Duration of pulmonary rehabilitation to achieve a plateau in quality of life and walk test in COPD

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KEYWORDS
Chronic obstructive pulmonary disease; Health-related quality of life; Respiratory rehabilitation; 6-Min walk test

Summary
Objective: To address the minimum duration of pulmonary rehabilitation necessary for patients with chronic obstructive pulmonary disease (COPD) to achieve a plateau in Health-Related Quality of Life (HRQL) and exercise tolerance.
Methods: COPD patients with a dyspnea rating of at least 2 on the Medical Research Council scale participated in an outpatient rehabilitation program of 3 weekly sessions for 12 weeks. Measurements included HRQL and exercise tolerance 2 weeks before the program started and every 2 weeks thereafter. Patients were considered to have reached a plateau if they showed no improvement beyond 20% of the minimal important difference between 2 consecutive evaluations on HRQL score or walk tests.
Results: Twenty-eight patients participated. The number of patients achieving stability after 8 weeks, showing continued improvement after 8 weeks, and demonstrating an erratic pattern of change was as follows: for physical function 16 (56%), 10 (37%) and 2 (7%) patients; for emotional function 22 (79%), 5 (18%) and 1 (4%); and for 6-min walk test 21 (75%), 5 (18%) and 2 (7%). More severe patients demonstrated a greater likelihood (76%) of achieving stability in physical function at 12 weeks than did less severe patients (27%; p on difference = 0.003). The likelihood of stability at 12 weeks in emotional function and the 6-min walk test did not differ by severity.

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Introduction

Pulmonary rehabilitation improves exercise tolerance and health-related quality of life (HRQL) in patients with chronic obstructive pulmonary disease (COPD). No consensus has emerged, however, regarding the optimal duration of the initial intense phase of rehabilitation.

Some authors have recommended programs of 3–5 sessions per week for 2–3 months. The most recent reviews of pulmonary rehabilitation by the American Thoracic Society and the European Thoracic Society called attention to the lack of evidence regarding optimal duration. The reviews nevertheless suggested the duration of effect is directly proportional to the duration of the program. Some evidence, however, suggests that shorter programs may be as effective as longer ones. Authors of a recent meta-analysis of 20 randomized controlled trials (RCTs) in 999 patients concluded that patients diagnosed with mild-to-moderate COPD could benefit from short rehabilitation programs, whereas those with severe disease needed at least 6 months to achieve the same benefits.

We hypothesized that the results of a pulmonary rehabilitation program could be evaluated based on serial measurements of HRQL and the 6-min walk test. Our aim was to establish the minimum time an outpatient pulmonary rehabilitation program should last to allow patients with moderate-to-severe COPD to achieve stability after initial improvement.

Methods and material

Study design

This is a longitudinal cohort study, in which we followed a group of COPD patients from 2 weeks before entering an outpatient rehabilitation program until the end of this program. We measured patients' health-related quality of life (HRQL) using the Chronic Respiratory Questionnaire (CRQ) and their 6-min walk test distance every two weeks.

Patients

Patients were recruited from among those attending our hospital’s outpatient clinic if they had COPD diagnosed according to the criteria of the Global Initiative for Chronic Obstructive Lung Disease (GOLD). Inclusion criteria were age under 65 years, shortness of breath rated as 2 or more on a modified Medical Research Council (MRC) scale, no need for home oxygen therapy, clinically stable nutritional status, no exacerbation in the last month or changes in medication in the last 4 months, and written informed consent to participate in the study.

All patients used an inhaled corticosteroid and an inhaled β2-agonist and/or an anti-cholinergic agent. Five patients with moderate COPD who had experiences at less 2 exacerbations last year used inhaled corticosteroid according to the judgment of their physicians.

Exacerbation, defined by the presentation of productive cough, purulent sputum, and increased shortness of breath in accordance with the criteria of Anthonisen et al. were grounds for withdrawal from the program.

The local institutional review board approved the study.

