Physiological Response to Moderate Exercise Workloads in a Pulmonary Rehabilitation Program in Patients With Varying Degrees of Airflow Obstruction*

Ioannis Vogiatzis, PhD; Andrew Frederick Williamson, BSc; Joanne Miles, BSc; and Ian Keith Taylor, MD

Study objectives: To investigate whether a 12-week pulmonary rehabilitation program that includes moderately intensive exercise training performed twice weekly can induce a training effect in patients with a wide variation of airflow limitation.

Participants: Sixty patients with COPD (38 men) with a mean ± SD FEV₁ % predicted of 55.1 ± 19.8 (range, 0.51 to 2.99). All patients performed identical incremental symptom-limited cycle ergometer testing before and after a 12-week study period.

Measurements and results: After 12 weeks, the patients demonstrated a significant (p < 0.05) increase in the peak values for work rate (WR; 77 ± 30 vs 91 ± 36 W) and oxygen uptake (1.14 ± 0.45 vs 1.20 ± 0.52 L/min). Furthermore, at a given WR during incremental symptom-limited cycle ergometer testing, there were significant (p < 0.05) reductions in minute ventilation (42.4 ± 16.1 vs 37.0 ± 13.6 L/min), carbon dioxide output (1.13 ± 0.49 vs 1.03 ± 0.42 L/min), ventilatory equivalent for oxygen (37.6 ± 8.1 vs 36.0 ± 6.3), and heart rate (135 ± 15 vs 128 ± 16 beats/min). None of the observed physiologic changes correlated with FEV₁ % predicted.

Conclusions: A pulmonary rehabilitation program performed twice weekly with moderate exercise workloads can lead to a physiologic training response irrespective of the degree of airflow limitation.

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Key words: COPD; exercise training; pulmonary rehabilitation

Abbreviations: AT = anaerobic threshold; HR = heart rate; SaO₂ = arterial oxygen saturation; V̇CO₂ = carbon dioxide output; V̇E = minute ventilation; V̇E/V̇O₂ = ventilatory equivalent for oxygen; V̇O₂ = oxygen uptake; WR = work rate

Patients with COPD are limited in their exercise tolerance by dyspnea, peripheral muscle weakness, and lactic acidosis at low levels of exercise.¹⁻³ The factors that contribute to dyspnea in these patients are related to a combination of high ventilatory requirement coupled with low ventilatory capacity. There is now a considerable body of evidence that rehabilitative exercise strategies in patients with COPD result in significant improvement in measures of exercise tolerance in contrast to those of pulmonary function.⁴⁻⁷ For example, Casaburi and colleagues³ reported that high-intensity exercise training performed 5 days per week for 8 weeks in 11 patients with moderate airflow limitation (mean FEV₁, 56% predicted) lowered the ventilatory requirement at a given level of exercise, thus increasing exercise tolerance. In contrast, a concurrent group of eight patients who exercised at a lower intensity failed to achieve comparable responses. The possibility of inducing training effects in patients with more severe COPD was originally investigated by Maltais et al,⁸ who exercised 11 patients (mean FEV₁, 36% predicted) three times a week for 12 weeks at moderate intensity. Again, this resulted in a reduced exercise ventilatory requirement accompanied by improved exercise tolerance. These results were recently confirmed by Casaburi et al,⁹ who applied a training program of rigorous exercise three times a week for 6 weeks in 25 patients with severe airflow limitation (mean FEV₁, 36% predicted).

While the above studies provide substantial evi-
idence of physiologic training effects over a wide objective spectrum of airflow limitation, these were achieved in small groups of patients. Recent studies have clarified previous uncertainty that twice-weekly pulmonary rehabilitation sessions were adequate to produce significant gains in exercise performance, as assessed simplistically by walking tests. However, the possibility of inducing training effects on measured objective physiologic exercise responses by the implementation of an exercise program featuring fewer than three sessions per week remains uncertain. In view of the cost and resource effort involved in conducting a rehabilitation program, we were particularly interested in designing and implementing an exercise regimen of moderate frequency and intensity that could be sufficient to induce measurable physiologic exercise responses and improvements in exercise tolerance. We therefore undertook a trial of pulmonary rehabilitation in 60 patients with a wide spectrum of airflow limitation who participated in a 12-week outpatient program that featured twice-weekly moderately intense exercise training sessions. While our primary outcome measure was the evaluation of physiologic training effects in these patients, by comparison we also report data in a smaller control group of 15 patients who did not participate in any training sessions.

