Depression and Functional Status Are Strongly Associated With Dyspnea in Interstitial Lung Disease

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Depression and Functional Status Are Strongly Associated With Dyspnea in Interstitial Lung Disease

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Word Count: 2,766
ABSTRACT

Background: Little is understood about the characteristics of dyspnea in patients with interstitial lung disease, and its severity is likely influenced by multiple factors. Depression and functional status are known to influence dyspnea in patients with chronic obstructive pulmonary disease. The aim of this study was to determine the relationship of dyspnea with clinical parameters including depression and functional status in patients with interstitial lung disease.

Methods: Dyspnea was measured with the Baseline Dyspnea Index and the University of California San Diego Shortness of Breath Questionnaire. Clinical parameters were recorded. Regression analysis was performed to determine independent correlates of dyspnea.

Results: Fifty-two subjects were enrolled. The two dyspnea scales were strongly correlated (r = -0.79, p < 0.00005). The mean levels of dyspnea were 6.5 and 41.0, representing a moderate degree of dyspnea. Clinically meaningful depressive symptoms were found in 23% of subjects. Independent correlates of dyspnea severity for each dyspnea scale were depression score (p = 0.002 and < 0.0005), 4-meter walk time (p = 0.001 and 0.06), forced vital capacity (p = 0.07 and 0.004), and diffusing capacity of carbon monoxide (p = 0.007). Body mass index had borderline significant association with the Baseline Dyspnea Index (p = 0.10).

Conclusions: In patients with interstitial lung disease, dyspnea is associated with depression score, functional status, and pulmonary function. These results suggest that attention to depression and functional status is important in these patients and that treatment directed at these comorbidities may improve dyspnea and quality of life.

Abstract Word Count: 247
ABBREVIATION LIST

6MWD, 6-minute walk distance
ANOVA, analysis of variance
BDI, Baseline Dyspnea Index
BMI, body mass index
BPI, Brief Pain Inventory
CES-D, Center for Epidemiologic Studies Depression
DLCO, diffusing capacity of carbon monoxide
FVC, forced vital capacity
ILD, interstitial lung disease
IPF, idiopathic pulmonary fibrosis
PSQI, Pittsburgh Sleep Quality Index
STAI, State-Trait Anxiety Inventory
TLC, total lung capacity
UCSD SOBQ, University of California San Diego Shortness of Breath Questionnaire
UCSF, University of California San Francisco
INTRODUCTION

Interstitial lung disease (ILD) is a diverse group of conditions that are characterized by inflammation and fibrosis of the pulmonary parenchyma. In general, the ILDs are chronic diseases that result in substantial morbidity and, in some instances, high mortality.\(^1,2\) In recognition of the significant morbidity and mortality associated with ILD, greater emphasis has recently been placed on assessing and improving the symptoms and quality of life of these patients.\(^3-7\)

Dyspnea is common in patients with ILD. It is present at the time of diagnosis in 90% of patients with idiopathic pulmonary fibrosis (IPF), a common subtype of ILD.\(^1,8\) Importantly, dyspnea severity has been shown to have a strong correlation with quality of life and mortality in patients with IPF.\(^9,10\) Consequently, dyspnea is increasingly recognized as an important outcome for both prognostic and therapeutic purposes in ILD. Unfortunately, dyspnea is often refractory to currently available therapies.\(^8\)

While restriction and impaired gas exchange likely influence the presence and degree of dyspnea, other factors such as depression and functional status likely contribute to its severity.\(^8\) Depression and functional status are known to influence dyspnea in patients with chronic obstructive pulmonary disease.\(^11,12\) Identification of the key correlates of dyspnea in patients with ILD could provide important insight into its management.

In the present study, we sought to determine the relationship of dyspnea with selected clinical variables including depression and functional status in patients with ILD. We hypothesized that the severity of dyspnea in patients with ILD is related to depression and decreased functional status, and that these relationships are independent of pulmonary function. We conducted a cross-sectional study of outpatients with ILD to examine these relationships.

METHODS
Study Subjects

Subjects were prospectively identified through the University of California San Francisco (UCSF) ILD Program between 2007 and 2009. Subjects were included if they had a diagnosis of ILD and the ability to provide informed consent. The final diagnosis was made by multidisciplinary review according to established criteria, considering clinical, radiologic, and pathologic findings. Subjects who were unable to read and write English were excluded. The study design was approved by the UCSF Committee on Human Research and all subjects provided written informed consent (Clinical trials.gov identifier: NCT00611182).

