Pulmonary Hypertension Related to Chronic Obstructive Pulmonary Disease and Diffuse Parenchymal Lung Disease

A Focus on Right Ventricular (Dys)Function

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KEYWORDS

• Pulmonary hypertension • Pulmonary fibrosis • COPD • Right ventricular dysfunction
• Diffuse pulmonary lung disease

KEY POINTS

- Pulmonary hypertension associated with diffuse pulmonary lung disease and chronic obstructive pulmonary disease is a frequent cause of exercise intolerance, progressive dyspnea, and worsening hypoxia.
- Right ventricular dysfunction and severe hemodynamic impairment, out of proportion pulmonary hypertension, is seen in a minority subset of this population and results in worsening survival.
- Limited data exists supporting the use of pulmonary hypertension-specific medical therapy for patients with diffuse pulmonary lung disease and chronic obstructive pulmonary disease associated pulmonary hypertension.

INTRODUCTION

Pulmonary hypertension (PH) is a relatively common complication of chronic obstructive pulmonary disease (COPD) and diffuse pulmonary lung disease (DPLD), inclusive of idiopathic interstitial lung disease, which may have serious implications on the function and structure of the right ventricle.[1–3] PH is defined by right heart catheterization as an mean pulmonary artery (mPA) of 25 mm Hg or greater; severe PH as an mPA of

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Table 1
Mild and severe pulmonary hypertension and clinical correlates

	Mild	Severe
Echocardiogram	TAPSE ≥2.0 ± RVH ≤ Mild RV Dysfunction RV:LV ≤1.0 No systolic notch	TAPSE ≤2.0 RVH ≥ Moderate RV Dysfunction RV:LV >1.0 Mid- to Late systolic notch
PFT	FVC/DLCO <1.5[a] ↓↓ DLCO	FVC/DLCO >1.5[a] ↓↓↓ DLCO
BNP/NT-proBNP	↑	↑/↑↑
V_E/V_{CO_2}	± ↑	↑↑
6MWT	↓	↓↓

Abbreviations: 6MWT, 6-minute walk test; BNP, brain natriuretic peptide; DLCO, diffusion capacity of carbon monoxide; DPLD, diffuse parenchymal lung disease; FVC, forced vital capacity; LV, left ventricle; NT-proBNP, *N*-terminal prohormone of brain natriuretic peptide; PFT, pulmonary function test; RV, right ventricle; RVH, right ventricular hypertrophy; TAPSE, tricuspid annular plane systolic excursion; V_{CO_2}, minute ventilation of carbon dioxide; V_E, minute ventilation.

[a] There is no correlation of DLCO with FVC in IPF, and no correlation of forced expiratory volume with DLCO in chronic obstructive pulmonary disease.

35 mm Hg or greater or an mPA ≥25 mm Hg or greater with a low cardiac index (≤2.0 L/min/m^2).[4]

PH associated with COPD and DPLD are classified as World Health Organization (WHO) group 3.[4,5] When present in these patients, PH is usually mild to moderate; however, regardless of severity, it is often associated with a decrease in exercise tolerance and a poor prognosis (Table 1). Available data suggest that the impact of PH-specific therapy in COPD and DPLD is limited and survival is poor despite attempted treatment.

PATHOPHYSIOLOGY

The pathophysiology of PH in chronic lung disease is complex and poorly understood. Prior studies have postulated that hypoxic vasoconstriction and chronic inflammation lead to increased tone and muscularization of small pulmonary arteries resulting in epithelial damage, small vessel destruction, and fibrosis. This vascular remodeling likely explains why there is only a partial reversal of the pulmonary vascular resistance in response to oxygen.[6] In addition, the loss of pulmonary vascular surface (ie, lung destruction) can serve as an additive increase in pulmonary vascular resistance. Finally, the morphogenic pulmonary vascular lesions in COPD and DPLD can appear strikingly characteristic of idiopathic pulmonary artery hypertension as the hemodynamic severity progresses, but may also reflect significant heterogeneity with additional features of venopathy and capillary duplication.[7]

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

PH is a frequent clinical manifestation associated with COPD and has been associated with a decrease in exercise capacity and increase

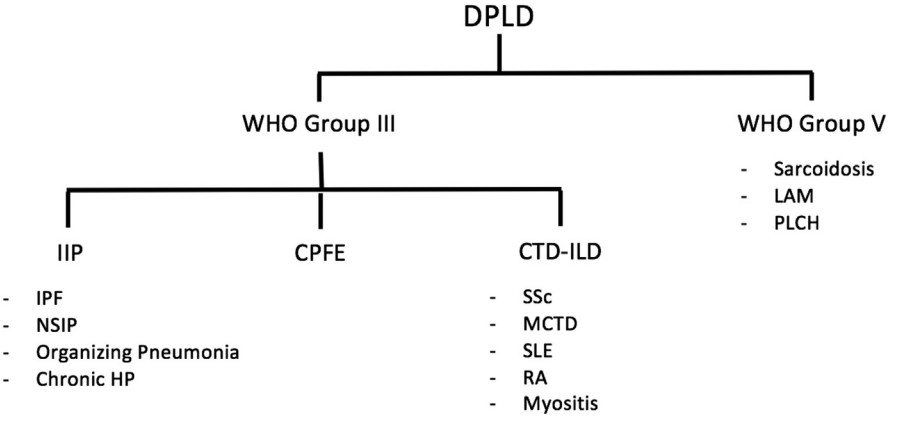

Fig. 1. Categories of diffuse parenchymal lung disease (DPLD) according to pulmonary hypertension World Health Organization (WHO) groups. CPFE, combined pulmonary fibrosis and emphysema; CTD-ILD, connective tissue disease-associated interstitial lung disease; DLPD, diffuse parenchymal lung disease; HP, hypersensitivity pneumonia; IPF, idiopathic pulmonary fibrosis; LAM, lymphangioleimyomatosis; MCTD, mixed connective tissue disease; NSIP, nonspecific interstitial pneumonia; PLCH, pulmonary Langerhans cell histiocytosis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; SSc, systemic scleroderma; WHO, World Health Organization.