The Minimal Important Difference in Borg Dyspnea Score in Pulmonary Arterial Hypertension

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Abstract

Rationale: Despite therapeutic advances, pulmonary arterial hypertension remains a disease without a cure. Focusing on symptoms, such as dyspnea, is an important part of assessing response to therapy.

Objectives: To determine the minimal important differences for the Borg dyspnea score and the Borg fatigue score in adult patients undergoing initial therapy for pulmonary arterial hypertension.

Methods: We studied 129 patients enrolled between 2003 and 2013 in the Pulmonary Arterial Hypertension Program registry at Johns Hopkins University Hospital in Baltimore, Maryland. We analyzed baseline demographics, clinical characteristics, 6-minute-walk test distance, and Borg dyspnea and fatigue scores at baseline and at follow up 3 months after initiation of pulmonary arterial hypertension therapy. The minimal important differences for the Borg dyspnea and fatigue scores were determined using distributional and anchor-based methods, using 6-minute-walk test distance as the anchor.

Measurements and Main Results: Most subjects were in New York Heart Association functional class II or III and had moderate to severe pulmonary arterial hypertension. The baseline Borg dyspnea score was 3.4 $\pm$ 1.9 units; the baseline Borg fatigue score was 2.8 $\pm$ 2.2 units. After therapy, the average change in the dyspnea score was -0.16 ± 1.9 units and the average change in the fatigue score was -0.21 ± 2.4 units. Using distributional methods, the minimum important difference for Borg dyspnea score ranged from 0.7 to 1.24 units and for Borg fatigue score ranged from 0.73 to 1.39 units. Using anchor-based methods, the minimum important difference for the Borg dyspnea scales was 0.36; this could not be calculated for the Borg fatigue score.

Conclusions: Using distributional and anchor-based methods, we estimate the minimum important difference for Borg dyspnea scale in pulmonary arterial hypertension is approximately 0.9 units. Using distributional methods only, we estimate the minimum important difference for the Borg fatigue scale is around 1 unit. Further studies are needed to determine the clinical utility of these scores in patients with pulmonary arterial hypertension.

Keywords: pulmonary hypertension; dyspnea; outcomes

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Pulmonary arterial hypertension (PAH) is a progressive disease of the pulmonary vasculature that leads to right heart failure and death (1). Unfortunately, despite advances in therapy, PAH remains a chronic disease without a cure (2). In chronic disease states such as PAH, patient-reported outcomes (PROs) are becoming increasingly important (3, 4). There are many facets of PAH that can lead to impaired health-related quality of life (HRQoL), including perceptions of dyspnea (5).

One method of measuring dyspnea that is commonly assessed in patients with PAH is the Borg dyspnea score (BDS). The BDS is a self-administered unidimensional assessment tool that analyzes breathlessness under exertion (6). In PAH, the BDS is often assessed as part of the 6-minute-walk test (6MWT), a submaximal exercise test widely used in PAH to assess functional

capacity and, until recently, the primary outcome measure for clinical trials of PAH therapies (7–14). In addition to the BDS, an assessment of leg fatigue, the Borg fatigue score (BFS), is often assessed during the 6MWT. Although change in BDS is often included as a secondary endpoint in a variety of PAH clinical trials, the threshold for clinically relevant change in this measure is not well described (7, 9, 12, 15, 16).

Deciding when to escalate PAH-specific therapies can be challenging and is often based on a variety of factors including but not limited to clinical deterioration resulting in hospitalization, worsening 6MWT, and worsening New York Heart Association (NYHA) functional class (17). Although it is important to modify therapy on the basis of functional capacity, it is also important to improve patient-important endpoints such as dyspnea. Defining the minimal important difference (MID), the smallest change or difference in an outcome measure perceived as beneficial that would justify a change in a patient's medical management (18), for the BDS and BFS would provide more pertinent information regarding patient perceptions on the efficacy of their PAH-specific therapies and possibly aid in subsequent therapeutic modifications. Therefore, we sought to estimate the MID for the BDS and BFS in patients with PAH using both anchor-based and distributional methods.

