Pulmonary rehabilitation is successful for COPD irrespective of MRC dyspnoea grade

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Received 11 September 2008; accepted 8 January 2009
Available online 13 February 2009

KEYWORDS
COPD;
Pulmonary rehabilitation;
Exercise;
MRC dyspnoea scale

Summary

Background: It is not clear whether the benefits of pulmonary rehabilitation (PR) apply equally to patients with Chronic Obstructive Pulmonary Disease (COPD) with different levels of starting disability. We have therefore investigated the effect of pulmonary rehabilitation stratified by the MRC dyspnoea scale in patients with COPD.

Methods: This is a retrospective, observational study of data collected from 450 consecutive patients with COPD attending outpatient PR: 247 male, mean (SD) age 69.5 (8.9) yrs and FEV1 44.6 (19.7)% predicted. The Incremental Shuttle Walk Test (ISWT) was performed before and after the seven-week course.

Results: 395 patients (88%) completed the programme. The mean (SD) baseline ISWT performance was 167 (113)m. The distribution of baseline MRC grades was 2 (15.4%), 3 (24.9%), 4 (27.3%) and 5 (32.4%). The mean (95% CI) improvement in ISWT after PR for each MRC scale grade was highly significant \(p < 0.0005\); 2 (66 (50–83)m, 3 (63 (50–75)m, 4 (59 (49–70)m, and 5 (54 (43–64)m.

Conclusions: Patients with COPD, of all MRC dyspnoea grades, benefit comparably from pulmonary rehabilitation achieving both statistically and clinically meaningful improvements in exercise performance. MRC grade should therefore not be used to exclude patients from pulmonary rehabilitation.

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Introduction

Patients with Chronic Obstructive Pulmonary Disease (COPD) commonly suffer from exertional breathlessness and fatigue resulting in reduced exercise tolerance. Over the last two decades strategies have been developed to decrease disability. Pulmonary rehabilitation (PR) has been shown to improve exercise performance and health status in COPD. Current guidelines suggest that ‘pulmonary rehabilitation should be considered for all patients with chronic respiratory disease who have persistent symptoms, limited activity, or are unable to adjust to illness in spite of...
optimal medical management. Guidelines have also suggested that the MRC dyspnoea scale may be an appropriate guide for patient selection for PR. The MRC Dyspnoea Scale is a simple to use, validated, reproducible, self-assessed tool of breathlessness. A threshold of disability of MRC dyspnoea scale grades 3–5 has been recommended for consideration for referral for rehabilitation.

Few papers have reported the characteristics of patients that respond favourably to rehabilitation. One study showed that patients with a ventilatory limitation to exercise and normal peripheral muscle strength were less likely to improve their exercise capacity after rehabilitation. This study did not investigate how baseline breathlessness affected the response to rehabilitation. There is also a suggestion that the more severely disabled patients (MRC grade 5) may do less well from traditional pulmonary rehabilitation and may need a longer duration programme. Some studies have recommended lower intensity training or passive training with neuromuscular exercise as much as patients with MRC grades 3 and 4, but the numbers were small. Currently patients with MRC grade 2 breathlessness are not included in the guidelines.

Our local pulmonary rehabilitation programme provides individually prescribed, high intensity short-term endurance training. We investigated, in a pragmatic setting, how disability influences the outcome of pulmonary rehabilitation in patients with COPD. Our hypothesis was that patients across the spectrum of disability would benefit equally from Pulmonary Rehabilitation. The specific aim was to answer two questions (1) do patients with severe disability (MRC grade 5) benefit from standard pulmonary rehabilitation or are other strategies always necessary? (2) Do patients with mild disability (MRC grade 2) benefit from pulmonary rehabilitation i.e. should they be referred for PR?

Methods

Participants

We completed a retrospective analysis of the data collected from consecutive patients with Chronic Obstructive Pulmonary Disease attending outpatient Pulmonary Rehabilitation at our institution over a two-year period. Patients were predominantly referred by respiratory physicians and had a clinical diagnosis of COPD supported by spirometry with an FEV₁/FVC ratio of <70% and an FEV₁ < 80% predicted and an MRC scale of 2–5. Patients had been stable for the preceding three months. Patients were excluded from rehabilitation if their limitation to exercise was primarily locomotor or neurological in origin. For safety reasons patients with unstable angina, a myocardial infarction in the preceding three months, or aortic stenosis were also excluded.

