From the microscopic to the macroscopic: clinical–radiological–pathological correlation in pulmonary hypertension

Robin Condliffe [1,2,3], Peter Dorfmüller [4,5], Deepa Gopalan [6], Olivier Sitbon [7,8,9] and Anton Vonk Noordegraaf [10]

[1]Sheffield Pulmonary Vascular Disease Unit, Royal Hallamshire Hospital, Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK. [2]Department of Infection, Immunity and Cardiovascular Disease, Medical School, University of Sheffield, Sheffield, UK. [3]National Institute for Health and Care Research Sheffield Biomedical Research Centre, Sheffield, UK. [4]Department of Pathology, University Hospital of Giessen and Marburg, Giessen, Germany. [5]Institute for Lung Health, Giessen, Germany. [6]Department of Radiology, Imperial College Healthcare NHS Trust, London, UK. [7]INSERM UMR_S 999, Hôpital Marie-Lannelongue, Le Plessis-Robinson, France. [8]Faculté Médecine, Université Paris Saclay, Le Kremlin-Bicêtre, France. [9]Service de Pneumologie et Soins Intensifs Respiratoires, Centre de Référence de l'Hypertension Pulmonaire, Hôpital Bicêtre, Assistance Publique Hôpitaux de Paris, Le Kremlin-Bicêtre, France. [10]Pulmonology, Amsterdam UMC, Amsterdam, The Netherlands.

Corresponding author: Robin Condliffe (robin.condliffe@nhs.net)

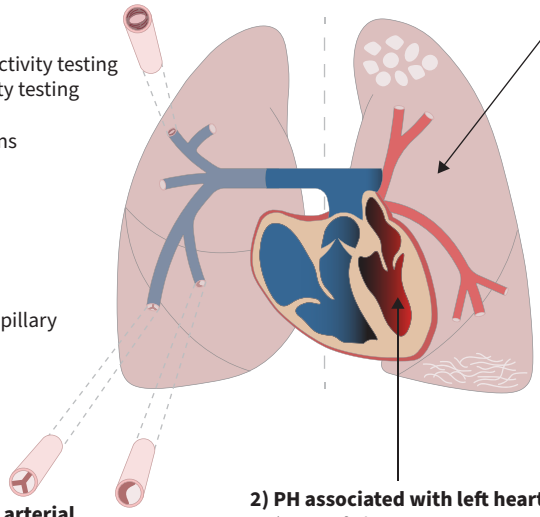
Shareable abstract (@ERSpublications)
This editorial introduces a new *European Respiratory Review* series focusing on clinical, radiological and histopathological features in pulmonary hypertension. https://bit.ly/3RtiFVK

Cite this article as: Condliffe R, Dorfmüller P, Gopalan D, *et al*. From the microscopic to the macroscopic: clinical–radiological–pathological correlation in pulmonary hypertension. *Eur Respir Rev* 2023; 32: 230237 [DOI: 10.1183/16000617.0237-2023].

Received: 16 Nov 2023
Accepted: 25 Nov 2023

Pulmonary hypertension (PH) is defined as the presence of a mean pulmonary arterial pressure >20 mmHg [1]. This simple haemodynamic definition encompasses a heterogenous collection of conditions. It is now appreciated that although treatable forms of PH are relatively rare, PH itself is not an uncommon entity, affecting ∼1% of the global population [1]. Current international guidelines describe five classification groups: group 1 (pulmonary arterial hypertension (PAH)), group 2 (PH associated with left heart disease), group 3 (PH associated with lung disease), group 4 (PH associated with pulmonary arterial obstructions) and group 5 (PH with unclear and/or multifactorial causes) figure 1 [1]. These groups are characterised by shared clinical, haemodynamic and radiological features which are underpinned by common histopathological changes. Pre-capillary PH (defined by a pulmonary arterial wedge pressure ⩽15 mmHg and a pulmonary vascular resistance >2 Wood units (WU)) may result from remodelling, obstruction or loss of the pulmonary arterial bed while post-capillary PH (defined by a pulmonary arterial wedge pressure >15 mmHg) results from passive backwards transmission of elevated left heart filling pressures into the pulmonary circulation (isolated post-capillary PH) [2]. Some patients with post-capillary disease may develop subsequent pulmonary vascular remodelling with a subsequent increase in pulmonary vascular resistance to >2 WU (combined pre- and post-capillary PH). Three main classes of PAH therapies have been shown to be of benefit in group 1 disease (targeting the nitric oxide, endothelin-1 and prostacyclin pathways) while chronic thromboembolic PH can be effectively treated with pulmonary endarterectomy surgery together with important roles for balloon pulmonary angioplasty and pulmonary vasodilators [3, 4]. The optimal treatment in the majority of patients in groups 2, 3 and 5 is less well defined. Recent advances in our understanding of the histopathological changes in different forms of PH have the potential to further inform classification and patient management [5].

