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Attenuation of Dyspnea and Improved Quality-of-Life through Exercise Training in Patients with COPD

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ABSTRACT

Carter R, Tiep B, Koh Y. Attenuation of Dyspnea and Improved Quality-of-Life through Exercise Training in Patients with COPD. **JEPonline** 2016;19(1):1-16. This study evaluated changes in dyspnea and health-related quality of life (HRQOL) before and after exercise training in a COPD cohort. One hundred and twenty-six patients with moderate to severe COPD ($\%PredFEV_1 = 45.9 \pm 12.5\%$) were evaluated before and after 16 wks of exercise training (ET). Patient assessments included: pulmonary function tests; gas exchange; cycle ergometry (CE); arm ergometry (AE); and the 6-min walk test (6MWT) with dyspnea measured using Borg scores and with the multidimensional Chronic Respiratory Disease Questionnaire (CRQ). Following ET, work performance was significantly increased for CE, AE, and the 6MWT (P<.0001) and these changes were considered clinically significant. Borg scores at peak exercise decreased for CE (-0.95 ± 2.8 units, P<.003); AE (-0.8 $\pm$ 2.6 units, P<.02), and 6MWT (-0.5 $\pm$ 2.3 units, P<.05) with greater work output. Borg scores for CE and AE at isotime demonstrated significant improvement (CE $-$ 1.4 $\pm$ 2.0, P<.0001 & AE $-$ 1.0 $\pm$ 2.1, P<.0001). Statistically significant and clinically relevant improvements in CRQ dyspnea (7.00 $\pm$ 5.76 (P<.0001)); emotional function (4.5 $\pm$ 6.3, P<.0001); fatigue (4.1 $\pm$ 4.1 P<.0001); mastery 3.1 $\pm$ 3.5, P<.0001), and total CRQ score (20.0 $\pm$ 15.9, P<.0001) were observed. The data suggest that a 13-watt or 12-watt or greater increase for CE and AE, respectively, represents clinically significant improvements. Exercise training improves upper and lower extremity work performance and reduces dyspnea during exercise while improving overall quality-of-life.

Key Words: Dyspnea, COPD, Exercise, HRQOL, 6MWT

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a leading cause of morbidity and mortality worldwide, with an escalating prevalence of more women than men (7,44). Patients with COPD suffer from several symptoms that adversely affect general health and quality-of-life (36). Identifying optimal methods for assessing COPD, making appropriate medical diagnosis and evaluating clinical outcomes remains somewhat controversial (56). Objective pulmonary function measurements, such as the forced expiratory volume in one second (FEV_1), provide important and timely information regarding the correct diagnosis, stage severity, and prognosis of COPD.

For patients with COPD, dyspnea is a key complaint that is causally interrelated with impaired exercise capacity by creating a major barrier to the patient's ability to live an active life. Dyspnea-on-exertion limits functional ability and is associated with depression and anxiety in promoting disability and negatively impacting health-related quality of life (HRQOL) (58). Further, dyspnea is typically the symptom that brings the patient to the physician.

In the clinical setting the assessment of dyspnea has gained a functional role for not only determining how short-of-breath an individual may be under a variety of conditions, but also to monitor the patient's response to therapy (63). While there are several approaches and multiple instruments for measuring dyspnea, a few have gained popularity in their ability to assess different aspects of dyspnea. For example, the chronic respiratory questionnaire (CRQ) is a quality-of-life instrument that includes a dyspnea measurement domain while Borg scores are routinely used to assess dyspnea during exertion (5,30,68). Generally, these instruments all purport to assess dyspnea, the Borg scale measures dyspnea during exertion when the rise of work of breathing reflects the increasing disparity between the decreased ventilator capacity and the increasing ventilatory requirement. However, little attention has been devoted to investigating changes in dyspnea using multiple instruments before and following exercise training in patients with COPD for both arm and leg exercises. Additionally, there is a scarcity of comparison data available for dyspnea scores collected during formal exercise testing with a cycle egometer or treadmill against that acquired during the 6-min walk test (6MWT). Because so many different assessments and exercise paradigms exist, a study where all measures are obtained in the same cohort may help explain the findings when only one set of data are available.

