

Cycle Ergometer and Inspiratory Muscle Training in Chronic Obstructive Pulmonary Disease

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In patients with chronic obstructive pulmonary disease (COPD) the intensity of aerobic training is limited by dyspnea. Improving strength of the inspiratory muscles could enhance aerobic exercise training by reducing exercise-related dyspnea. We examined effects of home-based inspiratory muscle training (IMT) and cycle ergometry training (CET) in 53 patients with moderate to severe COPD ($FEV_1\%$ pred, 50 ± 17 [mean \pm SD]). Patients were randomly assigned to 4 mo of training in one of four groups: IMT, CET, CET + IMT, or health education (ED). Patients were encouraged to train to the limits of their dyspnea. Inspiratory muscle strength and endurance increased in IMT and CET + IMT groups compared with CET and ED groups ($p < 0.01$). Peak oxygen uptake increased and heart rate, minute ventilation, dyspnea, and leg fatigue decreased at submaximal work rates in the CET and CET + IMT groups compared with the IMT and ED groups ($p < 0.01$). There were no differences between the CET and CET + IMT groups. Home-based CET produced a physiological training effect and reduced exercise-related symptoms while IMT increased respiratory muscle strength and endurance. The combination of CET and IMT did not produce additional benefits in exercise performance and exercise-related symptoms. This is the first study to demonstrate a physiological training effect with home-based exercise training. Larson JL, Covey MK, Wirtz SE, Berry JK, Alex CG, Langbein WE, Edwards L. Cycle ergometer and inspiratory muscle training in chronic obstructive pulmonary disease.

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Aerobic exercise training improves functional status (1-3), and if the intensity of training is adequate it produces a physiological training effect in patients with chronic obstructive pulmonary disease (COPD) (4-6). However, training effects are typically modest because the intensity of exercise training is limited by dyspnea and abnormal ventilatory mechanics (7, 8). Thus, greater training effects potentially could be achieved if the intensity of dyspnea were reduced. In addition, physiological training effects have been demonstrated only in hospital-based outpatient and inpatient exercise programs; it is not known if similar effects could be accomplished through more convenient home-based training.

At a given level of exercise the intensity of dyspnea is inversely related to strength of the inspiratory muscles (9-13). This relationship has been observed in healthy subjects and patients with COPD, suggesting that increases in inspiratory muscle strength could potentially reduce exercise-related dyspnea for people with normal and below-normal strength of the inspiratory muscles. In addition, it has been demonstrated that

inspiratory muscle training (IMT) increases strength of the inspiratory muscles and decreases the intensity of breathlessness, during loaded breathing or routine daily activities (14-17). With greater inspiratory muscle strength, a smaller fraction of maximal tension is generated with each breath and it has been suggested that this reduces the motor output to the respiratory muscles and decreases the perceived sense of the effort (9).

We reasoned that improved strength and endurance of the inspiratory muscles would reduce dyspnea, thereby improving the ability of patients to sustain high levels of ventilation for long periods of time. This would allow patients to increase the intensity of aerobic exercise training by increasing the duration of training sessions and thus the amount of total work accomplished during a training session. Moreover, the use of a home-based exercise program would be more convenient for patients and might enhance adherence to training.

Two controlled studies have addressed the issue of an additive effect for IMT and exercise training. Both were outpatient based, but their results were inconsistent. Berry and colleagues (18) found no additive effect whereas Weiner and coworkers (19) found a significant additive effect. In the first case patients did not demonstrate an improvement in respiratory muscle function, suggesting that the IMT protocol was not optimal (18). In the study by Weiner and colleagues (19), additive effects were noted in terms of performance on a 12-min distance walk test and endurance time on a bicycle at 66% of maximal work rate, both of which are subject to the effects of motivation.

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TABLE 1
DATA COLLECTION SCHEDULE

	Baseline Control Phase							Intervention Phase					
								Month 1	Month 2	Month 3	Month 4		
	LV 1	LV 2	LV 3	LV 4	LV 5	LV 6	LV 7	LV 8	LV 9	LV 10	LV 11	LV 12	LV 13
PFT	X												X
Exercise tests		X	X	X*						X		X	
Respiratory muscle tests					X	X	X	X	X		X		X
CRQ					X	X							X
Anthropometrics		X										X	
Breathlessness Scale		X											
SIP		X											

Definition of abbreviations: Breathlessness scale = American Thoracic Society/Division of Lung Disease Breathlessness Scale; CRQ = Chronic Respiratory Questionnaire; LV = laboratory visit; PFT = pulmonary function test; SIP = Sickness Impact Profile.

* The third exercise test was performed only if peak oxygen uptake was not within 9% of that measured during the first two tests.

The primary aim of this study was to determine if the combination of IMT and cycle ergometry training (CET) has additive effects, enabling patients to increase the intensity of CET and ultimately resulting in a greater improvement in aerobic capacity. The secondary aim was to determine if aerobic training effects could be accomplished in patients with COPD through a home-based cycle ergometry training program.

METHODS

This was a randomized, single-blind experimental study. Patients were assigned to one of four groups: IMT, CET, CET + IMT, and health education (ED). Patients were followed for 4 mo while undergoing exercise training or participating in health education. Outcome measures included respiratory muscle strength and endurance, exercise performance, dyspnea, and fatigue. The timing of measurements is described in Table 1. The study was approved by the appropriate institutional review boards, and informed consent was obtained from all patients before enrollment in the study.