It is, therefore, vital that clinicians who diagnose and manage patients with PH have a good understanding of the histopathological basis and radiological features associated with these different forms of PH. To this end, a series of reviews focusing on four of these diagnostic groups plus a bonus review specifically covering PAH with features of venous/capillary involvement (pulmonary veno-occlusive disease and pulmonary capillary hemangiomatosis) begins in this issue of the *European Respiratory Review* [6–10]. In these review articles, key histopathological and radiological patterns are explored using illustrative clinical



1) PAH
1.1) Idiopathic PAH
1.1.1) Non-responders at vasoreactivity testing
1.1.2) Responders at vasoreactivity testing
1.2) Heritable
1.3) Associated with drugs and toxins
1.4) Associated with:
1.4.1) Connective tissue disease
1.4.2) HIV
1.4.3) Portal hypertension
1.4.4) Congenital heart disease
1.4.5) Schistosomiasis
1.5) PAH with features of venous/capillary involvement (PVOD/PCH)
1.6) Persistent PH of the newborn

3) PH associated with lung disease and/or hypoxia
3.1) Obstructive lung disease or hypoxia
3.2) Restrictive lung disease
3.3) Lung disease with mixed restrictive/obstructive pattern
3.4) Hypoventilation syndromes
3.5) Hypoxia without lung disease (*e.g.* high altitude)
3.6) Developmental lung disorders

5) PH with unclear and/or multifactorial mechanisms
5.1) Haematological disorders
5.2) Systemic disorders
5.3) Metabolic disorders
5.4) Chronic renal failure
5.5) Pulmonary tumour thrombotic microangiopathy
5.6) Fibrosing mediastinitis

4) PH associated with pulmonary arterial obstructions
4.1) Chronic thromboembolic PH
4.2) Other pulmonary artery obstructions

2) PH associated with left heart disease
2.1) Heart failure
2.1.1) with preserved ejection fraction
2.1.2) with reduced ejection fraction
2.2) Valvular heart disease
2.3) Congenital/acquired cardiovascular conditions leading to post-capillary PH

FIGURE 1 Clinical classification of pulmonary hypertension (PH). PAH: pulmonary arterial hypertension; PVOD: pulmonary veno-occlusive disease; PCH: pulmonary capillary haemangiomatosis. Reproduced and modified from Kiely *et al.* [11] with permission, with updated classification reproduced from Humbert *et al.* [1] with permission.

case studies with particular attention being paid to the development of a systematic approach to radiological interpretation. It is hoped that the series will be an invaluable resource for all clinicians involved in the care of patients with PH.

Provenance: Commissioned article, peer reviewed.

Conflicts of interests: R. Condliffe reports consulting fees from Janssen and MSD, lecture fees and support for attending meetings and/or travel from Janssen, and participation on a data safety monitoring board or advisory board with Boston Scientific. A. Vonk Noordegraaf has received speaker fees for lectures and educational events from Janssen, MSD and United Therapeutics/Ferrer, and has received consulting fees from Janssen, MSD and United Therapeutics/Ferrer. The remaining authors declare no conflicts of interest related to this manuscript.

References

1 Humbert M, Kovacs G, Hoeper MM, *et al.* 2022 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension. *Eur Respir J* 2023; 61: 2200879.
2 Vachiéry JL, Tedford RJ, Rosenkranz S, *et al.* Pulmonary hypertension due to left heart disease. *Eur Respir J* 2019; 53: 1801897.
3 Galiè N, Channick RN, Frantz RP, *et al.* Risk stratification and medical therapy of pulmonary arterial hypertension. *Eur Respir J* 2019; 53: 1801889.
4 Kim NH, Delcroix M, Jais X, *et al.* Chronic thromboembolic pulmonary hypertension. *Eur Respir J* 2019; 53: 339–351.
5 Humbert M, Guignabert C, Bonnet S, *et al.* Pathology and pathobiology of pulmonary hypertension: state of the art and research perspectives. *Eur Respir J* 2019; 53: 1801887.
6 Condliffe R, Durrington C, Hameed A, *et al.* Clinical–radiological–pathological correlation in pulmonary arterial hypertension. *Eur Respir Rev* 2023; 32: 230138.
7 Lechartier B, Boucly A, Solinas S, *et al.* Pulmonary veno-occlusive disease: illustrative cases and literature review. *Eur Respir Rev* 2023; in press.
8 van de Veerdonk MC, Roosma L, Trip P, *et al.* Clinical–imaging–pathological correlation in pulmonary hypertension associated with left heart disease. *Eur Respir Rev* 2023; in press.
9 Verbelen T, Godinas L, Dorfmüller P, *et al.* Clinical–radiological–pathological correlation in chronic thromboembolic pulmonary hypertension. *Eur Respir Rev* 2023; 32: 230149.

10 Lichtblau M, Mayer L, Gopalan D, *et al.* Clinical–radiological–pathological correlation in pulmonary hypertension with unclear and/or multifactorial mechanisms. *Eur Respir Rev* 2023; 32: 230119.
11 Kiely DG, Elliot CA, Sabroe I, *et al.* Pulmonary hypertension: diagnosis and management. *BMJ* 2013; 346: f2028.