Short- and Long-term Effects of Outpatient Rehabilitation in Patients with Chronic Obstructive Pulmonary Disease: A Randomized Trial

Thierry Troosters, PhD, Rik Gosselink, PhD, Marc Decramer, PhD

PURPOSE: Pulmonary rehabilitation programs are effective in patients with severe chronic obstructive pulmonary disease (COPD) in the short term, but their long-term effects are not known. We investigated the short- and long-term effects of a 6-month outpatient rehabilitation program in patients with severe COPD.

SUBJECTS AND METHODS: One hundred patients were randomly assigned to receive either an exercise training program that included cycling, walking, and strength training (n = 50) or usual medical care (n = 50). Thirty-four patients in the training group were evaluated after 6 months (end of training), and 26 were evaluated after 18 months of follow-up. In the control group, 28 patients were evaluated at 6 months and 23 after 18 months. We measured pulmonary function, 6-minute walking distance, maximal exercise capacity, peripheral and respiratory muscle strength, and quality of life (on a 20 to 140-point scale), and estimated the cost-effectiveness of the program.

RESULTS: At 6 months, the training group showed improvement in 6-minute walking distance [mean difference (training — control) of 52 m; 95% confidence interval (CI), 15 to 89 m], maximal work load (12 W; 95% CI, 6 to 19 W), maximal oxygen uptake (0.26 liters/min; 95% CI, 0.07 to 0.45 liters/min), quadriceps force (18 Nm; 95% CI, 7 to 29 Nm), inspiratory muscle force (11 cm H2O; 95% CI, 3 to 20 cm H2O), and quality of life (14 points; 95% CI, 6 to 21 points; all P < 0.05). At 18 months all these differences persisted (P < 0.05), except for inspiratory muscle strength. For 6-minute walking distance and quality of life, the differences between the training group and controls at 18 months exceeded the minimal clinically-important difference.

CONCLUSION: Among patients who completed the 6-month program, outpatient training resulted in significant and clinically relevant changes in 6-minute walking distance, maximal exercise performance, peripheral and respiratory muscle strength, and quality of life. Most of these effects persisted 18 months after starting the program. Am J Med. 2000;109:207–212. ©2000 by Excerpta Medica, Inc.
with other severe medical problems, such as heart failure, myocardial infarction, cerebrovascular disease, cancer, or orthopedic disorders. The study was approved by the local ethics committee.

Measurements were made at enrollment, and at 6 months and 18 months after the start of the study. At all visits, patients underwent spirometry and whole body plethysmography (Body Box 1085, Medical Graphics, Inc., St. Paul, Minnesota). FEV1 and forced vital capacity were measured according to the European Respiratory Society guidelines for pulmonary function testing (10). In addition, the diffusing capacity for carbon monoxide was measured by the single breath method (Sensor Medic 6200, Bithoven, The Netherlands) at the initial visit. Results were expressed as a percentage of the predicted normal values (10).

Isometric quadriceps strength was measured using a Cybex II dynamometer (Lumex, Bay Shore, New York). Peak extension torque was evaluated at 60 degrees of knee flexion. Reference values for quadriceps force were developed in our laboratory (11). Tests were performed at least three times, and the best of two reproducible tests was used for further analysis.

Inspiratory and expiratory muscle strength was measured using standard techniques (12). At least five attempts were made to measure expiratory muscle strength from total lung capacity and to measure inspiratory muscle strength from residual volume. Both were determined as the pressure that could be sustained for at least 1 second. Tests were repeated until the variability among the three best attempts was less than 5%. The highest value was expressed as a percent of the predicted value (13).

Functional exercise performance was measured by a 6-minute corridor-walking test. Encouragement was standardized (14). A 54-m improvement was considered clinically important (15). To avoid learning effects, the best of two tests was used and expressed as percent of the predicted value (16).

Maximal exercise capacity was assessed by maximal cycle ergometry (Partn’air 5400; Medisoft, Dinant, Belgium). Patients cycled at an incremental workload (+10 W per minute) until exhaustion. Oxygen consumption, carbon dioxide output, and ventilation were measured breath by breath. Heart rate was monitored constantly. Maximal oxygen consumption was compared with normal values (17). At 6 months, data obtained from a maximal exercise test were analyzed at 60% of the initial workload.

The Chronic Respiratory Disease Questionnaire (18) was used to assess health-related quality of life. This 20-item questionnaire, which scores quality of life into four domains (dyspnea, mastery, emotional functioning, and fatigue) has been validated in the Dutch language (19).

