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Effects of Pulmonary Rehabilitation on Physiologic and Psychosocial Outcomes in Patients with Chronic Obstructive Pulmonary Disease

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■ *Objective:* To compare the effects of comprehensive pulmonary rehabilitation with those of education alone on physiologic and psychosocial outcomes in patients with chronic obstructive pulmonary disease.

■ *Design:* Randomized clinical trial.

■ *Setting:* University medical center.

■ *Patients:* 119 outpatients with chronic obstructive pulmonary disease that was stable while patients received a standard medical regimen.

■ *Intervention:* Patients were randomly assigned to either an 8-week comprehensive pulmonary rehabilitation program or to an 8-week education program. Pulmonary rehabilitation consisted of twelve 4-hour sessions that included education, physical and respiratory care instruction, psychosocial support, and supervised exercise training. Monthly reinforcement sessions were held for 1 year. The education group attended four 2-hour sessions that included videotapes, lectures, and discussions but not individual instruction or exercise training.

■ *Measurements:* Pulmonary function, maximum exercise tolerance and endurance, gas exchange, symptoms of perceived breathlessness and muscle fatigue with exercise, shortness of breath, self-efficacy for walking, depression, general quality of well-being, and hospitalizations associated with pulmonary diseases. Patients were followed for 6 years.

■ *Results:* Compared with education alone, comprehensive pulmonary rehabilitation produced a significantly greater increase in maximal exercise tolerance (+1.5 metabolic equivalents [METS] compared with +0.6 METS [$P < 0.001$]; maximal oxygen uptake, +0.11 L/min compared with +0.03 L/min [$P = 0.06$]), exercise endurance (+10.5 minutes compared with +1.3 minutes [$P < 0.001$]), symptoms of perceived breathlessness (score of −1.5 compared with +0.2 [$P < 0.001$]) and muscle fatigue (score of −1.4 compared with −0.2 [$P < 0.01$]), shortness of breath (score of −7.0 compared with +0.6 [$P < 0.01$]), and self-efficacy for walking (score of +1.4 compared with +0.1 [$P < 0.05$]). There were slight but nonsignificant differences in survival (67% compared with 56% [$P = 0.32$]) and duration of hospital stay (−2.4 days/patient per year compared with +1.3 days/patient per year [$P = 0.20$]). Measures of lung function, depression, and general quality of life did not differ between groups. Differences tended to diminish after 1 year of follow-up.

■ *Conclusions:* Comprehensive pulmonary rehabilitation significantly improved exercise performance and symptoms for patients with moderate to severe chronic obstructive pulmonary disease. Benefits were partially maintained for at least 1 year and tended to diminish after that time.

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The chronic obstructive pulmonary diseases are major causes of disability and death (1–3). Health statistics underestimate the prevalence of these diseases because of difficulties in definition and recognition and because of misclassification (4). Although standard medical therapy can alleviate symptoms, many patients with these diseases must cope with the distressing symptom of breathlessness that results from a chronic, irreversible, and disabling disease. These patients may use services in physician offices, emergency departments, hospitals, and intensive care units, in part because of a lack of understanding and inability to cope with frightening and disabling symptoms.

Since a comprehensive care program for patients with chronic obstructive pulmonary disease was first described (5), pulmonary rehabilitation has become an established way to enhance standard therapy to control symptoms, optimize functional capacity, and reduce the medical and economic burdens of patients with disabling chronic lung diseases (6–12). Comprehensive programs usually include education, instruction in respiratory and chest physiotherapy techniques, psychosocial support, and exercise training (13).

The primary goal of rehabilitation is to restore the patient to the highest possible level of independent function. This is accomplished by helping patients to become more knowledgeable about their disease, more actively involved in their own health care, more independent in performing daily activities, and less dependent on others, including health professionals. Previous studies have shown important benefits of pulmonary rehabilitation, including increased exercise tolerance and quality of life and a decreased number of symptoms and use of health care services (7). However, many of these findings are based on small numbers of patients and on observational, nonrandomized studies.

We compared the effects of comprehensive pulmonary rehabilitation on both physiologic and psychosocial outcomes with the effects of education alone. Our study featured random assignment and long-term, 6-year follow-up.

Methods

Patients

For 18 months, 352 patients with chronic obstructive pulmonary disease were screened for the study; 128 met entry criteria and were randomly assigned to either the comprehensive pulmonary rehabilitation program or an education program (control group). Patients were recruited through mechanisms similar to those used in regular clinical pulmonary rehabilitation, including written and personal contact with physicians and direct advertisement to the general public for persons with breathlessness. Nine patients who initially agreed to participate (6 in the rehabilitation group and 3 in the education group) but who withdrew from the study before completing 2 weeks of the interventions were considered to be pretreatment drop-outs. Reasons for dropping out included concurrent illness (four patients), a too-large time commitment (2 patients), and no clear explanation (3 patients). Patients who dropped out and those who remained in the study did not differ. The remaining 119 patients comprised 32 women and 87 men.

The following were the inclusion criteria:

1. Clinical diagnosis of mild to severe chronic obstructive pulmonary disease that was confirmed by history, physical examination, spirometry, measurement of arterial blood gases, and chest roentgenograms. Patients with diagnoses of emphysema, chronic bronchitis, or asthmatic bronchitis were accepted. Patients with primarily acute, reversible airway disease (asthma) but no chronic airflow obstruction were excluded.
2. Stable condition while the patient was receiving an acceptable medical regimen and was under the care of a primary care provider. Patients without a primary care physician who presented for evaluation were referred for appropriate evaluation and treatment before they enrolled in the study.
3. No other significant disabling lung disease, serious heart problems, or other medical condition that would interfere with the patient's participation.

Current smokers were not excluded if they showed a commitment to quitting smoking before enrollment. Smoking cessation counseling was incorporated into the rehabilitation program for patients assigned to that group.

Experimental Design

All eligible patients were randomly assigned to participate in either the comprehensive pulmonary rehabilitation program (n = 57) or the education program (n = 62). The randomization scheme was fixed before the trial with a block size of 8. Assignment was determined by a table of random numbers and was indicated on cards placed in sequentially numbered envelopes that were kept in a central office separate from the study site. Clinical personnel were unaware of the randomization scheme. After a patient agreed to enroll and signed the consent form approved by the University of California, San Diego, Human Subjects Committee, the central office was contacted by telephone and the next numbered envelope was opened.