Outpatient pulmonary rehabilitation program

Patients attended the rehabilitation center 3 days a week for 12 weeks. To optimize the use of respiratory muscles, a physiotherapist taught respiratory exercises during the first week. All patients received instruction regarding relaxation techniques, and those with significant sputum production received instruction on techniques to remove secretions. Lower extremity muscle training, which began in the second week, utilized a cycle ergometer in 30-min sessions at an initial load that represented 60% of the maximum load reached during an incremental exercise test. The exercise load was increased in keeping with tolerance. Upper extremity muscle training, also carried out in 30-min sessions, began with half-kilogram weights for each arm. The weight increased by 1 kg each week until patients reached maximum tolerance. Inspiratory and expiratory muscle training sessions lasted 15 min each with the patient breathing through a threshold resistive loading device (Threshold, Respironics, Cedar Grove, NJ, USA) with

Conclusions: A program of 3 weekly 3-h sessions of outpatient pulmonary rehabilitation program should last at least 8 weeks in order to achieve optimal HRQL and exercise tolerance for most patients. © 2008 Elsevier Ltd. All rights reserved.
a valve set to provide a pressure at least 30% of the maximum inspiratory pressure. The program included information sessions to explain the nature of the disease and ensure correct inhaler technique.

Statistical analysis

We chose a sample size based on resource and feasibility considerations rather than a formal sample size calculation.

Data were expressed as mean ± SD. Analysis of variance of repeated measures was applied to the CRQ and the 6-min walk tests recorded at 2-week intervals for patients who finished the program. We reasoned that, for both the CRQ and the walk test, if a patient showed no improvement beyond 20% of the minimal important difference (MID) then the patient had achieved all the improvement possible through rehabilitation as reflected in that outcome measure. We considered the MID for both the physical and emotional function domains of the CRQ as 0.5 and therefore considered patients to have achieved maximum benefit when 2 successive measurements showed no improvement beyond 0.1 points. For the walk test, we considered the MID to be 54 m and therefore considered that maximum benefit had been achieved if 2 successive 6-min walk tests showed no improvement beyond 10.8 m.

We classified patients as manifesting erratic behavior if the patient manifested deterioration in either walk test or CRQ of more than 10% in comparison to the previous measure on more than one occasion. We chose 10% as a threshold because it represents the coefficient of variation on 6-min walk test in our institution.

On the basis of previous results suggesting that optimal duration of rehabilitation may vary with the severity of COPD, we examined our results according to whether FEV₁ was ≤35% or >35%. We conducted a Fisher’s exact test to determine whether chance could explain the differences in the proportion of patients achieving stability by 12 weeks in the more and less severe patients.

Results

Of the 36 patients recruited, 2 withdrew before starting rehabilitation because of family- or work-related difficulties and 6 left during the course of the program: 1 because of starting continuous positive airway pressure treatment at 2 weeks and 5 due to exacerbation of disease requiring a treatment change or hospital admission. The analysis is therefore based on data from 28 patients.

