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Beyond the World Symposium on Pulmonary Hypertension: practical management of pulmonary arterial hypertension and evolving concepts

Jean-Luc Vachiéry[1]* and Nazzareno Galiè[2]

[1]*Department of Cardiology, Pulmonary Hypertension and Heart Failure Clinic, Cliniques Universitaires de Bruxelles—Hôpital Erasme, 808 Route de Lennik, 1070 Brussels, Belgium; and*
[2]*Department of Experimental, Diagnostic and Specialty Medicine, DIMES Alma Mater Studiorum University of Bologna, Via Zamboni, 33 - 40126 Bologna - Partita, Italy*

Pulmonary hypertension (PH) is a common complication of most cardiac and respiratory disorders.[1] It must not be confused with pulmonary arterial hypertension (PAH), a rare, incurable, and rapidly evolving condition.[1] With a median survival of 2.8 years when untreated,[1,2] PAH is without any doubt one of the most severe cardiovascular disorders. Despite its uncommon nature, it is remarkable that PAH has well-established guidelines for management and an evidence-based treatment algorithm.[1] These peculiar achievements witness decades of discoveries, resulting not only from intense collaborative research but also from industry/academic partnership to develop new therapies. In fact, scientific rigour, creativity and partnership probably best define the 'PH community'.

First held in 1973, then every 5 years since 1998,[3] the World Symposium on Pulmonary Hypertension (WSPH) is one of the key drivers of progress in PAH. Proceedings of the 6th WSPH provided the leading edge in PH, identified gaps in evidence and proposed important plans for the future. With this supplement, the authors aim to address some evolving paradigms and provide specific insights into the practical management of PAH, a year after the 6th WSPH.

The haemodynamic definition of PH has recently been debated extensively, from which a proposal for a revised definition has emerged. It is now recognized that a mean pulmonary artery pressure (mPAP) >20 mmHg and a pulmonary vascular resistance (PVR) ≥ 3 Wood units (WU) should be considered abnormal.[4] This revised definition has several advantages as it takes into account the impact of an increased mPAP on prognosis, helps early identification of patients in groups at risk who warrant attention and may allow early interventions for specific forms of PH.[5] This change in paradigm gives PVR a greater role in the characterization of pulmonary vascular disease (PVD), although more data are needed to establish how this truly reflects changes in the structure of the pulmonary vessels. In addition, this revised definition may allow a better management in patients with systemic sclerosis, carriers of genetic mutations associated with PAH and even chronic thromboembolic disease that may revisit the terminology of Group 4 PH in the future.[5]

The revised definition of PH will have an impact on screening strategies for PAH. Due to the rare nature of the disease, screening is defined as tests to aid early detection of PAH in asymptomatic patients belonging to groups at risk of developing PAH.[6] In fact, significant PVD may be present even in the absence of symptoms.[6] A structured screening programme positively impacts patient management by favouring early intervention. The current approach mostly relies on echocardiography and multidimensional assessment or scores. However, there is a growing interest in the use of blood-based biomarkers, exhaled volatile organic compounds, and new imaging techniques.[6] In addition, artificial intelligence and analysis of patients' healthcare utilization behaviour hold great promise.[6]

With the availability of specific therapies and better disease awareness, new issues are emerging in the management of PAH. Two of the most challenging issues are associated with the increased burden of comorbidities[7] and the care of elderly patients.[8] Both represent diagnostic challenges and potential difficulties in therapy maintenance. Cardiac and respiratory comorbidities are increasingly recognized in patients with PAH, both being confounding factors to establish a precise diagnosis: three quarter of patients over 65 years of age suffer from at least one coexisting condition that may negatively impact

*Corresponding author. Tel: +32 25554866, Fax: +32 2 555 4339, Email: jeanluc.vachiery@erasme.ulb.ac.be

outcome.[7,8] Interestingly, the burden of comorbidities has been well recognized as an important driver of outcome in patients with heart failure,[9] especially in patients with preserved ejection fraction (HFpEF) in whom it may also affect therapy.[10] A new approach may include specific recommendations on the management of specific comorbidities such as ischaemic heart disease, systemic hypertension, sleep-apnoea syndrome, and thyroid disorders in the context of PAH.[7] Real-life registries suggest that patients present at an older age in PH clinics: in the COMPERA registry, 63% of patients are aged over 65 years.[11] In contrast, such a subgroup of patients is unusual in randomized clinical trials (RCTs), even in the most recent studies: the mean age of patients included in the GRIPHON trial was 48.1 ± 15.37 years.[12] The higher prevalence of left heart diseases in the elderly remains a critical diagnostic challenge that has been addressed by a specific task force of the last WSPH.[13] In this supplement, a revised diagnostic algorithm is proposed, which puts in perspective the predisposition of HFpEF as a cause of PH and the role of fluid loading to uncover the contribution of diastolic dysfunction.[8] It also draws attention to the impact of age in blunting the effects of PAH therapies and the potential increase in risk of drug-induced side effects (including drug–drug interactions).[7,8]

The management of PAH involves a diversity of medical and surgical disciplines. In this context, portopulmonary hypertension (PoPH) and PAH associated with congenital heart diseases (PAH-CHD) represent unique challenges for physicians.[14] Both require specific attention to allow early detection and a decision-making process that involves correction of the underlying disorder. In addition, the current therapeutic algorithm applies to both situations.[1] Patients with portal hypertension may develop PH as a consequence of a high-output state or PVD, only the latter being a potential target for therapy. Although not an indication for liver transplantation per se, PoPH requires specific management when liver transplantation is indicated. In this context, combination therapies including a parenteral prostacyclin may successfully bridge patients to transplantation.[14,15] However, the evidence supporting a role for targeted therapies in PoPH is more experience-based than evidence-based as these patients were included in a handful of RCTs.[14] A similar comment can be made for PAH-CHD, as patients were allowed to be included only in the presence of small or corrected defects, with the exception of two RCTs in Eisenmenger syndrome.[14] In fact, the group of congenital heart disease is one of the most heterogeneous as the key question in the management is whether there is room for correction of the underlying defect.

A PH service is patient-centred and relies on the expertise of nurse specialists. Interestingly, one of the main complaints of PAH patients is fluid retention. Although it may have a major impact on quality of life, there is little evidence or guidelines for the management of this common manifestation of PAH. Nevertheless, a practical approach to this issue requires a high level of involvement of all caregivers.[16] Monitoring of weight gain, appropriate salt restriction, lifestyle adaptation, and administration of oral diuretics are common measures that allow a proper fluid balance. When fluid retention builds up, more aggressive measures such as intravenous diuretics and ultrafiltration may be considered. These measures are summarized on a well-articulated flow chart, which is readily applicable in the clinic.[16]

As healthcare providers, everything we do is dedicated to patients. It is therefore essential that their voice is heard, not only by all caregivers, but also by administrative staff members, hospital leadership teams and boards, as well as regulatory bodies. In short, the society we live in. This is why we wanted to leave the last word to patients who suffer from PAH. By sharing their journey, their fears but also their hopes and their trust in the future, we believe that the testimony of our patients will touch the heart and soul of our readers. We are together united to fight for them and with them, against this condition, which we hope, one day, will be cured.[17]

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