common form of PH, following the group 2 PH related to left heart diseases[4]. The prevalence of PH in ILDs is not well established. It varies widely across published studies, with reported rates between 3% and 86%[3,6-8]. This variability is primarily due to differences in ILD types, disease stages, ranging from general ILD populations to those evaluated for lung transplant – and the diagnostic method–TTE versus RHC. A 2015 review suggested a PH prevalence of 30-50% in ILD[6], but it currently remains unclear. However, fibrotic ILDs and PH frequently coexist in certain subgroups of patients. This high coincidence might be explained by common pathways between fibrosis and vascular remodeling[7], although this issue is not particularly addressed in this review.

Not only is PH common in the setting of ILDs, but it also significantly impacts its prognosis. PH in ILDs has been demonstrated to be associated with:

- Worsening of exertional dyspnea, cough, fatigue, emotional and social impacts[3,9,10].
- Increased need for long-term oxygen therapy[3,8,11].
- Reduced exercise capacity in the 6-min walking test (6MWT)[11,12] and cardiopulmonary exercise testing (CPET)[13].
- Increased risk of acute exacerbations and hospitalizations[3,12].
- Increased mortality[3,8,10,11,14].

Data from the European COMPERA registry showed a poor 1-, 2-, and 3-year survival of 73.3%, 51.2% and 34.1%, respectively[15]. Notably, the onset of PH in ILD significantly worsens prognosis, which seems to be similar across different fibrotic ILD types[3,8]. PH-ILD prognosis also differs from other group 3 causes, such as PH associated with chronic obstructive pulmonary disease (COPD). Interestingly, in the context of COPD, only severe PH increases mortality, whereas in ILD, even mild PH is associated with poorer outcomes[16].

WHEN SHOULD PH BE SUSPECTED IN ILD?

Detection of PH-ILD is challenging due to symptom overlap until advanced stages of the disease. Therefore, a multimodal assessment is essential, including clinical, functional, biologic, and morphologic domains[2].

Clinical suspicion and biomarkers

Specific signs and symptoms of PH-ILD are usually related to right heart failure. Their onset must raise the suspicion of PH and prompt further evaluation. However, PH-ILD is usually severe in this context, and it responds poorly to treatment. Consequently, early detection seems crucial, as the response to treatment could be better. Although there is currently no definitive evidence for this early-diagnosis/early-treatment approach, there is a rationale for it, extrapolated from PH associated with systemic sclerosis or group 1 pulmonary artery hypertension (PAH)[17,18].

Table 1 shows the signs and symptoms suggestive of PH-ILD, including those that are suggestive of right ventricular involvement and others that may be present earlier.

It is important for pulmonologists managing these patients to be familiar with these parameters and assess them regularly to detect PH-ILD as early as possible.

Currently, only two biomarkers have proven useful in detecting PH-ILD: brain natriuretic peptide (BNP) and N-terminal pro-BNP (NT-proBNP). Both correlate with right atrial pressure in RHC[2]. A recent Spanish Society of Pulmonology and Thoracic Surgery review proposed an algorithm for PH-ILD detection based on PH probability through TTE plus NT-proBNP levels > 300 pg/mL[19]. However, these biomarkers are usually elevated when it already exists some degree of right ventricle (RV) dysfunction. Thus, it would be important to detect PH-ILD before these biomarkers

Table 1. Signs and symptoms that should raise suspicion of PH-ILD

Signs and symptoms suggestive of right ventricle involvement[2,14]	Other signs and symptoms that may be present earlier
Pre-syncope/syncope. Peripheral edema. Tricuspid regurgitation murmur. Right ventricle third heart sound. Jugular venous distension. Parasternal heave.	A change in disease trajectory[2]. Disproportionate exertional dyspnea relative to the degree of ILD[2,14]. Discordance between symptom progression and lung function or chest imaging[19]. An increase in the number of ILD exacerbations[19].

