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Functional Performance in Chronic Obstructive Pulmonary Disease Declines with Time

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Abstract

Purpose—It is well known that people with chronic obstructive pulmonary disease (COPD) experience declines in functional performance, but little is known about the rate of decline. The purpose of this research was to describe the rate of decline in functional performance and to examine the contribution of disease severity, body composition, symptoms and functional capacity. Functional performance was defined as the activities that people choose to engage in on a day-to-day basis.

Methods—People (N=108) with COPD were enrolled and followed yearly for three years with: self-reported functional performance (Functional Performance Inventory), spirometry, lung volumes, diffusion capacity, body composition (dual energy x-ray absorptiometry), dyspnea and fatigue (Chronic Respiratory Disease Questionnaire) and functional capacity (six-minute walk distance (6MWD), isokinetic strength of knee flexors and extensors, handgrip strength and maximal inspiratory pressure). A total of 88 subjects completed a (mean ± SD) of 2.7 ± 0.9 years of follow-up.

Results—Significant negative slopes were observed for functional performance (P=0.001), spirometry (the ratio of forced expiratory volume in one second to forced vital capacity ((FEV_1/FVC), P<0.0001), diffusion capacity (P<0.0001) and muscle strength (P<0.0001). The slopes for dyspnea, fatigue and functional capacity were not significantly different from zero, but there was wide individual variation. Hierarchical regression demonstrated that 31% of the variance in the slope of functional performance was accounted for by the hierarchical model and the primary predictors were the slopes of the FEV_1/FVC, 6MWD and muscle strength (knee flexors/extensor and handgrip).

Conclusions—Subjects experienced a slow decline in functional performance, associated with declines in functional capacity and increases in body fat. Symptoms were relatively stable and not associated with declines in functional performance.

Keywords

functional status; activities of daily living; pulmonary rehabilitation; health outcomes

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INTRODUCTION

People with chronic obstructive pulmonary disease (COPD) experience a decline in functional status, but little is known about the rate of decline and factors that contribute to the decline. Of particular concern is the decline in functional performance, which can be defined as the activities that people choose to engage in on a day-to-day basis. Decreases in functional performance will ultimately lead to a sedentary life style, decreased health status and premature frailty. A better understanding of this process could be useful in guiding the development of targeted interventions to address the most salient modifiable factors.

From a theoretical/clinical perspective the process of decline has been described as a downward spiral of increasing disease severity, increasing symptoms, decreasing functional capacity and decreasing functional performance (16,21). The proposed relationships are empirically supported by cross-sectional studies (11,30,35) , though none have examined all of these variables simultaneously. Knowledge of this phenomenon is primarily based on cross sectional research with an emphasis on people in the later stages of the disease and the actual rate of decline in functional performance has never been measured.

Cross-sectional studies only provide an estimate of the change in variables of interest over time, whereas longitudinal studies provide a true measure of change over time. Cross-sectional studies are sensitive to past influences on the variables of interest, whereas longitudinal studies are sensitive to future influences. For example with spirometry data from COPD patients it has been demonstrated that cross-sectional studies predict a steeper annual decline than is actually measured in longitudinal studies (9).

The purpose of this research was to describe the rate of decline in functional performance for people with COPD and to examine the relationship between rate of decline and factors thought to contribute to the rate of decline, specifically changes in disease severity (spirometry, lung volumes and diffusion capacity), body composition (dual energy x-ray absorptiometry (DEXA)), symptoms (Chronic Respiratory Disease Questionnaire (CRQ) dyspnea and fatigue scales), and functional capacity (six-minute walk distance (6MWD), muscle strength and inspiratory muscle strength).

METHODS

This was a prospective longitudinal study with yearly measurements and three years of follow-up. Subjects were recruited through radio and print advertisements, word-of-mouth, and local pulmonologist offices. Potential subjects were screened for eligibility by phone and then in our clinical laboratory. Eligible subjects underwent baseline testing and returned to be tested approximately every 12 months for three more visits. The time interval between testing visits for some subjects exceeded 12 months to allow for recovery from an exacerbation. From visit to visit the time of day at which tests were performed was standardized.