Interventions

Pulmonary Rehabilitation Program

The comprehensive rehabilitation program included two phases. Phase I (core program) consisted of twelve 4-hour sessions given over 8 weeks. Each session included two periods of classroom or group support and supervised exercise training. The rehabilitation program included four main components:

1. Education. Groups of three to six patients were taught by experienced pulmonary rehabilitation staff and selected guest speakers. Topics included the following: How Normal Lungs Work, What Is Chronic Obstructive Pulmonary Disease?, Medications, Nutrition, Oxygen Therapy, Coping with Stress, Energy-saving Techniques, Self-Care Tips, Travel, Pollution and Environmental Hazards, When To Call Your Doctor, Smoking Cessation Techniques, Planning a Daily Schedule, and Breathing Techniques.
2. Physical and respiratory care instruction. Patients received individual instruction in respiratory care and chest physiotherapy techniques such as postural drainage, pursed lip and diaphragmatic breathing, oxygen therapy, and proper use of respiratory therapy equipment.
3. Psychosocial support. Patients and staff met in weekly group sessions facilitated by a psychiatrist. Spouses or partners of the patients were encouraged to attend. Sessions focused on difficulties commonly faced by patients, such as depression, anxiety, fear, and family or social problems. Relaxation techniques were introduced to help patients better cope with the emotional stress of dyspnea.
4. Supervised exercise training. After the baseline exercise test, each patient received an individualized exercise prescription based on the maximum, symptom-limited level (14). Patients with severe hypoxemia ($Pa_{O_2} < 55$ mm Hg at rest or < 50 mm Hg with exercise) were trained using supplemental oxygen. The primary exercise-training modality was walking. Training emphasized steady-state exercise consisting of continuous walking at the highest tolerated symptom-limited level for as long as 30 minutes. Patients were initially trained to walk on a motor-driven treadmill under supervision. The staff then instructed patients in translating the target treadmill speed to a pace for free walking. Patients were asked to walk at home at least twice daily and to keep a training log of time, distance, pace (steps per minute), and perceived symptoms of breathlessness and muscle fatigue.

Patients were also instructed and trained in upper-extremity exercise using an isokinetic upper-body ergometer during supervised sessions and a progressive program of arm lifts with weights for home training (15). Patients were asked to do upper-extremity training daily and to keep a daily log.

Phase II of the rehabilitation program involved monthly follow-up visits for 1 year. These visits provided reinforcement after the core phase of the program. These sessions included a supervised period of exercise, group sessions to discuss progress and problems, and the introduction of maintenance techniques.

Education Control Program

The goal of the education program was to conduct a series of health education classes that would provide information similar to that provided in the rehabilitation program, but in a shorter and less intensive program without the behavioral components, individualized instruction, and supervised exercise training. Patients in the education group attended four 2-hour sessions scheduled biweekly for 8 weeks. Each group consisted of approximately 10 to 15 patients.

At the beginning of each session, a videotape describing some aspect of chronic obstructive pulmonary disease management was presented (Pulmonary Self-Care Series, *Encyclopedia Britannica*, Vision Multimedia Communications, Inc., Winter Park, Florida). The four-part videotape series included the following programs: 1) Learning To Live with a Breathing Problem; 2) Building Your Strength and Endurance; 3) You Can Do It: Clearing Your Airways; and 4) Learning To Breathe Better. Patients also completed life events (16), social support (17), health locus of control (18), and sense of coherence (19) questionnaires and a semistructured smoking interview. The patients then participated in a group discussion about either the material covered in the videotape or the questionnaires. The final hour of the session included a lecture followed by a question and answer period presented by professionals in the fields of pulmonary medicine, pharmacology, respiratory therapy, and nutrition.

Assessment

Each patient had physiologic and psychosocial function evaluation before intervention (baseline), immediately after the program ended (2 months), and at regular intervals for 72 months. Physiologic measures, including laboratory pulmonary function and maximal treadmill exercise tests, were done 2, 12, 24, 48, and 72 months after the program began. Psychosocial measures and endurance exercise tests were done more frequently at 2, 6, 12, 18, 24, 36, 48, 60, and 72 months. Laboratory tests of pulmonary function and maximal treadmill exercise were done on 1 or 2 days, depending on patient preference. The treadmill endurance walk and psychosocial measures were obtained together on a separate day.

Physiologic Measures

Physiologic measures included tests of pulmonary function, maximum exercise tolerance, endurance exercise, and rest and exercise gas exchange.

Pulmonary function tests included spirometric measurements of vital capacity and expiratory flow rates, lung volumes and airway resistance measured by body plethysmography, single-breath diffusing capacity, maximal inspiratory pressure (at residual volume) and expiratory pressure (at total lung capacity) to assess respiratory muscle strength, and maximal voluntary ventilation. All testing and quality control procedures were done according to standard and recommended methods (20–22). To assess airway reactivity, spirometry, lung volume, and airway resistance measures were repeated only at baseline after patients received an inhaled bronchodilator.

Maximum exercise tolerance was measured with an incremental, symptom-limited exercise test of the maximal tolerable level on a treadmill. During this test, expired air was continuously analyzed to assess physiologic responses to exercise with measurements of oxygen uptake, carbon dioxide elimination, expired minute ventilation, and other related variables (23, 24). We calculated maximum exercise workload as the metabolic equivalent (estimated oxygen uptake values measured in metabolic equivalents) from the maximum treadmill speed and grade. We collected arterial blood samples from an indwelling radial artery catheter to measure arterial blood gases at rest and during exercise (Pa_{O_2}, Pa_{CO_2}, percentage of oxyhemoglobin, and percentage of carboxyhemoglobin). Cutaneous ear oximetry was used to monitor arterial oxygen saturation. Electrocardiography was used to monitor patients for ischemic cardiac changes and arrhythmias and to measure heart rate. Blood pressure was measured manually at periodic intervals. Perceived symptoms of breathlessness and muscle fatigue were rated at the end of the exercise test using a scale adapted from Borg (25) ranging from 0 (none) to 10 (maximum).