Sample

Participants were recruited by referral and local advertisements. A total of 1,872 people were screened for the study and from this pool 130 patients with COPD met the inclusion criteria and agreed to participate.

Patients between 45 and 75 yr of age were eligible if they met the following criteria: moderate to severe air flow obstruction ($FEV_1 < 65\%$ predicted and $FEV_1/FVC < 70\%$), complaints of dyspnea on exertion, clinically stable condition, and no participation in a pulmonary rehabilitation program in the last year. Patients were excluded if they had evidence of asthma, had experienced a major exacerbation in the 2 mo before enrollment, took more than 10 mg of prednisone per day, required home oxygen therapy or experienced oxyhemoglobin desaturation below 85% with exercise, and/or had other health problems that would interfere with exercise.

Of the 130 patients enrolled, 53 (35 male, 18 female) finished the study with usable data. Patients dropped out of the study or were disqualified from participation for the following reasons: exacerbation of lung disease ($n = 8$), other health problems ($n = 9$), lack of interest ($n = 6$), inability to perform training ($n = 4$), poor adherence to prescribed training ($n = 3$), response to the graded exercise test ($n = 34$), and other ($n = 13$). Those who were disqualified on the basis of their response to the graded exercise test experienced cardiovascular problems ($n = 23$), could not tolerate testing ($n = 7$), experienced oxyhemoglobin desaturation below 85% ($n = 2$), or had orthopedic problems ($n = 2$). There were no significant differences between those who completed the study and those who dropped out of the study in terms of demographics, pulmonary function tests, and arterial blood gases.

A description of the patients is presented in Table 2. There were no significant differences between the four groups at baseline. The

subjects were of average weight and reported mild functional impairment on the Sickness Impact Profile (20). At baseline all but five patients demonstrated evidence of a ventilatory limitation in terms of exercise as evidenced by a peak ventilation equal to less than 80% of the predicted peak ventilation, using the equation of Clark and co-workers (7).

Exercise Training

Exercise training programs were conducted in the home setting to reduce the effort required for participation.

Cycle ergometry training. Patients performed CET at home on a calibrated stationary cycle ergometer (BodyGuard 990; BodyGuard, Sandnes, Norway). Adherence to the prescribed home training regimen was monitored with a device that recorded the accumulated duration of training at the prescribed work rate.

Patients trained 5 d/wk, 20 min/d. An interval training protocol was used with patients performing four work sets, 5 min in duration, separated by rest intervals (2–4 min) of unloaded cycling. Training was initiated at 50% of the peak work rate, taken from the best baseline graded exercise test, and evaluated weekly with progressive increases as tolerated. Patients were instructed to pedal at a rate of 60 revolutions per minute (rpm) and they were encouraged to push themselves to the limits of their dyspnea, without exceeding a heart rate equal to 85% of the predicted maximal heart rate. Patients used pulse meters to monitor heart rate and they kept a log of training that included the duration, work rate, and highest heart rate for each training session. A nurse made weekly home visits to monitor training and adjust the exercise prescription. During each visit the nurse monitored one full training session.

Inspiratory muscle training. Patients trained with a threshold loaded breathing device (Threshold; HealthScan, Cedar Grove, NJ). The inspiratory orifice of this device is occluded with a spring-loaded poppet valve and the inspiratory pressure load is adjusted by varying the compression of the spring. The screw-type mechanism for compressing the spring was removed and different-sized spacers were used to compress the spring (21). This was done to keep patients from adjusting the inspiratory pressure setting. Stiffer springs were used as needed to establish the appropriate inspiratory pressure load. Adherence to the prescribed training regimen was monitored with a device that was plumbed into the inspiratory muscle trainer and recorded accumulated duration of inspiration at the prescribed load. Duration of training was estimated from the accumulated duration of inspiration and adherence was calculated as the estimated duration of training divided by the expected duration of training.

Patients trained 5 d/wk, for 30 min/d. The training was initiated at an intensity equal to 30% of maximal inspiratory pressure ($P_{I_{max}}$) with progressive increases as tolerated up to 60% of the current $P_{I_{max}}$. The goal was to have all patients training at 60% of $P_{I_{max}}$ during the fourth month of training. An interval training protocol was used with patients performing six work sets, 5 min in duration, separated by rest intervals lasting 1–3 min. Patients kept a log of their IMT and a nurse