A total of 108 subjects were enrolled and 88 provided longitudinal data, with 61 (69%) providing four data points (three years of follow-up), 14 (16%) providing three and 13 (15%) providing two. The reasons for dropping out after the baseline visit included: moved away = 2, personal or family reasons = 4, COPD-related health problems = 1, non-COPD related health problems = 4 (e.g. cancer, orthopedic disorders, etc), lost interest in the study = 3, lost to follow-up - unable to contact = 6. We compared the 20 dropouts with the 88 finishers and the two groups were not significantly different on pulmonary function, body mass index, DEXA lean percent or DEXA fat percent. Subjects were followed for a (mean ± SD) of 2.7 ± 0.9 years and data were collected when subjects were in their usual state of health.

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Subjects were eligible for inclusion if they were ≥ 45 years of age and had an FEV_1 of < 70 and ≥ 25 % of predicted normal values with no history of asthma, no evidence of restrictive lung disease on pulmonary function tests and no other major health problems that would affect functional status. The subjects were clinically stable at the time of enrollment into the study, defined as free of respiratory infection for at least two months prior to enrollment (no recent change in the color, consistency, or quantity of sputum, afebrile, and no recent change in medical therapy). Subjects were excluded if they had a potentially debilitating disease and/or a condition that would affect metabolism and nutritional status (cancer, Class 2 or greater functional status according to the New York Heart Association, congestive heart failure, kidney disease, liver failure or cirrhosis, alcohol or drug abuse, diabetes requiring insulin therapy, hyperthyroidism, and musculoskeletal or degenerative nerve disease with functional impairment). This research was approved by the local institutional review board and all subjects provided written consent.

Measurements

The Functional Performance Inventory (FPI) was used to measure self-reported functional performance, the extent to which people engage in their usual day-to-day activities (22,23) . It is a 65-item instrument with six subscales: body care, household maintenance, physical exercise, recreation, spiritual activities and social activities. Subjects report “how difficult it is” to do specific day-to-day activities, 1=no difficulty, 2=some difficulty, 3=much difficulty, and 4=don’t do because of health reasons. The data are transformed and the potential range for each subscale and the Total FPI is 0 to 3 with higher scores reflecting higher levels of functional performance. There is strong evidence to support the reliability and validity of the FPI when used with people who have COPD (20,22). Internal consistency reliability was high for this research; Cronbach’s alpha ranged from 0.90 to 0.93.

Functional capacity was measured in terms of functional capacity for walking, muscle strength and inspiratory muscle strength. The 6MWD reflects functional capacity for walking (3,13,14). The six-minute walk test was performed in an air conditioned corridor with 60 meter laps and standardized coaching, once a minute (3,13). A practice test (four-minute walk) was performed in the morning prior to the actual six-minute walk, which was conducted in the afternoon. Data were reported as a percentage of predicted normal values, normalizing for gender, age, height and weight (7).

Three measures of strength were combined to create an index of peripheral muscle strength: isokinetic strength of the knee flexors and extensors (Cybex 340 dynamometer; Cybex International, Medway, MA) and handgrip strength (Jamar dynamometer; Sammons Preston, Inc, Bolingbrook, IL). Isokinetic strength was assessed at a speed of 60 degrees per second and subjects were familiarized with the procedures by performing four practice repetitions before testing commenced. Data for each test were reported as the mean of three trials, taken from the right side of the body. The data were standardized for age and gender and reported as a percent of predicted normal values (5,28,31). Muscle strength was calculated by averaging the three values, thereby reflecting upper and lower body strength (17). The maximal inspiratory pressure (PI max) was employed as a measure of inspiratory muscle strength, using the Pmax mouth pressure monitor (P.K. Morgan Instruments Inc., Andover, MA) and techniques described by Black and Hyatt (2).

Symptoms of dyspnea and fatigue were measured with a modified version of the Chronic Respiratory Disease Questionnaire (12). The CRQ Dyspnea scale reflects the intensity of dyspnea experienced during activities that make the subject short of breath. For purposes of this research, the CRQ dyspnea scale was modified (CRQ-M Dyspnea) so that subjects reported dyspnea on the following six activities: walking with others, walking upstairs, carrying, hurrying, having a bath or shower, and bending. This modification was necessary

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because of the longitudinal nature of the study and concerns that with time subjects would no longer be capable of performing the activities that they initially identified, thereby making it difficult to compare dyspnea over time. Subjects indicated how much shortness of breath they experienced during the last month while performing the activity: 1= extremely short of breath to 7 = not at all short of breath. The modification was based on previous CRQ data provided by people with COPD. To identify the six activities we reviewed the CRQ data from 30 people with COPD and selected the low level activities which were most frequently identified as causing dyspnea. We used six activities because two were very close in frequency. The CRQ fatigue scale has four items, two that reflect the frequency of fatigue and two that reflect the intensity of fatigue.