Measurements

Baseline information was recorded and all questionnaires were completed at the study visit. Baseline data included age, gender, ethnicity, smoking history, and body mass index (BMI). Resting oxygen saturation was recorded. The physiologic assessment included standard techniques for the measurement of forced vital capacity (FVC), total lung capacity (TLC), and diffusing capacity of carbon monoxide (DLCO).

Dyspnea was measured using the self-administered Baseline Dyspnea Index (BDI) and the University of California San Diego Shortness of Breath Questionnaire (UCSD SOBQ). The BDI evaluates dyspnea in three categories including functional impairment, magnitude of task, and magnitude of effort. Patients designate a score of 0 to 4 for each of these categories, with a total possible range of 0 to 12. The UCSD SOBQ requires that patients rate the severity of dyspnea in 24 situations on a 0 to 5 scale, providing a total score of 0 to 120. A higher score indicates worse dyspnea for the UCSD SOBQ and a lower score indicates worse dyspnea for the BDI. Both indices were used since neither has demonstrated superiority in patients with ILD.

Depression, sleep quality, anxiety, and pain were measured using established self-administered questionnaires. Depression was measured using the Center for Epidemiologic Studies Depression (CES-D) score. A CES-D score above 15 was considered a clinically meaningful indicator of depressed mood. The referring physician was notified if a subject exceeded this score. Sleep
quality was measured with the Pittsburgh Sleep Quality Index, with a score above 5 considered clinically meaningful. An anxiety score above 40 was considered clinically meaningful. Pain was measured with the Brief Pain Inventory.

Kyphosis was measured using a flexometer and the kyphosis index was calculated. Muscle strength was measured using grip strength, an established geriatric metric of functional status. Grip strength was measured using a dynamometer (Jamar Hydraulic Hand Dynamometer, model 5030J1). The 4-meter walk time was used to assess muscle function. The 4-meter walk time was recorded as the time it took for subjects to walk 4-meters, starting from a standing position. Subjects were permitted the use of walking aids and supplemental oxygen. The 4-meter walk time is a validated geriatric measure of functional status. The 4-meter walk time was used instead of the 6-minute walk distance because the 4-meter walk is easier to perform and is less influenced by pulmonary and cardiovascular disease, thereby being a more accurate measure of peripheral muscle function in this population.

Data collection and testing was performed in the following order: demographic and clinical data, dyspnea, stress, anxiety, kyphosis index, gait speed, sleep, depression, pain, and grip strength.

Statistical Analysis

Data are described using the mean and standard deviation unless otherwise noted. Intergroup comparisons were performed using parametric or nonparametric methods as appropriate. Spearman’s correlation coefficients were calculated for bivariate analyses. The IPF subgroup was analyzed as a distinct subgroup as specified a priori, since it represented a large proportion of our cohort, is a common ILD, and likely has a unique pathophysiology. Backward stepwise linear regression analysis was performed using both the BDI and UCSD SOBQ as dependent variables, incorporating variables from bivariate analysis with each dyspnea metric that had a p value < 0.10. A p value cut-off of 0.10 was chosen to rule out confounding with greater certainty. The following predefined independent variables were evaluated: age, gender, ethnicity, smoking history, BMI, resting oxygen saturation, use of supplemental oxygen, FVC, TLC, DLCO,
kyphosis index, grip strength, 4-meter walk time, depression score, sleep quality score, anxiety score, and pain score. No variables were forced into the model. All data analysis was performed using STATA 11.0 (StataCorp, Texas, USA).

RESULTS

Study Subjects

Fifty two subjects were enrolled. The subjects’ demographic and clinical characteristics are summarized in Table 1. The most common diagnosis was IPF (n = 20, 38% of study population), followed by connective tissue disease-associated ILD (n = 17, 33%), and chronic hypersensitivity pneumonitis (n = 7, 13%). Other subtypes of ILD included sarcoidosis (n = 4), idiopathic non-specific interstitial pneumonia (n = 3), and organizing pneumonia (n = 1). On average, subjects were 64 years old, predominantly male, and predominantly current or former smokers. Subjects had a mild reduction in FVC (74% predicted) and TLC (74% predicted), with a moderate reduction in DLCO (51% predicted). Clinically meaningful depressive symptoms were found in 23% of subjects. Clinically meaningful anxiety symptoms and abnormalities in sleep quality were found in 27% and 58%, respectively. Subjects with IPF were significantly older and more likely to be male. No significant difference was found in lung function between subjects with and without IPF.

