The new definition and diagnostics of P(A)H

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Increased understanding of the pathophysiology of pulmonary arterial hypertension (PAH) has led to the development of several PAH-specific therapies that target the different pathophysiological pathways. As treatment options continue to increase, evidence-based treatment strategies are evolving to optimize the management of PAH.

Pulmonary arterial hypertension (PAH) is defined as an increase in mean pulmonary arterial pressure (mPAP) ≥25 mmHg (assessed by right heart catheterization [RHC]), a pulmonary arterial wedge pressure (PAWP) of ≤15 mmHg and normal or reduced cardiac output (CO)\(^1\). Based on recent registries, the prevalence of PAH is estimated at 15 cases/million adult population, with approximately 6 cases/million adult population of idiopathic PAH (IPAH)\(^2,3\). The French registry, which included 674 PAH patients, reported a mean age at diagnosis of 50 ± 15 years\(^2\). In addition, the female to male sex ratio was 1.9, highlighting the predominance of PAH in females.

PAH represents one of the 6 clinical classifications of PH, and includes heritable forms of PAH, clinically sporadic IPAH, and PAH associated with other conditions (APAH). Diagnosis of a patient with suspected PAH is performed through a process of exclusion, involving a series of step-wise tests. Current ESC/ERS guidelines provide an integrated algorithm for the diagnosis of PAH. RHC – which directly measures pulmonary artery pressure and cardiac function – is currently the only
method to offer a definitive diagnosis. Following diagnosis, additional tests may be necessary to characterize the functional and haemodynamic impairment, and to establish the specific aetiology. These include transthoracic echocardiography (TTE), high-resolution computed-tomography (HRCT), cardiac magnetic resonance, liver function tests and assessment of biochemical markers. In addition, consideration of the clinical history of the patient may be important, for example in drug/toxin-induced PAH and PAH associated with connective tissue disease (PAH-CTD).

Screening has an important role in the early identification of PAH in at-risk populations. For example patients with systemic sclerosis (SSc) are at increased risk of developing PAH and screening by TTE is therefore recommended for symptomatic patients. TTE is currently the most established tool for screening populations at high risk for PAH. As evidence continues to emerge, it is important that established screening programs are adapted accordingly. This has recently been illustrated following a 3-year follow-up of the ItinérAIR-Sclérodermie study. Specificity of this screening algorithm has been increased by raising the threshold for systolic regurgitant tricuspid flow velocity from <2.5 to \( \leq 2.8 \text{ m/s} \).

In addition to improving existing screening methods, introduction of novel methods may facilitate better detection of PAH in at-risk populations. N-terminal pro-brain natriuretic peptide (NT-proBNP) has been shown to correlate with survival in PAH. Furthermore, in addition to exercise capacity and NYHA/WHO functional class (FC),
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NT-proBNP showed good correlation with pulmonary vascular resistance (PVR), mean right arterial pressure (mRAP) and cardiac index (CI) in PAH-SSc patients. However, the use of this peptide as a screening and diagnostic tool needs to be validated in large-scale studies. The DETECT study is currently evaluating the role of NT-proBNP along with electrocardiography and echocardiography against RHC in screening for PAH in SSc patients.

Given the progressive nature of PAH, timely diagnosis and prompt treatment initiation is critical. The results of the EARLY study showed for the first time that PAH progression can be significantly delayed, even in FC II. These findings emphasize the importance of early treatment and reinforce the need for screening programs in high-risk groups such as SSc patients. A better understanding of the subtypes of PAH along with new diagnostic methods will contribute to improved patient management.

References
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