PH-ILD: pulmonary hypertension secondary to interstitial lung diseases.

rise. Furthermore, BNP and NT-proBNP can be elevated in other conditions such as left heart diseases, renal failure, acute pulmonary embolism, and coronary syndrome[2], so they are not truly specific for PH.

Functional impairment related to PH-ILD

Pulmonary function tests (PFTs) – spirometry, lung volumes, and diffusion capacity – and the 6MWT are commonly used at diagnosis and during follow-up of ILDs. Furthermore, these tests could also be useful for suspecting PH-ILD.

ILDs may show a wide range of functional impairment on PFTs. Most of them show a restrictive ventilatory pattern, although some of them may show a mixed or obstructive pattern. The majority of ILD patients have decreased diffusion capacity measured by diffusion capacity for carbon monoxide (DLCO) and carbon monoxide transfer coefficient (KCO). PH can also be the cause of a decrease in DLCO and KCO. The impairment of DLCO and KCO appears more markedly in patients with PH-ILD, though the difference between low DLCO/KCO in ILD and PH-ILD is often difficult to distinguish. However, in ILD patients, a significant DLCO or KCO decrease not associated with a corresponding reduction of forced vital capacity (FVC) may be the sign of possible associated PH.

ILDs with and without PH are associated with reduced distance and higher oxygen desaturation in 6MWT. These findings tend to be more severe in PH-ILD compared to ILD alone, but it is sometimes difficult to differentiate between them. Heart rate recovery is defined as the reduction of the heart rate 1 min after completing the 6MWT, and its decrease may suggest PH-ILD[2].

An electrocardiogram is not routinely obtained in ILDs' follow-up, but it is easy to perform and could help identify patients at risk for PH-ILD. Right axis deviation and/or incomplete right bundle branch block are signs that may raise suspicion for PH-ILD[14,19].

CPET can be useful for PH detection, although its availability may be limited depending on the center where PH-ILD patients are followed. The presence of a cardio-circulatory limitation pattern with exhausted circulatory reserve is indicative of PH in ILD patients[19].

Table 2. Functional finding that should raise suspicion for PH-ILD[2,14,19]

DLCO and/or KCO < 40%
Decrease of DLCO > 15%
FVC/DLCO ratio > 1.6
6MWT distance < 350 m and/or oxygen desaturation > 4%, disproportionate to ILD severity.
HRR < 13 beats/min (bpm).
Increased Borg dyspnea score.
Right axis deviation and/or incomplete right bundle branch block at ECG.
Cardio-circulatory limitation pattern with exhausted circulatory reserve on CPET.

PH-ILD: pulmonary hypertension secondary to interstitial lung diseases; DLCO: diffusion capacity for carbon monoxide; FVC: forced vital capacity; KCO: carbon monoxide transfer coefficient; 6MWT: 6-min walking test; HRR: heart rate recovery; ECG: electrocardiogram; CPET: cardiopulmonary exercise testing.

Key functional findings that should raise suspicion for PH-ILD are shown in table 2.

Radiological features associated with PH-ILD

Chest radiography may provide clues to the presence of PH in ILDs, although it lacks sensitivity and specificity for the diagnosis of either condition. Findings such as pulmonary artery (PA) dilatation and enlarged heart silhouette with "water-bottle" shape may indicate the presence of PH-ILD[2,19].

High-resolution computed tomography (CT) scan is routinely performed in the diagnosis and follow-up of ILD patients. The most frequently described CT scan features suggestive of PH-ILD include PA enlargement and increased PA-to-ascending aorta (PA/Ao) diameter ratio[2,14,19-21]. PA diameter correlates with the mPAP in RHC[21]. Other suggestive findings include peripheral vascular pruning, right atrial and RV enlargement, and RV/left ventricle ratio > 1[2]. A CT scan is also essential to assess the extent of ILD and/or emphysema[2]. In addition, contrast-enhanced chest CT can rule out pulmonary embolism as an alternative cause of PH.