This work was previously presented in abstract form at the American Thoracic Society Meeting 2014, San Diego, CA (19).

Methods

Subjects

A cohort of patients evaluated and treated at Johns Hopkins from September 2003 through September 2013 was identified from the Johns Hopkins Pulmonary Hypertension Program registry. The registry was approved by the Johns Hopkins Institutional Review Board (NA_00027124) and all subjects included in the registry provided informed, written consent. The data were collected prospectively for this cohort and analyzed retrospectively.

Subjects with complete demographic, clinical, and hemodynamic data establishing a diagnosis of PAH were included. PAH was defined as mean pulmonary artery pressure greater than or equal to 25 mm Hg, pulmonary capillary wedge pressure less than or equal to 15 mm Hg, and pulmonary vascular resistance greater than 3 Wood units in the absence of significant obstructive or restrictive lung disease and chronic thromboembolic disease (2, 20).

6-Minute-Walk Testing

6MWTs were performed according to consensus guidelines (21). 6MWT was obtained at baseline, which was defined as time of PAH diagnosis or while on stable PAH-specific therapy for a minimum of 3 months (21). A second 6MWT was performed within 18 months of the first 6MWT and after initiation of PAH therapy or after any of the following in patients on background PAH therapy: dose change in PAH therapy or addition of PAH therapy, behavioral modifications (medication adherence, weight loss), adjustment of non–PAH-specific medications/treatments (diuretics, negative inotropes, oxygen therapy, etc.), enrollment in pulmonary rehabilitation, or randomized controlled trials for PAH. As per the practice of the Johns Hopkins Pulmonary Function Laboratory, BDS and BFS were collected at the end of each 6MWT.

Statistical Analysis

Continuous variables were summarized as the mean ± SD, or the median and range, and compared using Student *t* test. Categorical variables were compared using the chi-square statistic. P values < 0.05 (two-tailed) were considered significant. Dichotomous and categorical data were summarized using proportions.

The MIDs of the BDS and BFS were calculated using both anchor- and distributional-based methods. Using anchor-based methods to calculate the MID relies on selection of an anchor, that is, a measure for which an MID has already been established (22). This anchor is then used to estimate the MID for another measure provided the anchor has a relatively strong linear relationship with the measure of interest; therefore, the MID for the 6MWT was chosen as the anchor, as it has previously been described within PAH (23, 24).

Clinically relevant changes in patient-reported outcomes have yet to be defined within PAH and thus were not used as anchors for the purposes of this study (22). Mathai and colleagues have defined the MID of the 6MWT in PAH as 33 m using both anchor-based and distributional methods (23). The MIDs for the BDS and BFS were then determined with this anchor using the linear regression of change in 6MWT against change in BDS and BFS.

Distributional methods were also used to calculate the MIDs for the BDS and BFS. These included: (*1*) effect size, (*2*) standardized response mean (SRM), (*3*) SE of the measurement, and (*4*) the SD of the baseline measure multiplied by 0.5 (0.5 SD). Effect size is defined as the average of the difference between end-of-treatment and baseline scores subsequently divided by the SD of the baseline scores (25).

The SRM uses the SD of the change of the measure over time with therapy and therefore accounts for the covariance between the baseline and end-of-study measures (26). The standard error of the measurement is calculated by multiplying the SD of the baseline measurement by the square root of the difference of 1 minus the intraclass coefficient, or the test-retest reliability coefficient, of the measure (27). In addition, we used another distributional method, 0.5 SD, which involves multiplying the SD of the baseline measurement by 0.5 (28).

These estimates of MID for the BDS and BFS were then triangulated to determine a clinically and statistically significant measure of change for these measures (29). All analyses were performed using Stata version 12.0 (College Station, TX).

