TABLE 304-1 COMPONENTS OF THE PATHOGENESIS OF PULMONARY ARTERIAL HYPERTENSION

Alterations in regulators of proliferation
• Growth factors
• Platelet-derived growth factor
• Fibroblast growth factor
• Vascular endothelial growth factor
• Epidermal growth factor
• Transforming growth factor β (TGF-β)
• Bone morphogenetic protein
• Transcription factors
• Matrix metalloproteinases
• Cytokines
• Chemokines
• Mitochondria
Alterations in inflammatory mediators
• Altered T cell subsets
• Monocytes and macrophages
• Interleukin (IL) 1β
• IL-6
• MCP-1
• RANTES
• Fractalkine
Alterations in vascular tone
• Endothelin
• Nitric oxide
• Serotonin
• Prostaglandin
• K^+ channels
• Ca^{2+} channels
Hypoxia-induced remodeling
• HIF-1α
• ROS
• Mitochondria
TGF-β signaling
• BMPR2
• ALK1
• Endoglin
• Smad9
• TGF-β1

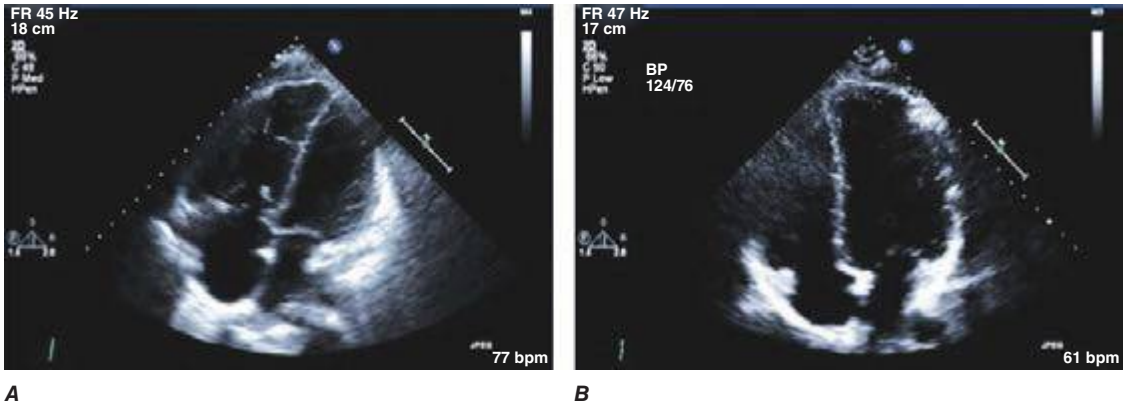
Abbreviations: PDGF, platelet-derived growth factor; EGF, epidermal-derived growth factor; FGF, fetal-derived growth factor; VEGF, vascular endothelial-derived growth factor; MCP-1, monocyte chemoattractant protein-1; IL, interleukin.

is also important to evaluate the degree of exertional hypoxemia and limitation and to monitor progression and response to therapy.

Sleep-disordered breathing is another important cause of PH, but a sleep study is generally necessary only when indicated by the patient's history. Nocturnal desaturation is a common finding in PH, even in the absence of sleep-disordered breathing. Thus, all patients should undergo nocturnal oximetry screening, regardless of whether classic symptoms of obstructive sleep apnea or obesity-hypoventilation syndrome are observed. Laboratory tests that are important for screening include an HIV test when clinically indicated. In addition, all patients should have antinuclear antibodies, rheumatoid factor, and scl-70 antibodies assessed to screen for the most common rheumatologic diseases associated with PH if clinically indicated. Liver function and hepatitis serology tests are important to screen for underlying liver disease. Finally, there is an increasing role for brain natriuretic peptide (BNP) testing in the diagnosis and management of PH. BNP and the N-terminus of its propeptide (NT-proBNP) correlate with right ventricular function, hemodynamic severity, and functional status in PAH.

Right heart catheterization with pulmonary vasodilator testing remains the gold standard both to establish the diagnosis of PH and to enable selection of appropriate medical therapy. The definition of precapillary PH or PAH requires (1) an increased mean pulmonary artery pressure (mPAP ≥25 mmHg); (2) a pulmonary capillary wedge pressure (PCWP), left atrial pressure, or left ventricular end-diastolic pressure ≤15 mmHg; and (3) PVR >3 Wood units. Postcapillary PH is differentiated from precapillary PH by a PCWP of ≥15 mmHg; this is further differentiated into passive, based on a transpulmonary gradient <12 mmHg, or reactive, based on a transpulmonary gradient >12 mmHg and an increased PVR. In either case, the CO may be normal or reduced.

Vasodilators with a short duration of action, such as inhaled nitric oxide, inhaled epoprostenol, or intravenous adenosine, are preferred for vasodilator testing. A decrease in mPAP by ≥10 mmHg to an absolute level of ≤40 mmHg without a decrease in CO is defined as a positive pulmonary vasodilator response, and responders are considered for long-term treatment with calcium channel blockers (CCBs). Less than 12% of patients are deemed vasoreactive during testing, and even fewer exhibit long-term responsiveness to CCBs. Acute vasodilator-induced reductions in PVR and mPAP predict better long-term survival even among patients not treated with CCBs. The need for invasive hemodynamic measurements to diagnose PH accurately poses an additional problem when evaluating older patients. Physicians are often reluctant to refer older patients for invasive procedures. However, the diagnosis of PH is increasing in the older population, at least in part because of increased awareness of this disease in the elderly and increased use of screening echocardiograms. Furthermore, the increased availability of oral and less complicated therapeutic options has encouraged the referral of older patients for evaluation and treatment.



A ***B***

FIGURE 304-2 ***A.*** Representative echocardiogram showing the apical four-chamber view from a patient with pulmonary hypertension demonstrating an enlarged right atrium and ventricle with some compression of the left side of the heart. ***B.*** Same echocardiographic view showing a normal echocardiogram.