Exercise Outcomes After Pulmonary Rehabilitation Depend on the Initial Mechanism of Exercise Limitation Among Non-Oxygen-Dependent COPD Patients*

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Study objectives: **Pulmonary rehabilitation (PR) that includes exercise training can improve exercise tolerance and quality of life for patients with COPD. However, the degree of benefit from PR is variable. We hypothesized that the exercise response to PR varies depending on the initial factors that limit exercise.**

Design, setting, participants, and measurements: **We retrospectively analyzed the change in exercise capacity after PR in 290 nonhypoxemic patients with COPD. We classified patients into the following subgroups based on the primary limitation seen on initial exercise testing: (1) ventilatory-limited (VL); (2) cardiovascular-limited (CVL); (3) mixed ventilatory/cardiovascular-limited (VLCVL); and (4) non-cardiopulmonary-limited (NL). We compared outcomes among subgroups.**

Results: **In the entire study population, PR led to increased timed walk distance (30.3%; $p < 0.0001$) and maximal oxygen consumption ($\dot{V}O_2max$) [84.8 mL/min; $p < 0.0001$]. Stepwise multiple regression selected age, ventilatory reserve at peak exercise, and exercise arterial oxygen pressure as individual predictors of improvement in $\dot{V}O_2max$. $\dot{V}O_2max$ increased in the VL subgroup (30.4 mL/min; $p = 0.008$), the CVL subgroup (109.0 mL/min; $p < 0.0001$), the mixed VLCVL subgroup (61.3 mL/min; $p < 0.0001$), and NL subgroups (110.5 L/min; $p < 0.0001$). The improvement in $\dot{V}O_2max$ was greater in the CVL subgroup than in the VL subgroup ($p < 0.0001$). Timed walk distance improved to a similar degree in all subgroups (26 to 36%).**

Conclusions: **Patients with nonventilatory exercise limitations experience the greatest increase in $\dot{V}O_2max$ after PR. However, even patients with severe ventilatory limitation can improve exercise tolerance with PR.** ***(CHEST 2005; 127:110–116)***

Key words: exercise therapy; exercise tolerance; lung diseases; obstructive; oxygen consumption; walking

Abbreviations: CVL = cardiovascular-limited; $ExPO_2$ = PO_2 at peak exercise; HR = heart rate; MVV = maximum voluntary ventilation; NL = non-cardiopulmonary-limited; PR = pulmonary rehabilitation; $\dot{V}E$ = minute ventilation; VL = ventilatory-limited; VLCVL = ventilatory/cardiovascular-limited; $\dot{V}O_2max$ = maximal oxygen consumption; VR = ventilatory reserve

Patients with COPD often complain of exercise intolerance. While ventilatory limitation to exercise is often present, other factors are also important. These include cardiovascular deconditioning, skeletal muscle dysfunction, gas exchange abnormalities, right ventricular dysfunction, and psychological factors.[1]

Pulmonary rehabilitation (PR) is designed to reverse these exercise-limiting factors through supervised exercise training, respiratory care, and education. Exercise training in COPD patients can lead to improved aerobic fitness with increases in muscle aerobic enzyme content,[2] and reductions in lactate levels, heart rate (HR), and minute ventilation ($\dot{V}E$) at isowork rates.[3] Other benefits include improved motivation and exercise technique, desensitization to dyspnea, and an optimized breathing pattern.[4] A prospective, randomized, controlled trial[5] showed that PR improves endurance tests, peak work rate, maximal oxygen consumption ($\dot{V}O_2max$), and quality of life. The American Thoracic Society recommends PR for

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Manuscript received April 2, 2004; revision accepted August 12, 2004.

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patients with persistent exercise intolerance despite receiving optimal medical therapy.[6]

Despite these overall benefits, the response to PR varies significantly among individuals. This variation may result from individual differences in the factors limiting exercise. For example, Zu Wallack et al[7] showed that ventilatory reserve (VR) is positively correlated with an improvement in 12-min walk distance after PR. Similarly, physiologic training effects may be more pronounced in patients limited primarily by cardiovascular and skeletal muscle deconditioning (poor aerobic fitness).

The aim of this study was to describe the relationship between initial exercise limitation and exercise response to PR. We hypothesized that the degree of benefit from PR and the mechanisms of improvement vary depending on the primary factor limiting exercise. Specifically, we expected patients who were limited by poor aerobic fitness to have a greater increase in exercise capacity than ventilatory-limited (VL) patients. To test this hypothesis, we performed a retrospective analysis of 290 COPD patients who had undergone PR.