Patients with severe resting hypoxemia (Pa_{O_2} < 55 mm Hg) or exercise hypoxemia (Pa_{O_2} < 50 mm Hg) repeated the treadmill exercise test while receiving supplemental oxygen so that a safe level for subsequent exercise training could be defined.

Exercise endurance was measured on a separate day. This test was done at a constant work level chosen from the incremental exercise test to estimate each patient's maximum, symptom-limited capacity for steady-state walking. On average, the target exercise level represented 95% of the initial maximal exercise tolerance (14). Patients were instructed to walk for as long as 20 minutes at this level and, if possible, for an additional 10 minutes at the next higher level. The total treadmill time at the target levels was recorded (maximum, 30 minutes); perceived breathlessness and muscle fatigue were rated (on a scale of 0 to 10) at the end of the exercise test (25).

Psychosocial Measures

Patients completed psychosocial measures 10 times during the 6 years of follow-up. These included the following:

1. Self-efficacy questionnaire. Self-efficacy was defined as the expectation that a specific behavior can be executed. The self-efficacy questionnaire was adapted from one used in a previous study by Kaplan and colleagues (26). The scale emphasizes walking and includes 9 statements of increasing exercise intensity: Walk 1 block (approximately 5 minutes), walk 2 blocks (10 minutes), walk 3 blocks (15 minutes), ... walk 3 miles (90 minutes). Patients were asked to rate their expectation of completing that activity on a 100-point probability scale, ranging in 10-point intervals from 0 (complete uncertainty) to 100 (complete certainty). The score reflects the highest level at which the patient expressed 100% confidence.

2. Quality of Well-Being scale. This comprehensive measure of health-related quality of life includes several components. First, it obtains observable levels of functioning at a point in time. The levels of functioning are obtained from three separate scales: mobility, physical activity, and social activity. Second, reports of symptoms and disturbances are noted. The patients identify the most undesirable symptom or problem from a standard list. Then, the observed level of function and symptom report are weighted by preference or by the desirability of the state on a scale ranging from 0 (for dead) to 1.0 (for optimum function). The weights are obtained from independent samples of judges who rate the desirability of the observable health status and symptom–problem combinations. This system has been used extensively in various medical and health services research applications (27, 28). Findings from specific validity and reliability studies that have used this measure for patients with chronic obstructive pulmonary disease have been reported (29). These studies show that the Quality of Well-Being scale is generally

Table 1. Results for Selected Variables by Group at Initial Evaluation*

Variable	Rehabilitation Group	Education Group
Patients, *n*	57	62
Men/women, *n/n*	42/15	45/17
Age, *y*	61.5 ± 8.0	63.6 ± 6.3
Smoking status		
Current, *n* (%)	8 (14)	6 (10)
Former, *n* (%)	41 (72)	50 (81)
Never, *n* (%)	8 (14)	6 (10)
Pack-years, *n*	45 ± 38	52 ± 35
Carboxyhemoglobin level >3%, *n* (%)	10 (18)	10 (16)
Pulmonary function		
FEV_1, *L*	1.21 ± 0.55	1.24 ± 0.56
FEV_1/FVC, %	45 (13)	43 (10)
$FEF_{25\%-75\%}$, *L/s*	0.53 ± 0.45	0.48 ± 0.31
RV/TLC, %	60 (11)	61 (10)
R_{AW}, *cm H_2O/L per s*	3.0 ± 1.4	3.2 ± 1.2
D_LCO, *mL/min per mm Hg*	14.2 ± 7.5	14.0 ± 6.8
MIP, *cm H_2O*	94.6 ± 29.3	86.2 ± 27.5
MVV, *L/min*	46.3 ± 24.0	48.5 ± 24.5
Resting Pa_{O_2}, *mm Hg*	74.0 ± 11.9	74.1 ± 11.8
Resting Pa_{CO_2}, *mm Hg*	38.5 ± 5.5	39.0 ± 5.1
Resting V_D/V_T, %	49.5 (6.9)	47.3 (9.7)
Maximum exercise		
$V_E$max, *L/min*	44.9 ± 19.5	43.6 ± 18.5
VO_2max, *L/min*	1.24 ± 0.51	1.24 ± 0.54
Perceived symptom score		
Breathlessness	5.3 ± 1.6	5.1 ± 2.0
Muscle fatigue	4.3 ± 2.3	4.0 ± 1.8
Endurance exercise		
Duration, *min*	12.4 ± 8.4	11.8 ± 8.0
Perceived symptom score		
Breathlessness	5.0 ± 2.2	4.5 ± 2.1
Muscle fatigue	4.3 ± 2.2	4.3 ± 2.2
Psychosocial measures		
Self-efficacy, walking, *n*	3.7 ± 3.2	4.1 ± 3.3
Quality of Well-Being score	0.666 ± 0.096	0.652 ± 0.067
CES-D depression score	14.0 ± 8.7	15.3 ± 10.0
Score > 18, *n* (%)	15 (26)	14 (23)
Shortness of Breath Questionnaire response	35.8 ± 18.5	32.8 ± 19.2
Health care utilization		
Patients reporting any hospitalizations or emergency department visits for lung problems in the past 12 months, %	53	45
Hospital days per patient, *n*	6.4 ± 12.6	3.6 ± 6.6
Total hospital days, *n*	362	196

*CES-D = Centers for Epidemiologic Studies Depression scale; D_LCO = Single-breath diffusing capacity for carbon monoxide; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; $FEF_{25\%-75\%}$ = forced expiratory flow rate over the midportion (25% to 75%) of the vital capacity; MIP = maximal inspiratory pressure; MVV = maximal voluntary ventilation; Pa_{CO_2} = arterial partial pressure for carbon dioxide; Pa_{O_2} = arterial partial pressure for oxygen; R_{AW} = airway resistance; RV = residual volume; TLC = total lung capacity; V_D = dead space ventilation; $V_E$max = maximal expired minute ventilation; VO_2max = maximal oxygen uptake; V_T = tidal volume. Values are expressed as the mean ± SD. All comparisons between groups are nonsignificant ($P > 0.05$).