There has been some controversy about which is the optimal threshold for PA diameter and PA diameter/Ao diameter ratio to raise the suspicion of PH in this population. PA and Ao diameters should be measured at the level of the PA bifurcation, perpendicular to the long axis of the main PA[22,23]. Despite inconsistent previous reports, a position paper of the Fleischner Society suggested a threshold of PA diameter > 30 mm and PA/Ao diameter ratio > 0.9 for populations with high risk of PH, including those with ILD[21]. In contrast, the Group 3 PH task force from the 7th World Symposium on PH recommended a threshold PA diameter > 32 mm and a PA/Ao diameter ratio > 1[2]. In this regard, to standardize measurements and the use of the same thresholds remains an unmet need[21].

Magnetic resonance imaging (MRI) has also been investigated for its potential role in detecting PH-ILD. PA size measurements are comparable to those obtained in a CT scan[21]. The diagnostic capacity of MRI appears to be better than CT scan, as it can quantify additional structural and functional cardiovascular parameters indicative of PH – interventricular septal angle, RV ejection fraction, ventricular mass index, and PA pulsatility[21]. However, similarly to CPET, it is an expensive and less widely available technique, and it is not routinely used in the evaluation of ILD patients.

HOW TO DETECT AND CONFIRM PH IN ILD?

Once there is clinical suspicion of PH, TTE should be performed to estimate the echocardiographic probability of PH-ILD. In a third step, depending on the TTE findings and the strength of clinical suspicion, RHC may be indicated to confirm or rule out PH, particularly if this confirmation impacts management[2].

A modified Delphi consensus[24] and Group 3 Task Force from the 7th World Symposium on PH[2] proposed similar diagnostic algorithms for PH-ILD. In both, clinical suspicion was divided into low, moderate, and high, based on non-invasive parameters described in the previous section. However, these frameworks do not clearly define how to distinguish among these categories and which parameters carry the highest weight in the decision-making process. As such, this approach is largely subjective, and there is potential for variability between evaluators.

In this context, the development and validation of a predictive score to objectively identify patients with a higher risk of PH-ILD would be highly valuable, helping to optimize TTE and RHC indications. So far, no such validated scoring system exists for PH-ILD.

Role of TTE to detect PH-ILD

The probability of PH on TTE is estimated by evaluating tricuspid regurgitation velocity (TRV), along with indirect signs of PH. Fig. 1 illustrates the algorithm to assess the probability of PH, adapted from the 2022 ESC/ERS PH guidelines[4].

In those patients with high probability or with intermediate probability but significant clinical suspicion, RHC must be considered to confirm or rule out PH.

While TTE is a key tool to detect PH-ILD, it has some limitations. First, it has only shown a moderate correlation with RHC results[25-27]. Second, TRV cannot be adequately measured in a significant proportion of ILD patients due to technical limitations or a poor acoustic window due to the ILD itself[19,26]. Third, this test is in high demand and may pose an excessive healthcare burden[19]. These problems highlight the need to improve non-invasive PH detection beyond TTE, so that RHC requests could be optimized.

RHC indications and interpretation

As stated before, RHC should be performed if results impact management. RHC indications are the following[2]:

- PH-ILD phenotyping.
- Prognostic evaluation.
- Guidance for therapeutic interventions.
- Pre-operative assessment with perioperative management.
- Clinical trial enrolment.
- Evaluation for lung transplantation.