**Materials and Methods**

**Patients**

Outpatients with COPD were referred to the rehabilitation program by their attending chest physicians at the Sunderland Royal Hospital. Prior to entering the program, all patients met the following criteria: (1) a FEV\(_1\) < 70% predicted and a FEV\(_1\)/FVC < 65%; (2) nonsmokers for a minimum of 2 months; (3) their medical therapy had been optimized; and (4) no clinical evidence of exercise-limiting cardiovascular or neuromuscular diseases. The patients enrolled into the study were clinically and physiologically stable; patients who had been hospitalized or had suffered an exacerbation of their airflow limitation within 2 months prior to the start of the study were excluded. A total of 70 patients were originally recruited to the rehabilitation program. Only 60 patients (35 men; FEV\(_1\), range, 0.55 to 2.90 L) completed the regimen (the training group) and are presented in this report; the remaining 10 patients failed to complete because of intercurrent pulmonary infection and noncompliance with the training schedule. An additional 15 patients (8 men; FEV\(_1\), range, 0.55 to 2.91 L) who originally declined to participate in the rehabilitation program because of time constraints agreed to undertake the required assessments before and after the 12-week study period (the nontraining control group). The demographic characteristics of both the training and nontraining control groups are given in Table 1. The study protocol was approved by the University of Sunderland and Sunderland Health Authority ethics committees, and all patients gave informed consent prior to participation in the study.

**Table 1**—Physical Characteristics, Lung Function, and Exercise Capacities of the Patients in the Training and Nontraining Control Groups at the Outset of the Study

<table>
<thead>
<tr>
<th>Variables</th>
<th>Training Group (n = 60)</th>
<th>Nontraining Control Group (n = 15)</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>64 ± 1</td>
<td>56 ± 31</td>
<td>8 (0.1, 15)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>71.4 ± 2.2</td>
<td>68.3 ± 5.1</td>
<td>3.1 (–8.8, 15.0)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>1.65 ± 0.01</td>
<td>1.64 ± 0.01</td>
<td>0.01 (–0.03, 0.05)</td>
</tr>
<tr>
<td>% predicted FEV(_1)</td>
<td>55.1 ± 2.6</td>
<td>54.8 ± 4.8</td>
<td>0.3 (–10.9, 11.5)</td>
</tr>
<tr>
<td>FEV(_1)/FVC, %</td>
<td>47.9 ± 1.8</td>
<td>47.3 ± 3.0</td>
<td>0.6 (–6.6, 7.9)</td>
</tr>
<tr>
<td>Peak WR, W</td>
<td>77 ± 4</td>
<td>71 ± 8</td>
<td>6 (–13.3, 26.3)</td>
</tr>
<tr>
<td>Peak VO(_2), L/min</td>
<td>1.14 ± 0.05</td>
<td>1.08 ± 0.12</td>
<td>0.06 (–0.22, 0.34)</td>
</tr>
<tr>
<td>Peak VE, L/min</td>
<td>42.4 ± 2.1</td>
<td>41.1 ± 4.5</td>
<td>1.3 (–9.1, 11.6)</td>
</tr>
</tbody>
</table>

*Data are expressed as mean ± SEM (95% confidence interval). tp < 0.05.

**Outcome Measurements**

The patients visited the pulmonary function laboratory at Sunderland Royal Hospital for a half-day session and performed pulmonary function and identical incremental symptom-limited cycle ergometer tests immediately before and after the 12-week study period.

**Pulmonary Function Tests:** Pulmonary function evaluation was carried out 10 min after actuation from a metered-dose inhaler of two inhalations of both ipratropium bromide, 40 µg, and salbutamol, 200 µg. With the patients in a sitting position, spirometry was performed using an autolink spirometer (Transfer Test SN 293; P.K. Morgan; Haverhill, MA). The patients were required to perform three satisfactory spirometric techniques within 5% of each other by FVC; from the best of these maneuvers, FEV\(_1\) and FVC were determined. The transfer factor for carbon monoxide was determined via the single breath method; in contrast to the spirometric data, the results of three maneuvers were averaged. Pulmonary function data of the 60 patients in the training group at the outset and termination of the study are detailed in Table 2. Additionally, comparable data from the 15 patients in the nontraining control group are shown in Table 2.