**Intervention**

Patients assigned to the training program were invited to attend the outpatient sessions three times a week in the first 3 months; during the subsequent 3 months, training frequency was reduced to twice weekly. Each session had a duration of 1.5 hours. Training items were cycling, treadmill walking, stair climbing, and peripheral muscle training. Patients started the program at 60% of the initial maximal workload on the cycle ergometer and at 60% of their maximal walking speed during the 6-minute walking test. During the first 3 months, this workload was increased up to 80% of the maximal workload and maximal walking speed. In each session, patients also performed arm cranking and stair climbing in 2-minute blocks (1 to 3 repetitions). Peripheral muscle strength training on a multi-gym device was performed in three series of 10 repetitions at 60% of the one repetition maximum for each muscle group (triceps, latissimus dorsi, pectoralis, and quadriceps muscle). Physiotherapists ensured close supervision and continuous encouragement of the patients. Oxygen saturation and heart rate were measured during the training sessions. Supplemental oxygen was given to maintain oxygen saturation above 90%.

**Cost-effectiveness**

The program had a cost of $57 per session per patient, based on the charges as reimbursed by the National Health Insurance, which covers the salary for 1.5 hours of treatment from a physical therapist. The total cost of the program per patient was determined by multiplying this cost by the number of sessions.

**Statistical Analysis**

Baseline characteristics of the two groups were compared using unpaired t tests. The effects of treatment (training or control) were analyzed with a repeated measures analysis of variance. Unpaired t tests were used to evaluate the effects of treatment at the end of training (6 months) and follow-up (18 months). Statistical significance was set at \( P < 0.05 \). All tests were performed with the Statistical Analysis System (SAS Institute, Cary, North Carolina).

**RESULTS**

One hundred consecutive eligible patients fulfilled inclusion criteria and were randomly assigned to either the training group (n = 50) or the control group (n = 50). Three patients (1 in the training group and 2 in the control group) refused initial testing, leaving 97 patients who underwent initial tests. Of these, 12 patients refused to participate in the training sessions, and 15 patients in the control group refused further follow-up. Except that they were older [mean (± SD) age of 66 ± 7 years vs 61 ± 9 years, \( P < 0.004 \)], these patients did not differ from the patients with follow-up. In addition, 3 of the remaining
37 patients in the training group (2 of whom died) and 5 of the remaining patients in the control group (3 of whom died) were not able to comply with short-term follow-up (6 months). Long-term (18-month) follow-up could not be performed in 11 of the 37 patients in the training group (9 of whom died) and in 10 of the 33 patients (7 of whom died) in the control group. There were no differences in 18-month mortality between the two groups (P = 0.79).

All patients had severe COPD with moderate peripheral and respiratory muscle weakness and with impaired functional and maximal exercise capacity. There were no significant differences in the characteristics of the 70 patients who participated in the training and control groups (Table 1). Patients who died during the trial (n = 16) had a significantly lower FEV\textsubscript{1} (32% ± 12% vs 45% ± 13% of predicted, P <0.001), diffusing capacity for carbon monoxide (41% ± 19% vs 64% ± 25% of predicted, P <0.001), walking distance (357 ± 117 vs 429 ± 124 m, P <0.05), and maximal exercise capacity (58 ± 30 vs 79 ± 34 W, P <0.02) than those who survived.

### Rehabilitation Program

Patients in the training group participated in a mean of 46 ± 11 sessions (attendance rate 77% ± 19%). Training intensity for walking and cycling reached a plateau, on average, after 3 months (Figure 1). Heart rate during the training session averaged 92% ± 9% of the maximal achieved heart rate during the incremental maximal exercise test. Workload during treadmill walking is expressed as percent of the speed achieved during the initial 6-minute walking test. Lower panel: total training time (mean ± SD) during training sessions, by week of training.

### Effects of Training

Compared with usual care, there were no significant effects of the training program on measures of pulmonary function. The training program did, however, improve 6-minute walking distance, maximal work load, maximal oxygen uptake, quadriceps force, and quality-of-life score.
Table 2. Effects of a Pulmonary Rehabilitation Training Program at 6 Months, Compared with Control

