Insights and Advances in the Diagnosis, Treatment, and Management of Pulmonary Hypertension

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The earliest description of a patient with pulmonary hypertension (PH) was published in 1891 by Dr. Ernst von Romberg, a German physician. However, it was not until the early 1970s—when there was an epidemic of pulmonary arterial hypertension (PAH) in young women—that the medical community broadly recognized PH as a deadly disease. Around the same time, the World Health Organization (WHO) had its first meeting to assess what was known about PAH. Subsequently, the National Institutes of Health (NIH) started a national registry for PAH. Over the next 40 years, the once-orphan disease saw rapid development in therapeutics and management, and today we have 14 drugs to treat PAH. In addition, we have improved our understanding of the pathogenesis of PH with the creation of five etiologic subgroups. This progress has broadened our therapeutic quest to find treatment and management strategies in other groups of PH and develop novel treatments targeting other pathways of disease. In this edition of the *Methodist DeBakey Cardiovascular Journal*, we review the challenges and progress in all aspects of PH, from advances in diagnostics, theranostics, and understanding the genetic basis of disease to the latest development and controversies in management of each subgroup.

In the first article, Dr. Sarah Beshay leads a concise summary of the latest classifications of PH based on the World Symposium on Pulmonary Hypertension. In this article, we discuss the latest updates in classification, such as long-term responders to calcium channel blockers and other suggested changes. We also focus on the key elements of evaluation and diagnosis.

Homing in on fine tuning the diagnostic algorithm, Drs. Isaac Tea and Imad Hussain provide tips and tricks to further our understanding of the role of right heart catheterization (RHC) in the diagnosis of PH. Specifically, they delve into the waveforms and their interpretation with regard to differentiating PH subgroups and the latest data illuminating the role of provocative techniques in RHC.

Understanding the genetic basis of PH gives us insight into pathways implicated in the pathogenesis of disease, possibly opening up newer paradigms of treatment. Dr. C. Gregory Elliot masterfully summarizes these novel genetic mutations and explores ethical considerations and counseling of families affected by hereditary PAH.

Moving on to PH treatment, Drs. Kanza Qaiser and Adriano Tonelli present exciting new therapies in the pipeline to treat PH. Despite advances in PH management over the last decades, median survival is still only 7 years. Fortunately, deepening understanding of the disease has led to the development of newer disease-modifying drugs, some of which are currently in phase 2 and 3 trials. These novel pharmaceuticals targeting pathophysiologically unique pathways such as BMPR2, TGF-beta, and metabolic modulation hold great promise for improving PH outcomes.

The expansion of therapeutic options has uncovered a need to personalize treatments based on both risk of disease progression and patient preference. Drs. Sandhya Murthy and Raymond Benza discuss risk scores such as the 2015 European Society of Cardiology (ESC)/European Respiratory Society (ERS) risk assessment strategies and Registry to Evaluate Early and Long-Term PAH Disease Management (REVEAL) risk score, highlighting multivariable approaches to managing and treating PAH. They underline the pros and cons and the future of PAH risk prediction.

Next, Drs. Francesca Macera and Jean-Luc Vachiéry open a series of articles discussing management of PH related to specific disease states. In their review, they focus on the most prevalent group of PH—that due to left heart disease (PH-LHD). They elaborate on PH's negative impact on heart failure prognosis and explore how PH-LHD and PAH have distinct differences in pathophysiology and clinical presentation despite similarities in mechanics. They also summarize the findings of multiple therapies that have been studied in the treatment of PH-LHD.

Continuing this theme, Drs. Jordan Sugarman and Jason Weatherald review PH as a complication of diffuse lung parenchymal disease, including chronic obstructive pulmonary disease, interstitial lung diseases, and hypoxia-related PH. The authors discuss principle management strategies in chronic-lung-disease–associated PH and the use of therapies for treating PH in this group of patients.

Adults with congenital heart disease (ACHD) are another patient group that requires special focus. As the population of ACHD survivors ages, the complexities of PH management in these

patients have gained increasing recognition. Drs. Hassaan Arshad and Valeria Duarte guide us through the evaluation and management of common scenarios of PAH in the ACHD patient population and describe the novel use of pulmonary vasodilators in Fontan physiology.

In this issue's two online reviews—available at journal.houstonmethodist.org—subject-matter experts discuss chronic thromboembolic PH (CTEPH), an underappreciated complication of acute pulmonary embolism. A multidisciplinary approach is key to a successful CTEPH program. To that end, Drs. Qasim Al Abri, Alexander Lu, and Mahesh Ramchandani provide an introductory review of CTEPH and guide us through multidisciplinary surgical approaches to treatment.

Although pulmonary thromboendarterectomy is the only cure for CTEPH, up to 40% of patients may not qualify for the operation. Fortunately, medical management options are available. Drs. Ryan Logue and Zeenat Safdar provide an excellent summary of medical management for inoperable CTEPH patients and those who have a residual PH after surgery.

As the medical community continues to improve our understanding of PH and its subgroups and expand treatment and long-term management options, the immediate future is ripe with opportunities to improve patient outcomes in this deadly disease. We hope this issue's reviews broaden your knowledge of PH, PAH, and CTEPH, and we encourage you to visit journal.houstonmethodist.org to read additional content and leave comments to further this important conversation.