Dyspnea scores and measured clinical variables are shown in Table 2. Subjects had a wide range of dyspnea severity (Figure 1). The average level of dyspnea was 6.5 (out of 12) and 41.0 (out of 120) as measured by the BDI and UCSD SOBQ respectively, representing a moderate degree of dyspnea. The mean BDI and UCSD SOBQ scores were similar between subjects with and without IPF (p = 0.13 and 0.30).

Correlation of dyspnea and clinical variables

The BDI was strongly correlated with the UCSD SOBQ (r = 0.79, P < 0.00005; Figure 2). This
relationship was similar when analyzing only IPF. The BDI had significant correlation with depression, anxiety, 4-meter walk time, and FVC (Table 3). The UCSD SOBQ was significantly correlated with depression, sleep quality, anxiety, pain, 4-meter walk time, and gender. Of the variables tested, depression had the strongest correlation with both the BDI and UCSD SOBQ (r = -0.43 and 0.50 respectively, p < 0.002) (Figure 3). Analysis of only subjects with IPF revealed similar relationships, as did analysis of subjects with non-IPF conditions (data not shown).

**Multivariate Analysis**

Variables associated with dyspnea using multiple regression analysis are shown in Table 4. Five variables were considered potential independent correlates of dyspnea as measured by the BDI: depression score, 4-meter walk time, DLCO, FVC, and BMI. These five parameters had a cumulative $r^2$ of 0.54 (adjusted $r^2$ 0.48). FVC and BMI had borderline statistically significant association with BDI. The strength of these associations were not altered by considering the possibility of threshold effects (e.g. that only a BMI above a certain threshold impacted dyspnea). Removal of FVC and BMI from the model did not alter the strength of association of BDI with the remaining three variables. Three variables were independent correlates of dyspnea as measured by the UCSD SOBQ: depression score, 4-meter walk time, and FVC. These three parameters had a cumulative $r^2$ of 0.40 (adjusted $r^2$ 0.35). The direction and degree of association of dyspnea with DLCO and BMI was similar using both dyspnea scales. The results were unchanged with backward or forward stepwise regression, when using transformed or non-transformed variables, and when considering the impact of interactions among included variables.

The 4-meter walk time had the strongest association with the BDI (p = 0.001) and depression had the strongest association with the UCSD SOBQ (p < 0.0005). A one second increase in the 4-meter walk time was associated with a 0.8 point (6.9%) decrease in the BDI score and a 5.2 point (4.3%) increase in UCSD SOBQ score. A one point (1.7%) increase in depression score was associated with a 0.10 point (0.8%) decrease in BDI score and a 1.3 point (1.0%) increase in UCSD SOBQ score.
DISCUSSION

This study demonstrates that dyspnea is common in patients with ILD and is strongly correlated with depression and 4-meter walk time (a measure of functional status). Further, this study illustrates the prevalence of clinically significant depressive symptoms in patients with ILD. Depression and functional status may be common modifiable therapeutic targets in ILD, a disease group that often lacks effective disease modifying therapy. Treatment directed at these targets may improve dyspnea and, by extension, quality of life.

Studies in COPD have demonstrated a close relationship of dyspnea with depression and functional status. The consistency of these findings with our results suggests that factors modifying the severity of dyspnea may be similar in COPD and ILD. These similarities have important implications for the future study and treatment of dyspnea in chronic lung diseases, suggesting that strategies for the treatment of dyspnea in COPD may be applied to patients with ILD. This is of particular importance since the relatively small patient population in ILD limits the ability to perform large clinical trials. A shared treatment approach to dyspnea would be analogous to the treatment of chronic pain syndromes which is often consistent across diseases with widely varying etiologies.

Dyspnea and depression

The prevalence of clinically meaningful depressive symptoms in the current study (23%) is similar to the prevalence in a previous study of IPF (23-27%), and above the expected prevalence for minor depression in a general population of the elderly (9.8%). Over 40% of patients with an above average UCSD SOBQ score had clinically meaningful depressive symptoms, compared to only 4% of patients with a below average UCSD SOBQ score. These data suggest that patients with ILD and a moderate degree of dyspnea may have a high frequency of depression and that routine screening for depression may be justified.

