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REVIEW

Left Heart Disease and Pulmonary Hypertension: Are We Seeing the Full Picture?

Kevin Chung, MBBS [a*], Geoff Strange, PhD [a,b], Jim Codde, PhD [f], David Celermajer, MBBS, PhD [b,c,d,e], Gregory M. Scalia, MBBS, MMedSc [g,h], David Playford, MBBS, PhD [a,b]

[a]The University of Notre Dame Australia, School of Medicine, Perth, WA, Australia
[b]Pulmonary Hypertension Society, Australia and New Zealand, Sydney, NSW, Australia
[c]Department of Cardiology, Royal Prince Alfred Hospital Sydney, Sydney, NSW, Australia
[d]The University of Sydney, School of Medicine, Sydney, NSW, Australia
[e]Heart Research Institute, Sydney, NSW, Australia
[f]Institute for Health Research, The University of Notre Dame Australia, Perth, WA, Australia
[g]The Prince Charles Hospital, Brisbane, Qld, Australia
[h]The University of Queensland, School of Medicine, Brisbane, Qld, Australia

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Pulmonary hypertension (PH) is common, under diagnosed and associated with a high mortality. There are significant delays in the diagnosis of pulmonary hypertension leading to increased morbidity and delays in the initiation of treatment. Once PH is diagnosed, establishing the degree of pulmonary vascular resistance (PVR) enables clinicians to broadly divide the underlying pathology into pre-capillary or post-capillary causes, a crucial step in tailoring management.

Pulmonary hypertension is most commonly due to left heart disease (PH-LHD) and echocardiography (echo) is the most widely accessible investigation in its diagnosis. Regardless of the underlying pathophysiology of LHD, the sequelae lead to pressure overload on the left heart and a reactive increase in pulmonary pressures.

In this review article, we will discuss the prevalence of PH, examine the pathophysiology of PH-LHD, establish how echo can be used to identify patients with PH-LHD and discuss surrogate echo markers of PVR.

Keywords Pulmonary Hypertension (PH) • Left heart disease (LHD) • Diastolic dysfunction • Echocardiography • Heart failure with preserved ejection fraction (HFpEF) • Pulmonary vascular resistance (PVR)

Introduction

Pulmonary hypertension (PH) is common, under diagnosed and associated with a high mortality. Even when PH is suspected, there are significant delays in final diagnosis [1,2], resulting in more severe disease when the diagnosis is eventually made. PH, regardless of cause, is an independent risk factor for death and disability [3,4]. Appropriate treatment, started early in the disease, may improve survival and quality of life. Echocardiography (echo) is the most commonly used initial investigation for PH. This review focusses on PH due to left heart disease (PH-LHD), and discusses current echo techniques, including methods to simplify the diagnosis and measures of pulmonary vascular resistance (PVR). Although many different left heart diseases (LHD) have been described, from the perspective of

*Corresponding author at: The University of Notre Dame, School of Medicine, 47 Henry St, Fremantle, Western Australia 6160, Australia.
Tel.: +61 8 9433 0228., Email: kevin.chung1@my.nd.edu.au

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Table 1 Haemodynamic definitions of PH (adapted from Galie et al., 2016) [5].

Definition	Characteristics	NICE Clinical groups
PH	mPAP ≥25 mmHg	All
Pre-capillary PH	mPAP ≥25 mmHg	1. PAH
	PCWP <15 mmHg	3. PH due to chronic lung disease
		4. Chronic thromboembolic PH
		5. PH with unclear and/or multifactorial mechanism
Post-capillary PH	mPAP ≥25 mmHg	2. PH-LHD
	PCWP >15 mmHg	5. PH with unclear and/or multifactorial mechanism
a) Isolated Post-capillary PH	DPG <7 mmHg and/orPVR ≤3 WU	
b) Combined post and pre-capillary PH	DPG ≥7 mmHg and/or PVR >3 WU	

Abbreviations: DPG: diastolic pressure gradient (diastolic PAP – mean PCWP); PVR: pulmonary vascular resistance; WU: Wood units

pulmonary hypertension, all LHD exert their influence on the pulmonary circulation via increased pulmonary venous pressure. These effects may differ (e.g. mitral regurgitation vs left ventricular diastolic dysfunction) but in general, PH-LHD may be grouped together to separate them from pulmonary vascular causes. This review does not focus on individual treatment of specific LHDs.

Pulmonary hypertension is defined as a mean pulmonary artery pressure (mPAP) ≥25 mmHg, measured by right heart catheterisation [5]. Based on the NICE classification, there are five main forms of PH. The commonest of these is PH-LHD [6,7]. Haemodynamically, PH can be divided into pre-capillary, due to increased PVR, or post-capillary due to increase left heart filling pressure [5]. Post-capillary PH is further stratified into isolated post-capillary PH (Normal PVR) or combined post and pre-capillary PH (Increased PVR (Table 1)).

Pulmonary Hypertension from Left Heart Disease

Epidemiology

Australia

While up to four out of five people with diagnosed PH have PH-LHD [8], the true prevalence of PH-LHD in Australia remains unknown but in the current milieu of an ageing population and the increasing prevalence of systemic hypertension, diabetes, sleep apnoea and metabolic syndrome, significant work is required to establish the current burden of this disease. In the absence of community based studies, measures about the prevalence and disease burden of PH have come from other clinical registries and targeted studies.

To date, the Armadale Echo Study is the largest study in Australia to investigate PH prevalence and mortality. Results from this study confirmed that PH-LHD was the commonest form of PH (70%), and that patients with this diagnosis had the worst prognosis of all forms of PH, with a median time from echo detection to death of only 4.1 years [3].

Compounding the gravity of this situation, a related study reported significant delays from symptom onset to final diagnosis (average time: 47 months) with patients reporting an average of five GP visits and three specialist reviews before being seen at a PH centre [2]. The large database of PH managed by the Pulmonary Hypertension Society of Australia and New Zealand (PHSANZ), comprising over 2500 patients, includes almost exclusively patients with groups 1, 3, 4 and 5 PH, with only a small proportion with LHD [9].

Severity of PH is associated with increased mortality (see Figure 1). Compared to patients with mild PH, those with moderate or severe PH are respectively at 1.89 times and 3.29 times greater risk of death [3]. This highlights the need for early diagnosis and treatment, particularly in those with mild PH, including finding markers of disease progression to more severe PH.

Worldwide Epidemiology of PH-LHD

International prevalence of PH-LHD is lacking due to poor reporting of the disease and a lack of registry data available on the demographics and clinical course [5]. Prevalence data derived from tertiary referral centres mostly have PAH as the reason for referral, whereas population prevalence studies appear most suited to identifying the true prevalence of PH-LHD. Therefore, the current literature on pulmonary hypertension is disproportionately focussed on data available from PAH registries whilst lacking in group two (PH-LHD) and group three (PH due to lung disease), who make up most of the PH population.

In the United States, population based data from the Olmsted County study found that the prevalence of PH was 6.6%. Eighty-three per cent of patients with heart failure with preserved ejection fraction (HFpEF) had PH and the predictors for developing PH were increasing age and systemic hypertension [10].

In the United Kingdom (UK) the reported prevalence of PH is 97 cases per million with women 1.8 times more likely to have the disease [5]. This is likely to be an underestimate of the true population prevalence, particularly PH-LHD. The Assessing the Spectrum of Pulmonary hypertension Identified at a REferral centre (ASPIRE) registry from the Royal Hallamshire Hospital is the largest UK based PH registry.

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