TABLE 2
CHARACTERISTICS OF PATIENTS IN SAMPLE*

Variable	IMT (n = 13)	CET (n = 14)	CET + IMT (n = 14)	ED (n = 12)
Age, yr	66 ± 5	66 ± 6	68 ± 6	62 ± 7
BMI, kg/m ²	28 ± 4	26 ± 4	27 ± 4	26 ± 5
FEV ₁ , % pred	55 ± 17	46 ± 17	46 ± 17	55 ± 18
FEV ₁ /FVC [†]	44 ± 9	39 ± 9	40 ± 9	42 ± 16
MVV, % pred	51 ± 17	42 ± 17	45 ± 17	49 ± 15
TLC, % pred	125 ± 17	129 ± 15	124 ± 21	129 ± 21
RV, % pred	193 ± 41	217 ± 56	203 ± 53	197 ± 49
$\dot{V}_{E_{peak}}$, % pred [†]	107 ± 22	113 ± 29	126 ± 37	112 ± 37
Sa _{O₂} , mm Hg	94 ± 2	94 ± 2	93 ± 2	94 ± 3
Pa _{O₂} , mm Hg	77 ± 8	76 ± 6	74 ± 8	78 ± 9
Pa _{CO₂} , mm Hg	40 ± 4	39 ± 3	41 ± 3	39 ± 4
SIP				
Physical dimension, % impairment [†]	3 ± 3	1 ± 2	4 ± 3	3 ± 3
Psychosocial dimension, % impairment [†]	5 ± 7	3 ± 4	5 ± 6	4 ± 4
Total, % impairment	6 ± 5	4 ± 4	6 ± 4	5 ± 5

Definition of abbreviations: BMI = body mass index; MVV = maximal voluntary ventilation; RV = residual volume; SIP = Sickness Impact Profile; TLC = total lung capacity; $\dot{V}_{E_{peak}}$, % pred = peak minute ventilation divided by the predicted peak minute ventilation, calculated as $\dot{V}_{E_{peak}}/(FEV_1 \times 35)$, according to Clark and coworkers (7).

* Values presented are means ± 1 SD. MANOVA revealed no significant group effect, $F(30, 118) = 0.78$.

[†] These variables were not included in the MANOVA because they are a function of one or more dependent variables that were included in the MANOVA.

made weekly home visits to monitor training and adjust the training load. During each visit the nurse monitored one full training session.

CET and IMT. Patients in the CET + IMT group trained 5 d/wk, 20 min/d (CET) and 30 min/d (IMT) as described above. Some patients split the training sessions, performing one in the morning and the other in the evening.

Health education. The control group participated in a structured program of health education with emphasis on how to live a healthier life and how to manage COPD. Health education was conducted on a one-to-one basis with a nurse in the home setting. Eight home visits were conducted, one every other week, and each session lasted approximately 1 h.

Outcome Measures

Respiratory muscle strength. The $P_{I_{max}}$ and maximal expiratory pressure ($P_{E_{max}}$) were measured as indicators of inspiratory and expiratory muscle strength, using techniques described by Black and Hyatt (22). Mouth pressures were measured with a pressure transducer and recorded on a strip chart recorder. A tube-type mouthpiece was connected to the transducer by 61 cm of pressure tubing, and an air leak was positioned in the lateral wall of the mouthpiece (small hole, diameter of 1.6 mm) to minimize the contribution of buccal muscles during the maneuver. Just before each test, the transducer was calibrated against a column of water.

$P_{I_{max}}$ and $P_{E_{max}}$ were defined as the largest negative (vacuum) and positive pressure, respectively, sustained for 1 s against an occluded airway. The tube-type mouthpiece was pressed against the face, with the lips inside the mouthpiece, and measurements were taken from residual volume (RV) and total lung capacity (TLC) for $P_{I_{max}}$ and $P_{E_{max}}$, respectively. A minimum of 10 maneuvers was performed for each measurement, with rest periods between maneuvers. All maneuvers were performed while sitting upright in a chair.

Respiratory muscle endurance. Respiratory muscle endurance was measured with a discontinuous-incremental threshold loading (DC-ITL) test as described earlier (23). Breathing patterns were monitored continuously throughout the work period of each stage of the test.

The protocol for the DC-ITL test was structured with 3-min stages, each of which included a 2-min work period followed by a 1-min rest period off the mouthpiece. The initial inspiratory load was 30% of each patient's $P_{I_{max}}$ and for each stage the load was increased by -5.7 cm H₂O, the change in inspiratory pressure load associated with the addition of 50 g on the platform. Results were reported as the inspiratory pressure generated at the mouth during the last completed stage

of the test (P_m , -cm H₂O). In addition, results were reported as the maximal load relative to inspiratory muscle strength ($P_m/P_{I_{max}}$).

The same sequence of measurements was used at each test of respiratory muscle function. The $P_{I_{max}}$ and $P_{E_{max}}$ were measured first, followed by a 20-min rest and the DC-ITL test. Three tests of respiratory muscle function were performed at baseline to familiarize subjects with the testing protocol. Baseline tests were performed at least 1 wk apart and data representing best performance were used for analysis.

Exercise performance. Graded exercise tests and submaximal exercise tests were conducted on an electronically braked cycle ergometer (CPE 2000; Medical Graphics, Minneapolis, MN) and the same variables were measured during the two tests. Metabolic data and air flow were collected breath by breath with a metabolic cart (model 2900; Sensor Medics, Yorba Linda, CA). Analyzers were calibrated against known gases before each exercise test and calibration was verified immediately after each test. Air flow was calibrated daily with a 3-L syringe. Heart activity (via a 12-lead electrocardiogram), oxyhemoglobin saturation, and blood pressure were monitored during all exercise tests (MAX-1 [Marquette Electronics, Milwaukee, WI], model 3740 [Ohmeda, Boulder, CO], and model 9350 [Paramed Technologies, Mountain View, CA], respectively).

