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Pulmonary Arterial Hypertension in the Southern Hemisphere

Results From a Registry of Incident Brazilian Cases

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BACKGROUND: Pulmonary arterial hypertension (PAH) is a rare and ultimately fatal disorder of the pulmonary vasculature. There is increasing interest in the worldwide characteristics of patients with PAH, although data coming from the Southern Hemisphere remain scarce. The objective of this study was to describe a cohort of incident patients with PAH from a large reference center in Brazil.

METHODS: All consecutive patients who received a diagnosis of PAH by right-sided heart catheterization between 2008 and 2013 were included in the study.

RESULTS: A total of 178 patients with newly diagnosed PAH were enrolled in the study (mean age, 46 years; female/male ratio, 3.3:1; 45.5% in New York Heart Association functional class III or IV). Idiopathic PAH (IPAH), connective tissue disease (CTD), and schistosomiasis-associated PAH (Sch-PAH) accounted for 28.7%, 25.8%, and 19.7% of all cases, respectively. The patients were treated with phosphodiesterase type 5 inhibitors (66%), endothelin receptor antagonists (27%), or a combination of both (5%). For the PAH group as a whole, the estimated survival rate 3 years after diagnosis was 73.9%. The prognosis for the patients with CTD was worse than that for the patients with IPAH and Sch-PAH ($P = .03$).

CONCLUSIONS: The distribution of PAH causes and the baseline characteristics in our registry clearly differ from the previously published European and US-based registries. These differences highlight the importance of regional registries and also raise questions regarding the need to better account for such differences in future clinical trials.

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ABBREVIATIONS: CTD = connective tissue disease; FC = functional class; IPAH = idiopathic pulmonary arterial hypertension; mPAP = mean pulmonary arterial pressure; PAH = pulmonary arterial hypertension; PVR = pulmonary vascular resistance; REVEAL Registry = Registry to Evaluate Early and Long-term PAH Disease Management; Sch-PAH = schistosomiasis-associated pulmonary arterial hypertension

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Pulmonary arterial hypertension (PAH) is a rare and ultimately fatal disorder of the pulmonary vasculature.[1,2] The disease is associated with various underlying causes but is diagnosed by the presence of an elevated mean pulmonary arterial pressure (mPAP) and normal pulmonary occlusion arterial pressure at rest, in the absence of significant lung or left-sided heart disease.[3,4]

The past decade has witnessed an increasing interest in the worldwide characteristics of PAH. Data from national registries have been published and have contributed to the understanding of regional characteristics regarding the epidemiology, demographics, etiology, clinical course, hemodynamics, disease management, and treatment outcomes.[5-12] Nevertheless, data remain scarce with respect to such aspects for the population living in the Southern Hemisphere.

Most pulmonary hypertension registries enroll a mixed population of patients, including both prevalent and incident cases. "Prevalent" indicates those who have already been diagnosed and treated at the time the registry is started, whereas "incident" designates those diagnosed and treated during the generation of the registry ("newly diagnosed cases"). This distinction is relevant because prevalent patients have a better prognosis compared with incident patients and may be overrepresented in registries.[13,14] The objective of this study was to describe the epidemiology, baseline characteristics, and outcomes of a population of incident patients with PAH in Brazil with respect to the underlying causes.

Materials and Methods

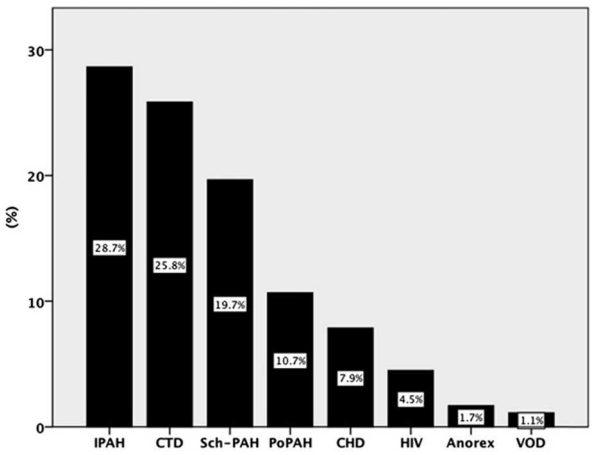
From January 2008 to December 2013, a total of 178 consecutive patients with PAH, diagnosed according to the Nice classification,[15] were enrolled in this study. PAH diagnosis was established in accordance with current international guidelines.[4] The date of the first right-sided heart catheterization was defined as the date of diagnosis.[9] Other causes of pulmonary hypertension were excluded by echocardiography, pulmonary function testing, chest CT scans, and ventilation-perfusion scans. The investigators who enrolled the subjects into the registry classified the subjects into the PAH subgroups based both on laboratory tests and their impressions of the most likely causes of the PAH. Baseline clinical, functional, and hemodynamic data were collected, and all patients were followed until December 2013. Data collection was approved by the institutional review board of the University of Sao Paulo Clinical Hospital (approval number 0832/07).

The continuous variables were expressed as mean values and SDs and were compared using paired *t* tests. One-way analysis of variance with Bonferroni correction for multiple comparisons was used to identify differences among the patient groups. The categorical variables were expressed as proportions and compared using the χ^2 test or Fisher exact test, as appropriate. The survival was described using Kaplan-Meier curves; the log-rank test was used for curve comparison. The predicted survival according to the French equation[13] was also calculated for the idiopathic PAH (IPAH) patient group. A *P* value of .05 was considered to be significant.

Results

A total of 178 patients with PAH were included in the study. Figure 1 shows the proportion of the patients in each PAH subgroup. IPAH, connective tissue disease (CTD), and schistosomiasis-associated PAH (Sch-PAH) represented the most prevalent subgroups, accounting for 28.7%, 25.8%, and 19.7% of all cases, respectively. From the 46 patients with CTD-PAH, 23 patients had systemic sclerosis, 14 patients had systemic lupus erythematosus, five patients had mixed CTD, and the remaining four patients had other CTD.

The clinical and hemodynamic data at diagnosis for the main subgroups of PAH are displayed in Table 1. Although pulmonary vascular resistance (PVR) was not used as part of the definition of PAH, only three patients with PVR < 3 Wood units were included in the cohort, all presenting portopulmonary hypertension (PVR of 2.8, 2.5, and 2.2 Wood units for each one of the individuals). The mean age of all patients enrolled in the cohort was 46 years, and the female to male ratio was 3.3:1. At diagnosis, 45.5% of the patients were classified as New York Heart Association functional class (FC) III or IV. Compared with the subjects with Sch-PAH and IPAH, patients with CTD presented with a worse FC, despite



IPAH: idiopathic pulmonary arterial hypertension; CTD: connective tissue disease-associated pulmonary arterial hypertension; Sch-PAH: schistosomiasis-associated pulmonary arterial hypertension; PoPAH: portopulmonary arterial hypertension; CHD: congenital heart disease-associated pulmonary arterial hypertension; HIV: human immunodeficiency virus-associated pulmonary arterial hypertension; Anorex: anorexic drugs-associated pulmonary arterial hypertension; VOD: veno-occlusive disease

Figure 1 – *The proportion of patients in each subgroup of pulmonary arterial hypertension (PAH) by cause.*