Table 2. Baseline Values and Changes from Baseline in Rehabilitation and Education Groups*

Variable	Baseline	2 Months	6 Months
Patients, *n*			
Rehabilitation	57	53	52
Education	62	57	54
FEV_1, *L*			
Rehabilitation	1.21 ± 0.55	0.12 ± 0.38	
Education	1.24 ± 0.56	0.06 ± 0.29	
D_LCO, *mL/min per mm Hg*			
Rehabilitation	14.2 ± 7.5	0.7 ± 2.2	
Education	14.0 ± 6.8	0.1 ± 2.3	
Maximum treadmill workload, *metabolic equivalents*			
Rehabilitation	4.6 ± 2.8	1.5 ± 1.3†	
Education	4.7 ± 2.7	0.6 ± 1.2	
Maximum oxygen uptake, *L/min*			
Rehabilitation	1.24 ± 0.51	0.11 ± 0.23§	
Education	1.24 ± 0.54	0.03 ± 0.17	
Treadmill endurance, *min*			
Rehabilitation	12.4 ± 8.4	10.5 ± 9.9†	7.6 ± 11.2†
Education	11.8 ± 8.0	1.3 ± 6.1	1.2 ± 7.0
Perceived breathlessness score			
Rehabilitation	5.0 ± 2.2	−1.5 ± 2.1†	−1.5 ± 2.0†
Education	4.5 ± 2.1	0.2 ± 2.0	0.3 ± 1.6
Perceived muscle fatigue score			
Rehabilitation	4.3 ± 2.2	−1.4 ± 2.3‖	−1.4 ± 2.6‖
Education	4.3 ± 2.2	−0.2 ± 2.0	0.1 ± 2.1
Self-efficacy for walking score			
Rehabilitation	3.7 ± 3.2	1.4 ± 3.1‡	0.8 ± 3.5‡
Education	4.1 ± 3.3	0.1 ± 2.9	−0.5 ± 2.3
CES-D depression score			
Rehabilitation	14.0 ± 8.7	−0.1 ± 10.0	0.3 ± 7.2
Education	15.3 ± 10.0	−0.4 ± 7.3	−1.4 ± 6.2
Quality of Well-Being score			
Rehabilitation	0.666 ± 0.096	0.004 ± 0.098	−0.032 ± 0.159
Education	0.652 ± 0.067	0.016 ± 0.084	−0.001 ± 0.071
Shortness of Breath Questionnaire			
Rehabilitation	35.8 ± 18.5	−7.0 ± 14.0‖	−6.8 ± 13.0‖
Education	32.8 ± 19.2	0.6 ± 13.1	0.3 ± 11.3
Mean hospital days for lung disease in the past 12 months, *n*			
Rehabilitation	6.4 ± 12.6	–	–
Education	3.6 ± 6.6	–	–

* CES-D = Centers for Epidemiologic Studies Depression scale; D_LCO = single-breath diffusing capacity for carbon monoxide; FEV_1 = forced expiratory volume in 1 second. Values are expressed as the mean ± SD.
† $P \leq 0.001$.
‡ $P \leq 0.05$.
§ $P \leq 0.10$.
‖ $P \leq 0.01$.

sensitive to changes in health status and is correlated with various physical and functional measures.

3. Centers for Epidemiologic Studies Depression Scale (CES-D). We measured depression with the CES-D scale, which is a general measure of depressive symptoms that has been used extensively in epidemiologic studies (30, 31). The scale includes 20 items and taps dimensions of depressed mood, feelings of guilt and worthlessness, appetite loss, sleep disturbance, and energy level. These items are assumed to represent the major components of depressive symptoms. To avoid patterned responses, 16 of the symptoms are worded negatively and 4 are worded positively. Patients are asked to report how often they experienced a particular symptom during the past week on a four-point scale ranging from 0 to 3 (0 = rarely or none of the time—less than 1 day; 1 = some or a small amount of the time—1 to 2 days; 2 = occasionally or a moderate amount of time—3 to 4 days; and 3 = most or all of the time—5 to 7 days). The responses to the four positive items are reverse scored, and the total sum of the responses is calculated. Scores on the CES-D scale can range from 0 to 60. We considered a score greater than 18 to indicate clinically significant depression. The CES-D scale has been found to have high internal consistency and test–retest reliability (31), and it is highly correlated with other standardized depression scales (30).

4. University of California, San Diego, Shortness of Breath Questionnaire. The questionnaire was developed and has been used extensively in the Pulmonary Rehabilitation Program at the University of California, San Diego (32). Patients are asked to indicate on a 6-point scale how frequently they experience shortness of breath (0 = 0% of the time or never, 1 = 25% of the time or sometimes, 2 = 50% or half of the time, 3 = 75% or most of the time, 4 = 100% or all of the time, and NA = not applicable or unable to do) during 21 activities of daily living that are associated with varying levels of exertion. The questionnaire includes three additional questions about limitations caused by shortness of breath, fear of harm from overexertion, and fear of shortness of breath, for a total of 24 items. Responses were summed to produce a total score. Missing responses or responses marked "not applicable" were scored as 0.

Health Care Utilization

Information about hospitalization and emergency department visits was obtained by self-report at each annual follow-up evaluation. Patients were asked to provide information about the number and duration of hospitalizations and emergency department visits for lung problems during the previous 12 months.

Statistical Analysis

For baseline data, we calculated descriptive statistics and used independent *t*-tests to compare groups. For each follow-up eval-