The graded exercise test was conducted with 2-min stages increasing by 10 W at each stage. Patients warmed up by pedaling for 3 min at 10 W following by 2 min at 20 W. After the warm-up, patients rested for 5 min while remaining seated on the cycle ergometer. The graded exercise test was initiated at 30 W. Patients were coached to maintain pedaling at 60 rpm and to continue cycling until they were either too breathless or too tired to continue. If during the first graded exercise test a patient completed 1 min of cycling at 100 W or more, subsequent tests were initiated at 60 W instead of 30 W.

The submaximal exercise test was a two-stage steady-state test, conducted 2 h after the end of the graded exercise test. The protocol included two 5-min work stages separated by a 5-min rest. The two stages were 25 and 50% of the baseline peak work rate, taken from the graded exercise test.

Exercise test conditions were standardized for time of day, medication administration, diet for the 24 h preceding the test, seat height, test instruction, and degree of coaching. Patients were instructed to avoid heavy physical exertion for 24 h before each exercise test. Usual medications were taken in the morning and two puffs of albuterol were administered 30 min before the beginning of the test. The same test instructions were administered at each visit by script. The exercise specialist was blinded to the treatment condition and coached all patients to give their best effort.

At least two exercise tests were conducted during the baseline period to establish stable baseline measures. Tests were separated by at least 7 d and a third test was conducted if the difference in peak O_2 uptake was $\geq 9\%$. All patients requiring a third test had $< 9\%$ difference between test 2 and 3. Data for analysis were taken from the baseline graded exercise test with the highest peak O_2 uptake.

Dyspnea and fatigue. The Borg Category-Ratio Scale (24) was used to measure symptoms during the DC-ITL test, graded exercise test, and steady-state submaximal exercise test. During the DC-ITL test patients rated perceived breathing difficulty at the end of each 2-min work stage. During the graded exercise test and steady-state submaximal exercise tests patients rated perceived breathlessness and perceived leg fatigue at the end of each minute of exercise. The Borg Category-Ratio Scale has a range of 0 to 10 and is highly reproducible when used to measure respiratory sensations during exercise in patients with COPD (25).

The Chronic Respiratory Questionnaire (CRQ) was used to measure the intensity of dyspnea and fatigue experienced by patients on a daily basis. Guyatt and colleagues (26) recommended that subjects be informed of their most recent answer on each item before giving their current answer. For the purposes of this study we blinded patients to their responses on previous visits. This was done to minimize the bias to report improvement, because most patients anticipate benefits from exercise training. The reliability of this modified technique was supported by acceptable test-retest reliability when the instrument was administered twice to patients with COPD, with a 1-wk interval between administrations. The test-retest reliability coefficients were as follows: CRQ Dyspnea, $r = 0.73$, $df = 48$; CRQ Fatigue, $r = 0.69$, $df = 68$ (our unpublished data, 1998). The CRQ has been widely used in surveys of patients with COPD and its validity has been established (26, 27).

Pulmonary function tests. Air flow obstruction and lung volumes were measured with a spirometer and whole body plethysmograph (model 6200; Sensor Medics). Tests were conducted according to American Thoracic Society (ATS) guidelines (28). Predicted normal values were calculated from equations developed by Morris and colleagues (29) and Goldman and Becklake (30) for spirometry and lung volumes, respectively.

Procedures

Tests were conducted under identical conditions at the same time of day and a single investigator collected all of the respiratory muscle data from any given patient. Similarly, the same investigators conducted all exercise tests for a given patient. Respiratory muscle tests and exercise tests were conducted during different visits to the laboratory.

Data Analysis

Data were analyzed with descriptive statistics, multivariate analysis of variance (MANOVA), and univariate repeated measures analysis of variance (ANOVA) using BMDP/DYNAMIC software (release 7.0; BMDP Statistical Software, Cork, Ireland). Descriptive statistics are reported as means \pm SD. The MANOVA statistic was used to control for potential inflation of the overall type I error rate. To compare sample characteristics across groups the MANOVA was performed with one grouping variable. To examine repeated measures across groups, MANOVA was performed with two grouping variables: treatment (IMT, CET, CET + IMT, and ED) and time (before and after the intervention). Univariate ANOVAs and post hoc contrasts were performed to identify the source of significant effects (31). For respiratory muscle function data, post hoc contrasts included between group comparisons for IMT and CET + IMT versus CET and ED, followed by a comparison between IMT and CET + IMT. For exercise data, contrasts included between group comparisons for CET and CET + IMT versus IMT and ED, followed by a comparison between CET and CET + IMT. An α level of < 0.05 was used for all statistical tests.

Performance at the highest equivalent load was used to compare submaximal exercise responses on the graded exercise test and DC-ITL test. For both analyses performance at baseline and the end of the study was examined for individual subjects to identify the highest load attained at both test sessions. This was referred to as the highest equivalent load.

RESULTS

There were no significant changes in body weight, spirometry, or lung volumes after the intervention. At the end of the study all patients demonstrated evidence of a ventilatory limitation to exercise with a mean peak ventilation of $114 \pm 23\%$ of predicted peak values (7).

