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Pulmonary hypertension: Real-world data from a Portuguese expert referral centre

A. Gomes[a], C. Cruz[a], J. Rocha[a], M. Ricardo[a], M. Vicente[b], A. Melo[c], M. Santos[c,d], L. Carvalho[a,c], F. Gonçalves[a,c], A. Reis[c,*]

[a] *Internal Medicine Service, Medicine Department, Centro Hospitalar do Porto – Hospital de Santo António, Porto, Portugal*
[b] *Department of Health Sciences, University of Aveiro, Aveiro, Portugal*
[c] *Pulmonary Vascular Disease Unit, Medicine Department, Centro Hospitalar do Porto Hospital de Santo António, Porto, Portugal*
[d] *Cardiology Service, Medicine Department, Centro Hospitalar do Porto – Hospital de Santo António, Porto, Portugal*

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Abstract
Background: Pulmonary hypertension (PH) is a heterogeneous, debilitating condition with highly relevant impact on functional capacity, quality of life, and life-expectancy.
Objectives: This study aims to provide long-term data on the Portuguese PH population, by characterising the clinical presentation, evolution, and outcomes of PH patients in a specialised referral centre.
Methods: Retrospective analysis of a cohort of 101 patients with pre-capillary PH (pcPH) referenced to an expert tertiary care referral centre in northern Portugal from 2002 to 2013. Diagnosis was confirmed by right heart catheterisation (RHC). PH classification followed consensus criteria from the 5th World Symposium in Nice, 2013.
Results: The most frequent causes of pcPH were Group 1 PH – pulmonary arterial hypertension (PAH) (54.4%) and Group 4 PH – Chronic thromboembolic pulmonary hypertension (CTEPH) (25.7%); importantly, 17.8% of patients presented PH associated with multiple aetiologies. Targeted therapy was used in 91.1% of patients (48.5% combination therapy). 1-, 3-, and 5-year survival was estimated at 86.6%, 76.7%, and 64.1%, respectively. Survival was significantly better for those $\leq$40 years old (10.5 vs. 6.4 years; $P = 0.003$) and for women with I/HPAH (9.3 vs. 4.5 years; $P = 0.039$).

* Corresponding author at: Pulmonary Vascular Disease Unit, Centro Hospitalar do Porto – Hospital de Santo, António, 4099-001 Porto, Portugal.
E-mail address: reisabilio@gmail.com (A. Reis).

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Conclusions: This study provides long-term, real-world data for the management of PAH and CTEPH in Portugal and demonstrates the importance of dedicated electronic medical records and well defined clinical management protocols for better patient outcomes. Patients presented mostly with intermediate or high risk of mortality, which suggests delayed diagnosis and highlights the need to increase awareness among clinicians.

Introduction

Pulmonary hypertension (PH) is an heterogeneous condition associated with various underlying disorders, which is defined as at rest mean pulmonary arterial pressure (mPAP) ≥25 mmHg confirmed by right heart catheterisation (RHC).[1] The pathophysiological processes associated with the development of PH are complex and more than likely multifactorial, why explains why several types of classification have been proposed over the years. The most recent international consensus from the 5th World Symposium held in Nice in 2013, classifies PH according to five general groups of aetiologies.[2] Group 1 PH refers to pulmonary arterial hypertension (PAH) and includes idiopathic pulmonary arterial hypertension (IPAH), heritable pulmonary arterial hypertension (HPAH), and drugs and toxin induced; PH associated with diseases such as connective tissue disease (CTD), HIV infection, portal hypertension, congenital heart disease (CHD) and schistosomiasis are also included in Group 1. Group 1′ and Group 1″ refer to pulmonary veno-occlusive disease and/or pulmonary capillary haemangiomatosis and persistent pulmonary hypertension of the newborn, respectively. Group 2 PH includes PH due to left heart disease (LHD). Group 3 refers to PH due to lung diseases or hypoxia, such as chronic obstructive pulmonary disease (COPD) or interstitial lung disease. Group 4 PH includes chronic thromboembolic pulmonary hypertension (CTEPH) and other pulmonary artery obstructions. Group 5 refers to PH with unclear and/or multifactorial mechanisms.

Group 1 (PAH) aetiologies, except schistosomiasis associated PAH, are considered rare diseases; IPAH being an exclusion diagnosis, is the most studied form of PAH and the model for clinical management of PAH forms which are indicated for targeted therapy.[3,4] Treatment of PH involves both conventional, symptom-based therapy and targeted therapy, which is indicated for specific PH aetiologies. Conventional treatment involves the use of digoxin to improve right ventricular function, diuretics to reduce peripheral oedema, supplemental oxygen, and in specific cases anticoagulants.[3] Calcium channel blockers (CCBs) can be used to lower PAP, but their use is restricted to a small percentage of patients (3–5%) showing positive response to acute pulmonary vasodilator (ARVT) challenge.[5,6] Targeted therapy includes the use of endothelin-1 receptor antagonists (ERA),[7–9] phosphodiesterase-5 inhibitors (PDE-5I),[10,11] soluble guanylate cyclase (sGC) stimulators,[12,13] and prostacyclin analogues or receptor agonists,[14–19] surgical treatment, like lung or heart-lung transplantation is reserved to refractory cases of PAH; pulmonary angioplasty and pulmonary endarterectomy is reserved to CTEPH patients.

The proliferation of studies assessing long-term prognosis of PH has helped identify considerably different patients and disease characteristics both over time and for populations in different geographical regions.[20] These findings suggest the need for specific regional data, to fully characterise local disease populations, inform clinical practice, and to help define local/regional political strategies.

In Portugal, a national PH registry has been, but given its recent implementation, only short-term data have been published.[21] Recently, another study characterised the survival over a longer follow-up period but the sample size remained relatively small ($n = 66$).[22]

This study aims to provide long-term data for the Portuguese PH population, by characterising the clinical presentation, evolution, and outcomes of PH patients in a specialised referral centre in Portugal.

Materials and methods

Study population

We conducted a retrospective analysis of a cohort of PH patients referenced to an expert tertiary care referral centre in northern Portugal (Pulmonary Vascular Disease Unit, Centro Hospitalar do Porto – Hospital de Santo António, Porto, Portugal) from 2002 to 2013. At this centre, patients followed a defined protocol for the clinical management of PH, which was adjusted to the applicable national[23] and international guidelines during the period of the study. The protocol specified mandatory clinical assessments, which were prospectively collected in dedicated PH software developed by the centre (PAHTool®, Inovultus Lda, Santa Maria da Feira, Portugal).

PH was confirmed by right heart catheterisation (RHC), with a mean pulmonary artery pressure (mPAP) ≥25 mmHg; pulmonary arterial wedge pressure (PAWP) ≤15 mmHg was used to define pre-capillary PH. For the purposes of this study, clinical classification of PH followed standard criteria according to the consensus from the 5th World Symposium in Nice, 2013. Patients with left heart disease (LHD) (Group 2 PH) were not included in this study, due to the