**Cycle Ergometer Test:** Exercise testing was performed on an electromagnetically braked cycle ergometer (ER 900; Jaeger; Hoechberg, Germany) and was always preceded by a familiarization test on a different occasion. The patients breathed through a mouthpiece with a nose clip in place. Oxygen uptake (VO\(_2\)), carbon dioxide output (VCO\(_2\)), minute ventilation (VE), and the ventilatory equivalent for oxygen (VE/VO\(_2\)) were determined at intervals of 15 s by a respiratory mass spectrometer featuring a mixing chamber (Airspec QP9000; Case: Kent, UK). Gas exchange and expired minute volume were measured using the concentration of injected argon at a rate of 600 mL/min into the expirate upstream of the mixing chamber, while the resulting composition downstream was used to deduce the mass flows of all its components. The anaerobic threshold (AT) was determined from a plot of VCO\(_2\) vs VO\(_2\) by the modified gas exchange V-slope technique described by Sue and coworkers. The identification of the AT was made blindly and independently by two observers from duplicate copies of the data. We recently reported a significant agreement between the V-slope technique and another noninvasive gas exchange method (plots of VE and VE/VO\(_2\) vs VO\(_2\)) for the determination of the AT in COPD patients with a high interobserver agreement. Heart rate (HR)
was recorded every minute by a monitor (PE 4000 Sports Tester Transmitter; Polar; Kempele, Finland) and arterial oxygen saturation (SaO₂) was measured using a pulse oximeter (Biox 3760; Datex-Ohmeda; Louisville, CO).

The patients performed an incremental symptom-limited cycle ergometer test that included a 3-min rest period and 3 min of unloaded pedaling, followed by an increase in work rate (WR) of 10 W every minute from a starting work rate of 20 W until exhaustion was apparent from the inability to maintain the pedaling cadence above 40 revolutions/min. The peak WR was defined as the highest work level reached and maintained for a full minute.

Rehabilitation Program

The rehabilitation strategy was a comprehensive program that included modalities of exercise training, breathing control techniques, disease education, and instruction in the use of medication. There was no weight training component. The exercise training component consisted of the following sequence: (1) cycling on a calibrated cycle ergometer (824E; Monark; ); (2) walking on level ground; and finally (3) walking on an inclined nonmotorized treadmill (Woodway; Waukesha, WA) for a total of 60 min (including periods of rest) twice weekly for 12 consecutive weeks. The exercise training protocol is shown in Figure 1. Monitoring during exercise sessions was conducted by a physiotherapist and involved measurements of HR and SaO₂.

The initial exercise level for cycling was defined as previously described by Niederman et al., namely 50% of the maximal WR attained in the baseline incremental symptom-limited cycle ergometer evaluation. Hence, at the first exercise session, patients cycled at this workload for 20 min unless symptomatic (leg pain, severe dyspnea) or physiologic end points (a HR ≥ 80% of the maximal age-predicted HR or SaO₂ < 85%) were exceeded earlier. At subsequent sessions, this same WR was applied until the patient could sustain it for 20 min.