We show a strong relationship between dyspnea and depression score. Dyspnea (measured using the Bath Breathlessness Scale) has previously been correlated on unadjusted (i.e. bivariate)
analysis with clinically meaningful depression in one of the four domains of the Beck Depression Inventory and two of the four domains of the Cognitive Depression Inventory. We build upon this study by demonstrating the independent nature and strength of the relationship between dyspnea and depression by adjusting for other important clinical variables. The strength of the relationship between depression and dyspnea suggests that treatment of depression could lead to improvement in dyspnea and quality of life in these patients. This hypothesis has important implications since dyspnea is the predominant symptom in ILD, is disabling, and often persists despite therapy. Further studies are required to determine if treatment of depression in ILD will improve dyspnea and quality of life.

**Dyspnea and functional status**

This study reports the novel finding that dyspnea correlates with the 4-meter walk time, a measure of lower extremity muscle mass and function, and an important marker of functional status. Prior studies of patients with ILD have demonstrated the correlation of dyspnea with other measures of functional status, including the 6-minute walk distance (6MWD) and 6-minute step test. We chose to use the 4-meter walk test instead of the 6MWD for several reasons. First, the 4-meter walk test is an established metric of functional status in the geriatric population. Second, the 6MWD has been questioned as a reliable outcome measure in patients with ILD, in part due to its sensitivity to change in non-pulmonary conditions (e.g. cardiac or musculoskeletal disease). Third, in patients with ILD the 6MWD is likely influenced by dyspnea (i.e. not an independent variable), whereas the 4-meter walk time is not.

**Dyspnea and pulmonary function**

We found that the severity of dyspnea correlated with the FVC and DLCO. This finding is consistent with previous studies that have evaluated the relationship between dyspnea and lung function. Interestingly, the correlation between dyspnea and pulmonary function is relatively weak and this relationship does not explain the majority of variance in dyspnea.

**Dyspnea and body mass index**
A high BMI had borderline association with worse dyspnea on bivariate and multivariate analysis when dyspnea was measured by the BDI, but not when measured by the UCSD SOBQ. In ILD, the cumulative mechanical load placed on the lungs by parenchymal fibrosis and obesity would be expected to worsen dyspnea. This contrasts with the effects seen in COPD, where obese subjects experience less dyspnea during exercise and achieve a higher peak oxygen consumption compared to non-obese subjects. This reduction in dyspnea may have been due to the mechanical effects of obesity that counterbalanced the hyperinflation that is typical of COPD, resulting in normalization of lung volumes. Despite what appear to be opposite effects on dyspnea, the impact of BMI on mortality is similar in COPD and IPF, with a lower BMI predicting higher mortality rates in both conditions. A relationship between dyspnea and BMI has not been previously reported in ILD and the weak association with only one dyspnea index in the current study is insufficient to draw conclusions. However these results do suggest that further research is warranted to better characterize the impact of BMI on dyspnea in ILD.

There are several limitations to this study. First, due to its cross-sectional nature we were able to comment on association, but not on causation. We cannot comment directly on the effect of depression on the experience of dyspnea. We hypothesize that depression contributes to dyspnea severity, but it is also possible that worse dyspnea leads to worse depressive symptoms. Second, we used several indices and clinically meaningful values that have not been validated in patients with ILD. While this may affect the prevalence of these abnormalities, this would not alter the correlative relationships. Third, subjects were recruited from a tertiary ILD clinic and it is possible that the characteristics of these subjects are not representative of the general ILD population. Fourth, our analysis did not include all potential determinants of dyspnea and it is possible that other factors (e.g. pulmonary hypertension) could confound our findings. Finally, the sample size limits the analysis of subgroups and it is possible that the relationships among the measured variables differ based on the type of ILD. However, both the IPF and non-specific interstitial pneumonia subgroups were large enough to permit bivariate analysis, showing similar relationships compared to the entire ILD population (data not shown).
In summary, dyspnea in ILD is common and is strongly correlated with depression and functional status. Future longitudinal assessment of the interactions of dyspnea, depression, and functional status should investigate if and how changes in these variables are inter-related and whether treatment of depression and functional status can improve quality of life. The strong association between dyspnea and depression suggests that treatment of depression in patients with ILD may not only improve mood but may also improve dyspnea. The similar relationship between depression, functional status, and dyspnea in COPD and ILD suggests that effective strategies for dyspnea relief (e.g. standardized exercise programs) in one pulmonary disease may be beneficial in other chronic lung diseases, regardless of etiology. With an improved understanding of dyspnea in patients with ILD, it is hoped that novel therapeutic interventions can be developed that positively impact clinically important outcomes.
Acknowledgements:

HRC, CSL, VLC, and SZP conceived the study design. CJR and HRC performed the data analysis and produced the initial draft of the manuscript. All authors participated in interpretation of the analysis and final preparation of the manuscript. All authors read and approved the final manuscript.

The authors would also like to thank Talmadge E. King Jr. for his thoughtful comments and review of the manuscript, Debra Koehler and the providers and staff of the UCSF Interstitial Lung Disease Program for their assistance in recruiting subjects for this study, the members of the UCSF Interstitial Lung Disease Consortium for their continued referral of patients to our center, and the patients with ILD who, through their generosity and efforts, allow us to conduct clinical research studies such as this in an effort to improve the lives of patients with ILD.
REFERENCES

6 King TE, Jr., Behr J, Brown KK, et al. BUILD-1: a randomized placebo-controlled trial of bosentan in idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 2008; 177:75-81
28 De Vries J, Kessels BL, Drent M. Quality of life of idiopathic pulmonary fibrosis patients. Eur Respir J 2001; 17:954-961
FIGURE LEGENDS

Figure 1. Distribution of dyspnea scores.
(A) Distribution using the UCSD SOBQ.
(B) Distribution using the BDI.

Abbreviations: BDI, Baseline Dyspnea Index; IPF, idiopathic pulmonary fibrosis; UCSD SOBQ, University of California San Diego Shortness of Breath Questionnaire.

Figure 2. Relation between the UCSD SOBQ and BDI scores.
Significant correlation was observed between the dyspnea scores in all patients ($r = -0.79$, $p < 0.00005$) and in patients with IPF ($r = -0.65$, $p = 0.002$).

Abbreviations: BDI, Baseline Dyspnea Index; IPF, idiopathic pulmonary fibrosis; UCSD SOBQ, University of California San Diego Shortness of Breath Questionnaire.

Figure 3. Relation between the UCSD SOBQ and depression scores.
Significant correlation was observed between dyspnea and depression scores in all patients ($r = 0.50$, $p = 0.0002$) and in patients with IPF ($r = 0.57$, $p = 0.009$).

Abbreviations: IPF, idiopathic pulmonary fibrosis; UCSD SOBQ, University of California San Diego Shortness of Breath Questionnaire.
Table 1.
Baseline Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (n = 52)</th>
<th>Patients with IPF (n = 20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>63.9 (11.6) 33 - 84</td>
<td>70.3 (7.9) 52 - 81</td>
<td>0.001</td>
</tr>
<tr>
<td>Males</td>
<td>56%</td>
<td>80%</td>
<td>0.005</td>
</tr>
<tr>
<td>Current or former smoker</td>
<td>60%</td>
<td>75%</td>
<td>0.07</td>
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<tr>
<td>Body mass index, kg/m²</td>
<td>29.0 (6.1) 19 - 45</td>
<td>28.8 (5.3) 20 - 39</td>
<td>0.84</td>
</tr>
<tr>
<td>Oxygen saturation at rest, %</td>
<td>96.2 (2.1) 91 - 99</td>
<td>96.0 (1.9) 92 - 99</td>
<td>0.56</td>
</tr>
<tr>
<td>Long-term oxygen therapy</td>
<td>8%</td>
<td>10%</td>
<td>0.62</td>
</tr>
</tbody>
</table>

**Pulmonary function tests**

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>Range</th>
<th>Value</th>
<th>Range</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC, % predicted</td>
<td>74.3</td>
<td>42 - 115</td>
<td>78.0</td>
<td>48 - 115</td>
<td>0.29</td>
</tr>
<tr>
<td>TLC, % predicted</td>
<td>73.5</td>
<td>40 - 114</td>
<td>73.1</td>
<td>44 - 95</td>
<td>0.87</td>
</tr>
<tr>
<td>DLCO, % predicted</td>
<td>50.8</td>
<td>27 - 90</td>
<td>49.6</td>
<td>33 - 67</td>
<td>0.69</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD) unless otherwise indicated. P value is for the difference between IPF and non-IPF patients.

