



# Self-reported physician practices in pulmonary arterial hypertension: Diagnosis, assessment, and referral



Susan Polanco-Briceno<sup>\*</sup>, Daniel Glass, Alexis Caze

Deerfield Institute, 780 Third Avenue, 37th floor, New York, NY, 10017, USA

## ARTICLE INFO

### Article history:

Received 23 November 2015  
Received in revised form  
21 December 2015  
Accepted 23 December 2015  
Available online 30 December 2015

### Keywords:

Pulmonary arterial hypertension  
Clinical practice  
Right heart catheterization  
Vasoreactivity testing  
Pulmonary hypertension

## ABSTRACT

**Background:** Numerous clinical trials have contributed to rapid advancements in the diagnosis and management of pulmonary arterial hypertension (PAH), yet patients often do not undergo right heart catheterization (RHC) with vasoreactivity testing and may receive a delayed or incorrect diagnosis. Efforts to improve standards of care include the designation of Pulmonary Hypertension Association (PHA)-Accredited PH Care Centers (PHCCs). This study evaluated current practices in the diagnosis and assessment of PAH.

**Methods:** A survey of 167 physicians who had  $\geq 1$  claim for PAH in the past 3 months was conducted. **Results:** Of 167 respondents, 15% were affiliated with a PHCC, 40% had referred  $\geq 1$  patient with diagnosed PAH, and 79% had  $\geq 1$  patient referred to them by another physician who they then newly diagnosed with PAH. More than half (52%) reported having  $\geq 1$  patient who was previously misdiagnosed with PAH referred to them by another physician. RHC and vasoreactivity testing, respectively, were performed in 43% and 33% of patients with PAH who respondents referred to another physician, 86% and 67% of patients newly diagnosed by respondents, and 84% and 57% of patients who respondents considered accurately diagnosed prior to being referred to them. Respondents affiliated with a PHCC were more likely to try to refer to another physician affiliated with a PHCC, and to perform RHC and vasoreactivity testing.

**Conclusions:** Self-reported clinical practices often deviated from established guidelines. Future research should focus on both clinical efficacy and ways to encourage clinicians to bring their practices in line with well-supported, evidence-based recommendations.

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## 1. Introduction

Data from a multitude of clinical trials have contributed to rapid advancements in the management of pulmonary arterial hypertension (PAH) [1–5], and PAH is the focus of many ongoing trials [6–11]. However, the benefits of these advances for patients can be limited by the capacity of physicians to adopt practices supported by evidence from well-designed studies.

PAH is a rare type of pulmonary hypertension (PH) and is

specifically defined as increased pulmonary vascular resistance that can ultimately lead to right ventricular failure and death [2–4,12,13]. Four classes of functional status have been defined by the World Health Organization. Patients with Functional Classification (FC) Class I PH are the least affected whereas those with Class IV PH are significantly functionally impacted [14,15].

PAH is defined by hemodynamic measures, including a mean pulmonary artery pressure  $>25$  mm Hg at rest or  $>30$  mm Hg with exercise [2,15]. Right heart catheterization (RHC) is the diagnostic gold standard for PAH, in part because echocardiography can only provide an estimate of pulmonary artery pressure [2,13,15,16].

Accurate diagnosis of PAH and exclusion of other types of PH is crucial to optimal management [14]. PAH-specific therapies have not been shown to benefit patients with other forms of PH, and inappropriate treatment can prevent or delay the introduction of more beneficial treatment and/or directly harm the patient [13,14].

Ideally, vasoreactivity testing is done during RHC to determine whether the patient might benefit from treatment with a calcium

**Abbreviations:** CCB, calcium channel blocker; FC, functional classification; PAH, pulmonary arterial hypertension; PCPs, primary care physicians; PH, pulmonary hypertension; PHA, Pulmonary Hypertension Association; PHCCs, Pulmonary Hypertension Care Centers; RHC, right heart catheterization; SHS, Symphony Health Solutions.

<sup>\*</sup> Corresponding author.

E-mail addresses: [spolanco-briceno@deerfield.com](mailto:spolanco-briceno@deerfield.com) (S. Polanco-Briceno), [dglass@deerfield.com](mailto:dglass@deerfield.com) (D. Glass), [acaze@deerfield.com](mailto:acaze@deerfield.com) (A. Caze).

channel blocker (CCB) [2,15]. Patients who do not respond with an adequate level of vasoreactivity are unlikely to benefit from CCB therapy yet would still be at risk for treatment side effects [15]. Although only a small subset of patients with PAH will demonstrate vasoreactivity sufficient to justify CCB treatment, short-term vasoreactivity testing is currently the only method of identifying those patients [2,15].