We hypothesized that patients may reflect dyspnea differently depending on the context and/or the stress encountered to invoke dyspnea and that exercise training will reduce the sensation of dyspnea differently depending on the instrument used for assessment. This study seeks to quantify self-reported dyspnea, using multiple instruments before and following exercise rehabilitation, when medical delivery is optimized. Further, the impact of exercise induced changes in physiologic function will be evaluated for arms and legs and by use of field testing (6-min walk) to further explore their interaction with Borg scores and HRQOL indices. Lastly, based on the exercise training schema used, we wanted to determine if any of the changes associated with exercise training could be considered as a clinically significant.

METHODS

Subjects
One hundred twenty-six COPD patients in stable condition (92 males and 34 females; mean age and range, 66.8 ± 7.3 yrs and 46 to 80 yrs, respectively) volunteered to participate in this study.

Informed consent was obtained following the guidelines established by the Institutional Ethics Committee. All subjects: (a) had a history of COPD (emphysema or bronchitis); (b) were in stable medical condition with no acute exacerbations during the 3 months prior to the study; (c) were able to engage in exercise; and (d) were mentally suited for completion of the protocol. The exclusion criteria included: (a) acute or chronic heart disease that would limit exercise; (b) primary diagnosis of asthma; (c) significant vascular or metabolic problems; (d) a bleeding disorder; or (e) the inability to give informed consent.

Severity of pulmonary dysfunction ranged from moderate to severe (20). Prior to exercise testing, the subjects' medication regime was optimized by a pulmonologist. All subjects were instructed to use their medications as prescribed. They were told to use their bronchodilator therapy 30 min prior to exercise testing or training. Pre- and post-bronchodilator evaluations were performed and dyspnea ratings obtained in the post-bronchodilator condition. Subjects who were hypoxemic were tested without supplemental oxygen during the gas exchange studies and during the 6-min walk. Oxygen was administered at a liter flow setting to minimize desaturation for 9 subjects.

Pulmonary Function Tests
Spirometry was performed with a SensorMedics Vmax 20C spirometry system (SensorMedics, Yorba Linda, CA) that was calibrated prior to each test and compared to the predicted values of Crapo (18). Lung diffusion capacity for carbon monoxide (DL_{CO} mL·min^{-1}·mmHg^{-1}) was measured by the single breath technique of Jones and Mead (34) using a SensorMedics system (SensorMedics, Vmax 22, Autobox, Yorba Linda, CA). Lung volumes were determined by body plethysmnography (SensorMedics, Vmax 22, Autobox, Yorba Linda, CA). Lung diffusion capacity for carbon monoxide (DL_{CO}) was compared to the data from Miller et al. (48) while normal predicted lung volumes were derived from the equations of Goldman and Becklake (23) (females) and of Boren et al. (4) (males). All studies were performed post bronchodilation following Albuterol (90 mcg x 2) administration via a meter dose inhaler (MDI). Pulmonary function testing and severity classification was performed following the standards outlined by the ERS-ATS (20).

Exercise Testing
All subjects performed an incremental arm test (5 to 15 watts·min^{-1} square wave adjustment) to a symptom limited peak work capacity. The difference in workload selected was based on predicted functional capacity and a desire to exercise patients for about 9 min total; the higher the functional predicted capacity the higher the initial workload selected. A modified Monarch arm crank ergometer (Quinton Instruments, Bothell, WA) was used to deliver precise arm workloads. Each subject was given a 3-min 0 load accommodation period followed by a 5 to 15 watts·min^{-1} increment in workload adjustment to a symptom limited peak. Gas exchange data were obtained using the instrumentation described below. Borg dyspnea scores were obtained at the end of each minute of exercise.

For the leg exercise test, the subjects peddled on an electronically braked cycle ergometer (CE) (Medical Graphics, Minneapolis, MN) according to a ramp protocol as described by Wasserman and Whipp (65). Again, the workload selected was based on predicted values so that about 9 min of exercise would maximize the performance. The arm and leg exercise tests were separated by at least 2 hrs of rest and 30 min following bronchodilator therapy. Both leg and arm ergometry testing were completed prior to the 6-min walk test, which was completed 1 to 2 d later.

To evaluate dyspnea during exercise, we used isotime at 4 min using identical exercise testing protocols with the subjects. This comparison allowed for changes in both physiological function

and dyspnea to be evaluated within each subject. Thus, each subject served as his or her own control.