Abbreviations: DLCO, diffusion capacity of carbon monoxide; FVC, forced vital capacity; IPF, idiopathic pulmonary fibrosis; TLC, total lung capacity.
## Table 2

**Dyspnea Scores and Measured Clinical Variables**

<table>
<thead>
<tr>
<th>Variable</th>
<th>All patients (n = 52)</th>
<th>Patients with IPF (n = 20)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dyspnea scores</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BDI</td>
<td>6.5 (2.4) 3 - 11</td>
<td>7.2 (2.5) 3 - 11</td>
<td>0.13</td>
</tr>
<tr>
<td>UCSD SOBQ</td>
<td>41.0 (25.3) 1 - 103</td>
<td>36.4 (24.4) 1 - 103</td>
<td>0.30</td>
</tr>
<tr>
<td><strong>Clinical variables</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety (STAI)</td>
<td>34.8 (9.4) 20 - 60</td>
<td>33.1 (9.5) 20 - 50</td>
<td>0.29</td>
</tr>
<tr>
<td>Depression (CES-D)</td>
<td>10.5 (9.2) 0 - 37</td>
<td>9.1 (7.8) 0 - 22</td>
<td>0.39</td>
</tr>
<tr>
<td>Pain (BPI)</td>
<td>6.0 (7.3) 0 - 22</td>
<td>5.0 (6.1) 0 - 21</td>
<td>0.43</td>
</tr>
<tr>
<td>Sleep quality (PSQI)</td>
<td>7.0 (3.9) 1 - 17</td>
<td>6.6 (3.9) 2 - 17</td>
<td>0.56</td>
</tr>
<tr>
<td>4-meter walk time, seconds</td>
<td>4.4 (1.2) 3 - 9</td>
<td>4.4 (0.9) 3 - 7</td>
<td>0.94</td>
</tr>
<tr>
<td>Grip strength, % predicted</td>
<td>111.4 (23.2) 48 - 167</td>
<td>124.1 (20.7) 94 - 162</td>
<td>0.01</td>
</tr>
<tr>
<td>Kyphosis index</td>
<td>11.7 (3.1) 6 - 21</td>
<td>11.9 (3.8) 6 - 21</td>
<td>0.80</td>
</tr>
</tbody>
</table>

Data are presented as mean (SD) unless otherwise indicated. P value is for the difference between IPF and non-IPF patients.

Abbreviations: BDI, baseline dyspnea index; BPI, Brief Pain Inventory; CES-D, Center for Epidemiologic Studies Depression score; PSQI, Pittsburgh Sleep Quality Index; STAI, State-Trait Anxiety Inventory; UCSD SOBQ, University of California San Diego Shortness of Breath Questionnaire.
### Table 3.
Association of Dyspnea with Clinical Parameters