Patient characteristics

Twenty-four of the 28 patients (86%) were men. The mean age of patients enrolled was 63 ± 9.7 years. According to GOLD criteria, 5 patients (18%) had moderate COPD, 11 (39%) had severe disease, and 12 (43%) had very severe disease. The MRC score was 2 for 10 patients (36%), 3 for 14 patients (50%), and 4 for 4 patients (14%). All were in a state of good nutrition. Table 1 shows patient baseline characteristics.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Mean</th>
<th>SD</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
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<tbody>
<tr>
<td>Age, year</td>
<td>62.8</td>
<td>9.7</td>
<td>37</td>
<td>74</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>25.2</td>
<td>3.2</td>
<td>20</td>
<td>33.2</td>
</tr>
<tr>
<td>Upper arm circumference</td>
<td>29.9</td>
<td>8.3</td>
<td>24</td>
<td>70</td>
</tr>
<tr>
<td>Triceps skin fold, cm</td>
<td>13</td>
<td>5</td>
<td>6</td>
<td>25</td>
</tr>
<tr>
<td>Albumin, g/L</td>
<td>43</td>
<td>3</td>
<td>38</td>
<td>48</td>
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<tr>
<td>FEV₁ pbd, % predicted</td>
<td>36</td>
<td>15</td>
<td>17</td>
<td>70</td>
</tr>
<tr>
<td>FEV₁ pbd ≤ 35% (n = 17)</td>
<td>26</td>
<td>7</td>
<td>17</td>
<td>34</td>
</tr>
<tr>
<td>FEV₁ pbd &gt; 35% (n = 11)</td>
<td>51</td>
<td>11</td>
<td>38</td>
<td>70</td>
</tr>
<tr>
<td>FVC pbd, % predicted</td>
<td>72</td>
<td>17</td>
<td>42</td>
<td>104</td>
</tr>
<tr>
<td>FEV₁/FVC pbd, %</td>
<td>35</td>
<td>8.9</td>
<td>19</td>
<td>66</td>
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<tr>
<td>TLC, % predicted</td>
<td>114</td>
<td>15</td>
<td>80</td>
<td>141</td>
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<td>RV, % predicted</td>
<td>185</td>
<td>42</td>
<td>96</td>
<td>262</td>
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<tr>
<td>Kco, % predicted</td>
<td>59</td>
<td>19</td>
<td>24</td>
<td>96</td>
</tr>
<tr>
<td>Pimax, % predicted</td>
<td>96</td>
<td>27</td>
<td>40</td>
<td>133</td>
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<tr>
<td>PEmax, % predicted</td>
<td>117</td>
<td>40</td>
<td>34</td>
<td>195</td>
</tr>
<tr>
<td>PaO₂, mmHg</td>
<td>74</td>
<td>10</td>
<td>55</td>
<td>95</td>
</tr>
<tr>
<td>PaCO₂, mmHg</td>
<td>41</td>
<td>4.7</td>
<td>33</td>
<td>54</td>
</tr>
<tr>
<td>Dyspnea rating</td>
<td>2.8</td>
<td>0.7</td>
<td>2</td>
<td>4</td>
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<tr>
<td>MVC 1−5i</td>
<td></td>
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<td></td>
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<tr>
<td>6MWT, m</td>
<td>399</td>
<td>82.5</td>
<td>250</td>
<td>550</td>
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<tr>
<td>Wmax, kpm</td>
<td>547</td>
<td>170</td>
<td>300</td>
<td>900</td>
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<tr>
<td>VO₂max, mL</td>
<td>0.58</td>
<td>0.26</td>
<td>0.19</td>
<td>1.09</td>
</tr>
<tr>
<td>CRQ scoresc</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>16.51</td>
<td>3.56</td>
<td>9.44</td>
<td>21.77</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>3.04</td>
<td>0.75</td>
<td>1.40</td>
<td>4.40</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4.20</td>
<td>0.98</td>
<td>2.50</td>
<td>6.00</td>
</tr>
<tr>
<td>Emotion</td>
<td>4.49</td>
<td>1.17</td>
<td>1.86</td>
<td>6.00</td>
</tr>
<tr>
<td>Mastery</td>
<td>4.79</td>
<td>1.30</td>
<td>2.25</td>
<td>7.25</td>
</tr>
</tbody>
</table>

a BMI = body mass index; FEV₁ = forced expired volume in 1 second; FVC = forced vital capacity; pbd = post-bronchodilator; TLC = total lung capacity; RV = residual volume; Kco = carbon monoxide transfer coefficient; Pimax = maximal inspiratory pressure; PEmax = maximal expiratory pressure; MRC = Medical Research Council; 6MWT = 6-min walk test; Wmax = work capacity; VO₂max = maximal oxygen consumption; CRQ = Chronic Respiratory Questionnaire.

b The score on the MRC ranges from 1 (best situation) to 5 (worst).
c The total score on the Chronic Respiratory Questionnaire ranges from 4 (worst situation) to 28 (best); each domain score ranges from 1 (worst situation) to 7 (best).

Seven patients (25%) improved on both domains of CRQ and on the 6-min walk test (4 of them at 4th week, 1 at 8th week and 2 at 10th week). Eleven patients (39%) improved in two of the outcomes (the 2 CRQ domains and the walk test) (1 of them at 2nd week, 4 at 6th week, 3 at 8th week and 3 at 10th week). Two (7%), 2(7%) and 4 (14%) patients only improved in one of three outcomes. Two patients (7%) didn’t improve on any outcome.