Gas Exchange Measurement

Following a detailed explanation of the testing procedure and a practice trial pedaling/cranking, all subjects were prepared for testing using standard procedures (8). Normal predicted values were computed according to the method of Wasserman and Whipp (64). Peak predicted V_E was estimated from the measured FEV_1 using the method of Carter and colleagues (11). Heart rate was calculated using the R-R ECG intervals.

6MWT

We conducted the 6MWT as described by Guyatt et al. (28,29), which is a modification of the 12-min walk test originally described by McGavin et al. (47). A 100 foot (30.5 m) hospital corridor course was used and marked by colored tape at each end of the corridor. Subjects were instructed to walk from end to end at their own pace, while attempting to cover as much distance as possible in the allotted 6-min. A research assistant timed the walk and recorded the distance traveled, rating of perceived exertion (RPE) for dyspnea and leg fatigue, heart rate and SpO_2 for each minute of walking completed. For subjects requiring supplemental oxygen (9 patients), the research assistant carried the portable oxygen cylinder during the walk and oxygen was titrated to maintain SpO_2 above 90%.

Assessment of Dyspnea
Direct Measures of Dyspnea — Borg Scores

A modified Borg scale was used to measure perceived breathlessness/dyspnea (1,6,24,69). The modified Borg scale administered in this study has been used extensively in exercise related studies, and it is known to be a valid, reliable, and sensitive instrument to change (37,41,59). Two Borg score ratings were used in the evaluation of exercise dyspnea. The first was obtained at peak exertion. The second was rated at the end of the 4th min of exercise (isotime Borg score) using identical testing protocols for baseline and post-exercise. Thus, the subject was evaluated at the same workload prior to and following rehabilitation. The 4th min (isotime) of exercise was selected from the first exercise study to compare identical workloads for rating dyspnea and other important physiologic indices before versus after training. This selection reflects the limited work capacity anticipated for subjects with moderate to severe COPD prior to training and a work output that would be modified with training and is in line for expected activities of daily living energy costs.

Chronic Respiratory Disease Questionnaire (CRQ)

The chronic respiratory disease questionnaire (CRQ) is a reliable and valid disease specific measurement tool for evaluating Health Related Quality-of-life (HRQL) in patients with respiratory disease (15). It was developed in 1987 by Guyatt et al. (26) for the assessment of quality-of-life for patients with lung disease. It evaluates four dimensions of HRQL including dyspnea, emotional function, fatigue, and mastery. The subjects were asked to select the five most bothersome activities that elicited breathlessness and/or dyspnea during the preceding 2 wks. Severity of dyspnea was measured by selecting numeric values ranging from 1 [extremely short of breath] to 7 [not at all short-of-breath]. Individual scores were then summed to derive an overall CRQ dyspnea score (range 5 to 35), with 5 representing the most severe dyspnea and 35 the least significant dyspnea. An important aspect of the CRQ is its ability to quantify clinically important change resulting from an intervention. A change of 0.5 for each item represents a clinically important change (33). Thus, for dyspnea a change of greater than 2.5 (0.5 x 5 questions) would be clinically

significant. The same scoring holds for fatigue (0.5 x 4), emotional function (0.5 x 7), and mastery (0.5 x 4).

Exercise Training
The exercise training program consisted of a supervised training program that included treadmill walking, leg cycling, arm cranking, light arm weights (1 to 2 lbs), and arm and leg ergometry using a Schwinn Airdyne® cycle. The subjects exercised 3 times·wk^{-1} for 16-wks at 20 to 60 min·session^{-1} depending on individual ability as measured during the initial exercise testing. Intensity of training was derived from the subjects' estimated or measured anaerobic threshold from their initial exercise test for arms and legs, respectively. When the subjects were just initiating training the workloads were set at approximately 80% of their anaerobic threshold. All subjects completed the 20 min of exercise trainig at multiple stations. Duration of training was increased as tolerated till 40 min of exercise training could be completed. Thereafter, intensity was increased as tolerated so as to maintain the 40-min exercise training duration.

Clinically Significant Changes in Work Performance
Because the subjects were evaluated using several testing modalities, it was important to identify if any of the reported changes were considered as clinically significant. To address this issue, the 6MWT was used, as the surrogate, for investigating corresponding changes in arm and leg ergometry. Using the data from Toosters and colleagues (61) for a clinically meaningful change, we extrapolated the 6 MWT data to that obtained for the bike and arm crank. From these comparisons, an attempt was carried out to identify the minimal threshold for clinically significant changes.