<table>
<thead>
<tr>
<th>Variable</th>
<th>BDI</th>
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<th>UCSD SOBQ</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>P value</td>
<td>r</td>
<td>P value</td>
</tr>
<tr>
<td>Age, years</td>
<td>0.19</td>
<td>0.18</td>
<td>-0.20</td>
<td>0.17</td>
</tr>
<tr>
<td>Gender*</td>
<td>-</td>
<td>0.30</td>
<td>-</td>
<td>0.03</td>
</tr>
<tr>
<td>Ethnicity†</td>
<td>-</td>
<td>0.86</td>
<td>-</td>
<td>0.43</td>
</tr>
<tr>
<td>Current or former smoker*</td>
<td>-</td>
<td>0.57</td>
<td>-</td>
<td>0.98</td>
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<tr>
<td>Body mass index, kg/m²</td>
<td>-0.25</td>
<td>0.09</td>
<td>0.18</td>
<td>0.23</td>
</tr>
<tr>
<td>Oxygen saturation at rest</td>
<td>0.13</td>
<td>0.37</td>
<td>-0.06</td>
<td>0.65</td>
</tr>
<tr>
<td>Long-term oxygen therapy*</td>
<td>-</td>
<td>0.27</td>
<td>-</td>
<td>0.34</td>
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<tr>
<td>Anxiety (STAI)</td>
<td>-0.33</td>
<td>0.02</td>
<td>0.34</td>
<td>0.02</td>
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<tr>
<td>Depression (CES-D)</td>
<td>-0.43</td>
<td>0.002</td>
<td>0.50</td>
<td>0.0002</td>
</tr>
<tr>
<td>Pain (BPI)</td>
<td>-0.09</td>
<td>0.55</td>
<td>0.29</td>
<td>0.04</td>
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<tr>
<td>Sleep quality (PSQI)</td>
<td>-0.20</td>
<td>0.15</td>
<td>0.37</td>
<td>0.007</td>
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<tr>
<td>4-meter walk time, seconds</td>
<td>-0.36</td>
<td>0.009</td>
<td>0.37</td>
<td>0.006</td>
</tr>
<tr>
<td>Grip strength, % predicted</td>
<td>0.16</td>
<td>0.25</td>
<td>-0.13</td>
<td>0.34</td>
</tr>
<tr>
<td>Kyphosis</td>
<td>0.03</td>
<td>0.84</td>
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<td>0.90</td>
</tr>
<tr>
<td><strong>Pulmonary function tests</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FVC, % predicted</td>
<td>0.29</td>
<td>0.05</td>
<td>-0.26</td>
<td>0.08</td>
</tr>
<tr>
<td>TLC, % predicted</td>
<td>0.03</td>
<td>0.86</td>
<td>0.05</td>
<td>0.76</td>
</tr>
<tr>
<td>DLCO, % predicted</td>
<td>0.27</td>
<td>0.06</td>
<td>-0.24</td>
<td>0.10</td>
</tr>
</tbody>
</table>

* Variables with P values obtained using a Student's t-test.
† Variables with P values obtained using oneway ANOVA.
Data are presented as r values using Spearman's correlation coefficients, unless otherwise indicated.

Abbreviations: BDI, Baseline Dyspnea Index; BPI, Brief Pain Inventory; CES-D, Center for Epidemiologic Studies Depression score; DLCO, diffusion capacity of carbon monoxide; FVC, forced vital capacity; PSQI, Pittsburgh Sleep Quality Index; STAI, State-Trait Anxiety Inventory; TLC, total lung capacity; UCSD SOBQ, University of California San Diego Shortness of Breath Questionnaire.
Table 4. Multivariate models of dyspnea

<table>
<thead>
<tr>
<th>Variable</th>
<th>BDI Coefficient</th>
<th>95% CI</th>
<th>P value</th>
<th>UCSD SOBQ Coefficient</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body mass index</td>
<td>-0.08</td>
<td>-0.18 to 0.02</td>
<td>0.10</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>FVC % predicted</td>
<td>0.03</td>
<td>-0.002 to 0.06</td>
<td>0.07</td>
<td>-0.5</td>
<td>-0.8 to -0.2</td>
<td>0.004</td>
</tr>
<tr>
<td>DLCO % predicted</td>
<td>0.05</td>
<td>0.01 to 0.09</td>
<td>0.007</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Depression score</td>
<td>-0.10</td>
<td>-0.17 to -0.04</td>
<td>0.002</td>
<td>1.3</td>
<td>0.6 to 1.9</td>
<td>&lt; 0.0005</td>
</tr>
<tr>
<td>4-meter walk time</td>
<td>-0.83</td>
<td>-1.31 to -0.35</td>
<td>0.001</td>
<td>5.2</td>
<td>-0.1 to 10.6</td>
<td>0.06</td>
</tr>
</tbody>
</table>

Data are presented as coefficients and their 95% CIs from stepwise multiple regression analysis, incorporating variables from bivariate analysis that had a p value < 0.10. Values not shown indicate variables that did not remain in the model following multivariate analysis.

Abbreviations: BDI, Baseline Dyspnea Index; CI, confidence interval; DLCO, diffusion capacity of carbon monoxide; FVC, forced vital capacity; UCSD SOBQ, University of California San Diego Shortness of Breath Questionnaire.
Figure 2
Figure 3
Depression and Functional Status Are Strongly Associated With Dyspnea in Interstitial Lung Disease
Christopher J. Ryerson, Jane Berkeley, Virginia L. Carriéri-Kohlman, Steven Z. Pantilat, C. Seth Landefeld and Harold R. Collard
Chest; Prepublished online August 5, 2010; DOI 10.1378/chest.10-0608

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