IMT and CET

The intensity of IMT was not significantly different for the two IMT groups, IMT and CET + IMT. The prescribed IMT load increased from a mean of 31 ± 8 and $30 \pm 3\%$ of baseline $P_{I_{max}}$ at the start of the study to 70 ± 21 and $70 \pm 18\%$ of baseline $P_{I_{max}}$ during the last month for the IMT and CET + IMT groups, respectively. This was the equivalent of 63 ± 9 and $56 \pm 9\%$ of the current $P_{I_{max}}$. Adherence to the IMT prescription was high, ranging from a mean of 81 ± 18 to $92 \pm 21\%$ for the IMT group and from a mean of 94 ± 27 to $106 \pm 34\%$ for the CET + IMT group.

The intensity of CET was not significantly different for the two CET groups, CET and CET + IMT. The intensity of training increased from 52 ± 8 and $44 \pm 9\%$ of the baseline peak work rate at the start of the study to 92 ± 21 and $78 \pm 14\%$ of the baseline peak work rate during the fourth month for the CET and CET + IMT groups, respectively. Because of technical difficulties the monitoring device for adherence was not reliable for low training loads. Consequently, the data were used as a gross indicator of adherence to CET, but actual adherence could not be calculated. Anecdotal observations indicated that some patients had difficulty fulfilling the training requirements for the combined CET + IMT group.

Respiratory Muscle Strength and Endurance

Outcomes for respiratory muscle function are presented in Table 3. After 4 mo of training $P_{I_{max}}$ increased significantly, 10 and 20% in the IMT and CET + IMT groups, respectively, with no change in the CET and ED groups. The DC-ITL load

TABLE 3
RESPIRATORY MUSCLE FUNCTION, COMPARING
EFFECTS OF IMT AND CET + IMT TO CET AND ED*

Variable	Time	IMT (n = 13)	CET (n = 14)	CET + IMT (n = 14)	ED (n = 12)
$P_{I_{max}}$, -cm H ₂ O	T1	91 \pm 26	83 \pm 30	75 \pm 22	86 \pm 16 ¹⁵
	T2	100 \pm 25	86 \pm 27	90 \pm 16	86 \pm 17
DC-ITL P_m , -cm H ₂ O	T1	54 \pm 15	47 \pm 12	45 \pm 15	48 \pm 18 ^{15#}
	T2	69 \pm 15	58 \pm 20	68 \pm 15	49 \pm 16
$P_m/P_{I_{max}}$, %	T1	61 \pm 14	61 \pm 18	62 \pm 18	56 \pm 19 [†]
	T2	70 \pm 8	68 \pm 14	76 \pm 12	57 \pm 17
RPBD**	T1	7.4 \pm 2.5	6.0 \pm 3.6	6.4 \pm 3.5	6.1 \pm 2.6 [†]
	T2	4.8 \pm 2.4	4.7 \pm 2.9	3.5 \pm 2.4	4.5 \pm 2.2

Definition of abbreviations: DC-ITL = discontinuous incremental threshold loading test; $P_{I_{max}}$ = maximal inspiratory pressure; P_m = mouth pressure; RPBD = rating of perceived breathing difficulty measured during the DC-ITL test (possible range, 0-10); T1 = end of the baseline phase, before interventions; T2 = end of the study, after 4 mo of interventions.

* Values presented are means \pm 1 SD. MANOVA group effect $F(9, 115) = 1.10$, not significant; time effect $F(3, 47) = 25.32$, $p = 0.000$; interaction (group and time) $F(9, 115) = 2.69$, $p = 0.007$.

[†] Univariate ANOVA time effect significant, $p < 0.001$.

[‡] Univariate ANOVA interaction effect (group and time) significant, $p < 0.05$.

[#] Univariate ANOVA interaction effect (group and time) significant, $p < 0.001$.

[§] Post hoc contrasts of IMT and CET + IMT versus CET and ED were significant, $p < 0.01$; those of IMT versus CET + IMT were not significant.

^{||} Mouth pressure was measured at the last completed stage.