Results

A total of 129 subjects were included in this study (Table 1). The majority of subjects were white women who were, on average, 51 years old at the time of diagnosis. Nearly 50% had idiopathic PAH (IPAH), and 44% had PAH related to a connective tissue disease (CTD-PAH). The majority of subjects had NYHA functional class II (49%) or III (36%) disease. The mean 6MWT at baseline was 359 ± 128 m, suggesting moderate functional impairment. Overall, the cohort had moderate to severe PAH with a right atrial pressure of 9 ± 5 mm Hg, a mean pulmonary artery pressure of 47 ± 14 mm Hg, a cardiac index of 2.6 ± 0.7 L/min/m^2, a pulmonary capillary wedge pressure of

Table 1. Baseline characteristics

Demographics	All Patients (*N* = *129*)
Diagnosis age, yr	51 ± 14
Female sex	112 (87)
White race	107 (83)
NYHA functional class of patients	
I	13 (11)
II	55 (49)
III	41 (36)
IV	4 (4)
PAH etiology	
Idiopathic	62 (48)
Connective tissue diseases	57 (44)
Other	10 (8)
Right atrial pressure, mm Hg	9 ± 5
Mean pulmonary artery pressure, mm Hg	47 ± 14
Pulmonary capillary wedge pressure, mm Hg	11 ± 4
Cardiac output, L/min	4.7 ± 1.5
Cardiac index, L/min/m^2	2.6 ± 0.7
Pulmonary vascular resistance, Wood units	9 ± 5

Definition of abbreviations: NYHA = New York Heart Association; PAH = pulmonary arterial hypertension.
Data presented as n (%) or mean ± SD.

11 ± 4 mm Hg, and a pulmonary vascular resistance of 9 ± 5 Wood units.

Forty-five (35%) of the subjects were treatment naive at the start of the study. More than half of these subjects were started on a single-agent phosphodiesterase type 5 inhibitor (n = 24 [53%]). Five of the treatment-naive patients with IPAH were found to be vasoreactive during inhaled nitric oxide challenge on diagnostic right heart catheterization and thus were subsequently started on calcium channel blockers (2). One subject endured a prolonged hospitalization for volume overload and was treated with diuretic therapy before repeat 6MWT. The remainder of the cohort was on various PAH-specific therapies at the start of the study as shown in Table 2. Of those who were on stable PAH-specific therapy at time of baseline 6MWT, 26 (31%) were on a prostacyclin. Seventeen percent of subjects in the study had a prostacyclin added to their therapeutic regimen before follow-up 6MWT. Additional data regarding added therapies are shown in Table 2.

Table 2. Therapy

	Background Therapy (*n* = *84*)	Subsequent Therapy (*n* = *129*)
Treatment naive (n = 45)		Of 45 patients: 24 (53) PDE5I 8 (18) ERA 5 (11) CCB 2 (4) PROST 4 (9) PDE5I and ERA 1 (2) PROST and ERA 1 (2) diuretics alone
Background therapy	Of 84 patients: 23 (27) PDE5I 19 (23) ERA 11 (13) PROST 16 (19) PDE5I and ERA 10 (12) PDE5I and PROST 1 (1) PROST and ERA 4 (5) PDE5I, ERA, PROST	Of 84 patients: 8 (10) PDE5I 13 (15) ERA 12 (14) PROST 3 (3) PDE5I and ERA 1 (1) PDE5I and PROST 2 (2) PROST and ERA 0 PDE5I, ERA, PROST 21 (25) PAH therapy dose change 6 (8) Behavioral modifications 9 (11) Adjustment in non-PAH therapy 9 (11) Enrollment in clinical trials or PR

Definition of abbreviations: CCB = calcium channel blocker; ERA = endothelin receptor antagonist; PAH = pulmonary arterial hypertension; PDE5I = phosphodiesterase type 5 inhibitor; PR = pulmonary rehabilitation; PROST = prostacyclin.
Data presented as n (%).

Borg Dyspnea and Fatigue Scores

For this cohort, the BDS was 3.4 ± 1.9 units and the BFS was 2.8 ± 2.2 units at baseline (Table 3). After initiation or addition of PAH-specific therapy, both the BDS and BFS improved, with the average change in BDS of −0.16 ± 1.9 units and −0.21 ± 2.4 units in the BFS. This corresponded with a mean improvement in 6MWT of 13 ± 67.1 m overall. Sixty-four (49.6%) of the cohort demonstrated a change in 6MWT distance greater than the MID (33 m), consistent with prior studies of PAH-specific therapy (30). During the observation period, a total of 48 (37%) patients died.