Repeated measures of the CRQ were administered without informing subjects of their previous answers. The CRQ is widely used in studies of chronic lung disease and there is strong evidence for its reliability and validity (12,15). Internal consistency was high for this research; Cronbach's alpha ranged from 0.86 to 0.89 for CRQ-M dyspnea and CRQ fatigue subscales.

Disease severity was measured with pulmonary function tests including spirometry, lung volumes and diffusion capacity (6200 Autobox and Vmax22, Sensor Medics, Yorba Linda, CA). Pulmonary function tests were conducted according to established standards (1,26) and data were reported as percentage of predicted normal values using established equations (4,10,27).

Body composition was measured with dual energy x-ray absorptiometry (QDR4500W; Hologic Inc., Bedford, MA) to document the percentage of body fat (8,25). Body mass index was calculated as weight [kg]/height [m^2].

Procedures

A day and a half of testing was required to complete the measurements. Subjects completed the majority of measures on day one and spent the night in the UIC Clinical Research Center. The remaining measures were completed the morning of day two.

Data Analysis

The data analysis was performed using SPSS 17 software (SPSS Inc, Chicago, IL) and the significance level was set at $P<0.05$. For each individual subject we calculated the slope of change over time for each key variable and these were used in the regression analysis (32). Pearson correlations among the independent variables (the slopes of disease severity, body composition, symptoms and functional capacity) and the dependent variable (the slope of functional performance) were examined. Hierarchical linear regression (HLR) was employed to determine significant predictors of the slope of functional performance. The independent variables were entered into the regression model by blocks in the following order: disease severity (slopes of FEV_1/FVC, lung volume and diffusion capacity), slope of percent body fat, symptoms (slopes of dyspnea and fatigue) and functional capacity (slopes of 6MWD, muscle strength and PI max). The variables that are not readily modifiable with interventions were entered first and those that are more easily modified were entered last.

RESULTS

Sample characteristics and baseline values are presented in Tables 1 and 2. Subjects had a (mean ± SD) FEV_1, % predicted of 51±19. Of the 88, there were 7 subjects in GOLD class I, 38 at class II, 29 at class III and 14 at class IV. People with significant co-morbidities were not included in the study. Approximately 80% of the subjects were smoke free at all available time points. Smoking status was not related to the decline in functional

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performance ($F_{(2, 84)} = 1.09$, $P=0.34$). At baseline subjects reported intermediate levels of functional performance (FPI total = 2.2±0.4) and moderate symptoms of dyspnea (CRQ-M dsypnea = 4.4±1.1) and fatigue (CRQ fatigue = 4.2±1.1). Functional performance declined and disease severity increased over the course of follow-up as reflected by slopes that were significantly different from zero (Table 2). Functional capacity and symptoms did not change significantly, but there was substantial individual variation.

The slope of functional performance was not related to baseline values of independent variables at entry into the study, but it was negatively associated with the slope of body composition (percent body fat) and positively associated with the slope of disease severity and the slopes of two of the three measures of functional capacity, 6MWD and muscle strength (Table 3). The slope of functional performance was not correlated with the slope of dyspnea and was weakly correlated with the slope of fatigue. Variance inflation factor values ranged from 1.03 to 1.32 and Pearson correlations among key variables ranged from $r=0.15$ to $r=0.44$, indicating a lack of multicollinearity (Table 3).

The hierarchical regression model for the slope of functional performance is presented in Table 4. The slope of disease severity accounted for 6% of the variance in the slope of functional performance and the addition of body fat and symptoms accounted for an additional 6%, improving the regression model. When functional capacity variables were added they accounted for an additional 19% of the variance in the slope of functional performance. The final model explained approximately 31% of the variance in the slope of functional performance and the primary predictors were the slopes of 6MWD and muscle strength.