** RPBD was measured at the highest equivalent inspiratory threshold load at T1 and T2.

TABLE 4
PEAK EXERCISE PERFORMANCE, COMPARING EFFECTS
OF CET AND CET + IMT TO IMT AND ED*

Variable	Time	IMT (n = 13)	CET (n = 14)	CET + IMT (n = 14)	ED (n = 12)
Work rate, W	T1	70 ± 20	62 ± 25	66 ± 26	75 ± 27 ^{†‡§}
	T2	68 ± 17	75 ± 30	77 ± 32	73 ± 26
\dot{V}_E , L/min	T1	57.1 ± 18.5	44.4 ± 16.9	50.2 ± 19.0	53.5 ± 17.2
	T2	54.4 ± 16.0	47.7 ± 16.9	50.9 ± 16.1	52.9 ± 13.4
\dot{V}_{CO_2} , L/min	T1	1.37 ± 0.37	1.11 ± 0.42	1.26 ± 0.50	1.29 ± 0.48
	T2	1.32 ± 0.32	1.17 ± 0.40	1.35 ± 0.52	1.27 ± 0.43
\dot{V}_{O_2} , L/min	T1	1.38 ± 0.38	1.14 ± 0.38	1.26 ± 0.45	1.26 ± 0.43 [§]
	T2	1.30 ± 0.31	1.25 ± 0.38	1.33 ± 0.44	1.29 ± 0.42
HR, beats/min	T1	141 ± 22	140 ± 19	129 ± 21	146 ± 14
	T2	140 ± 23	141 ± 16	128 ± 22	142 ± 14
RPB	T1	7.0 ± 2.6	6.6 ± 2.8	6.2 ± 2.8	7.0 ± 1.8
	T2	7.5 ± 2.7	5.9 ± 3.1	6.3 ± 2.8	7.3 ± 2.7
RPLF	T1	6.8 ± 2.9	6.0 ± 3.0	5.8 ± 2.7	5.8 ± 2.4
	T2	7.4 ± 2.6	4.8 ± 2.7	5.8 ± 3.2	6.4 ± 1.8
\dot{V}_E/\dot{V}_{O_2} [#]	T1	42 ± 9	40 ± 9	40 ± 4	43 ± 6
	T2	42 ± 9	38 ± 6	38 ± 4	41 ± 7
V_T , L [#]	T1	1.6 ± 0.3	1.3 ± 0.5	1.4 ± 0.5	1.5 ± 0.5
	T2	1.6 ± 0.3	1.3 ± 0.4	1.5 ± 0.5	1.4 ± 0.4
RR, breaths/min [#]	T1	36 ± 9	35 ± 6	36 ± 6	36 ± 6
	T2	34 ± 7	37 ± 5	34 ± 3	38 ± 7

Definition of abbreviations: HR = heart rate; RPB = rating of perceived breathlessness; RPLF = rating of perceived leg fatigue; RR = respiratory rate; \dot{V}_E = minute ventilation; \dot{V}_E/\dot{V}_{O_2} = ventilatory equivalent for oxygen uptake; \dot{V}_{O_2} = oxygen uptake. For other definitions see Table 2.

* Values presented are means ± 1 SD. MANOVA group effect F(21, 124) = 1.52, not significant; time effect F(7, 43) = 2.32, p = 0.04; interaction (group and time) F(21, 124) = 2.43, p = 0.001.

[†] Univariate ANOVA time effect significant, p < 0.01.

[‡] Univariate ANOVA interaction effect (group and time) significant, p < 0.01.

[§] Post hoc contrasts of CET and CET + IMT versus IMT and ED, p < 0.05; those of CET versus CET + IMT were not significant.

^{||} Univariate ANOVA interaction effect (group and time) significant, p < 0.05.

[#] These variables were not included in the MANOVA because they are a function of one or more dependent variables that were included in the MANOVA.

(P_m , -cm H₂O) at the last completed stage increased significantly, 28 and 51% in the IMT and CET + IMT groups, respectively. Maximal expiratory pressure did not change during the study.

Breathing patterns at the highest equivalent work load were not significantly different between groups, but all groups used a larger tidal volume and smaller duty cycle on the DC-ITL test at the end of the study. There was no change in minute ventilation.

Exercise Performance

Results of the graded exercise tests are presented in Table 4. The CET and CET + IMT groups demonstrated significant increases in peak work rate and peak oxygen uptake. There were no significant changes in heart rate, tidal volume, or rating of perceived breathlessness and leg fatigue at peak exercise, supporting the assumption that patients pushed themselves to similar points of exhaustion on both graded exercise tests before and after training.

Results from submaximal exercise performance at the highest equivalent work rate are presented in Table 5. Because of space limitations descriptive statistics are not presented for the two steady-state tests, 50 and 25% of the baseline peak work rate. The highest equivalent work rate for the four groups ranged from 62 ± 25 to 68 ± 26 W. The work rate for steady-state tests at 50 and 25% of the baseline peak work rate ranged from 31 ± 11 to 37 ± 14 W and from 16 ± 6 to 19 ± 7 W, respectively, for the four groups.

Minute ventilation decreased significantly at the highest equivalent work rate for CET and CET + IMT groups, but not in the steady-state tests at 50 and 25% of the baseline peak work rate. Heart rate decreased significantly for the CET and CET + IMT groups at all three submaximal work rates. There were no differences between the CET and CET + IMT groups at the highest equivalent work rate and 50% baseline peak work rate. At 25% baseline peak work rate the decrease in heart rate was significantly greater for the CET group as compared with the CET + IMT group. Heart rate decreased by 9 beats per minute (bpm) in the CET group and by 1 bpm in the CET + IMT group. This finding at the 25% work rate is not considered significant because it did not occur consistently at the other work rates.

Dyspnea and Fatigue

Exercise-related dyspnea was improved after training with cycle ergometry. At all three submaximal work rates the CET and CET + IMT groups demonstrated a significant decrease in rating of perceived breathlessness as compared with the IMT and ED groups, but there were no differences between the CET and CET + IMT groups.