Table 2—Continued

12 Months	18 Months	24 Months	48 Months	72 Months
47	46	41	27	26
43	48	43	31	23
0.16 ± 0.48		0.09 ± 0.46	0.08 ± 0.57	0.14 ± 0.51
0.03 ± 0.36		0.09 ± 0.42	0.15 ± 0.48	0.0 ± 0.42
0.7 ± 2.2		0.5 ± 2.7	−0.3 ± 2.5	0.3 ± 3.7
0.2 ± 2.0		0.0 ± 2.4	−0.7 ± 3.0	−0.1 ± 2.8
1.5 ± 1.9‡		0.7 ± 1.5	0.5 ± 2.2	−0.9 ± 3.1
0.6 ± 1.8		0.1 ± 1.9	−0.2 ± 1.5	−0.4 ± 3.0
0.02 ± 0.32		−0.09 ± 0.34	−0.12 ± 0.42	−0.31 ± 0.34
−0.05 ± 0.25		−0.08 ± 0.23	−0.18 ± 0.31	−0.38 ± 0.32
5.8 ± 10.9§	5.0 ± 14.3§	1.8 ± 11.1	−0.1 ± 11.4	−5.4 ± 11.8
1.8 ± 8.0	0.5 ± 8.6	1.2 ± 8.6	−0.5 ± 4.9	−5.7 ± 6.9
−1.4 ± 2.2‡	−1.3 ± 2.2	−1.1 ± 2.1‡	−0.7 ± 2.0	−0.8 ± 2.5
−0.3 ± 2.0	−0.5 ± 2.2	−0.1 ± 2.0	−0.2 ± 1.8	−0.5 ± 2.1
−1.0 ± 2.6	−0.7 ± 2.6	−0.6 ± 2.0	−0.3 ± 2.2	−1.1 ± 2.7
−0.4 ± 1.9	−0.5 ± 2.3	−0.2 ± 2.1	−0.1 ± 1.9	−0.8 ± 2.0
0.2 ± 3.3	0.0 ± 3.7‖	−0.3 ± 3.6	−0.9 ± 3.9	−1.3 ± 3.4
−0.8 ± 3.2	−1.9 ± 2.3	−1.2 ± 3.0	−1.5 ± 2.8	−2.7 ± 3.1
0.1 ± 9.2	1.4 ± 10.4	1.2 ± 10.4	1.6 ± 11.5	−0.4 ± 11.3
−2.7 ± 6.8	−0.2 ± 8.2	−1.4 ± 6.6	1.6 ± 10.6	−2.4 ± 7.6
−0.053 ± 0.180	−0.091 ± 0.204	−0.103 ± 0.238	−0.254 ± 0.324	−0.305 ± 0.324
−0.027 ± 0.154	−0.049 ± 0.149	−0.057 ± 0.199	−0.230 ± 0.316	−0.348 ± 0.344
−6.0 ± 15.2	−3.1 ± 15.3	−5.1 ± 11.2	−4.2 ± 15.1	1.2 ± 14.2
−0.9 ± 15.0	−0.3 ± 15.5	−2.6 ± 14.7	−1.5 ± 17.5	4.4 ± 18.3
−2.4 ± 15.4	–	−2.9 ± 16.1	2.9 ± 13.1	2.9 ± 5.5
1.3 ± 10.7	–	1.6 ± 12.8	0.9 ± 8.7	−0.2 ± 5.3

uation, the change from the baseline value was calculated. We also used independent *t*-tests to analyze group comparisons of the changes from baseline for the rehabilitation and education interventions at each time interval. In addition, for variables for which the two groups significantly differed, we evaluated within-group change from baseline with paired *t*-tests at each follow-up time interval.

We did survival analyses using the Kaplan–Meier product-limit method and compared the two groups with the log-rank test. We used the Cox proportional hazards model to evaluate the influence of six selected variables on survival. For these analyses, experimental group assignment was entered as a dummy variable, baseline age was entered as a fixed covariate, and four repeated measures were entered as time-dependent covariates. We did the multivariate analysis using a forward stepwise procedure.

Results

Results of selected baseline measures are summarized in Table 1. There were no significant differences between the rehabilitation and education groups at study entry. Eighty-eight percent of the patients formerly or currently smoked. Although 14 patients (12%) admitted to being current smokers at baseline, 20 (17%) were found to have carboxyhemoglobin levels greater than 3% on blood gas testing, levels that suggested current smoking status. Seven patients (6%) were receiving long-term oxygen therapy at baseline (two patients in the rehabilitation group and five in the education group).

The major results of the study are summarized in Table 2 and Figures 1, 2, 3, and 4. Compared with the education program alone, a 2-month program of pulmonary rehabilitation produced significantly greater improvement in exercise endurance, maximum exercise tolerance, symptoms of perceived breathlessness and muscle fatigue during exercise, reported shortness of breath with daily activities, and self-efficacy for walking. After the 2-month core rehabilitation program and the 1-year monthly reinforcements, group differences gradually declined. The benefits persisted for as long as 6 months for perceived muscle fatigue ratings during exercise and breathlessness with daily activities, for as long as 12 months for maximum treadmill workload and exercise endurance, for as long as 18 months for walking self-efficacy, and for as long as 24 months for ratings of perceived breathlessness during exercise.

There were no significant differences between the groups in changes from baseline for measures of pulmonary function, depression, general quality of life, or hospital days. Quality of Well-Being scores decreased progressively over time because of death, which is incorporated into

this measure of general health-related quality of life. The difference between the groups in the decrease in the number of hospital days in the year after rehabilitation compared with the year before rehabilitation were not significant (P = 0.2); however, this result is somewhat difficult to interpret because the rehabilitation group had a slightly greater (but nonsignificant) number of hospital days at baseline.

The overall survival curves for both experimental groups are shown in Figure 4. All patients are accounted for without censoring. After 6 years of follow-up, 73 of the original 119 patients were alive (survival rate, 61%). Thirty-eight of the 57 patients in the rehabilitation group (67%) and 35 of the 62 patients in the education group (56%) survived. This group difference was not statistically significant (P = 0.3).

The effects of six selected variables on survival for both the univariate and multivariate analyses are shown in Table 3. We chose the following six variables: experimental group assignment, baseline age, and four time-dependent covariates—forced expiratory volume in 1 second (FEV_1), exercise endurance time, Quality of Well-Being score, and shortness of breath with daily activities (based on responses to the Shortness of Breath Questionnaire). The analysis was limited to six variables because of the number of deaths (46 deaths, approximately 8 cases per variable). We chose the variables on the basis of an assessment of their importance and representativeness for the main significant outcomes in the clinical trial. For the time-dependent Quality of Well-Being variable, we included in this analysis only quality-of-life measures obtained while the patients were alive (that is, we excluded codings of 0 for dead patients). We selected the following as clinically meaningful intervals of change: 5 years of age, 0.05 units for the Quality of Well-Being scale, 0.1 liters for FEV_1, 5 minutes for endurance exercise time, and 5 units for the Shortness of Breath Questionnaire.