Minimum Important Differences

A summary of the MID calculations using both distributional and anchor-based methods is outlined in Table 4 for the BDS. After establishing a significant correlation ($r = -0.33$, $P < 0.01$) between change in 6MWT and change in BDS, shown in Figure 1, the MID for BDS was found to be 0.36 units using anchor-based methods. However, this could not be calculated for BFS when using 6MWT as an anchor given insufficient correlation ($r = -0.08$, $P = 0.36$). The distributional method estimates were similar for both the BDS and BFS, with BDS ranging 0.70 to 1.24 units and BFS estimates ranging 0.73 to 1.39 units.

Sensitivity analyses performed in the treatment-naive cohort, IPAH cohort, and CTD-PAH cohort yielded similar results for both BDS anchor and distributional estimates, as shown in Table 4. These estimates were then triangulated to generate a clinically and statistically relevant measure of change in the BDS and BFS, estimated to be around 0.9 units and around 1 unit, respectively (29).

Table 3. Study outcome measures

	Baseline	End of Study	Change
6MWT (m)	359 ± 128	372 ± 129	+13 ± 67.1
Borg dyspnea score	3.4 ± 1.9	3.1 ± 1.8	−0.16 ± 1.9
Borg fatigue score	2.8 ± 2.2	2.5 ± 2.2	−0.21 ± 2.4

Definition of abbreviation: 6MWT = 6-minute-walk test.
Data are presented as mean ± SD.

Discussion

In this study, we report estimates of the MID for the BDS and BFS in PAH. To our knowledge, this is the first report of the MID for the BDS in PAH using both anchor- and distributional-based methods. The range of MID estimates for both BDS and BFS are small relative to the range of the Borg scales and are consistent across measures, suggesting robustness of these estimates. Based on our data using triangulation methodology, we estimate the MID of the BDS in PAH to be about 0.9 and to be around 1 unit for the BFS.

Dyspnea is a common symptom in PAH. In the REVEAL (Registry to Evaluate Early and Long-term PAH Disease Management) registry, a prospective registry of more than 3,500 patients with PAH, more than 80% of patients noted dyspnea on exertion as an initial symptom (31). In a study by Matura and colleagues, 191 participants with self-reported PAH rated 17 symptoms based on severity (32). The study found that the most prevalent symptoms in these patients were dyspnea on exertion (98%) and fatigue (95%). Furthermore, these symptoms were also found to be the most severe, even when adjusting for age. Thus, dyspnea is not only common but also an important symptom in PAH.

Although the BDS has not been validated as an assessment tool for dyspnea within PAH, it has, in general, been shown to be reliable, reproducible, and cost effective (6). Despite this lack of validation in PAH populations, the BDS is one of the most commonly obtained and described PROs in PAH as it is often administered as part of the 6MWT, both in clinical trials and in clinical practice. Still, only a few studies have examined the clinical relevance of BDS in PAH. In a study by Cenedese and colleagues in patients with various forms of precapillary pulmonary hypertension, BDS at baseline predicted time to adverse clinical event, defined as death, lung transplantation, or pulmonary endarterectomy, in univariate analysis (hazard ratio, 1.24; 95% confidence interval, 1.03–1.5; $P = 0.027$) (33). Furthermore, BDS demonstrated moderate associations with HRQoL assessed by the Minnesota Living with Heart Failure Questionnaire and the Short-Form Health Survey-36 in two cohorts of patients with PAH (33, 34).

The BDS examines breathlessness under exertion, with higher scores indicating more intense perceptions of dyspnea (6). It ranges from 0 to 10 with increments of 1 for the most part aside from the initial 0.5 increment. The MID estimate of 0.9 found in this study is small compared with the range of the scale, suggesting that relatively minor changes in BDS may be clinically relevant. Interestingly, as shown in Table 5, the reported changes in BDS in clinical trials of PAH therapies are also small. In fact, only the change in BDS noted in the Ambrisentan in Pulmonary Arterial Hypertension, Randomized, Double-Blind, Placebo-Controlled, Multicenter, Efficacy Studies (ARIES) 1 and 2 studies equaled or exceeded the MID estimate in this study. This is not surprising given the recent systematic review by Rival and colleagues demonstrating the absence of clinically relevant responses to PAH therapies in other PROs such as HRQoL in randomized clinical trials (35). Thus, although directed PAH therapies may improve functional capacity and hemodynamics and reduce hospitalizations, there is scant evidence that these therapies lead to clinically relevant improvements in patient symptoms or HRQoL.