Advancements in the diagnosis and management of PAH have produced novel treatments and improved patient outcomes, and could have an even greater positive impact on healthcare [2,4,17]. However, in many cases evidence-based recommendations such as published guidelines are not followed [12,14,17–19]. A substantial delay between symptom onset and diagnosis still occurs in many patients, with the majority of patients diagnosed when they are already in FC Class III or IV, despite better outcomes being associated with FC Classes I and II [4,17,19]. Other issues include misdiagnosis and inappropriate therapy [19]. To improve standards of care, the Pulmonary Hypertension Association (PHA) has developed a program for accreditation of centers demonstrating expertise in PH, with particular emphasis on PAH [17].

The objective of this study was to evaluate actual practices in the diagnosis, assessment, and treatment of PAH. The goals were to understand: which physicians are diagnosing PAH; the methods used for diagnosis, evaluation, and treatment; how patients with diagnosed or suspected PAH are referred between physicians; and at which point in the progression of the disease patients tend to be diagnosed and/or referred.

## 2. Methods

### 2.1. Survey sample design

A universe sample frame of PAH-treating physicians in the US was created by sourcing 2013 insurance–claims activity for PAH therapies from Symphony Health Solutions (SHS). SHS is a leading source of nationally representative and comprehensive physician prescribing information in the US. A total of 2594 physicians who had at least one insurance claim for PAH were invited by postal mail and email to participate in an online study regarding PH. At this point, physicians voluntarily self-screened based on knowledge, interest, and experience level in PH. As it is unknown how many physicians successfully received, reviewed, and self-screened for this survey invitation, a true response rate cannot be calculated for this recruitment methodology. However, it is assumed that participation in this survey was random and represented basic interest and knowledge in this disease area.

In order to qualify for the survey, physicians had to personally have made treatment decisions and/or adjustments for at least one patient specifically to manage PAH in the previous three months. They also had to be willing to provide accurate responses to questions about their professional experiences.

### 2.2. Ethics, consent, and permission

Physicians were offered an industry-standard honorarium for their time to complete the survey. By opting in to the survey, the respondents provided consent to use their anonymized responses to the survey questions. Because this study did not involve patients or patient data, Institutional Review Board approval and patient consent were not required.

### 2.3. Survey and data collection

The survey was live between June 11 and July 12, 2015, and was comprised of 22 quantitative and eight qualitative questions.

Quantitative questions addressed the total volume of patients treated for PH and PAH, the type of physician who diagnosed/referred patients, tools used for diagnosing, and functional class at time of diagnosis. Additional quantitative questions that were unrelated to this analysis include volume of current patients in each functional class, current therapy (by functional class), and overall treatment approach by line of therapy; these results will not be presented here. Qualitative questions included those relating to how a diagnosis was determined among patients who did not have an RHC and why patients who did not receive vasoreactivity testing were not tested. Additional questions not included in this analysis related to the rationale for their treatment approach among FC Class I and FC Class IV patients, rationale for brand preference (if any), and rationale for whether they use PAH-specific medications to treat patients with PH. The survey also contained a short demographic section that asked respondents to provide their gender, the number of years in practice, the location and the setting of their practice, affiliation with any academic medical center, and percentage of professional time spent in direct patient care vs research and teaching vs other professional duties (e.g., hospital/practice administration).

### 2.4. Data analysis

All survey data were analyzed in the aggregate, and study authors were blinded to the individual identities of physician survey respondents. Responses to the closed questions were analyzed quantitatively. Responses to open-ended questions were coded into predetermined categories that were developed based on four telephone interviews with two pulmonologists and two cardiologists with current experience treating PAH. A response that addressed multiple categories was counted as multiple comments. SPSS Version 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) was used to perform the appropriate statistical analyses in order to test for significant differences between two subgroups (those affiliated with a PHA-Accredited PHCC and those not affiliated with a PHA-Accredited PHCC), although the sample size for one group (those affiliated with a PHA-Accredited PHCC) was lower than ideal for this comparison. Two-sided test p-values less than 0.05 were considered statistically significant. Multiple comparisons were not adjusted.

## 3. Results

Of the 184 physicians who entered the screener, 136 were pulmonologists, 33 were cardiologists, 11 were primary care physicians (PCPs), and four were rheumatologists (Table 1). Of the 136 pulmonologists who entered the screener, 129 qualified and completed the survey (although one was excluded for data quality issues), two qualified but did not complete the survey, and one did not qualify due to not personally making treatment decisions or adjustments specifically to manage PAH in the past three months. A total of 32 cardiologists completed the screener, 28 qualified and completed the rest of the survey, three qualified but did not complete the rest of the survey, and one did not qualify due to not personally making treatment decisions or adjustments specifically to manage PAH in the past three months. Out of the 11 PCPs who entered the screener, eight qualified and completed the survey, one qualified but did not complete the rest of the survey, and two did not qualify due to not personally making treatment decisions or adjustments specifically to manage PAH in the past three months. Finally, all three of the rheumatologists who completed the screener qualified and completed the rest of the survey. An additional four pulmonologists, one cardiologist, and one

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