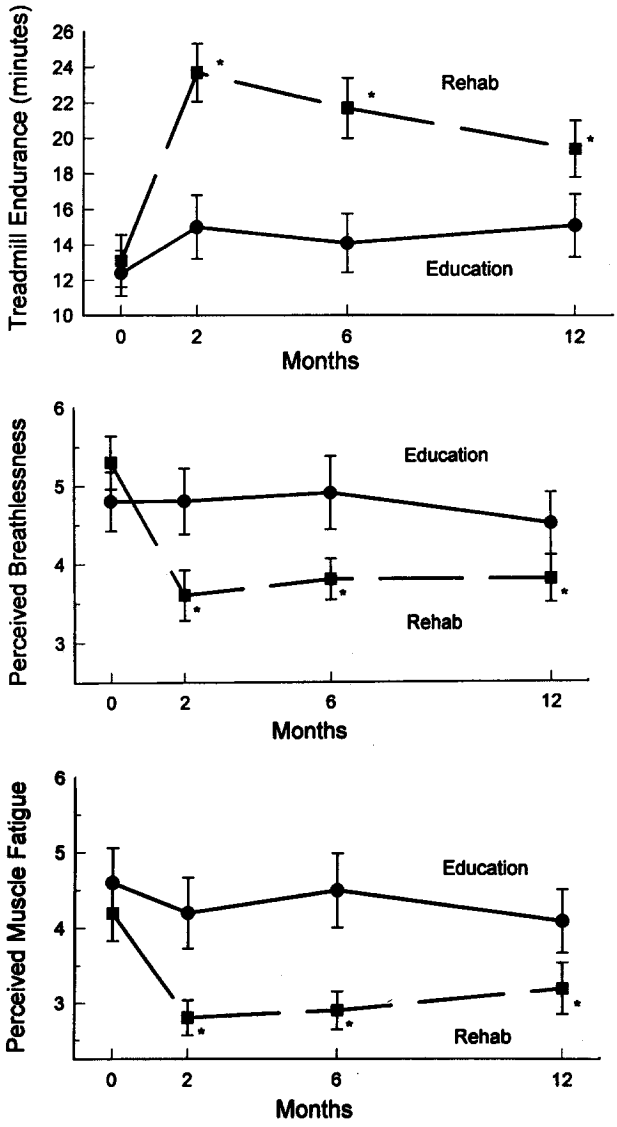

Figure 1. Results of treadmill endurance exercise tests for patients in the rehabilitation (*Rehab*) and education groups at baseline and for 12 months of follow-up. A. Exercise endurance time. **B.** Perceived breathlessness rating at the end of exercise. **C.** Perceived muscle-fatigue rating at the end of exercise. Asterisks indicate $P < 0.05$ for within-group change from baseline; values and error bars represent the mean ± SE.

In the univariate analyses, three of the four time-dependent covariates were significantly associated with survival (exercise endurance time was of borderline significance). Experimental group assignment was not significantly associated with survival (hazard ratio, 0.74 [95% CI, 0.41 to 1.34; P = 0.32]), a finding that is consistent with the log-rank test comparison of the Kaplan–Meier survival curves (P = 0.32). For these patients, age at baseline was not associated with survival.

In the stepwise, multivariate analysis with these same variables, FEV_1 and Quality of Well-Being scores were found to be the most significant independent predictors of survival.

Discussion

Our findings indicate definite benefits of comprehensive pulmonary rehabilitation for patients with chronic obstructive pulmonary disease. Compared with patients who participated in the education program, rehabilitation participants had highly significant changes in exercise performance and important symptoms after the program. In particular, pulmonary rehabilitation produced significantly greater changes in measures of exercise endurance, maximal exercise tolerance, ratings of perceived breathlessness and muscle fatigue during exercise, reported shortness of breath with daily activities, and self-efficacy for walking. After rehabilitation, slight nonsignificant trends of improvement were seen in survival rates and the number of hospital days. Rehabilitation did not affect measures of pulmonary function, general quality of life, or depression.

The improvements noted in exercise performance and in symptoms support the findings of previous studies. However, ours is the first randomized trial of this size and duration of follow-up to show these substantial beneficial effects of pulmonary rehabilitation. Two recently published reports of randomized trials showed shorter-term benefits favoring pulmonary rehabilitation over conventional treatment. Goldstein and coworkers (33) reported significant improvement in exercise tolerance, dyspnea, and quality of life after 6 months in 45 patients participating in an 8-week inpatient pulmonary rehabilitation program followed by 16 weeks of supervised outpatient

care compared with 44 patients who received conventional care from their own physicians. Wijkstra and coworkers (34) reported significant improvement in exercise tolerance and quality of life in 28 patients who were randomly allocated to a home pulmonary rehabilitation program for 12 weeks compared with 15 patients who received no rehabilitation. These randomized trials and ours show important and significant improvements in exercise performance, symptoms, and key elements of quality of life in patients with chronic obstructive pulmonary disease.

Both groups in this trial received considerably more than "usual care." The education "control" group participated in an education program with content similar to that provided to rehabilitation participants but that was covered in less depth. The education program also lacked individualized attention, behavioral components, and supervised exercise training. We believed that conducting a study of this sort would be impossible without providing any treatment for control patients. The information provided, as well as the attention and encouragement given to patients to attend these education sessions, may have affected the outcomes.

The improvement observed in exercise endurance is notable for the magnitude of the effect (an 82% increase in endurance time) but is consistent with our previous experience with an exercise program that emphasizes endurance training at the maximum limits tolerated by symptoms. In fact, the endurance test probably underestimated the true treatment effect. For this test, patients were allowed to walk for a maximum of 30 minutes—20 minutes at a high-intensity target (an average of 95% of the baseline maximal workload) plus 10 minutes at a higher level. Because many of the rehabilitation patients reached the 30-minute maximum time limit after the rehabilitation program, their scores were artificially capped at 30 minutes despite their potential to continue.