<table>
<thead>
<tr>
<th>Measurement</th>
<th>Absolute Values</th>
<th>Difference between Groups in Change from Baseline</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forced expiratory volume in 1 second (L)</td>
<td>Control Group (n = 28)</td>
<td>Training Group (n = 34)</td>
<td>(95% Confidence Interval)</td>
</tr>
<tr>
<td></td>
<td>1.3 ± 0.4</td>
<td>1.2 ± 0.5</td>
<td>0.04 (−0.09–0.12)</td>
</tr>
<tr>
<td>Quadriceps force (Nm)</td>
<td>121 ± 52</td>
<td>144 ± 45</td>
<td>18 (7–30)</td>
</tr>
<tr>
<td>Maximal inspiratory pressure (cm H₂O)</td>
<td>68 ± 23</td>
<td>83 ± 28</td>
<td>11 (3–20)</td>
</tr>
<tr>
<td>6-minute walking distance (m)</td>
<td>438 ± 104</td>
<td>468 ± 125</td>
<td>52 (15–89)</td>
</tr>
<tr>
<td>Maximal work load (watts)</td>
<td>85 ± 37</td>
<td>88 ± 36</td>
<td>12 (6–19)</td>
</tr>
<tr>
<td>Maximal oxygen uptake (L/min)</td>
<td>1.54 ± 0.63</td>
<td>1.63 ± 0.64</td>
<td>0.256 (0.07–0.45)</td>
</tr>
<tr>
<td>Disease-specific quality of life (points)</td>
<td>82 ± 25</td>
<td>90 ± 18</td>
<td>14 (6–21)</td>
</tr>
</tbody>
</table>

* Results are presented both as absolute values at 6 months and as the difference (change in treatment group − change in control group) from baseline.
† For the comparison of difference in change from baseline.

DISCUSSION

We found that a 6-month outpatient rehabilitation program that involved moderate-to-high training intensity did not alter pulmonary function, but did improve functional and maximal exercise performance, peripheral and respiratory muscle strength, and quality of life when compared with usual care in patients with severe COPD. Improvements in functional and maximal exercise performance and quality of life were clinically relevant (15) and were maintained 18 months after the onset of training. However, 31% of patients dropped out of the study by 6 months, and 36% by 18 months. Goldstein et al (2) reported similar dropout and refusal rates. In our study, the main reasons for dropping out were unwillingness to participate in the rehabilitation sessions, refusal to participate in further assessments, or death. Patients who died during the trial had severe disease, as manifested by low values for FEV₁ and diffusing capacity for carbon monoxide, and a low exercise capacity (20–22). As reported by others, the pulmonary rehabilitation program did not prevent short-term mortality (3).

The training regimen that we used differed somewhat from other trials. Patients trained at a slightly greater intensity than reported by Maltais et al (23), but the training time for each session was substantially shorter in our study. The mean attendance rate in our study (77% ± 19%) was similar to that in the study of Bendstrup et al (6), although less than that reported by others (23).

The magnitude of the training effect (approximately 20% improvement) in this study is similar to other trials, as measured by improvement in functional exercise capacity (5,24–26) and maximal exercise capacity (8,24,27,28). Although some trials have not demonstrated improvements in maximal oxygen uptake (4,24,28,29), the increase (12% ± 29%) that we achieved...
resembles that reported in studies that used strenuous, individually-tailored cycle exercise (3,23,30,31). The improvements that we observed in all four dimensions of quality of life were similar to those reported in a recent meta-analysis (1).

Most of the benefits of training in this study persisted for 12 months after the training program had been completed. Swerts et al (9) reported that the improvements seen after an 8-week program declined gradually during 1 year of follow-up, whereas patients who continued the training program for 20 weeks (60 sessions) maintained improvements in walking distance. Two other studies that had shorter training periods were unable to show long-term benefits (3,8). Whether this apparent discrepancy is the result of the duration of the training program is not clear. In our study, the maintained improvement at 18 months not only reached statistical significance, but also the difference with controls exceeded the minimal clinically-important difference for improvements in quality of life and functional exercise capacity. For the latter test, it was estimated to be 54 m (19). In our study, after the rehabilitation period had been completed, the average improvement—which was approximately 90 m in walking distance—persisted in those subjects who returned for the 1-year follow-up. Similar and persistent improvements in quality of life were also seen, whereas there was a significant and clinically-important deterioration of mean quality of life in the control group.

Our outpatient-based program had a mean cost per patient of approximately $2,600 to achieve a mean improvement of 52 m in 6-minute walking distance at 6 months. A previous study reported that a hospital-based program cost approximately $7,800 per patient and resulted in a 37m improvement in 6-minute walking distance (2). Thus, outpatient rehabilitation appears to be more cost-effective than an inpatient program. Compared with home rehabilitation, which was reported to cost approximately $660 per patient and resulted in approximately a 39m improvement in 6-minute walking distance (8), the costs of our rehabilitation program were great. However, the patients in our study had more severe disease than those in the study of the home-care program and might need more careful monitoring during training. Indeed, prudent training strategies in a home setting were not effective in one study that enrolled patients with severe COPD (7).

We conclude that a 6-month outpatient rehabilitation program with high-intensity training resulted in clinically-relevant improvements in functional and maximal exercise capacity, peripheral and respiratory muscle strength, and quality of life in patients with severe COPD (7).

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