Statistical Analysis

Descriptive statistics (mean ± SD) was used to calculate variables of interest using the Statistical Analysis System for Windows version 8E (The SAS Institute, Cary, North Carolina). Parametric (Pearson) and non-parametric (Spearman) correlations were used to evaluate the relationship of one variable to another. Paired *t*-tests were used to determine if significant differences exist within an individual over time (paired *t*-test). All data are presented as mean ± SD and a value of P<.05 was considered significant.

RESULTS

Subjects
One hundred and twenty-six males (n = 92) and females (n = 34) with moderate to severe COPD completed this study. The subjects' characteristics, baseline pulmonary function, and total baseline dyspnea scores are presented in Table 1. The COPD cohort was weighted to the severe airway obstruction category (n = 90) with the remaining subjects classified as moderate (ATS ERS Guidelines).

Table 1. Subject Characteristics and Indices of Pulmonary Function.

Variable	Overall Mean ± SD	Moderate Mean ± SD	Severe Mean ± SD
Age (yrs)	67.0 ± 7.04	70.1 ± 6.4	66.1 ± 7.0
Ht (in)	67.82 ± 3.63	68.2 ± 3.9	67.3 ± 3.6
Wt (lbs)	179.66 ± 37.66	172.8 ± 39.3	176.2 ± 36.6
BMI (units)	27.15 ± 5.17	28.9 ± 6.3	26.7 ± 4.7
Pack Years Smoking (yrs)	65.95 ± 30.88	68.45 ± 35.9	65.3 ± 29.6
FEV_1 (L)	1.34 ± 0.42	1.71 ± .48	1.24 ± .35
% Pred FEV_1 (%)	45.32 ± 11.77	60.3 ± 9.2	41.5 ± 9.0
FVC (L)	3.31 ± 0.90	3.02 ± .88	3.38 ± .90
% Pred FVC (%)	83.27 ± 15.39	78.1 ± 11.8	84.5 ± 16.0
FEV_1/FVC (%)	41.31 ± 10.10	57.1 ± 4.6	37.2 ± 6.5
% Pred FEV_1/FVC (%)	55.40 ± 13.86	77.3 ± 5.8	49.8 ± 8.8
FRC (L)	4.67 ± 1.02	4.03 ± .98	4.8 ± .97
IC (L)	2.61 ± 0.78	2.67 ± .77	2.59 ± .78
RV (L)	3.81 ± 0.90	3.45 ± .97	3.90 ± .86
RV/TLC (%)	52.2 ± 8.04	51.0 ± 7.8	52.5 ± 8.12
ERV (L)	0.81 ± 0.43	0.61 ± .35	0.86 ± .44
TLC (L)	7.31 ± 1.36	6.75 ± 1.52	7.44 ± 1.30
V_A (L)	4.97 ± 1.21	4.98 ± 1.29	4.97 ± 1.19
RAW (CMH_2O/L/SEC)	3.00 ± 1.04	2.47 ± .94	3.13 ± 1.03
SGAW (L/CMH_2O/SEC)	0.07 ± 0.03	0.1 ± .04	0.06 ± .03
DL_{CO} ($mL·min^{-1}·mmHg^{-1}$)	13.3 ± 5.58	17.6 ± 6.4	12.3 ± 4.9
DL_{CO}/VA ($L·min^{-1}·mmHg^{-1}$)	1.92 ± 1.17	2.15 ± 1.56	1.87 ± 1.06

BMI = Body Mass Index; FEV_1 = Forced Expiratory Volume in 1 Sec; FVC = Forced Vital Capacity; FRC = Functional Residual Capacity; IC = Inspiratory Capacity; RV = Residual Volume; ERV = Expiratory Reserve Volume; TLC = Total Lung Capacity; V_A = Alveolar Ventilation; RAW = Airway Resistance; SGAW = Specific Airway Conductance; DL_{CO} = Diffusing Capacity for Carbon Monoxide.