The changes in maximum exercise tolerance (peak workload and maximum oxygen uptake) were significant and similar in magnitude to that observed in other studies (7) but were smaller than the changes in exercise endurance. This was expected because training in the rehabilitation program emphasized exercise endurance (time) over exercise level. In addition, the greater improvement in maximum workload (33%) compared with peak oxygen uptake (9%) for the patients in the rehabilitation group is consistent with previous findings and with our experience that mechanical efficiency of walking (for example, longer stride length) improves after rehabilitation in many patients with pulmonary disorders (35, 36). This would produce a greater increase in maximum treadmill work level than in oxygen uptake.

We anticipated the lack of significant change in pulmonary function. Most previous studies have also failed to show significant changes in lung function (7). However, the absence of significant changes in measures of general quality of life, the number of hospitalizations, and depression was unexpected.

The failure to show significant changes for quality-of-life measures used in our study is difficult to interpret. There are at least two alternative explanations for this finding. One is that pulmonary rehabilitation did not improve quality of life or health status. Although this is possible, such a conclusion would be inconsistent with the observations of significant changes on other measures of function and symptoms. An alternative explanation is that the Quality of Well-Being scale is insensitive to the specific quality-of-life changes that result from pulmonary rehabilitation. Although this scale is correlated with other outcomes for patients with lung diseases (29, 37), it may not detect subtle changes that occur as a result of rehabilitation (38). For example, one result of a rehabilitation program may be a meaningful reduction in the intensity of such symptoms as dyspnea. These changes might not be captured by general health-status measures that note only the presence or absence of symptoms. Quality-of-life measures that are more specific to lung disease may provide a more sensitive assessment of rehabilitation for patients with disabling lung diseases. These changes, although small in the context of overall health status, may be meaningful and important for patients with disabling lung disease. There is clearly a need for additional methodologic studies comparing general and disease-specific outcome measures in patients with chronic lung diseases.

The nonsignificant changes in hospital days between groups also differed from the findings in previous studies (7). Although the trend was in the expected direction

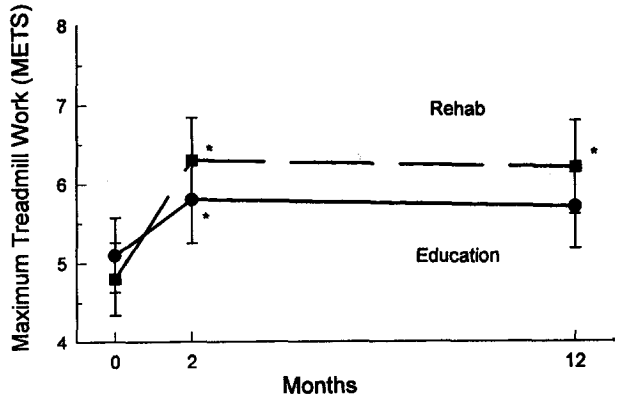

Figure 2. Maximum treadmill workload (measured as estimated oxygen uptake in metabolic equivalents [*METS*]) for patients in the rehabilitation (*Rehab*) and education groups at baseline and for 12 months of follow-up. Asterisks indicate $P < 0.05$ for within-group change from baseline; values and error bars represent the mean ± SE.

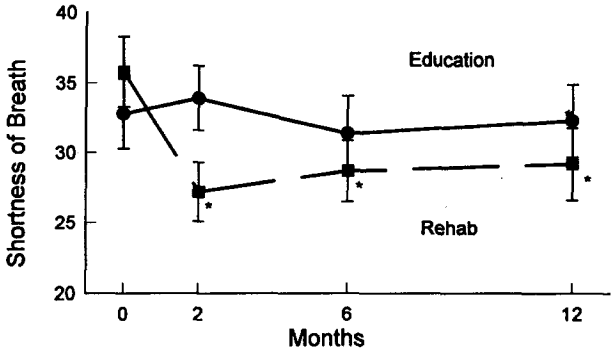

Figure 3. Self-reported shortness of breath with daily activities for patients in the rehabilitation (*Rehab*) and education groups at baseline and for 12 months of follow-up. Asterisks indicate $P < 0.05$ for within-group change from baseline; values and error bars represent the mean ± SE.

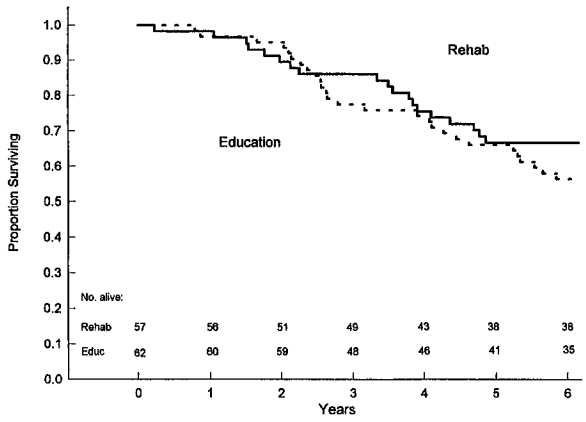

Figure 4. Kaplan–Meier survival curves for patients in the rehabilitation (*Rehab*) and education (*Educ*) groups during 6 years of follow-up. All patients are accounted for without censoring. Numbers at the bottom of the graph indicate the number of patients alive in each group at the beginning of each year.

(that is, the number of hospital days for the rehabilitation group decreased), the results were not statistically significant. In our study, we relied on self-reports because the patients came from several different hospital and health care systems. Many of the patients used more than one hospital for inpatient and other medical care. In addition, because hospitalizations for chronic obstructive pulmonary disease tend to be concentrated in a minority of patients, a few patients can have a considerable effect on the results.

Investigators have reported both significant reductions in the number of hospitalizations and resulting cost savings in the years after pulmonary rehabilitation compared with the year before rehabilitation. Lertzman and Cherniack (39) reported that pulmonary rehabilitation resulted in an average decrease of 20 hospital days per year. Petty and coworkers (5) found that the total number of hospital days among 85 patients with chronic obstructive pulmonary disease who were evaluated 1 year after pulmonary rehabilitation decreased 38% (from 868 days in the previous year to 542 days). In a randomized controlled study, Jensen (40) found that pulmonary rehabilitation led to significantly fewer hospitalizations over 6 months of follow-up in patients with chronic obstructive pulmonary disease and "high-risk" markers for psychosocial problems. In an evaluation of an inpatient pulmonary rehabilitation program, Agle and coworkers (41) reported 30 hospital admissions among 24 patients in the year before rehabilitation compared with only 5 admissions in the subsequent year. Johnson and colleagues (42) observed a 55% decrease in the number of hospital days in the year after an inpatient pulmonary rehabilitation program in 96 patients with severe chronic obstructive pulmonary disease (mean FEV_1, 0.87 L).