The exercise prescription was revised weekly by a physiologist. Once an individual could exercise at the prescribed work level for 20 min, the WR was increased by approximately 25%, and again this level was continued until it could be sustained for 20 min. Following the completion of cycling exercise, the patients walked on the horizontal for 10 min at a training intensity that was targeted at the highest pace that could be tolerated by each individual patient. The targeted walking speed was gauged to result in a HR of approximately 70% of the maximal age-predicted HR. Walking on the horizontal was subsequently followed by five 1-min bouts on a treadmill with 10% inclination at a speed of 3.0 km/h, unless the previously described symptomatic or physiologic end points were exceeded earlier. The patients who were unable at the beginning of the program to exercise for a full minute were allowed to stop before attempting again. Each 1-min bout was followed by 1 min of rest. The walking exercise prescription was kept constant throughout the 12 weeks. The patients exercised at a fairly steady WR for the entire duration of the three exercise modes, with only 5 min of cool-down periods on the bicycle ergometer at a low pedaling frequency, and three 5-min rest periods in between the remaining exercise modes (Fig 1).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Training Group (n = 60)</th>
<th>Nontraining Control Group (n = 15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>64 ± 6</td>
<td>56 ± 12</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>71.4 ± 17.2</td>
<td>68.3 ± 17.7</td>
</tr>
<tr>
<td>Height, cm</td>
<td>1.65 ± 0.09</td>
<td>1.64 ± 0.06</td>
</tr>
<tr>
<td>FEV₁, L</td>
<td>1.45 ± 0.62</td>
<td>1.61 ± 0.71</td>
</tr>
<tr>
<td>% predicted FEV₁</td>
<td>55.1 ± 19.8</td>
<td>54.8 ± 18.4</td>
</tr>
<tr>
<td>FVC, L</td>
<td>3.00 ± 0.80</td>
<td>3.20 ± 1.02</td>
</tr>
<tr>
<td>FEV₁/FVC, %</td>
<td>47.9 ± 14.2</td>
<td>47.3 ± 11.6</td>
</tr>
<tr>
<td>% predicted TLCO</td>
<td>67.02 ± 25.39</td>
<td>69.82 ± 20.39</td>
</tr>
<tr>
<td>Peak WR, w</td>
<td>77 ± 30</td>
<td>71 ± 33</td>
</tr>
<tr>
<td>Peak VO₂, L/min</td>
<td>1.14 ± 0.45</td>
<td>1.08 ± 0.47</td>
</tr>
<tr>
<td>Peak VCO₂, L/min</td>
<td>1.13 ± 0.49</td>
<td>1.04 ± 0.54</td>
</tr>
<tr>
<td>Peak WR, L/min</td>
<td>42.4 ± 16.1</td>
<td>41.1 ± 17.4</td>
</tr>
<tr>
<td>Peak HR, beats/min</td>
<td>135 ± 15</td>
<td>134 ± 24</td>
</tr>
<tr>
<td>Peak % SaO₂</td>
<td>92 ± 2</td>
<td>91 ± 2</td>
</tr>
</tbody>
</table>

*Values are presented as mean ± SD; TLCO = transfer factor for carbon monoxide.
†p < 0.05.

Table 2—Data on Postbronchodilator Pulmonary Function and Peak Exercise Responses Before and After the 12-Week Study in the Training (n = 60) and Nontraining Control (n = 15) Groups*
Statistical Analysis

Prior to statistical analysis, normality frequency plots were performed to examine the data distribution. Data are presented as means ± SD, unless otherwise indicated. Percentage differences in physiologic variables before and after the training intervention were calculated according to the following formula: (poststudy mean value-prestudy mean value/prestudy mean value) × 100. Comparisons between baseline and outcome measurements in the training group were made using paired t tests. Additionally, within the training group, comparisons for a number of physiologic variables were evaluated as a function of baseline airway function (FEV₁ > 40% predicted vs < 40% predicted) by unpaired t tests. Correlations between measured physiologic variables and airway function were assessed by Pearson’s correlation coefficient.

As secondary outcome assessments, physiologic measurements between the training and nontraining control groups were compared using Student’s unpaired t tests at the beginning of the study prior to the training intervention; between-group mean differences are presented with 95% confidence intervals. Additionally, paired t test comparisons were made at baseline and at 12 weeks for a number of physiologic variables within the nontraining control group. The level of significance was set at p < 0.05.

Results

Although the training and nontraining control groups were not prospectively randomized, they were well matched for all variables other than age (Table 1). Among the 60 patients assigned to the training group over the 12-week period, 20 patients improved on their baseline training prescription by 50%, 27 patients improved by 25%, and 13 patients did not improve. The percentage attendance for the training cohort throughout the study was 90 ± 9.

There was significant improvement in exercise tolerance as assessed by the incremental cycle ergometer test within the training group. Peak WR increased by a mean of 18%; this was accompanied by significantly higher peak values for VO₂, VCO₂, VE, and HR (Table 2; Fig 2). By contrast, none of these variables significantly changed in the nontraining control group (Table 2; Fig 2).

For each patient in the training group, peak physiologic measurements at the WR attained at the end of tolerable exercise in the baseline ergometer test were compared to measurements at an identical WR during the outcome test. Accordingly, significant mean reductions in VE (13%), VCO₂ (9%), VO₂ (8%), VE/VO₂ (4%), and HR (5%) were found (Table 3). Furthermore, the AT as detected by the V-slope technique significantly increased by 10% following training (Table 3; Fig 2). Changes in VCO₂ were significantly correlated with changes in VE at a given

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**Figure 2.** Changes from baseline in a number of physiologic responses during the incremental exercise test following the 12-week study period for the training (square) and nontraining control (circle) groups. *p < 0.05; comparisons are within, not between, group.
exercise WR (r = 0.63; p = 0.002). Significant changes in the above physiologic variables within the nontraining control group were not observed (Fig 2).