On the DC-ITL test all four groups reported significantly less breathing difficulty after 4 mo of intervention, and this was associated with changes in breathing pattern. At the highest equivalent load, change in rating of perceived breathing difficulty correlated moderately with change in duty cycle (r =

TABLE 5
SUBMAXIMAL EXERCISE PERFORMANCE AT THE HIGHEST EQUIVALENT WORK RATE BY GROUP*

Variable	Time	IMT (n = 13)	CET (n = 14)	CET + IMT (n = 14)	ED (n = 12)
Work rate, W		67 ± 18	62 ± 25	65 ± 26	68 ± 26
\dot{V}_E , L/min	T1	52 ± 17	43 ± 17	47 ± 18	46 ± 12 ^{†‡§}
	T2	51 ± 14	38 ± 12	42 ± 12	47 ± 13
\dot{V}_{CO_2} , L/min	T1	1.25 ± 0.34	1.06 ± 0.44	1.19 ± 0.50	1.14 ± 0.40 [†]
	T2	1.25 ± 0.30	0.96 ± 0.36	1.13 ± 0.44	1.16 ± 0.41
\dot{V}_{O_2} , L/min	T1	1.26 ± 0.34	1.10 ± 0.40	1.20 ± 0.45	1.14 ± 0.38
	T2	1.24 ± 0.30	1.06 ± 0.35	1.15 ± 0.37	1.19 ± 0.39
HR, beats/min	T1	132 ± 23	135 ± 19	125 ± 19	137 ± 14 ^{‡#}
	T2	134 ± 23	126 ± 13	114 ± 17	132 ± 14
RPB	T1	5.5 ± 2.4	5.5 ± 3.0	5.2 ± 2.4	5.3 ± 2.1 ^{‡#}
	T2	5.3 ± 2.2	3.4 ± 2.2	4.1 ± 2.1	5.1 ± 2.4
RPLF	T1	5.0 ± 2.4	5.5 ± 3.0	5.3 ± 2.4	5.2 ± 2.2 ^{§ **}
	T2	5.5 ± 2.1	2.9 ± 1.7	3.9 ± 2.4	5.0 ± 2.3
\dot{V}_E/\dot{V}_{O_2} ^{††}	T1	41 ± 8	39 ± 8	40 ± 4	41 ± 5 [†]
	T2	41 ± 8	37 ± 5	37 ± 4	41 ± 7
V_T , L ^{††}	T1	1.7 ± 0.4	1.3 ± 0.4	1.4 ± 0.5	1.5 ± 0.4 [†]
	T2	1.7 ± 0.3	1.4 ± 0.4	1.5 ± 0.5	1.5 ± 0.4
RR, breaths/min ^{††}	T1	32 ± 8	32 ± 5	33 ± 6	31 ± 5 ^{§ **}
	T2	30 ± 6	29 ± 4	28 ± 4	32 ± 6

For definition of abbreviations, see Table 4.

* Values presented are means ± 1 SD. MANOVA group effect $F(18, 125) = 1.07$; $p = 0.394$; time effect $F(6, 44) = 3.13$, $p = 0.012$; interaction effect $F(18, 125) = 2.30$, $p = 0.004$.

[†] Univariate ANOVA time effect significant, $p < 0.05$.

[‡] Univariate ANOVA interaction effect (group and time) significant, $p < 0.05$.

[§] Post hoc contrasts CET and CET + IMT versus IMT and ED, $p < 0.01$; and IMT versus CET + IMT, not significant.

^{||} Univariate ANOVA time effect significant, $p < 0.01$.

[#] Post hoc contrasts CET and CET + IMT versus IMT and ED, $p < 0.05$; and CET versus CET + IMT, not significant.

^{**} Univariate ANOVA interaction effect (group and time) significant, $p < 0.01$.

^{††} These variables were not included in the MANOVA because they are a function of one or more dependent variables that were included in the MANOVA.

0.44, $df = 51$), and weakly with change in tidal volume ($r = -0.15$, $df = 51$).

The symptom of exercise-related leg fatigue was improved after training with cycle ergometry at all three submaximal work rates. The rating of perceived leg fatigue decreased significantly for patients in the CET and CET + IMT groups, but not for patients in the IMT and ED groups. There was no difference between the CET and CET + IMT groups.

Improvements in exercise-related dyspnea and leg fatigue were not reflected in patient perception of dyspnea and fatigue experienced on a daily basis (Table 6). The CRQ Dyspnea Scale reflected a significant decrease in dyspnea from the beginning to the end of the study, but no differences between the groups. There were no significant changes in CRQ Fatigue Scale.

DISCUSSION

The results of this study demonstrated that home-based CET can produce a physiological training effect in patients with moderate to severe COPD as reflected by an increase in peak oxygen uptake on a graded exercise test and decrease in heart rate and minute ventilation with no change in oxygen uptake for identical work rates at submaximal levels. But the combination of CET and IMT did not yield significant additional benefits in exercise performance.

TABLE 6
CHRONIC RESPIRATORY QUESTIONNAIRE BY GROUP*

Variable	Time	IMT (n = 12) [†]	CET (n = 14)	CET + IMT (n = 14)	ED (n = 12)
Dyspnea Scale [‡]	T1	19.3 ± 5.8	20.4 ± 5.4	21.3 ± 4.8	22.8 ± 6.5 [§]
	T2	21.8 ± 6.5	23.9 ± 4.4	23.3 ± 5.0	22.7 ± 5.3
Fatigue Scale	T1	19.6 ± 4.7	18.9 ± 3.1	17.7 ± 3.0	18.9 ± 5.3
	T2	19.8 ± 4.7	19.4 ± 4.5	19.8 ± 2.8	19.7 ± 4.5

* Values presented are means ± 1 SD. Note the CRQ is scored in reverse, so that an increase in the score reflects a decrease in dyspnea and fatigue. The potential range is 5–35 for the Dyspnea Scale and 4–28 for the Fatigue Scale. MANOVA group effect $F(6, 86) = 0.30$, not significant; time effect $F(2, 43) = 5.41$, $p = 0.008$; interaction (group and time) $F(6, 86) = 1.28$, not significant.