The MID estimate for BDS in PAH found in the current study is remarkably similar to the MID estimate of the BDS in chronic obstructive pulmonary disease (COPD) (around 1 unit) (36). Although the significance of BDS in PAH is not well described, within COPD, some studies have shown that the BDS is an independent predictor of distance achieved on the 6MWT (37, 38), and some have also demonstrated close relationships between the BDS measured during the 6MWT and HRQoL as well as with dyspnea during daily life (39, 40). Furthermore, the BDS has been found to be an independent predictor of HRQoL in subjects with sarcoidosis (41). In a study of 25 patients with idiopathic pulmonary fibrosis, the BDS was found to be associated with blood oxygenation at rest and during exercise in addition to diffusing capacity (42). Interestingly, in another study of patients with idiopathic pulmonary fibrosis, the BDS has been found to be an important prognostic factor for survival (hazard ratio, 1.285; 95% confidence interval, 1.091–1.514; $P = 0.0027$) (43).

Although fatigue is a common symptom in PAH, few studies have reported changes in this symptom with therapy. The MID estimate in this study suggests that relatively small changes in fatigue are noticeable to patients. Fatigue is particularly relevant in subjects with chronic respiratory diseases and may be a target for therapy. In COPD, dimensions of subjective fatigue

Table 4. Estimates of the minimum important difference for the Borg dyspnea scale

Method	MID for Entire Cohort (*n* = 129)	MID for Treatment Naive (*n* = 45)	MID for IPAH (*n* = 62)	MID for CTD-PAH (*n* = 57)
Anchor	0.36	0.42	0.33	0.42
ES	0.70	0.91	0.71	0.61
SRM	0.98	1.24	1.12	0.93
SEMeas	0.96	1.46	1.20	1.45
0.5 (SD)	1.24	0.97	0.93	1.14

Definition of abbreviations: CTD-PAH = connective tissue disease–associated pulmonary arterial hypertension; ES = effect size; IPAH = idiopathic pulmonary hypertension; MID = minimum important difference; SEMeas = SE of the measurement; SRM = standard response mean.