Clinically, there was a very modest, though statistically significant, increase in both FEV1 and FVC by 4% and 6%, respectively, following training (Table 2). No significant correlations were found between the degree of airflow limitation (as quantified by % predicted FEV1) with changes in any of the measured physiologic parameters at peak or identical levels of exercise (r < 0.4; p > 0.05 for all variables evaluated). Furthermore, following 12 weeks of training, the magnitude of improvement in peak WR and reductions in VCO2, VE, and HR at an identical WR during the incremental test were comparable and independent of baseline pulmonary dysfunction (Table 4).

### Discussion

This study provides evidence that a 12-week pulmonary rehabilitation program with moderate exercise workloads performed twice weekly can lead to a physiologic training response irrespective of the degree of airflow limitation. Furthermore, in contrast to other studies,4–7 there was a significant but very modest clinical impact on ventilatory capacity.

The improvements in exercise tolerance were manifest not only by attainment of higher peak exercise responses (in WR, VE, and VCO2), but also by reduced ventilatory requirement at a given level of exercise. Furthermore, the magnitude of improvement in exercise tolerance was comparable over a spectrum of airflow limitation.

There is considerable evidence (approaching 40 studies)17 that documents the benefits of exercise regimens in pulmonary rehabilitation strategies. However, there are only a minority of exercise programs3,8,9,18–23 that have been specifically designed to elicit as primary outcome measures the physiologic changes within the exercising muscles and other organ systems. The present training program design differed importantly from other programs3,8,9,18–20 in two respects. First, it featured only two exercise training sessions per week; second, it incorporated multimodality lower limb exercises. It may be argued that the variety of different exercises incorporated into the present program renders the interpretation of training improvements to be perhaps more problematic in contrast to those programs in which the training interventions were solely restricted to cycle ergometer activities.3,8,9,20 However, we believe that the diversity of the training modalities selected were more realistic and functionally more relevant to the daily activities of our study population.

Although the duration of this entire program (12 weeks) and the duration of the individual exercise training sessions (60 min) were well within the recommendations for exercise training programs,24 this study is notable not only for the number of patients studied in comparison to other recently published data,3, 8, 9 in which physiologic variables were used as primary outcome measures to assess the effects of training, but also by the wide spectrum of airflow limitation encompassed within the large study population.

The target training intensity of bicycle exercise in

### Table 3—Effects of Rehabilitative Exercise Training on Responses to Identical Levels of Exercise in the Incremental Exercise Test (n = 60)*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Before</th>
<th>After</th>
<th>% Change†</th>
</tr>
</thead>
<tbody>
<tr>
<td>V02, L/min</td>
<td>1.14 ± 0.45</td>
<td>1.05 ± 0.41†</td>
<td>8</td>
</tr>
<tr>
<td>VCO2, L/min</td>
<td>1.13 ± 0.49</td>
<td>1.03 ± 0.42†</td>
<td>9</td>
</tr>
<tr>
<td>VE, L/min</td>
<td>42.4 ± 16.1</td>
<td>37.0 ± 13.6†</td>
<td>13</td>
</tr>
<tr>
<td>VE/V02</td>
<td>37.6 ± 8.1</td>
<td>36.0 ± 6.3†</td>
<td>4</td>
</tr>
<tr>
<td>AT, L/min</td>
<td>0.86 ± 0.23</td>
<td>0.95 ± 0.26†</td>
<td>10</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>135 ± 15</td>
<td>128 ± 16†</td>
<td>5</td>
</tr>
</tbody>
</table>

*Values are presented as mean ± SD.
†Values are percentage changes from baseline.
‡p < 0.05.