HRQL

The mean change between baseline and the final evaluation of the CRQ physical function domain was 1.11 points (p < 0.001 on analysis of variance considering all
The physical component score at baseline (2 weeks before the first session) was 3.55 ± 0.76 points. Mean CRQ physical function had improved by more than 0.5 points by 4 weeks, when the score reached 4.23 ± 1.01 points. Mean score was stable between 6 and 8 weeks; scores on the last evaluation showed further improvement (5.46 ± 1.07 points) (Fig. 1).

Twenty-two patients (79%) achieved stability at 8 weeks of the program. Five patients (18%) did not achieve stability and one patient (4%) showed an erratic pattern of results.

Table 2 shows the number of patients exceeding the minimal important difference in improvement in HRQL on each determination.

<table>
<thead>
<tr>
<th></th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>6 weeks</th>
<th>8 weeks</th>
<th>10 weeks</th>
<th>12 weeks</th>
<th>Never achieved</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical</td>
<td>9</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>16</td>
</tr>
<tr>
<td>Emotional</td>
<td>4</td>
<td>9</td>
<td>0</td>
<td>4</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>22</td>
</tr>
<tr>
<td>6MWT</td>
<td>4</td>
<td>5</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>3</td>
<td>21</td>
</tr>
</tbody>
</table>

The mean change between baseline and the final evaluation of the CRQ emotional function was 0.86 points (p < 0.001 on analysis of variance). The emotional component score at baseline (2 weeks before the first session) was 4.60 ± 1.09 points. A mean improvement of greater than 0.5 points was seen at 6 weeks, when the score reached 5.26 ± 1.04 points. Mean score was stable between 6 and 8 weeks; scores on the last evaluation showed further improvement (5.46 ± 1.07 points) (Fig. 1).

Sixteen patients (57%) achieved stability with respect to physical function at 8 weeks. Ten patients (36%) did not achieve the stability and two patients (7%) showed an erratic pattern of results.

Six patients (21%) achieved stability at 8 weeks. Five patients (18%) continued to improve and two (7%) manifested erratic scores.

Table 2 shows the number of patients exceeding minimal important difference in improvement in the 6-min walk test at each determination.

**Pattern of response according to COPD severity**

Among 17 COPD patients with FEV₁ ≤ 35%, 13 (76%) achieved stability at 12 weeks in the physical and emotional function domain of the CRQ and 12 (71%) on the 6-min walk test.

Among 11 COPD patients with FEV₁ > 35%, 3 (27%) achieved stability on physical function domain of the CRQ and 9 (81%) on the emotional function domain and 6-min walk test at 12 weeks.

Chance is unlikely to explain the difference in frequency of stability at 12 weeks in CRQ physical function between patients with FEV₁ ≤ 35% (76%) and patients with FEV₁ > 35% (27%).
FEV₁ > 35% (27%) (p = 0.003). Differences between the two groups in emotional function and the 6-min walk test are easily explained by chance.

Discussion

We found patients with COPD completing an outpatient pulmonary rehabilitation program of 3 sessions per week for 12 weeks demonstrated improvement in HRQL and exercise tolerance. The majority of patients reached a plateau in physical function (57%), emotional function (79%), and walk test performance (75%) at 8 weeks.

Most of patients who achieved the stability during the program had achieved the MID before 6 weeks. Not all patients achieved the MID on each of the two domains of the CRQ and on the 6-min walk test, but almost all achieved the MID in one or more outcomes by the end of the program (Table 2).

The ATS/ERS¹³ recommended 20 sessions and the ACCP/AACVPR statement¹ suggests that programs of 6–12 weeks are beneficial. A single prior study including 13 COPD patients²⁴ used a design similar to ours to address the trajectory of changes in treadmill endurance and CRQ over a 12-week rehabilitation program (24 sessions). The authors conclude that 20 sessions are needed to reach optimal acute changes in exercise performance, but improvements in quality of life may occur earlier. While limited relative to our study in the smaller sample size, and the lack of focus on individuals, these authors’ results are consistent with ours.