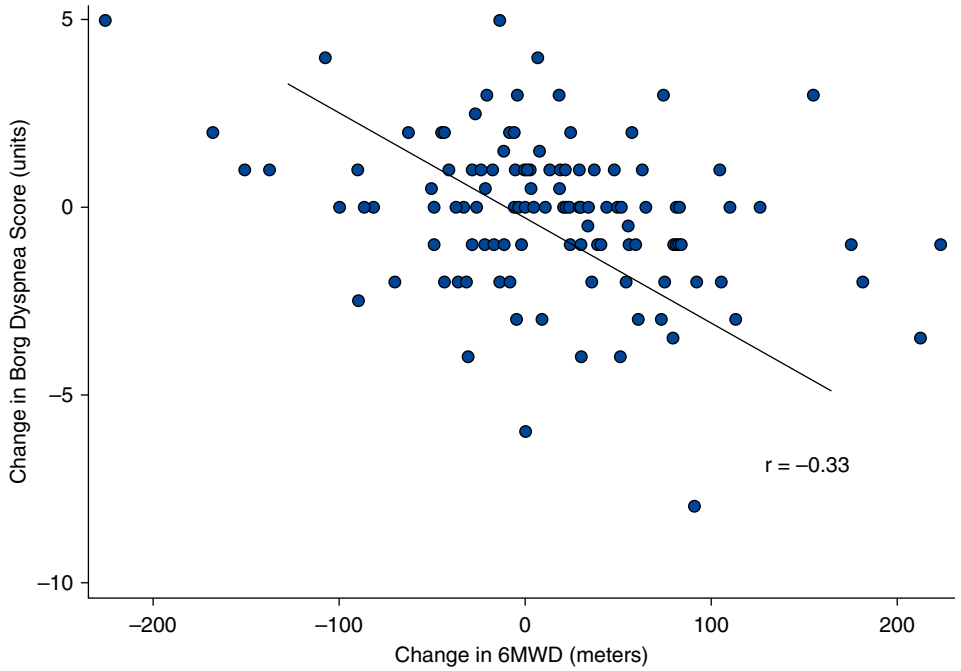

Figure 1. Change in Borg dyspnea scale versus change in 6-minute-walk test distance (6MWD).

have been related to pulmonary function, HRQoL, and skeletal muscle force (44, 45). The BFS has been associated with lower 6MWT, slower gait speed, more severe lung disease, increased dyspnea on exertion, and poorer HRQoL in patients with COPD (40, 46–48). In sarcoidosis, fatigue has been associated with decreased exercise capacity (49, 50). Further studies examining the role of fatigue in PAH and its responsiveness to PAH therapies are warranted.

We used both anchor-based and distributional methods to determine the MID in this study to develop a robust estimate. However, there is no consensus on which method (or methods) best represents the MID; there are strengths and limitations to each method (51). Although the estimates of the MID differ numerically between the anchor-based and distributional methods, this is to be

Table 5. Responsiveness of the Borg dyspnea score

Study	Reference	Baseline BDS	Change in BDS
Ambrisentan (ARIES 1&2)	12	4.0 ± 0.3	−0.9 ± 0.3* at 12 wk −1.3 ± 0.3* at 24 wk
Sildenafil (SUPER)	7	Not reported	At 12 wk: −1 (95% CI, −1 to 0) in 20 mg 0 (95% CI, −1 to 0) in 40 mg −1 (95% CI, −1.5 to 0) in 80 mg
Bosentan (BREATHE-1)	9		At 16 wk:
		3.3 ± 0.3 in 125 mg	−0.1 ± 0.2 in 125 mg
		3.8 ± 0.2 in 250 mg	−0.6 ± 0.2 in 250 mg
		3.8 ± 0.2 in placebo	+0.3 ± 0.2 in placebo
Combination ambrisentan + tadalafil for PAH (AMBITION)	16	Not reported	At 24 wk: median (IQR)
		Ambrisentan + tadalafil	−1.00 (−2.00 to 0.50)
		Ambrisentan	−0.50 (−1.50 to 0.50)
		Tadalafil	−0.50 (−2.00 to 0.88)
Riociguat (PATENT-1)	15		At 12 wk:
		4 ± 2 in 2.5 mg	−0.4 ± 1.7* in 2.5 mg
		3.9 ± 2.5 in placebo	+0.1 ± 2.1 in placebo

Definition of abbreviations: AMBITION = Ambrisentan and Tadalafil in Patients with Pulmonary Arterial Hypertension; ARIES = Ambrisentan in Pulmonary Arterial Hypertension, Randomized, Double-Blind, Placebo-Controlled, Multicenter, Efficacy Studies; BDS = Borg dyspnea score; BREATHE-1 = Bosentan Randomized Trial of Endothelin Antagonist Trial-1; CI = confidence interval; IQR = interquartile range; PAH = pulmonary arterial hypertension; PATENT-1 = Hypertension Soluble Guanylate Cyclase–Stimulator Trial 1; SUPER = Sildenafil Use in Pulmonary Arterial Hypertension.
*Indicates P value < 0.01.

expected due to the specific distributional methods used in this study. Compared with other distributional methods that use the SD of the change in a measure (e.g., SRM), the variation of the baseline measure is larger than the variation of the change of that measure over time or with intervention, and thus, the MID estimate will be larger. The anchor-based estimate uses a clinically relevant measure to group patients by magnitude of response (no change or small, moderate, or large change).