### Table 4—Effects of Rehabilitative Exercise Training on Peak WR and Physiologic Responses to Identical Levels of Exercise in the Incremental Exercise Test, Stratified by Severity of Airflow Obstruction*

<table>
<thead>
<tr>
<th>Variables</th>
<th>% Predicted FEV1 &lt; 40%</th>
<th>% Predicted FEV1 &gt; 40%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Peak WR, W</td>
<td>63 ± 4</td>
<td>76 ± 5†</td>
</tr>
<tr>
<td>VE, L/min</td>
<td>35.3 ± 2</td>
<td>29.7 ± 2.2†</td>
</tr>
<tr>
<td>VCO2, L/min</td>
<td>0.89 ± 0.06</td>
<td>0.80 ± 0.56†</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>129 ± 3</td>
<td>122 ± 2</td>
</tr>
</tbody>
</table>

*Values are presented as mean ± SEM.
†Values are percentage changes from baseline.
‡p < 0.05.
this program (50% of the baseline peak WR) was lower than comparative studies\(^3\,^9\), that featured target training intensities equivalent to 50% of the baseline peak WR. However, it has been previously shown that training intensity is often difficult to interpret because actual training loads may differ from the training prescription.\(^8\,^20\) The majority of patients in the current study were able to exceed their initial training prescription by up to 25%. Nevertheless, the relatively moderate training frequency and intensity employed in the present program possibly explain why improvements in exercise tolerance (peak WR by 18% and peak \(\text{VO}_2\) by 5%) were smaller than those previously reported by Casaburi et al\(^8\) (increased peak WR and \(\text{VO}_2\) by 35% and 16%, respectively), although patient demographics and training schedules were not directly comparable. In relation to other comparative studies,\(^3\,^3\,^3\,^20\) training improvements seen in this study were greater than those seen in a low WR (50% peak WR) and moderately obstructed training cohort,\(^3\) and were comparable to the improvements documented by Maltais et al\(^20\) (increases in peak WR and peak \(\text{VO}_2\) by 14% and 9%, respectively), albeit in a more severely impaired group of patients with COPD (training three times weekly for 12 weeks at an average exercise intensity equivalent to 50% of baseline WR).

In contrast to the improvements in exercise tolerance seen within the training cohort, peak values for WR, \(\text{VE}\), and \(\text{VO}_2\) within the nontraining control group were largely unchanged when reassessed after 12 weeks (Table 2; Fig 2). We are aware however, that a major limitation of this study was the lack of prospective randomization into the training and nontraining control groups. Allowing for the disparity in numbers, the two groups nevertheless were well matched, although the nontraining control cohort were younger (Table 1), with the implicit acceptance that age may be an important factor in disease progression. Furthermore, although the nontraining control group that was used may have been biased by patients who declined rehabilitation because of lack of motivation, the principal reason for the failure to participate was time constraint. Despite these limitations, we have included comparative data from the nontraining control cohort (Table 2), recognizing that statistical and clinical interpretation may be difficult.

Further evidence of training effects that were induced by the present exercise program can be seen from the physiologic responses to a given level of exercise. At an identical WR during the incremental exercise test, \(\text{VE}\), \(\text{VCO}_2\), \(\text{VE} / \text{VO}_2\), and HR were all significantly lower after 12 weeks of training (Table 3). Moreover, we observed increases in the AT after training, implying that the training program might have induced functional changes in the exercising muscles, most notably allowing them to increase their capacity for aerobic work and forestall the onset of lactic acidosis. Indeed, recent evidence obtained by comparable exercise programs has demonstrated that training improved cellular bioenergetics and resulted in increased levels of aerobic enzymes within the leg muscles of patients with severe COPD\(^8\,\,^22\), these adaptations were associated with reduced exercise-induced lactic acidosis. Reduced lactic acidosis could benefit patients with COPD by removing, at least in part, some of the acid stimulus to breathe, thereby lowering the ventilatory requirement at a given exercise level.\(^3\) The reduction in \(\text{VE} \) (13%) is in a good agreement with two previous studies of Casaburi et al\(^3\,\,^9\) (12% and 9%, respectively), and is considerably greater than in two further comparative studies by Maltais et al\(^20\) (5% and 6%, respectively). Reductions in \(\text{VO}_2\) at identical levels of exercise seen in this study were also comparable (8%) to previously reported data.\(^3\)

We are aware however that the reduction in \(\text{VE}\) could be multifactorial and could relate to diverted substrate utilization or diminished catecholamine production, or that it could be due to the increased efficiency of peripheral muscle oxygen extraction, with lower resultant lactate and \(\text{CO}_2\) generation from bicarbonate buffering.\(^25\) Although the significant correlation \((r = 0.63)\) that was found between changes in \(\text{VE}\) and \(\text{VCO}_2\) suggests that a considerable component of the reduction in \(\text{VE}\) is related to decreased \(\text{VCO}_2\) after training, we also cannot exclude the possibility of a more efficient breathing pattern (reduced physiologic dead space/tidal volume ratio) and decreased hyperinflation following a training program being contributory.\(^9\) In the absence of physiologic dead space/tidal volume ratio measurements, we cannot confirm the previous observations.\(^9\)