DISCUSSION

We studied the rate of change (slope) for functional performance, disease severity, body composition, symptoms and functional capacity. Functional performance declined over three years and the rates of decline in functional capacity variables (6MWD and muscle strength) were the strongest predictors of decline in functional performance. Airflow obstruction increased and diffusion capacity decreased, but symptoms did not significantly change. Functional capacity variables did not significantly change for the group as a whole, but there was substantial variability in the slopes for individual subjects and this explains how it could serve as a predictor of functional performance. The observed relationship between slopes of functional performance and functional capacity variables are clinically important because changes in functional capacity can be modified through exercise and physical activity interventions.

Functional Performance

Functional performance at baseline was similar to levels previously reported for people with comparable disease severity, Total FPI scores 1.89 to 2.1 (20,22,30). In contrast Leidy observed lower scores, 1.50 ± 0.53 (mean ± SD), in a group of 71 subjects (N=71) with very severe disease (FEV_1 less than one liter) (22) and Yeh et al. (36) observed a mean score of 1.66 ± 0.44 in a group of subjects (N=138) with milder airflow obstruction (mean FEV_1 % predicted of 60 ± 33). Disease severity may account for the lower functional performance in the people studied by Leidy (22). Data from the current study do not support a relationship between disease severity and functional performance, but these results cannot be generalized to people with very severe disease such as the subjects studied by Leidy(22). Only 31 % of the subjects in the current study had an FEV_1 of less than one liter. The differences observed by Yeh and colleagues are not readily explained, except that they studied people in Taiwan using a Chinese version of the FPI and their sample of COPD subjects was a mixed group that included people with asthma (36). The translated version may not be equivalent and/or

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cultural differences may influence functional performance; and people with asthma may not experience the same changes in functional performance.

The observed decline in functional performance is consistent with the results from an earlier longitudinal study of health status in COPD where health/functional status declined over three years in all components of the Medical Outcomes Study, Short Form 36 (33). Our results are not consistent with those of a 30-month longitudinal study of COPD that employed the Sickness Impact Profile to document functional impairment (11). Graydon (11) documented no change in functional impairment for a group with more severe COPD (mean FEV_1 of 32 ± 9 % predicted). This is likely explained by an insensitivity of the Sickness Impact Profile, a generic measure of functional impairment, to the small gradual changes that are seen in people with COPD.

Longitudinal changes in disease severity, body composition, symptoms and functional capacity accounted for 31percent of the variance in longitudinal changes of functional performance, suggesting that other variables also influence deterioration in functional performance. We are aware of no previous research that examined a similar longitudinal model, but there have been cross sectional studies that examined predictors of functional impairment, a related term that reflects loss of function rather than the current level of function. Cross sectional studies with similar predictor variables accounted for a greater percentage of the variance (44% to 62%) in functional impairment, as measured by the Sickness Impact Profile (19,29). The observed differences are likely related to the differences in the two functional status variables and in the longitudinal and cross sectional nature of the studies. As noted earlier longitudinal studies measure change and cross sectional studies predict change. In this research we report on the extent to which changes in predictor variables are associated with concurrent changes in the outcome variable. Other factors that might influence change in functional performance include previous history of physical activity, environmental variables and personal characteristics.

The observed decline in functional performance reflects a gradual relinquishing of day-to-day activities. The annual rate of decline in functional performance was approximately three percent a year, three percent of the baseline FPI at entry into the study. If the decline is linear people could expect to experience approximately 30 percent decline within ten years. It is important to note that this estimate reflects an overly optimistic trajectory for most people with COPD because it does not include the decline in functional performance that would be caused by multiple comorbid conditions. The subjects in this research had no other major health problems that could affect functional performance, they were being treated with appropriate medications and all measurements were taken when people were clinically stable. People with multiple comorbid conditions and less than optimal health care could experience a faster rate of decline in functional performance.

Body Composition

Declining functional performance was accompanied by increasing body fat and this is not surprising. Functional performance is not synonymous with physical activity but it is likely that physical activity declines as people are less able to do the activities that they usually do during the course of daily life. Heretofore the relationships between changes in body composition and changes in functional performance have not been explored in people with COPD, but our results are consistent with longitudinal data in elderly people. Visser and colleagues (34) found that in older people fat mass rather than lean was predictive for physical disability over 3 years. Additionally, weight gains of ≥20 lbs significantly increased the odds ratio for functional decline over 3-4 years in older people (18). Further longitudinal study of the relationships between changes in body composition and functional performance in people with COPD are needed to explore the stability of this relationship.