Dyspnea/Quality-of-Life

The results of the CRQ dyspnea scores and the domains for emotional function, mastery, and fatigue for the CRQ are presented in Table 2, as are the patient's respective Borg scores. Spearman correlation coefficients were generated between dyspnea scores and physiologic indices at baseline. The FEV_1 was correlated with CRQ dyspnea (r = .21, P< .03), CE isotime Borg (r = -.27, P<.004) and AE isotime Borg (r = -.23, P<.01). Lung diffusion for carbon monoxide was correlated with CRQ dyspnea (r = .27, P<.01), CE Borg (r = .23, P<.02), CE isotime dyspnea (r = -.39, P<.0001), and AE isotime Borg (r = -.33, P<.0008). Further, CE work was correlated to CE isotime Borg (r = .56, P<.0001) and AE work to AE isotime Borg (r = .59, P<.0001).

Table 2. CRQ, Borg Scores and 6MWT Dyspnea Scores for Patients with Moderate to Severe COPD Before and After 16-Weeks of Exercise Training.

Variable	Baseline Mean ± SD	16-Weeks Mean ± SD	Clinically Significant Change	Pr >
CRQ Dyspnea	16.31 ± 5.28	23.14 ± 5.48	Yes	0.0001
CRQ Emotional Function	37.38 ± 7.87	41.99 ± 5.66	Yes	0.0001
CRQ Mastery	20.82 ± 5.26	24.22 ± 3.99	Yes	0.0001
CRQ Fatigue	16.77 ± 4.78	20.68 ± 4.29	Yes	0.0001
CRQ Total Score	90.06 ± 17.25	109.73 ± 15.44	Yes	0.0001
CE Peak Borg	4.48 ± 2.78	3.58 ± 1.69	ND	0.003
CE Isotime Borg	2.63 ± 2.21	1.22 ± 1.32	ND	0.0001
AE Peak Borg	4.31 ± 2.49	3.38 ± 1.77	ND	0.01
AE Isotime Borg	2.18 ± 2.20	1.14 ± 1.17	ND	0.0001
6MWT Borg	4.96 ± 2.66	3.93 ± 2.00	Yes	0.05

Isotime = 4th min of exercise at the same workload. **ND** = Not Detected

Exercise Testing/Training Responses

Exercise testing before and after exercise training yielded important and significant improvements in work capacity. On average, there was a 21.6% increase in CE watts (P<.0001), a 3.8% increase in VO_2 peak (mL·min^{-1}) (P<.0002), and a 7.3% increase in V_E (Liters) (P<.0003) with no change in peak heart rate noted (P>.05) (refer to Table 3). These findings were paralleled by a 13.9% increase in the 6MWT distance (P<.0001). Significant improvement in AE performance following training was also observed. There was a 31.5% increase in AE watts (P<.0001), a 4.7% improvement in VO_2 peak (mL·min^{-1}) (P<.0003), and a 5.5% increase in peak V_E (Liters) (P<.0004) at equivalent heart rates (P>.05).

A minimal clinically important difference (MCID) from 35 to 54 m or a 10% change in 6MWD has been suggested (2,55,57). Conversely, others have indicated that a 30 m decrease represents a clinically meaningful decrease in work performance. Yet, little data is available for cycle ergometry and there is a scarcity of data for arm crank ergometry with respect to MCID values. A change of 6.77 watts or a common effect size of 4 watts may indicate a MCID for cycle ergometry (39,54). Using our 6MWD and the published MCID criteria, we extrapolated the 6MWT data to leg and arm ergometry workload data. We found that a 13-watt increase in CE corresponds to the MCID from 6MWT for legs. A 12-watt increase in AE corresponds to MCID for arm crank ergometry. While the values for MCID are greater than previously reported, the values are in line with changes in metabolic costs for exercise, which is presumably partly responsible for improvement in perception and ability to perform work tasks.

Table 3. Gas Exchange and Work Performance Indices at Baseline and Following 16-Weeks of Exercise Training.