There are several other potential explanations for the reduction in \(\text{VE}\) following training. First, there may be a reduced metabolic requirement for a given exercise task, as evidenced by the lower \(\text{VO}_2\) at an identical WR. Second, since \(\text{VCO}_2\) decreased to the same extent as \(\text{VO}_2\) (from 8 to 9%; Table 3), the enhanced mechanical efficiency may also have contributed to the fall in the ventilatory requirement. However, at WRs above the AT, physiologic training is associated with reduced lactate production and, in turn, lower \(\text{VO}_2\) requirements (up to approximately 10%) and lower bicarbonate-elevated \(\text{VCO}_2\).\(^20\,\,^27\) In contrast to a comparative study,\(^3\) we did not evaluate serum lactate.

A review\(^17\) of many pulmonary rehabilitation programs identified only one program that featured a
variable training frequency of two or fewer sessions per week. While peak VO\textsubscript{2} and submaximal exercise performance improved following rehabilitation, there was no evidence of a lower ventilatory requirement at a given WR. Recently, studies featuring twice-weekly exercise rehabilitation sessions for 7 to 12 weeks reported significant improvements in exercise performance assessed by simple walking tests. The current study confirms the effects of twice-weekly training programs on enhancing exercise performance, not only in terms of objectively measured peak physiologic responses, but that such effects are accompanied by a reduced ventilatory requirement at a submaximal level of exercise.

The design of the initial training prescription in the present study was similar to that described by Niederman et al. who exercised 33 patients with a wide spectrum of airflow limitation (FEV\textsubscript{1} range, 0.33 to 3.8 L) three times a week for 9 weeks. It was shown that changes in maximal and submaximal exercise performance on a bicycle ergometer were not related to the magnitude of airflow impairment quantified as % predicted FEV\textsubscript{1}. In the present study, we were able to develop these observations in a larger cohort of patients but with a comparable wide spectrum of airflow limitation (FEV\textsubscript{1} range, 0.51 to 2.99 L). Our data show that training benefits are unrelated to and independent of underlying airflow limitation; comparable benefits were observed for patients with % predicted FEV\textsubscript{1} < 40% and for those whose FEV\textsubscript{1} exceeded this threshold (Table 4). Interestingly, in contrast to previous studies, there was a significant but very modest clinical impact on dynamic and static lung volumes. Even though the exercise program did not include weight training as a component, it is difficult to attribute the improvements in ventilatory capacity to the training schedule per se. A more likely explanation relates to indirectly derived educational benefits in the use of inhaled medication.

Primary outcome measures in pulmonary rehabilitation strategies include assessments of quality of life and psychosocial performance, quantification of domestic functional activity, in addition to the physiologic benefit derived from aerobic training. This study further emphasizes the important role of aerobic submaximal exercise training in patients with chronic pulmonary morbidity. Although the magnitude of the physiologic benefits observed in reducing ventilatory requirements may be considered small, they were nevertheless achieved irrespective of the degree of airflow limitation, and this has significant implications for clinical practice. We are unable to quantify which particular aspect of the exercise strategy is more important; additionally, we are unable to state with certainty whether or not the observed physiologic gains are directly extrapolatable to improved functional daily activity, since this was not our primary outcome measure. It is nevertheless likely, however, that in patients limited by dyspnea, peripheral muscle weakness and increased susceptibility to lactic acidosis, enhancement of exercise tolerance, and reduction in ventilatory and cardiovascular requirements at a defined level of exercise will extrapolate to improved domestic functioning. Of note, a recent study by Singh et al. did demonstrate objective improvements in domestic function following a rehabilitation strategy that resulted in improved exercise tolerance.

In summary, these data expand on the physiologically based principles of exercise prescription for patients with chronic airflow limitation and endorses the benefit of such strategies. We have shown that submaximal aerobic exercise training of moderate intensity performed twice weekly for 12 weeks in a large cohort of patients has significant potential benefits on a number of physiologic responses irrespective of the severity of the underlying obstructive pulmonary disease. The implications for clinical practice are tangible and compelling.

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