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Replication of these findings might suggest that weight maintenance to prevent increases in body fat could be used as a strategy to preserve functional performance.

Functional Capacity

Declines in functional capacity for walking, muscle strength and inspiratory muscle strength are well documented for people with COPD (6) but these variables have not been systematically studied from a prospective longitudinal perspective so the rate of decline was not previously known. One exception, Maher et al (24) documented a significant decline in maximal inspiratory pressure over two years (mean decrease = 3.4 cm H_2O) in men with moderate to very severe COPD. By comparison functional capacity variables were relatively well preserved in the current longitudinal study, possibly because this was a healthier group; subjects with more severe disease, FEV1 <25% of predicted normal values, were excluded.

Theoretically the causal direction between functional capacity and functional performance could go in either or both directions, declines in functional capacity could lead to deterioration in functional performance and declines in functional performance could lead to deterioration in functional capacity. Our subjects demonstrated a significant negative slope for functional performance, but not for functional capacity. While this longitudinal study cannot determine the causal direction of observed relationships the data are consistent with a temporal pattern where declining functional performance occurs prior to the decline in functional capacity. Further research is needed to clarify this relationship.

A moderate association was observed between the rate of change for the 6MWD and rate of change for functional performance. This is not as strong as previously reported from a cross sectional study (6MWD vs FPI, Total, r=0.71, P<.001) (36) and it could reflect differences in cross sectional estimates of decline and longitudinal measures of decline.

Symptoms of COPD

Dyspnea and fatigue are major symptoms for people with COPD but changes in dyspnea and fatigue did not appear to have an important role in limiting functional performance in this sample, possibly because we excluded people with the most severe disease and therefore the most severe symptoms. The group as a whole reported a moderate level of dyspnea and fatigue (7 = no dyspnea; 7 = no fatigue). Earlier in the course of the disease dyspnea is primarily associated with effort and people can reduce physical activity to minimize intensity of symptoms and this could explain the observed relative stability of dyspnea. Less is known about fatigue in COPD, but a similar phenomenon is plausible.

These findings are consistent with Leidy's framework for functional status which suggests that people respond differently to changes in functional capacity (21). According to this framework declining functional capacity can limit functional performance. Alternatively people can push themselves to maintain a given level of functional performance in the face of a declining functional capacity and this is accomplished at the expense of a decrease in functional reserve and increase in symptoms. The group as a whole did not experience a decline in functional capacity, but the significant relationships between functional capacity variables and functional performance were consistent with a decline in functional capacity that limits functional performance. The moderate strength of the observed relationship reflects the variability in individual responses and the fact that many subjects did not experience a decline in functional capacity. A more complex model will be required to fully explain the relationships, one that includes moderating and/or mediating variables.

The decline in functional performance is clinically important for two reasons; the increasingly sedentary lifestyle places people at increased risk for other health problems, most notably cardiovascular disease and premature development of frailty. Consequently

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multiple benefits could be derived from interventions that alter this downward trajectory. Our data highlight the importance of functional capacity, a modifiable variable, and improvements in functional capacity could lead to improvements in functional performance. Clearly there are other variables that are likely to influence the activities that people choose to do on a daily basis, variables such as their previous history of physical activity, environmental variables and personal characteristics. Continued study of this phenomenon is needed to guide the development of new interventions to alter the downward trajectory of functional performance.

In summary these data demonstrated a slow decline in functional performance that was associated with declines in functional capacity and increases in body fat. Symptoms and functional capacity were relatively stable for the group as a whole, with wide individual variation. The longitudinal nature of this research provides a real measure of the rate of decline as compared to the estimates that are derived from cross-sectional research. A modest amount of variance in functional performance was accounted for by the variables in this research, suggesting that more complex models are required to explain the relationships and other domains are likely to have a significant impact on rates of decline in functional performance.

