



Clinical Preview

An insider view on the World Symposium on Pulmonary Hypertension

The recent publication in the *European Respiratory Journal* of the proceedings of the 6th World Symposium on Pulmonary Hypertension (WSPH) is an important milestone in pulmonary vascular medicine. Since the first WHO meeting on primary pulmonary hypertension in Geneva in October, 1973, these World Symposia have taken place in Evian (France, 1998), Venice (Italy, 2003), Dana Point (USA, 2008), and twice in Nice (France, 2013, and 2018). These events have paved the way for better understanding and management of pulmonary hypertension worldwide. In 2018, a group of 124 experts were invited to describe the current state of the art and future directions in pulmonary hypertension. Chapters from 13 task forces have been written by leaders in their respective fields. In this brief overview, we highlight a few novelties from the proceedings.

Previously, pulmonary hypertension with right heart catheterisation was arbitrarily defined as 25 mm Hg mean pulmonary artery pressure (mPAP) or more. However, the upper limit of normal mPAP has been robustly defined to be 20 mm Hg, leaving a diagnostic gap between 21 and 24 mm Hg. It is important to underscore that any value of mPAP above 20 mm Hg defines pulmonary hypertension, which could be explained by different causes with or without pulmonary vascular disease. For example, an elevated pulmonary artery wedge pressure due to left heart disease is a common cause of pulmonary hypertension. In a minority of cases, pre-capillary pulmonary vascular disease will be the cause of elevated mPAP. The 6th WSPH task force definition stated clearly that pre-capillary pulmonary hypertension due to pulmonary vascular disease will be diagnosed when mPAP of over 20 mm Hg is associated with abnormal pulmonary vascular resistance of 3 or more Wood Units. Notably, a change in the haemodynamic definition of pulmonary hypertension due to pulmonary vascular diseases does not imply treating additional patients, but highlights the importance of close monitoring and further research. This is particularly true for patients with known risk factors for a pulmonary vascular disease, such as those with systemic sclerosis or carrying a *BMPR2* mutation, or in case of chronic thromboembolism. Another important message from this task force is that elevated mPAP is a biomarker of worse outcomes in different settings, irrespective of the presence of a treatable pulmonary vascular disease. This is the case in the large group of patients with pulmonary hypertension due to left heart disease or chronic lung diseases, in whom the use of drugs approved for pulmonary arterial hypertension (PAH) is

not recommended in the absence of positive randomised controlled trials.

Another highlight of the 2018 symposium was a new PAH treatment algorithm. Several medications targeting the endothelin, nitric oxide, and prostacyclin pathways have been approved for PAH in the past 25 years. The most important recent advances in the medical management of PAH have not been related to the discovery of new pathways, but to the development of new strategies for combination therapy and on escalation of treatments based on systematic assessment of clinical response. The new treatment strategy proposed at the 2018 symposium is based on the severity of disease in patients newly diagnosed with PAH, as assessed by a multiparametric risk stratification approach. Clinical, exercise, right ventricular function, and haemodynamic parameters are combined to define a low, intermediate, or high-risk status according to the expected 1-year mortality. The new treatment algorithm provides the most appropriate initial strategy, including monotherapy, or more often initial combination therapy (one or two oral drugs combined with an intravenous prostaglandin in the high-risk population and dual oral combination therapy with an endothelin receptor antagonist and a type 5 phosphodiesterase inhibitor in intermediate-to-low-risk cases). Further treatment escalation is required in case low-risk status is not achieved in planned follow-up assessments. Lung transplantation may be required in most advanced cases on maximal medical therapy.

The symposium also saw developments in the field of chronic thromboembolic pulmonary hypertension (CTEPH). In 1–3% of acute pulmonary embolism cases, abnormal persistent obstruction of proximal or distal pulmonary arteries by residual organised thrombi, combined with a variable microscopic pulmonary vasculopathy indistinguishable from that of PAH, may lead to CTEPH. Lung ventilation/perfusion scintigraphy is the screening test of choice and a normal lung scan rules out CTEPH. In the case of an abnormal perfusion scan, a high-quality pulmonary angiogram is necessary to confirm and define pulmonary vascular involvement. CT pulmonary angiography with or without digital subtraction angiography will characterise vessel morphology for assessment of operability. CTEPH treatment decisions will be made in an expert centre with multidisciplinary teams including experienced surgeons for pulmonary endarterectomy, interventional radiologists and cardiologists, radiologists experienced in pulmonary vascular imaging and pulmonologists and cardiologists with expertise in pulmonary hypertension. Besides lifelong anticoagulation



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For the **proceedings of the symposium** see *Eur Respir J* 2019; **53**: 1802148

For more on **pulmonary hypertension due to left heart disease** see *Eur Respir J* 2019; **53**: 1801897

For more on the **new pulmonary hypertension definition** see *Eur Respir J* 2019; **53**: 1801913

For more on **medical therapy for pulmonary hypertension** see *Eur Respir J* 2019; **53**: 1801889

For more on **chronic thromboembolic pulmonary hypertension** see *Eur Respir J* 2019; **53**: 1801915

For more on the importance of patient perspectives in pulmonary hypertension see *Eur Respir J* 2019; 53: 1801919

therapy, surgical endarterectomy is the treatment of choice in patients with proximal CTEPH affecting large pulmonary arteries. However, approximately half of patients with CTEPH are not operated on, mainly because of distal lesions inaccessible to surgery. Following the 2018 symposium, for technically inoperable cases, pulmonary hypertension medical therapy is now recommended with or without balloon pulmonary angioplasty performed in experienced centres. Riociguat, a guanylate cyclase stimulator targeting the nitric oxide pathway, is currently the only approved drug for inoperable CTEPH.

In summary, these chapters form the basis for development of new approaches aimed at treating the various forms of pulmonary hypertension. Hopefully, the next World Symposium on pulmonary hypertension will bring us one step closer to our quest for a cure for this condition. Meanwhile, we call for the development, expansion, and promotion of patient associations to support patients and caregivers, lobby for access to

best care and treatments, and provide input into the development of clinical trials and registries, focusing on the patients' perspective.

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