Considering the significant impact of PH in ILD, the authors consider that most ILD patients in whom PH is suspected would benefit from hemodynamic assessment if they are clinically fit enough to undergo RHC. Confirming the presence of PH-ILD provides valuable prognostic information, enables PH phenotyping, for instance, identifying

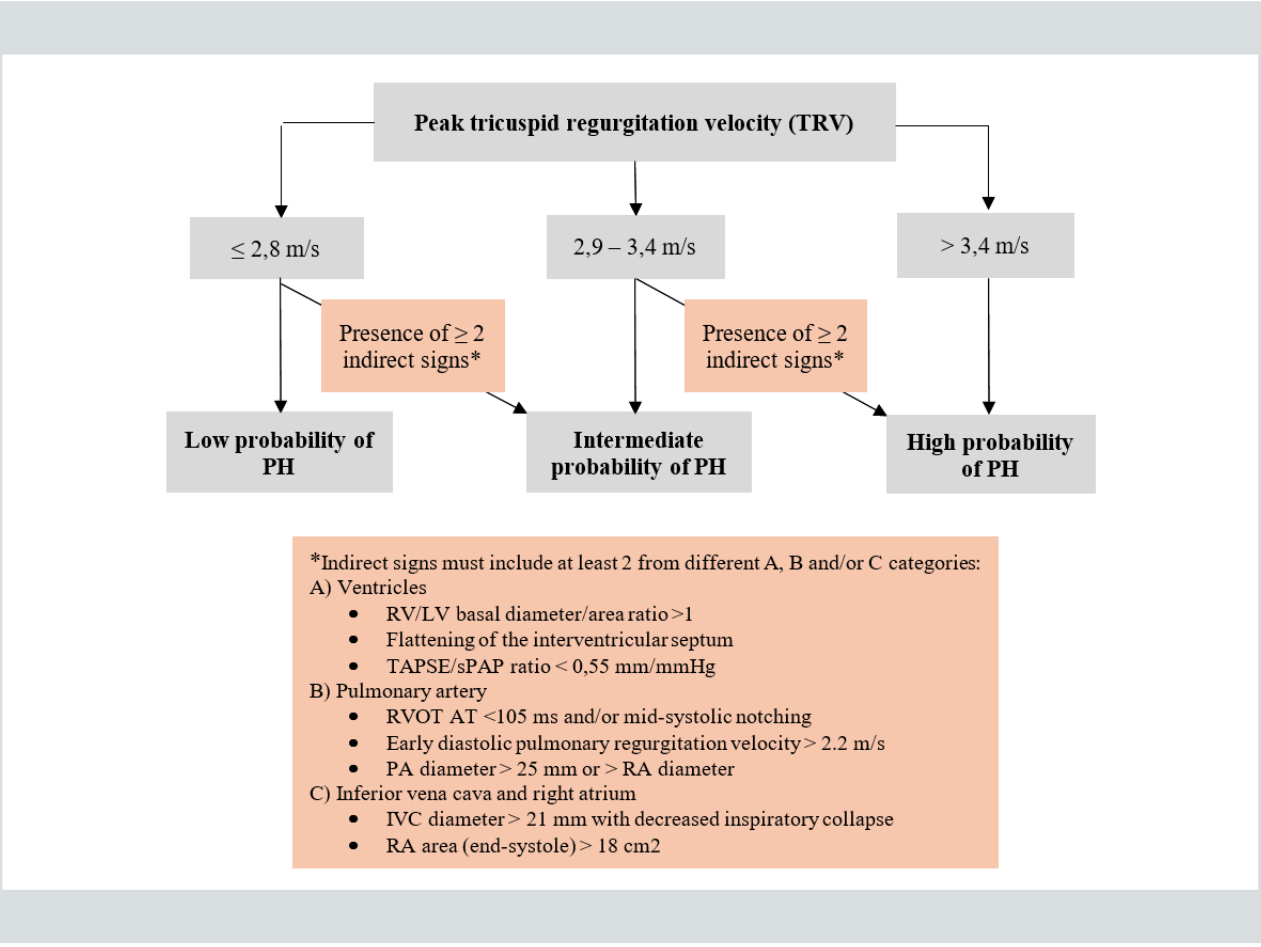

Figure 1. Probability of PH through TTE assessment (*adapted from Humbert et al.*[4]). PH: pulmonary hypertension; RV: right ventricle; LV: left ventricle; TAPSE: tricuspid annular plane systolic excursion; sPAP: systolic pulmonary artery pressure; RVOT AT: right ventricular outflow tract acceleration; PA: pulmonary artery; IVC: inferior vena cava; RA: right atrium.

post-capillary PH may lead to a formal diagnosis of heart failure with preserved ejection fraction and consequently, these patients could benefit from specific management, supports referral to a lung transplantation unit for potential eligible candidates, and facilitates the evaluation of PH-targeted therapies.