Materials and Methods

Subjects

We retrospectively reviewed a computerized database, which included all patients entering the Duke Pulmonary Rehabilitation Program between 1985 and 1999. This analysis included patients with a primary diagnosis of COPD or asthmatic bronchitis and a $\dot{V}O_2$max of $< 80\%$ of predicted. Patients with diagnoses of asthma, interstitial lung disease, or cystic fibrosis, or those who have undergone lung transplantation were excluded. We also excluded patients requiring supplemental oxygen during exercise because the level of oxygen used during exercise testing was not controlled. We thought that a difference in the amount of oxygen used at baseline and after rehabilitation exercise testing could be a significant confounding variable. Finally, patients were routinely excluded from the rehabilitation program for a history of unstable or exertion angina, frequent ventricular extrasystoles, or worsening ECG ST-wave or T-wave abnormalities with exercise. Approval for the use of the clinical data in this study was obtained from our institutional review board on human research.

During the period from 1985 to 1999, a total of 636 patients entered the Duke Pulmonary Rehabilitation Program. A total of 450 patients (71%) had a primary diagnosis of COPD or asthmatic bronchitis. Of these, we excluded 150 patients (33%) who required supplemental oxygen during exercise and 4 who lacked documentation of oxygen use. Finally, we excluded six patients due to missing initial exercise test data. This left 290 non-oxygen-dependent COPD patients (46.5% of all patients undergoing the Duke PR program) for inclusion in this study.

Of the 290 patients analyzed, 11 dropped out of the program for the following reasons: inguinal hernia requiring surgery (1 patient); back pain (1 patient); "groin pull" (1 patient); COPD exacerbation (1 patient); exercise-induced ST-segment changes on ECG (1 patient); hospitalization related to preexisting mitral valve disease (1 patient); palpitations (1 patient); new-onset atrial fibrillation/flutter (2 patients); and stable ventricular tachycardia during exercise (1 patient). One patient died at home 10 days after prematurely discontinuing the program. This death was presumed to have been due to myocardial infarction. In addition, nine patients were missing postprogram exercise test data. Six of these patients successfully completed the program but did not return for a final exercise test.

Design

The database included the following information: age; sex; primary diagnosis; pulmonary medications; supplemental oxygen use; spirometry; lung volumes; diffusing capacity; resting and exercise arterial blood gas levels; timed walk distance; and data from a maximal incremental exercise test. Spirometry, timed walk distance, and maximal exercise testing were performed before and after PR.

Primary outcome measures were the change in timed walk distance, $\dot{V}O_2$max, and oxygen pulse (*ie*, $\dot{V}O_2$max/peak HR) after completing PR. Secondary outcomes included changes in spirometry, peak $\dot{V}E$, and peak HR. Correlation between baseline variables and improvement in $\dot{V}O_2$max also were analyzed.

Pulmonary Function and Exercise Testing

Pulmonary function testing included spirometry, lung volume determinations, and single-breath diffusing capacity using standard equipment (model 2200 and $\dot{V}$max systems; SensorMedics; Yorba Linda, CA). Procedures were carried out according to American Thoracic Society standards.[8–12] The maximum voluntary ventilation (MVV) used in this study was directly measured using a 12-s MVV maneuver.

Graded bicycle exercise testing was performed with a system designed to measure oxygen consumption, carbon dioxide production, and $\dot{V}E$ in 20-s increments using polarographic, infrared, and mass flowmeter devices, respectively (system 2900 and $\dot{V}$max systems; SensorMedics). Workload was ramped at 12.5 W/min. Arterial blood gas levels and finger pulse oximetry were recorded at peak exercise. Eight-lead ECG was performed at rest and during all stages of exercise. Testing was usually performed in the week prior to entering the program and during the final week of the program.

Timed Walk Testing

Tests were performed on an indoor level track. Patients were instructed to walk as far as possible during the test and to "give it your best effort." A therapist kept time and counted laps but did not walk alongside the patient. No direct encouragement was offered during the test. Patients were allowed to use assistive devices (*eg*, walker or cane) for musculoskeletal or balance needs. Vital signs (*ie*, HR, BP, and oxygen saturation) were monitored at defined intervals during the test. During the 14-year study period, patients were evaluated with either a 12-min or a 15-min walk test, and the same type was used in individual patients before and after PR. Because the type of test may have differed between patients, we only report the percentage improvement in timed walk distance. The supervising therapist was not necessarily the same on pretesting and posttesting.

PR

PR was performed at Duke University Medical Center (Durham, NC) on an outpatient basis. It consisted of 20 sessions completed over a 4-week period. Sessions were 4 h in duration. The program emphasized respiratory care, education, and exercise. The exercise portion of each session consisted of at least 1 h