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Table 1

Sample characteristics at baseline (N=88)

Variable	**Mean ± SD**
Age, years	65 ± 6
FEV_1, liters	1.34 ± .51
FEV_1, % predicted	51 ± 19
RV, % predicted	181 ± 42
TLC, % predicted	123 ± 19
PaO_2, mm Hg*	78 ± 10
$PaCO_2$, mm Hg*	40 ± 4
HbO_2, % saturation*	93 ± 2
BMI	27 ± 4
Non-osseous fat-free mass, %	67 ± 6
Body fat, %	30 ± 7

*Arterial blood was not obtained from 6 subjects because of technical difficulties.

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Table 2

Baseline and slope values for dependent and independent variables (N=88)

Variable Measure	Baseline Mean ± SD	Slope (Units per year) Mean ± SD	Slope is different from zero P value
Functional Performance			
FPI, Total Score	2.2 ± 0.4	−0.06 ± 0.16	0.001
Disease Severity			
FEV_1/FVC	44 ± 9	−1.14 ± 2.47	< 0.0001
RV/TLC	0.6 ± 0.1	0.004 ± 0.04	0.33
DLco, % pred	69 ± 26	−1.92 ± 4.99	0.001
Body Composition			
Body Fat, %	30 ± 7	−0.05 ± 1.41	0.72
Symptoms			
CRQ-M dyspnea	4.4 ± 1.1	−0.06 ± 0.48	0.21
CRQ fatigue	4.2 ± 1.1	0.05 ± 0.36	0.20
Functional Capacity			
6MWD, % pred	88 ± 19	1.11 ± 5.76	0.07
Muscle strength, % pred	91 ± 15	0.03 ± 3.92	0.93
PImax, % pred	85 ± 26	1.67 ± 8.55	0.07

Functional Performance Inventory (FPI), forced expiratory volume in one second/forced vital capacity (FEV_1/FVC), residual volume/total lung capacity (RV/TLC), diffusion capacity (DLco), Chronic Respiratory Disease Questionnaire-modified (CRQ-M), CRQ Chronic Respiratory Disease Questionnaire (CRQ), six-minute distance walk distance (6MWD), maximal inspiratory pressure (PImax).

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Table 3

Pearson's correlations for the slopes of functional performance, disease severity, body fat, symptoms and functional capacity (n=88)

Variable Slope	1	2	3	4	5	6	7	8	9	10
Functional Performance										
1. FPI Total Score	1									
Disease Severity										
2. FEV_1/FVC	.23*	1								
3. RV/TLC	−.15	−.24*	1							
4. DLco, % pred	.17	.10	.24*	1						
Body Composition										
5. Body Fat, %	−.26*	−.04	−.14	−.43**	1					
Symptoms										
6. CRQ-M dyspnea	.20	.10	−.40**	−.03	−.05	1				
7. CRQ fatigue	.24*	−.16	.19	.21	−.20	.46**	1			
Functional Capacity										
8. 6MWD, % pred	.46**	.21*	−.36**	.06	−.07	.26**	.36**	1		
9. Muscle strength, % pred	.36**	.00	−.06	.01	.00	.09	.00	.21	1	
10. PImax, % pred	.20	−.13	−.30**	.08	.02	.26*	.32**	.11	.03	1

* P value < .05

** P value < .005

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Table 4

Hierarchical regression predicting change in functional performance (slope of total FPI) (N=87)

Independent variables, Slope of measures	Cum R^2 Adj	B±SE	P Value
Disease Severity	.06		
FEV_1/FVC		.013 ± .007	.051
DLco, % pred		.000 ± .004	.938
RV/TLC		.330 ± .488	.501
Body composition	.10		
Body Fat, %		−.024 ± .012	.061
Symptoms	.12		
CRQ-M dyspnea		.002 ± .038	.962
CRQ fatigue		.031 ± .054	.565
Functional Capacity	.31		
6MWD, % pred		.009 ± .003	.003
Muscle strength, % pred		.012 ± .004	.005
PI max, % pred		.004 ± .002	.072

Forced expiratory volume in one second/forced vital capacity (FEV_1/FVC), diffusion capacity (DLco), residual volume/total lung capacity (RV/TLC), Chronic Respiratory Disease Questionnaire-modified (CRQ-M), CRQ Chronic Respiratory Disease Questionnaire (CRQ), six-minute distance walk distance (6MWD), maximal inspiratory pressure (PI max).