EDITOR'S MEMO

Pulmonary Hypertension Due to Lung Disease: Between a Rock and a Hard Place

Pulmonary hypertension due to lung disease (Group 3 PH) represents one of the most challenging subsets of PH patients to evaluate and manage. Being afflicted by progressive severe lung disease compounded by PH places 3 strikes against the patient with dysfunctions in parenchyma and/or airway, pulmonary vasculature, and right heart function. Thus, we often hear desperation in the voices of patients struggling with severe Group 3 PH, when each breath taken becomes an act of labor.

These patients are often referred to PH centers in the hopes that pulmonary arterial hypertension (PAH) therapies can help them to improve the quality of their lives. Unfortunately, the presence of significant lung disease often poses both diagnostic and therapeutic challenges. It has been well established that echocardiograms are not very reliable as screening tools in patients with lung disease. Furthermore, accurate interpretation of hemodynamics with right heart catheterization usually requires additional scrutiny due to the effects from wide intrathoracic pressure changes.

As for treatment considerations, there is a strong desire to see if a patient would benefit from "off-label" use of pulmonary vasodilators. However, this group of patients is challenged because pulmonary vasodilators can worsen their hypoxia and clinical status due to underlying lung disease, and for many, there are no effective disease modifying treatments for most chronic pulmonary disorders. On the other hand, there are reports of carefully selected patients with significant pulmonary arterial vasculopathy and right heart dysfunction in the presence of lung disease responding to PAH treatments, causing us to question whether this disease process is a single or separate entity.

So it is with sincere pleasure that I present this issue of *Advances*, which focuses on the current status of Group 3 PH: covering questions yet to be answered, and pitfalls to avoid. I am sincerely grateful to our guest editor Dr Jeffrey Edelman for proposing the topic of Group 3 PH for this issue, and bringing together a distinguished group of experts to share their insights on this disease state—from an in-depth discussion of the pathophysiology of hypoxic pulmonary vascular disease to the impact of PH with underlying lung diseases such as COPD and pulmonary fibrosis. The Roundtable participants, led by Dr Edelman and joined by Drs Klinger, Levine, and Schilz, accurately articulate the difficulties in managing Group 3 PH. I hope you find the information in this issue helpful in caring for your patients.

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GUEST EDITOR'S MEMO

Over the last 2 decades we have seen tremendous progress in the understanding and treatment of World Health Organization (WHO) Group 1 pulmonary arterial hypertension (PAH). Sadly, the same is not true for WHO Group 3 PH. Despite an ever-expanding array of treatments for Group 1 patients, effective therapy for Group 3 patients is lacking, as is our understanding of how and why pulmonary hypertension (PH) develops in these patients.

In the first 2 articles of this issue of *Advances in Pulmonary Hypertension* Drs Bartolome and Rivera-Lebron focus on Group 3 PH patients with chronic obstructive pulmonary disease (COPD) and idiopathic pulmonary fibrosis (IPF). In the United States, prevalence of COPD in adults is estimated to be 6.3% (approximately 15 million US adults).[1] While PH is relatively uncommon in COPD patients, its incidence increases as disease progresses. Approximately half of patients with advanced disease manifest mild PH and 1% to 3% have moderate to severe PH.[2] IPF prevalence estimates in the United States range from 14-63/100,000 adults and PH has been reported in 20% to 46% of patients.[3,4] Thus, it can be inferred that there is a substantial population of COPD and IPF patients with PH or potential to develop PH, and therefore a substantial population that could benefit from future studies.

In general, treatment for WHO Group 3 patients consists of treatment of the underlying condition and treatment of hypoxia. The impact of this approach on the course of disease is not well defined. We currently do not have effective therapy for IPF, and COPD treatments other than smoking cessation do little to prevent or reverse disease progression. While the survival benefit of oxygen therapy has been demonstrated for hypoxic COPD patients, the impact of hypoxia treatment on the course of PH in COPD or other Group 3 patients is not clear. The mechanisms underlying hypoxic pulmonary vasoconstriction and its potential contribution to PH development are discussed by Dr Swenson in the third article of this issue.

"Off-label" use of PH drugs for Group 3 patients is frequently considered, but this approach must be tempered by the lack of demonstrated benefit, the associated costs, and the potential for harm. Twenty-two percent of patients who met the definition for WHO Group 1 PAH in the Registry to Evaluate Early And Long-term pulmonary arterial hypertension disease management (REVEAL) also had obstructive airways disease[5] and conversely, it may be argued that some

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