Variable	CE		AE		6MWT	
	Baseline Mean ± SD	16-Weeks Mean ± SD	Baseline Mean ± SD	16-Weeks Mean ± SD	Baseline Mean ± SD	16-Weeks Mean ± SD
Work (Watts)	64.0 ± 24.9	77.8 ± 25.8#	39.4 ± 19.9	51.8 ± 21.2#		
VO$_2$ (mL·min^{-1})	1103.7 ± 323.5	1145.9 ± 342.1**	916.0 ± 262.2	959.0 ± 261.0**		
VCO$_2$ (mL·min^{-1})	1067.5 ± 359.9	1137.5 ± 71.1#	882.9 ± 281.0	940.6 ± 265.5#		
V$_E$ (L)	39.8 ± 12.0	42.7 ± 13.4**	34.4 ± 9.5	36.5 ± 9.6**		
HR (beats·min^{-1})	117.1 ± 18.5	117.0 ± 16.4	114.0 ± 18.4	116.1 ± 16.2	112.7 ± 13.7	115.3 ± 13.6
SpO$_2$ (%)	95.5 ± 3.6	95.2 ± 3.6	96.4 ± 2.9	96.3 ± 2.8		
6MWT Distance (m)					403.6 ± 82.5	459.4 ± 92.9#

CE = Cycle Ergometry; **AE** = Arm Ergometry; **6MWT** = 6 Minute Walk Distance in meters; **VO$_2$** = Oxygen Uptake in m/min; **VCO$_2$** = Carbon Dioxide Production in ml/min; **V$_E$** = Ventilation in liters per minute; **HR** = Heart Rate in beats per minute; **SpO$_2$** = Oxygen Saturation in Percent. Significance level denoted by: # $P < .0001$, * $P < .001$, ** $P < .0005$

DISCUSSION

This prospective clinical trial demonstrates that upper and lower extremity exercise training improves work performance, increases exercise tolerance, and ameliorates dyspnea in several dimensions, while enhancing health related quality-of-life when medical delivery has been optimized. These changes may be attributed to peripheral muscle conditioning, dyspnea desensitization, or alterations in the anaerobic threshold as previously reported (12,43,51). More specifically, the use of both upper and lower body exercise training was accompanied by dyspnea reduction in both extremities evaluated yet this has not been the case when only leg or arm training is used (14).

Dyspnea was measured from different perspectives. First, we used Borg scores, pre- and post-peak exercise. Second, to investigate change at the same workload pre- versus post-rehabilitation, we evaluated isotime exercise dyspnea during CE and AE ergometry testing and used the 6MWT (functional test). Our results confirm that exercise training can improve function and lessen dyspnea as previously reported (3,49). The findings of this study also demonstrate significant increases in function (both statistical and clinically important) resulting from exercise training that directly lessens dyspnea on exertion and improves HRQOL by reducing the level of dyspnea associated with daily living. Therefore, while dyspnea indices may be multidimensional and their scaling properties different, the individual's perception may well reflect underlying physiologic changes associated with a training and/or detraining response as well as physiologic adjustments accommodated during acute exercise.

Impaired exercise capacity in COPD patients is strongly correlated with pulmonary hyperinflation as measured by the RV/TLC ratio, dyspnea, and the patient's age (21). In our COPD cohort, exercise capacity was diminished as compared to disease free individuals of the same age and gender (refer to Table 3). We used different measures of exercise capacity to evaluate patients (leg cycle and arm ergometry, 6-min walk test) where we noted consistent increases in function

following rehabilitation training. Changes in exercise performance were correlated with measures of dyspnea at both isotimes and at peak exertion, which suggests that dyspnea, as measured by the CRQ or through Borg scores, may reflect different dimensions of dyspnea perception and each appears to be sensitive to changes in physiologic function resulting from a physical training program. We speculate based on the data in the present study and others that exercise training constrains dynamic hyperinflation during exercise, thereby lessening the work-of-breathing, which in turn is perceived as a favorable response by the patient (40,52,53,62). Because of the reduction in dyspnea at less than maximal workloads, the patient may experience less dyspnea during activities of daily living. This finding translates to a better quality-of-life.

CRQ was used to assess quality-of-life and to evaluate dyspnea from the quality-of-life perspective. The findings indicate statistically and clinically significant improvements for dyspnea ratings following ET. This is an important clinical feature that often limits a patient's ability to engage in movement of any kind and may also influence other dimensions of quality-of-life. Other significant improvements were also noted in the other dimensions of health status as assessed by the CRQ including changes in fatigue, emotional functioning and mastery. Fatigue is a common complaint in about half of all patients with COPD that may be independent of changes in dyspnea and significantly impairs both functional performance and quality-of-life (35). For fatigue, a minimal change of 2.0 is required for a clinically significant change and we observed score of 4; emotional function required a change of 3.5 and 4.5 was measured; mastery required a change of 2.0 and ours was 3.2. Collectively, these findings are in agreement with Wedzicha et al. (66) who demonstrated that the CRQ is a sensitive instrument for detecting change in HRQOL resulting from ET. This sensitivity of the CRQ is also supported by the findings of Harper et al. (31) and Singh et al. (60).