Table 3 shows the normal ranges of the RHC parameters and criteria for pre- and post-capillary PH, based on the 2022 ESC/ERS guidelines for PH[4].

WHAT TO DO ONCE PH IS DIAGNOSED IN THE CONTEXT OF ILD?

Once PH-ILD is diagnosed with RHC, it is essential not only to consider the potential indication for PH-targeted therapies, but also to adopt a multidomain, holistic management strategy, including optimization of the underlying ILD, assessment of comorbidities, pulmonary rehabilitation (PR), oxygen supplementation, symptom control and evaluation for lung transplant if possible, depending on the patient's condition.

Table 3. Normal RHC values and PH hemodynamic criteria

RHC variables	Normal values
Systolic pulmonary artery pressure	15-30 mmHg
Diastolic pulmonary artery pressure	4-12 mmHg
Mean pulmonary artery pressure	8-20 mmHg
Pulmonary arterial wedge pressure	≤ 15 mmHg
Right atrial pressure	2-6 mmHg
Cardiac output	4-8 L/min
Cardiac index	2.5-4 L/min/m2
Pulmonary vascular resistance	0.3-2 WU
Stroke volume index	33-47 mL/m^2
Pulmonary arterial compliance	> 2.3 mL/mmHg
Mixed venous oxygen saturation (SvO_2)	65-80%
Type of PH	**Hemodynamic definition**
PH	mPAP > 20 mmHg
Pre-capillary PH	mPAP > 20 mmHg PAWP ≤ 15 mmHg PVR > 2 WU
Isolated post-capillary PH	mPAP > 20 mmHg PAWP > 15 mmHg PVR ≤ 2 WU mPAP > 20 mmHg PAWP > 15 mmHg
Combined post- and pre-capillary PH	PVR > 2 WU

RHC: right heart catheterization; PH: pulmonary hypertension; WU: Wood units.
Adapted from Humbert et al.[4]

Optimization of the underlying ILD and assessment of comorbidities

The first step after confirming PH-ILD is to optimize the management of ILD. If a definitive or high-confidence diagnosis of ILD has not yet been achieved, efforts should be made to accurately identify the specific ILD subtype to guide the most appropriate treatment. However, patients with PH-ILD are at higher risk when undergoing lung biopsy – both cryobiopsy and surgical biopsy – due to an increased likelihood of procedure-related complications such as bleeding and acute exacerbation of ILD, in addition to general risks such as pneumothorax. The presence of PH particularly increases the risk of major bleeding given the elevated pulmonary vascular pressures. Therefore, establishing a definitive diagnosis may be challenging in some cases.

Once a firm ILD diagnosis is made, treatment should be optimized accordingly. This includes antifibrotic treatment in patients with idiopathic pulmonary fibrosis (IPF) and non-IPF patients with progressive pulmonary fibrosis (PPF) and/or corticosteroids or other immunosuppressive treatments when indicated[1].

It is also essential to identify and manage other comorbidities that may influence the clinical course and prognosis of patients with PH-ILD. Those comorbidities include:

- Pulmonary embolism.
- COPD/emphysema.
- Obstructive sleep apnea.
- Obesity-hypoventilation syndrome.
- Gastroesophageal reflux.
- Lung cancer.
- Left heart disease.

Oxygen supplementation and PR

Exertional hypoxemia is commonly observed in PH-ILD patients during the 6MWT. If arterial oxygen saturation (SaO_2) persistently drops below 88%, long-term oxygen therapy (LTOT) at exertion is usually prescribed. Despite the lack of solid evidence for PH-ILD, this approach is supported by extrapolation from studies in COPD patients[28]. Given the potential role of hypoxemia in the pathogenesis of PH-ILD, this strategy appears to be reasonable.