[†] One subject did not complete the CRQ at the end of the study.

[‡] Data are missing on the CRQ Dyspnea Scale when subjects cannot rate their dyspnea for at least three of the activities that were identified at the beginning of the study. The sample size for this scale was as follows: IMT, $n = 11$; CET, $n = 13$; CET + IMT, $n = 14$; ED, $n = 10$.

[§] Univariate ANOVA time effect significant, $p < 0.01$.

Exercise Performance

For the first time a physiological training effect was demonstrated for aerobic exercise training in a home-based program with weekly supervision. In general, the magnitude of the effect was similar to that which was observed in outpatient programs, especially with respect to changes in minute ventilation and heart rate at the highest equivalent work rate (4, 5, 32).

The addition of IMT did not enhance the training effect. This is explained by the fact that IMT did not reduce exercise-related dyspnea, even though it increased strength of the inspiratory muscles. Others have reported that the intensity of dyspnea is inversely related to strength of the inspiratory muscles, even in healthy subjects (9–13). Using the Black and Hyatt prediction equations (22), the $P_{I_{max}}$ was 85 and 110% of predicted normal values for men and women, respectively, in this study. This suggests that functional weakness of the inspiratory muscles was not the primary cause of dyspnea in these patients.

In addition, the combination of CET and IMT was strenuous for all patients and anecdotal observations indicated that it may have been excessive for some. Of the four subjects who dropped out of the study because of the difficulty of training, all were in the CET + IMT group. We conclude that for some patients it may be more effective to provide the two types of training in series, with several months of IMT followed by several months of CET.

These results can be generalized to patients with moderate to severe COPD, but not to the sickest, oxygen-dependent patients with very severe COPD. The sickest patients were excluded from this study because of the potential risks associated with home-based aerobic exercise training.

Respiratory Muscle Strength and Endurance

Adherence to the IMT prescription was high, possibly encouraged by the presence of the monitoring device. The observed 10% (MT) and 20% (CET + IMT) increase in $P_{I_{max}}$ is consistent with increases reported in other studies that employed a similar intensity of IMT (14, 19, 33–35).

The results of the DC-ITL test reflect an increase in both respiratory muscle endurance and inspiratory muscle strength for the IMT and CET + IMT groups. But change in $P_{I_{max}}$ was weakly correlated with change in the peak load (P_m , cm H₂O) on the DC-ITL test ($r = 0.41$, $df = 51$), suggesting that it accounted for a relatively small portion of the increase in performance. At the end of the study, all four groups modified their

breathing pattern, using a shorter duty cycle and larger tidal volume. Theoretically, this is a more efficient breathing pattern (36), but it occurred in all four groups and therefore does not account for the improvement in performance that was observed only in the IMT and CET + IMT groups. In addition, the more efficient breathing pattern could explain the decrease in perceived breathing difficulty on the DC-ITL test at the end of the study (37).

Dyspnea and Fatigue

From previous research it is clear that general exercise training decreases dyspnea and leg fatigue measured during exercise testing. This was demonstrated in randomized controlled trials of pulmonary rehabilitation that incorporated general exercise training (1, 2, 8). Our findings are consistent with the results of these trials.

Patients reported a substantial amount of dyspnea during daily activities, yet improvement in exercise-related dyspnea did not generalize to improvements in dyspnea during activities of daily living. This is plausibly explained by the specificity of training. To improve performance in a given activity one must train specifically for that activity. The observed improvement in the intensity of dyspnea during exercise testing was measured at high work loads under controlled conditions. In contrast, dyspnea during activities of daily living was measured in terms of activities that require the use of multiple muscle groups at much lower work loads.

Similarly, patients reported a substantial amount of fatigue in daily life, but improvements in exercise-related leg fatigue did not influence fatigue in daily life. It is possible that patients were fatigued by the intense training schedule (5 d/wk). The inconsistent results from the two measures of fatigue are further explained by the nature of the instruments. The rating of perceived leg fatigue during exercise was more sensitive to changes in fatigue because measurements were conducted under controlled conditions during exercise at the same intensity. In contrast, the CRQ Fatigue Scale is a four-item scale with two items reflecting general intensity of fatigue and two items reflecting frequency of fatigue over the last 2 wk. In the daily life of patients the intensity and frequency of fatigue will be influenced by activity level, making it difficult to validate comparisons across time without controlling for activity level. Nevertheless, these results suggest that CET did not ameliorate fatigue in daily life.

In conclusion, home-based CET produced a physiological training effect, a reduction in dyspnea and leg fatigue during exercise, but no change in dyspnea and fatigue during activities of daily living. The IMT produced increases in inspiratory muscle strength and respiratory muscle endurance. But the combination of CET + IMT did not produce significant additive effects with respect to exercise-related dyspnea or the physiological training effect.

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