In the current study, we found a moderate linear relationship between BDS and 6MWT. Based on prior research in anchor-based estimation of MID, the strength of association was sufficient to warrant use of the 6MWT as the anchor (52). The estimate derived from this method is smaller in magnitude than the distributional method but has clinical relevance in PAH based on the anchor (6MWT). The similarity of the estimates derived from the entire cohort and the subset of treatment-naive subjects and subjects with IPAH and CTD-PAH supports the robustness of this estimate.

We chose to combine the anchor-based and distributional estimates to better represent the range of values based on prior studies that have shown the mean MID using distributional and anchor-based methods is a valid predictor of clinically significant change in disease.

Limitations

Despite the use of multiple methods to assess the MID for the BDS and BFS, there are several limitations within this study. First, the overall change in 6MWT was on average small (13 ± 67.1 m). However, although less than 50% of the cohort experienced a clinically relevant change in 6MWT (change > 33 m), this proportion is directly comparable to a prior large randomized controlled trial of PAH-specific therapy in a similar patient population that included patients who were treatment naive and on background therapy (8). Thus, the current cohort demonstrates similar composition and response to therapy as the PHIRST (Pulmonary Arterial Hypertension and Response to Tadalafil) trial despite a minimal average improvement in 6MWT distance overall. Although baseline 6MWT was not repeated among treatment-naive patients to minimize learning effect, patients on background therapy have had prior experience with the 6MWT. Given that there were no significant differences in the MID estimate for the BDS between the treatment-naive and background therapy patients in the sensitivity analyses, it is unlikely that learning effect had a significant impact on the MID estimate despite its potential impact on 6MWT distance.

Second, although the correlation between the BDS and the 6MWT ($r = -0.33$) was sufficient to perform anchor-based analyses based on expert recommendations and was consistent across the subgroup analyses (treatment-naive cohort, $r = -0.47$, $P = 0.001$; IPAH cohort, $r = -0.30$, $P = 0.03$; and CTD-PAH cohort, $r = -0.42$, $P = 0.001$), the strength of this association in the overall cohort approached the minimum acceptable level (52). However, the use of anchor-based, distributional, and triangulation methods to estimate the MID likely attenuates this limitation. Importantly, the association between BFS and 6MWT was below this minimum level. It is unclear as to why the correlation between the BFS and 6MWT was poor, but in a disease such as PAH, where patients often suffer from lower extremity edema in addition to cardiovascular limitations, a measure of leg fatigue seems particularly pertinent. It is possible that our data were influenced by inclusion of a high proportion of subjects with CTD-PAH (44% of total) who may experience fatigue as a result of extrapulmonary disease manifestations independent from the functional limitations imposed by PAH. However, correlations between BFS and 6MWT were poor even when examining the IPAH and CTD-PAH cohorts separately (data not shown). Published literature on the BFS within PAH is scant, and therefore interpretations of the significance of BFS and the change within this measure are limited.

Third, the study cohort was composed predominantly of patients with NYHA functional class II and III disease, which may impact the distributional MID estimates, as the SD of the BDS and BFS may be smaller than in a cohort that included more patients with NYHA functional class I and IV disease. Similarly, the predominance of women and white patients in the cohort may impact the generalizability of these findings. However, the characteristics of the study cohort compare favorably with the cohorts studied in clinical trials of PAH therapies, including the reported distribution of BDS (Table 5).

Finally, despite the common practice of reporting change in BDS in clinical trials of PAH therapies, no studies have compared BDS to other endpoints commonly assessed in PAH, such as hemodynamics or serum biomarkers. Thus, neither the BDS nor the BFS has been thoroughly evaluated in PAH, and, therefore, the clinical relevance of these findings requires further validation. However, defining the MID for these measures is an important component of this validation process (53).

Conclusions

Our findings suggest that small changes in Borg dyspnea and fatigue scores are noticeable to the patient, potentially clinically relevant, and therefore may serve as targets for therapeutic intervention. Thus, we believe the determination of the minimum important differences for the Borg dyspnea and fatigue scores has important implications for clinical management and future clinical trials of patients with PAH. However, further research is needed to fully validate and establish the clinical relevance of these measures in PAH. ■

Author disclosures are available with the text of this article at www.atsjournals.org.

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