The required oxygen flow (L/min) should be determined during the 6MWT. The target SaO_2 after exertion is generally > 85%, although it may

be difficult to achieve in advanced stages of the disease, even with supplementary oxygen.

LTOT at rest should be initiated in PH-ILD patients with hypoxemic respiratory failure, defined as a partial pressure of oxygen in arterial blood (PaO_2) < 60 mmHg[4]. It is generally administered through a nasal cannula for at least 15-h/day, similar to recommendations for patients with PH-COPD[28]. The SaO_2 target at rest is generally > 90%, although in selected cases 85-90% may be acceptable if well tolerated. In addition, in accordance with 2022 ESC/ERS PH guidelines, nocturnal oxygen therapy should be considered in case of sleep-related desaturation[4].

In addition to encouraging physical activity, a structured PR program should be considered for PH-ILD patients. Similar to LTOT, direct evidence for PR in these populations is lacking, and current recommendations are extrapolated from PAH, COPD, and ILDs[2]. However, PR may improve exercise capacity, muscular function, quality of life, and lung function parameters[29,30]. There is a current need for developing specialized PR programs for PH-ILD[4,29].

Supportive care and symptom management

PH-ILD patients usually experience exertional dyspnea, cough, fatigue, and reduced exercise tolerance. Despite appropriate management with both pharmacological and non-pharmacological therapies, these symptoms are often difficult to fully control. Therefore, it is essential to incorporate symptom-relieving medications, particularly opioids, to release dyspnea, cough, and improve quality of life[31]. In this regard, the involvement of palliative care teams is also crucial. Their expertise allows close follow-up and optimization of supportive care as part of the holistic management of patients with PH-ILD.

Referral to lung transplantation

According to the consensus document for the selection of lung transplant candidates[32], the diagnosis of PH in the setting of ILDs is a criterion for referral for transplant evaluation and potential listing in eligible patients. As in PAH, most patients could benefit from bilateral lung transplantation, whereas heart-lung transplantation is reserved for those with additional non-corrected cardiac conditions[4].

Pharmacological treatment

Despite the fact that mortality from PH-ILD is higher than in PAH[33], until recently, there were no available therapeutic options for this condition. The use of PH-targeted drugs is only recommended in cases of severe PH, currently defined by PVR > 5 WU. The existence of a "vascular phenotype" has been proposed, which is characterized by better preserved spirometry, low DLCO, hypoxemia, and a circulatory limitation to exercise[4]. However, as previously mentioned, any degree of PH worsens prognosis[16]. According to the Task Force for Group 3 PH in the 7th World Symposium, the degree of vascular impairment may need to have different thresholds when applied to prognostication versus indications for treatment[2].

The basis for this recommendation is that, until late 2021, no clinical trial evaluating PH

therapies in ILD patients had met its primary endpoint. Bosentan did not demonstrate efficacy in the BUILD-1 to -3 trials, and macitentan also failed to meet its primary endpoint in the MUSIC trial, although both showed non-significant improvements in quality-of-life secondary outcomes[4,14]. Ambrisentan and riociguat are not recommended for this population as they showed an unfavorable risk-benefit profile in their respective studies[4]. Phosphodiesterase type 5 inhibitors (PDE5i) also failed to meet primary endpoints. However, a post hoc analysis of the STEP-IPF trial showed that in patients with right ventricular dysfunction on TTE, sildenafil (compared to placebo) preserved exercise capacity, improved quality of life, oxygen saturation, and DLCO, and was safe and well tolerated[34]. More recently, a retrospective cohort study showed that sildenafil may improve survival in patients with PH-ILD, particularly in those without right ventricular dysfunction[35].