Several investigators have examined follow-up data for more than the first year after rehabilitation. Hudson and coworkers (43) studied hospitalizations for pulmonary disease in 64 patients who participated in a comprehensive pulmonary rehabilitation program and who had known follow-up after 4 years (44 patients were alive and 20 were dead). In the 44 patients alive 4 years after the program had ended, the number of hospital days in the year before the program began (529) was reduced by 73% (145 days) in year 1, 49% (270 days) in year 2, 47% (278 days) in year 3, and 61% (207 days) in year 4. In a study of 80 patients, Hodgkin and coworkers (12) found that the number of hospital days decreased from 196 in the year before rehabilitation to 6 days in the first year after the program. The improvement was maintained during 8 years of follow-up.

The difference between our findings and those of previous studies could be due in part to the changes in hospitalization patterns for patients with chronic obstructive pulmonary disease that have occurred in recent years, particularly in managed care environments. With stricter admission criteria, inpatient care has been increasingly limited to fewer patients with more severe and acute disease. For ambulatory patients participating in outpatient pulmonary rehabilitation, hospitalization rates may not accurately reflect health care utilization patterns. In this situation, it may be important to focus on health care utilization beyond just inpatient hospital stays and examine the efficacy with which and manner in which patients use their particular health care system.

Neither group showed reductions in the CES-D measure of depression. In patients in both groups, depression was highly prevalent (29 patients [24%] with CES-D scores >18). Using data from the present study, we previously reported that depression may be an important variable that affects outcome for patients in pulmonary rehabilitation and that the overall results may mask associations for subsets of patients (44). Rehabilitation participants whose depression decreased showed greater improvements in exercise performance than those whose measured depression increased. For patients who participated in the education program, changes in depression were unrelated to changes in exercise. This finding contrasts with the improvements in several measures of psy-

Table 3. Effects of Six Selected Variables on Survival*

Variable	Results of Univariate Analysis		Results of Multivariate Analysis	
	Hazard Ratio (95% CI)	*P* Value	Hazard Ratio (95% CI)	*P* Value
FEV_1 (per 0.1 L)†	0.84 (0.78 to 0.90)	≤0.0001	0.85 (0.80 to 0.92)	<0.0001
Quality of Well-Being scale (per 0.05 units)†	0.71 (0.58 to 0.87)	≤0.001	0.78 (0.62 to 0.98)	0.03
Exercise endurance (per 5 minutes)†	0.87 (0.72 to 1.04)	0.11	0.87 (0.72 to 1.05)	0.14
Shortness of Breath Questionnaire (per 5 units)†	1.14 (1.06 to 1.24)	≤0.001	–	0.37
Group (rehabilitation compared with education)	0.74 (0.41 to 1.34)	0.32	–	0.53
Age at baseline (per 5 years)	1.09 (0.89 to 1.32)	0.40	–	0.91

*FEV_1 = forced expiratory volume in 1 second.
†Variables entered as time-dependent covariates.

chological function, including depression, reported by Emery and colleagues (45) in a nonrandomized study of rehabilitation in patients with chronic obstructive pulmonary disease. Patient populations in the two studies differed. More than half of the patients in our study were recruited from general clinic populations at three area hospitals (University of California, San Diego, Medical Center; San Diego Veterans Affairs Medical Center; and Balboa Naval Hospital); our study also included more men than women (87 of 119 patients [73%]). Patients in the study by Emery and colleagues were self-referred and included more women (29 of 64 patients [45%]) whose lung disease was more severe than that of the men. Further studies of depression as a mediating variable are warranted.

In our study, the benefits observed after the 8-week pulmonary rehabilitation program followed by monthly reinforcement sessions for 1 year tended to diminish over time and were largely absent after 12 to 18 months. Longer-term benefits were seen only for measures of self-efficacy and perceived breathlessness, but these benefits were not significant after 24 months. This duration of benefit after a short-term intervention such as rehabilitation might be expected in patients with morbidity and mortality as high as that in many of these patients (39% in 6 years). One likely explanation is that a short-term behavioral intervention such as rehabilitation may be inadequate for producing long-term change. Long-term maintenance of behavior change has also been difficult to show in research on smoking cessation (46), weight loss (47), and adherence to exercise programs (48). The finding that patients experience behavior change during treatment that is not maintained after treatment has been observed with the use of several other behavioral interventions (49).

Results of the survival analyses indicate that there was a slight but nonsignificant difference in survival between the rehabilitation (67%) and the education (56%) groups. Ours is the first randomized clinical trial of pulmonary rehabilitation to examine survival over this period of time. Varying results were reported in previous retrospective, nonrandomized survival analyses (7).

Despite the absence of significant treatment effect on survival, several of the important time-dependent variables measured in this trial were significantly associated with survival. As expected, FEV_1 was the most significant predictor of survival. This measure has been shown in previous studies to be a significant predictor of survival in patients with chronic obstructive pulmonary disease (50, 51). However, other measures of symptoms and function were also significantly associated with survival. In the multivariate analysis, after adjustment for FEV_1, each of the other time-dependent variables (Quality of Well-Being score, Shortness of Breath Questionnaire responses, and exercise endurance) were independently associated with survival. The Quality of Well-Being score proved to be the most statistically significant; after adjustment for this score, Shortness of Breath Questionnaire responses and exercise endurance became less significant. These findings indicate that symptom and functional measures are important predictors of survival beyond physiologic measures of lung disease severity.

In summary, our findings support prescriptions of pulmonary rehabilitation for patients with chronic obstructive pulmonary disease. Measures of exercise performance, dyspnea, exercise-associated symptoms of breathlessness and muscle fatigue, and self-efficacy significantly improved after the core rehabilitation program. Benefits were partially maintained for 1 year with monthly reinforcement but decreased after that time. Future rehabilitation programs should emphasize behavioral interventions that may help to maintain beneficial outcomes for longer periods of time.

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