Preface

Challenges in Pulmonary Hypertension

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Editors

Pulmonary hypertension (PH) is a clinical condition that has gained mounting attention in the last two decades. The development of several effective drugs has led to a remarkable improvement in quality of life and prognosis of patients with pulmonary arterial hypertension (PAH), which in fact is no longer considered an orphan disease as it was in the 1990s. However, there are several outstanding diagnostic and therapeutic issues that need to be addressed by clinical research in PAH and other forms of PH. This issue of *Heart Failure Clinics* includes a series of reviews on burning problems in the field of PH. Moreover, interesting original preliminary data regarding PH diagnosis and therapy are presented. In the opening article, the group of Marra and colleagues discusses the topic of mildly elevated PH, taking into account the new lower threshold of 20 mmHg for the diagnosis of PH. Next, Pilote and collaborators provide an overview on PH in women, bringing gender medicine into PH. Unusual PH forms (such as schistosomiasis, sarcoidosis, veno-occlusive disease, Langerhans cell histiocytosis, and hemoglobinopathies) are addressed by Souza and colleagues in their review. This contribution is of utmost importance considering that these patients are underrepresented in clinical trials. The cardiopulmonary exercise test is an important tool to assess treatment response and prognosis in PH, and Sherman and Saggar describe all the meaningful information that can be gathered by this technique. Visovatti covers the diagnostic and therapeutic issues regarding PAH associated with connective tissue diseases others than systemic sclerosis. Portopulmonary hypertension is another relevant PAH form in which the decision making regarding liver transplant is usually challenging, and this is the object of the article by Jose and colleagues. In their original work, Upadhyay and colleagues report intriguing data on microscopic examination of clots from percutaneous mechanical embolectomies in pulmonary embolism (PE). They analyzed 13 thrombectomy aspirates from patients with acute PE and determined the age of the clots according to histologic characteristics. Patients with "younger" thrombi had higher initial oxygen requirement, while those with "older" PE tended to require long-term oxygen therapy. Mei and colleagues discuss critical aspects of PH during pregnancy, from preconception to risk stratification through pregnancy and postpartum. The German group headed by Eichstaedt and colleagues presents an interesting overview of the genetic background of high-altitude pulmonary edema. Oral anticoagulation has long been a mainstay of supportive therapy in idiopathic PAH, and it is mandatory in chronic thromboembolic PH. This topic is covered by Demelo-Rodriguez and colleagues in their article. The COVID-19 pandemic impacted dramatically on the health care system worldwide. The questions of how to manage PAH patients during COVID-19 and whether COVID-19 may lead to future development of PH are answered by Giannakoulas and Farmakis. A preliminary report regarding the hormonal abnormalities in PAH is

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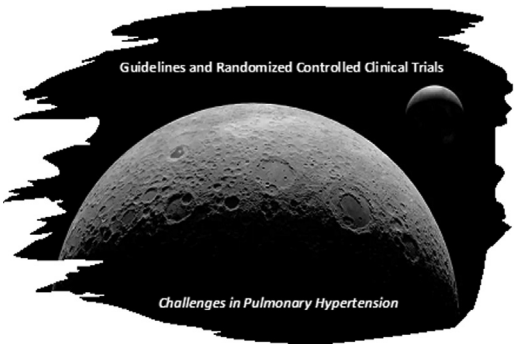

Fig. 1. In this issue, we covered PH topics commonly neglected by medical literature, including mildly elevated PH, sex and gender issues, unusual forms, cardiopulmonary exercise testing, rarer connective tissue diseases, liver transplant and portopulmonary hypertension, pregnancy, high-altitude pulmonary edema, anticoagulation, COVID-19, right-ventricular failure, noncoding RNAs, and novel research regarding embolectomy specimens and hormonal abnormalities in PH. Such issues are like the dark side of the moon, something usually not seen by observers from the earth. (*Modified from* Wright E. The Moon's Far Side. February 12, 2015. https://svs.gsfc.nasa.gov/11747.)

provided by Marra and colleagues. According to this study, patients presenting two or more hormonal deficiencies (testosterone, Dehydroepiandrosterone sulfate, insulin-like growth factor-1, insulin resistance, and thyroid hormones) cluster in a subgroup with worse exercise capacity, pulmonary hemodynamics, and right-ventricular size and function, generating the hypothesis that hormonal replacement therapy may be useful. Cittadini and colleagues overview the occurrence of right-ventricular failure and its management. In the last article of this issue, Ameri and colleagues address the emerging topic of noncoding RNAs in PH.

In conclusion, this issue brings attention to novel or unsolved aspects of PH that are commonly encountered in clinical practice (**Fig. 1**), with the ambition of keeping the reader updated on the main lines of research and, possibly, clinical changes in the challenging arena of PH.

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