Improvement in exercise capacity is reflected in multiple organ physiological adjustments (heart, lung, muscle, bioenergetics, etc.) that collectively signify improved overall efficiency of the human body to tolerate increased work demands or resist premature fatigue. We measured V_E, VO_2, VCO_2, V_T, and HR during leg and arm cycle ergometry performance, as well as, resting pulmonary function indices. Improvements in these measured indices are indicative of positive improvements in cardiopulmonary function. Overall, the indices changed significantly in a positive manner, which is agreement with the findings of Carter and Nicotra (10).

A unique feature of this study was the assessment of dyspnea using Borg dyspnea scores for three different acute bouts of exercise along with HRQOL dyspnea assessment before and following ET. Most clinicians agree that dyspnea is the most debilitating symptom for COPD patients. Hence, improvement in this outcome is a very important therapeutic objective (19). Further, COPD patients complain of accentuated dyspnea sensation when using their arms to work. Arm work associated dyspnea does not dissipate for patients who are trained with lower extremity exercise alone (13,17). These heightened sensations of dyspnea limit the patient's ability to perform muscular work, which promotes ongoing debilitation (9). We have demonstrated that ET incorporating arm exercise promotes similar reductions in dyspnea for CE, AE, and the 6MWT in trained subjects using Borg scores. These are important and timely results confirming the need for muscle specific training to counter decreasing function imposed by progressive COPD, evolving dyspnea and deteriorating quality-of-life.

Another unique feature of this study was the assessment of exercise capacity and dyspnea using multiple instruments. We sought to address the issue of whether leg and arm ergometry results would translate to a common day activity, walking or ambulation. The 6MWT has been used

extensively to assess function in COPD and other chronic diseases with good reliability and sensitivity (32,46). Recent evidence suggest that an increase of about 50 m in walk distance represents the minimal distance for patients to notice a clinically significant improvement in their functional status (57,61). The overall average improvement for the patients in the this study was 55 m. Patients with moderate disease improved by 77 m, while the severe group averaged 51 m. These findings are important since they occurred in patients with severe airflow obstruction. Additionally, our 6MWT findings were accompanied by a significant workload increase in both CE and AE. From these data, we were able to investigate workload changes for leg and arm ergometry that would reflect the minimal clinically significant changes in workload for our cohort. The data suggest that a 13-watt increase for leg and a 12-watt increase for arm workload represent a clinically significant improvement.

Among the important and complex findings in this study were the correlation coefficients noted between changes in dyspnea and work performance as assessed by CE, AE, and 6MWT. Our data demonstrate that the direction of change is consistent for all measures (demonstrating improved correlations) and that the different measures are sensitive overall. Some may argue that the reported changes for dyspnea were not highly correlated with objective indices of work performance even though they were statistically significant (P<.05). These findings suggest the uniqueness of each exercise modality and instrument in assessing the various dimensions of dyspnea and functional performance. When the data is compared to previous findings, we find that our results complement those described by Mahler et al. (42), Wegner et al. (67), and Fuchs-Climent et al. (22). Further, our data are similar in many respects to that of Guyatt et al. (27) and compared to prior studies, our correlation coefficients are somewhat higher. Collectively, these data appear to indicate that the sensation of dyspnea may be arising from many integrated physiologic and/or psychologic signals as suggested by prior research (16,25,38,42,45).

CONCLUSION

Dyspnea is reduced following exercise training using multiple instruments. The exercise training protocol used in the present study promoted an increase in overall functional performance as measured by the 6MWT with an associated reduction in dyspnea. The 6MWT distance reached clinical and statistical significance with respect to functional capacity as did the HRQOL dimensions of dyspnea, fatigue, emotional function, and mastery as measured by the CRQ. Further, we were able to identify the threshold for minimally important changes for leg and arm ergometry, a 13-watt and 12-watt increase, respectively.

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