

Executive Summary*

Diagnosis and Management of Pulmonary Arterial Hypertension: ACCP Evidence-Based Clinical Practice Guidelines

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(*CHEST* 2004; 126:4S–6S)

Abbreviations: ACCP = American College of Chest Physicians; CTEPH = chronic thromboembolic pulmonary hypertension; PAH = pulmonary arterial hypertension; PPH = primary pulmonary hypertension

An expert committee representing multiple disciplines has developed “Diagnosis and Management of Pulmonary Arterial Hypertension: ACCP Evidence-Based Clinical Practice Guidelines.” This committee was impaneled at the request of the American College of Chest Physicians (ACCP) Health and Science Policy Committee, with the endorsement of the ACCP Board of Regents, who had selected pulmonary hypertension as a priority for evidence-based guideline development in 2001. Ten years ago, the ACCP formed a consensus panel on primary pulmonary hypertension (PPH), which provided a well-received and concise general review of the pathobiology, diagnosis, and treatment of PPH. The objective of the current project was to create a guideline broader in scope and more evidence based than the earlier consensus statement. The Duke University Center for Clinical Health Policy Research provided the review and summaries of the current evidence on this subject. The resulting evidence-based recommendations are targeted toward an audience of cardiologists, pulmonologists, rheumatologists, and primary care physicians, as well as other health-care providers who treat pulmonary arterial hypertension (PAH).

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This guideline has been reviewed and endorsed by the American College of Cardiology Foundation, the Pulmonary Hypertension Association, The American Heart Association, and the American College of Rheumatology.

For financial disclosure see page 1S.

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PANEL SELECTION AND COMPOSITION

Lewis J. Rubin, MD, FCCP, served as the chair of this international panel of 19 experts representing five medical specialties. Representatives from other medical and patient advocacy associations were also invited to join the panel (including the American College of Cardiology, American College of Rheumatology, and the Pulmonary Hypertension Association). These experts convened on several occasions, including the culminating panel conference in September 2003, in which they deliberated over the composition of the final recommendations and grading of the current state of the evidence, benefits to the patient, and the strength of the recommendations.

SCOPE

The panel chose PAH as the topic of this guideline, adopting the nomenclature developed at the 1998 World Health Organization International Conference and recently updated at the Third World International Conference in 2003. In so doing, the panel broadened the topic compared with the consensus statement on PPH 10 years earlier, but excluded other causes of pulmonary hypertension from their analysis, including chronic parenchymal or airways disease and left-sided heart disease. Although there is no uniformly accepted definition for PAH, we recognize and adopt the hemodynamic definition developed by the National Institutes of Health Registry on Primary Pulmonary Hypertension, which has been widely used in subsequent clinical trials: a mean pulmonary artery pressure ≥ 25 mm Hg, with a pulmonary capillary wedge pressure ≤ 15 mm Hg, both measured at rest by right-heart catheterization. While the panel is unable to provide specific, evidence-based guidelines addressing thresholds for the timing of diagnostic and therapeutic interventions in suspected or proven PAH, respectively, we wish to emphasize that PAH is a serious and frequently life-threatening condition that should be approached aggressively once its presence is suspected. The panel chose the following topics for review and analysis, based on the consen-

sus impression that these topics were clinically important and had sufficient evidence to support recommendations: (1) screening, early detection, and diagnosis; (2) medical therapies; (3) surgical therapies; (4) sleep-disordered breathing; and (5) prognosis.

The section on screening addressed diagnostic and genetic tests to evaluate asymptomatic individuals at risk, including family members and patients with diseases that predispose them to the development of PAH. The section on diagnosis addresses the approach to patients suspected of having pulmonary hypertension, including history and physical examination and a variety of noninvasive and invasive diagnostic studies. Therapy was divided into medical and surgical components. Medical therapies included all currently available medications and supplements for which there is evidence of benefit in PAH. Surgical therapies were restricted to transplantation, pulmonary thromboendarterectomy, and atrial septostomy.

Since obstructive sleep apnea may be an independent risk factor for pulmonary hypertension, the evaluation for this condition and the effects on PAH of treating sleep apnea were reviewed, analyzed, and documented separately. Since the prognosis of PAH has changed substantially over the past few years as a result of new therapies, the parameters that predict prognosis and how they can be utilized in treatment choice decisions were also addressed.

The panel liberally incorporated tables and algorithms into the text, which is also extensively referenced. The recommendations were all reached by consensus of the entire panel and reflect both extensive investigation and discussion. As with other complex diseases, it is impossible to provide detailed and highly specific recommendations that apply to all patients with PAH at all stages of their illness. Rather, these Guidelines provide the physician caring for patients with PAH with a general map; directions for each trip must be left to individual circumstances. Although all of the recommendations made by the Panel are highly relevant to the care of patients with PAH, there are several key recommendations that are worthy of repetition because they address key aspects of care that, in our experience, physicians either overlook or find confusing.

SCREENING, EARLY DETECTION, AND DIAGNOSIS

In patients with a clinical suspicion of PAH, Doppler echocardiography should be performed as a noninvasive screening test that can detect pulmonary hypertension, though it may be imprecise in determining actual pressures compared to invasive evaluation in a portion of patients.

In patients with unexplained PAH, testing for connective tissue disease and HIV infection should be performed.

In patients with PAH, ventilation-perfusion scanning should be performed to rule out chronic thromboembolic pulmonary hypertension (CTEPH); a normal scan effectively excludes a diagnosis of CTEPH.

In patients with suspected pulmonary hypertension, right-heart catheterization is required to confirm the presence of pulmonary hypertension, establish the specific diagnosis, and determine the severity of pulmonary hypertension.

In patients with suspected pulmonary hypertension, right-heart catheterization is required to guide therapy.

MEDICAL THERAPIES

Patients with idiopathic PAH should undergo acute vasoreactivity testing using a short-acting agent such as IV epoprostenol, adenosine, or inhaled nitric oxide.

Patients with PAH should undergo vasoreactivity testing by a physician experienced in the management of pulmonary vascular disease.

Patients with idiopathic PAH, in the absence of right-heart failure, demonstrating a favorable acute response to vasodilator (defined as a fall in mean pulmonary artery pressure of at least 10 mm Hg to ≤ 40 mm Hg, with an increase or unchanged cardiac output), should be considered candidates for a trial of therapy with an oral calcium-channel antagonist.

In patients with PAH, calcium-channel blockers should not be used empirically to treat pulmonary hypertension in the absence of demonstrated acute vasoreactivity.

Patients with PAH in functional class III who are not candidates for, or who have failed, calcium-channel blocker therapy are candidates for long-term therapy with: (1) endothelin receptor antagonists (bosentan); (2) IV epoprostenol; (3) subcutaneous treprostinil; (4) inhaled iloprost; (5) beraprost.

SURGICAL THERAPIES

Patients with suspected CTEPH should be referred to centers experienced in the procedure for consideration of pulmonary thromboendarterectomy.

PAH patients with New York Heart Association functional class III and IV symptoms should be referred to a transplant center for evaluation and listing for lung or heart-lung transplantation.

For patients with PAH who are undergoing transplantation, the procedure of choice is a bilateral lung transplant.

SLEEP-DISORDERED BREATHING

In the evaluation of patients with PAH, an assessment of sleep-disordered breathing is recommended.

The panel believes that these guidelines will provide a useful framework for clinicians to diagnose and treat patients with PAH using contemporary, evidence-based information. We appreciate the opportunity to work on this project on behalf of the ACCP, and we hope that we have achieved the goals set out for us.