# Pulmonary Hypertension and Thrombembolism—Long-Term Management and Chronic Oral Anticoagulation

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**KEYWORDS**

• Pulmonary hypertension • Pulmonary artery hypertension • Anticoagulation
• Warfarin

**KEY POINTS**

- Pulmonary hypertension (PH) is a complex disease that is characterized by an elevated mean pulmonary arterial pressure of greater than or equal to 25 mm Hg.
- PH has a wide variety of etiologies, all with specific therapies.
- Presenting symptoms are generally nonspecific and can include fatigue, lethargy, angina, weakness, signs of right heart failure, and increasing shortness of breath.
- Pulmonary artery hypertension is associated with increased thrombosis and disrupted coagulation and fibrinolysis, making anticoagulation an attractive and frequently used therapeutic modality.
- Pulmonary vasodilator therapy and oral anticoagulation are the main tools of long-term medical therapy.

## INTRODUCTION

Pulmonary hypertension (PH) is a complex disease that is characterized by an elevated mean pulmonary arterial pressure (mPAP) of greater than or equal to 25 mm Hg (**Table 1**). In the United States, there are approximately 200,000 hospitalized patients annually who have PH as a primary or secondary diagnosis.[1] Before introducing new treatments, the average life expectancy of the patients with PH was 2.5 years.[2] Due to the complexity of the disease and the multiple etiologies of

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**Table 1**
**Right heart catheterization evaluation**

| Hemodynamic Parameter | Hemodynamic Cutoff | Diagnosis |
|---|---|---|
| mPAP | <20 mm Hg | Normal |
| PAWP | ≤15 mm Hg | Normal, when mPAP <25 mm Hg |
| mPAP | ≥25 mm Hg | PH |
| PAWP | ≤15 mm Hg | Precapillary PH[a] |
| PAWP | >15 mm Hg | Postcapillary PH [a] |
| Transpulmonary pressure gradient (mPAP-PAWP) | ≤12 mm Hg | Passive postcapillary PH |
| Transpulmonary pressure gradient (mPAP-PAWP) | >12 mm Hg | Reactive postcapillary PH |
| PVR | >3 Wood units | PAH[b] |

[a] When mPAP is ≥25 mm Hg.
[b] When mPAP is ≥25 mm Hg and PAWP <15 mm Hg.

the disease, the World Health Organization (WHO) has classified PH into 5 classes with the purpose of helping guide diagnosis and treatment (**Table 2**). There has been a total of 5 World Symposia on PH since 1973.[3–8] The most recent, the Nice Classification in 2013, has further refined previous works to develop the new clinical classification of PH. In this classification there are 5 major groupings and several subgroups that further define etiology with the aim to guide diagnosis and treatment.

## GROUP 1—PULMONARY ARTERY HYPERTENSION

Pulmonary artery hypertension (PAH) is defined by a pulmonary vascular resistance (PVR) greater than 3 Wood units with mPAP greater than or equal to 25 mm Hg and pulmonary artery wedge pressure (PAWP) less than 15 mm Hg[9] determined by a right heart catheterization (RHC) at rest.

PAH affects the small pulmonary arteries with vascular obstruction by intimal and media proliferation and increased vascular resistance though complex multifactorial pathways. This results in increased right ventricular afterload and eventual failure.[10]

The cardiopulmonary effects of PAH can be debilitating and worsen health-related quality of living,[11] resulting in inactive lifestyles.[2]

In the REVEAL[12] study of 2176 patients enrolled with PAH, the 1-year survival rate with PAH at 1 year after enrollment was 91%. Increased mortality is seen with PVR of greater than 32 Wood units, portal hypertension, modified New York Heart Association (NYHA)/WHO functional class IV, men greater than 60 years old, and family history of PAH. Connective tissue disease, renal insufficiency, modified NHYA/WHO functional class III (**Table 3**), resting systolic blood pressure of less than 110 mm Hg, resting heart rate greater than 92 beats per minute, 6-minute walk distance less than 165 m, B-type natriuretic peptide (BNP) greater than 180 pg/mL, presence of pericardial effusion, percent predicted diffusing capacity of the lungs for carbon monoxide ($D_{LCO}$) less than or equal to 32%, and mean right arterial pressure greater than 20 mm Hg within the year preceding enrollment.

Conversely, a modified NHYA/WHO functional class I, 6-minute walk distance greater than or equal to 440 m, BNP less than 50 pg/mL, and $D_{LCO}$ greater than or equal to 80% have an increased 1-year survival rate.[12]

PAH is a broad term is further characterized by several subgroups based on etiology that have recently been updated by the Nice Classification.[7]

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