Other prior studies address the optimal duration of rehabilitation by making direct comparisons of specific alternative durations with the same intensity of intervention throughout. Berry et al.²⁵ conducted an RCT comparing a 3-month program versus 18 months. Patients in both programs achieved their greatest gains in self-reported disability and physical function at 3 months. However, patients in the longer program showed less disability and better physical function at 18 months. Sewell et al.²⁶ undertook an RCT in patients with COPD to assess whether a 4 weeks pulmonary rehabilitation program was equivalent to conventional 7 weeks pulmonary rehabilitation program. The authors found no important differences between the programs at 7 weeks and 6 months. Foy et al.²⁷ conducted an RCT comparing 3 months of exercise training to 18 months. Men, but not women, experienced greater benefit with the longer program.

Programs with fewer than 2 weekly sessions sometimes²⁸, but not always,¹⁵ led to minimal improvement in health status and the 6-min walk test. Most programs that have shown benefit in RCTs conducted more frequent training sessions. Thus, although the evidence is meager, one might expect patients to reach a plateau more rapidly with programs with greater frequency of training sessions. The ATS/ERS statement¹³ suggests programs should offer at least three sessions per week to achieve physiologic benefit. They qualify this recommendation by stating that twice-weekly supervised plus one unsupervised home session may also acceptable.

There are three RCTs addressing the influence of training intensity on the benefits reached by the pulmonary rehabilitation program. Gimenez et al.²⁹ and Vallet et al.³⁰ found that higher intensity training in COPD patients resulted in a greater physiologic improvements than low-intensity training. Normandin et al.³¹ compared, in a randomized trial, the short-term effectiveness high-intensity program with a lower-intensity one. The high-intensity group trained on a stationary bicycle and treadmill and the lower-intensity group performed classroom exercises. Both groups participated in twice-weekly sessions for 8 weeks. The high-intensity group showed greater increases in treadmill endurance and greater reductions in exertional dyspnea, and low-intensity showed greater increases in arm endurance. Both groups had similar improvements in overall dyspnea, functional performance and health status. The differences between groups may have been due as much or more to differences in the muscular groups trained training rather than differences in intensity training.

No study has addressed the effect of training intensity on time to maximal improvement. The ACCP/AACVPR statement¹ suggests that high and low-intensity training are beneficial. Moreover, whether program intensity influences the rapidity with which patients reach a plateau remains uncertain.

Finally, disease severity may influence the rapidity with which patients’ reach their optimal status. Wedzicha et al.³² found that patients with a high degree of dyspnea (MRC rating of 5) obtained less benefit from rehabilitation than patients with mild or moderate dyspnea. The authors speculated that it is possible that patients with more severe dyspnea may require longer or more intense training. These results are consistent with the meta-analysis of Salman et al.¹⁶ The authors analyzed 20 RCTs with a total of 999 symptomatic COPD patients and concluded that mild and moderate COPD (FEV₁ > 35%) patients obtain benefits from short and long rehabilitation programs while severe COPD (FEV₁ < 35%) patients need at least 6 month of rehabilitation. Our results do not, however, support the conclusion of Salman et al. meta-analysis. A substantially larger proportion of patients with more severe COPD in our study
achieved stability in CRQ physical function by 12 weeks than did patients with less severe COPD. We found no differences in time to stability in both groups in either CRQ emotional function or 6-min walk test distance.

These studies demonstrate that factors other than the duration of the program can determine the point at which patients have reached a plateau in the benefits from the pulmonary rehabilitation. These factors include session frequency, training intensity and severity of the disease. The optimal balance between intensity, frequency and duration remains unclear and requires further study.

The most important strengths of this study are the careful repeated measurement of functional exercise capacity and HRQL, the rigorous analyses focusing both on the total patient group and on individuals. Our study has three important limitations. First, the sample size is small. Second, approximately 25% of the patients were still improving at 12 weeks. When such patients would have reached their plateau remains uncertain. Third, it is possible that continuing the intensive phase of rehabilitation after patients reach a plateau may impact on the long-term benefits, and the persistence of those benefits.

Nevertheless, our results support a conclusion that an 8-week outpatient pulmonary rehabilitation program with 3 sessions per week is sufficiently long for most patients with moderate-to-severe COPD (GOLD class II—IV) and dyspnea (MRC rating, 2—4), to reach a plateau in HRQL and walk test distance. A minority of patients will continue to demonstrate improvement after 8 weeks, and for at least as long as 12 weeks.

Conflict of interest

The authors have no conflict of interest.

References