In late 2021, the results of the first positive randomized controlled trial (INCREASE) for the treatment of PH-ILD were published. This study demonstrated the safety and efficacy of inhaled treprostinil compared to placebo in that population. It showed significant improvements at 16 weeks in the primary endpoint (6MWT distance), as well as in secondary endpoints, including NT-proBNP and the number of clinical worsening events (hospitalizations, decline in exercise capacity, lung transplantation, and death)[5,36]. Furthermore, a *post hoc* analysis of the INCREASE study revealed an improvement in FVC in the treprostinil-treated group, especially among patients with IPF[37,38]. These findings provided the rationale for investigating potential antifibrotic effects of treprostinil in the ongoing TETON trial for IPF and PPF without PH. Results from the INCREASE open-label extension study confirmed the long-term safety and efficacy of inhaled treprostinil at 52 weeks, with sustained improvements in 6MWT distance, NT-proBNP levels, oxygenation, and FVC[39].

Taking into account all this information, the main pharmacological therapies available for PH-ILD are:

- PDE5i: sildenafil and tadalafil. Although there are no clinical trials with positive results, there is evidence from retrospective studies that supports that they are safe and effective for PH-ILD. They have been generally reserved for severe PH-ILD with PVR > 5 WU, although they might be prescribed in non-severe PH-ILD following an individualized approach.
- Inhaled treprostinil. It is the only therapy with a positive result in clinical trials and can be prescribed in PH-ILD with PVR > 3 WU (following the inclusion criteria of the INCREASE trial), with better results in those with PVR ≥ 4 WU. However, it has not yet been approved by the European Medicines Agency, and its availability may be limited in some centers.

Assessing fibrosis versus vasculopathy: guidance for targeted therapy

Within the multimodal assessment of PH-ILD, the decision to start a PH-targeted therapy can be difficult. Clinical and/or functional worsening could be due to both fibrosis and vasculopathy, and this distinction may often be challenging. In this regard, it is important to assess these decisions in a PH-ILD committee using a multimodal approach.

Table 4. Items that should be considered for the decision about PH-ILD therapy

Domains	Favors PH therapy	Favors no PH therapy
Clinical domain	Worsening symptoms due to PH Underlying CTD	Relevant comorbidities
Hemodynamics	PVR ≥ 4 WU and mPAP ≥ 25 mmHg	PVR 2-3 WU and mPAP 20-25 mmHg
Functional domain	Mild-to-moderate restrictive ventilatory defect, vascular limitation to exercise	Severe restrictive ventilatory defect FEV1/FVC < 0.7
Biological domain	Elevated BNP/NT-proBNP	Normal BNP/NT-proBNP
Morphological domain	Non-severe fibrotic ILD on CT	Extensive fibrotic ILD on CT, Emphysema extent > 15%

PH-ILD: pulmonary hypertension secondary to interstitial lung diseases; PH: pulmonary hypertension; CTD: connective tissue disease; PBR: pulmonary vascular resistance; mPAP: mean pulmonary artery pressure; FEV1: forced expiratory volume in the first second; FVC: forced vital capacity; ILD: interstitial lung disease; CT: computerized tomography.
Adapted from Shlobin et al.[2]

Table 4 summarizes the items that are useful for PH therapy evaluation and that should be considered before taking the decision[2].

CONCLUSION

PH-ILD is a serious condition that impacts very significantly on patients' symptoms, exercise tolerance, quality of life, and survival. Early detection is crucial to act as soon as possible and try to prevent the development of severe PH and a poorer outcome. A predictive score would be highly valuable for early detection of PH-ILD and optimizing TTE and RHC indications. Once PH-ILD is diagnosed, a holistic approach is needed, considering optimization of the underlying ILD, assessment of comorbidities, PR, oxygen supplementation, symptom control, evaluation for lung transplantation, and PH therapy. The decision about PH-targeted therapies should be made using a multimodal approach in a multidisciplinary PH-ILD committee.

FUNDING

None.

CONFLICTS OF INTEREST

None.

ETHICAL CONSIDERATIONS

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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