Outcomes

All patients attended an assessment prior to commencing the course. The patients’ demographics were recorded, height and weight measured and spirometry performed. The primary outcome measure was the Incremental Shuttle Walk Test (ISWT) distance. Patients completed two ISW Ts, the first for familiarisation, with a 30 min rest between tests. Standardised instructions were given on how to complete the test. Patients reported their disability resulting from breathlessness using the five-point Medical Research Council (MRC) dyspnoea scale.

Intervention: pulmonary rehabilitation (PR)

The seven-week course combined physical training and self-management education and complies with international recommendations. It involved two hospital visits a week for 2 h (1 h of exercise and 1 h of education) and daily home training. The exercise component was predominantly endurance training. A daily walk was prescribed at 85% VO₂ peak determined from the peak performance on the ISWT. Patients were advised to increase their walking time by a few seconds each day and record their time in a daily diary (the speed remained constant). The diary and the individual’s walking speed were checked at each supervised session. Peripheral strength exercises were prescribed three times a week using free weights performed once at hospital and twice at home. The education sessions were multidisciplinary. A patient had completed the course after attending 14 sessions.

Statistical analysis

Data was analysed using SPSS v. 14.0. One way analysis of variance (ANOVA) was used to assess any difference in the baseline ISWT distance, FEV₁, or age per MRC grade. Post hoc analysis, with Bonferroni’s correction factor for multiple comparisons, was performed for the between group (MRC grade) differences for the same variables. Chi squared (with Cramer’s V measure for strength of association) was used to assess the differences in gender distribution between each MRC grade. Chi squared test was used to assess any differences between the number of dropouts for any MRC grade. Spearman’s correlation analysis was used to compare the baseline ISWT performance and the improvement in ISWT with PR. Two way ANOVA was used to assess the change in ISWT distance after pulmonary rehabilitation per MRC grade and per GOLD stage. Univariate analysis was used to assess the effect of ISWT, age, FEV₁, age or gender on change in ISWT after rehabilitation. ANCOVA was applied to test the effect of MRC grade on the change in ISWT, accounting for the difference in FEV₁, age, and gender between the MRC grades. A p value of <0.05 was taken as the level of statistical significance.

Results

Data from 450 consecutive patients over two years was collected and entered onto a database; 247 male, mean (SD) age 69.5 (8.9) yrs, FEV₁ 1.0 (0.5)L, FEV₁ 40.0 (17.5)%
predicted. The mean (SD) baseline ISWT performance was 167 (113)m. The MRC grade was recorded in 92% \((n = 415)\) of patients. The baseline demographics and distribution of the MRC dyspnoea scale grades are shown in **Table 1**.

Nearly a third of patients described their breathlessness as MRC grade 5 and 15% of patients recorded MRC grade 2. One patient described MRC grade 1 dyspnoea and has been excluded from further analysis. The baseline ISWT distance, for each MRC grade, is also shown in **Table 1**. There was no difference in mean age of the patients between the MRC grades; range 68.3–70.1 yrs \((\text{ANOVA } p = 0.550)\). There were more males in MRC grade 2 than in the other grades \((p = 0.008)\) (Table 1). The mean (SD) FEV\(_1\) (L) significantly decreased with increasing MRC grade, range 1.21 (0.49)L to 0.89 (0.44)L \((\text{ANOVA } p < 0.0005)\), but there was no difference in FEV\(_1\) percent predicted between MRC grades \((\text{ANOVA } p = 0.168)\). The mean ISWT distance decreased with increasing MRC dyspnoea grade \((\text{ANOVA } p < 0.0005)\) with no overlap between the 95% confidence intervals (Fig. 1). Post hoc analysis confirmed that the baseline ISWT distance was significantly different between each MRC grade \((p < 0.0005)\).

There was no significant difference in mean (SD) ISWT distance between the groups when stratified by spirometry according to the GOLD criteria\(^\text{13}\) although there was a trend for a decrease in distance walked with increasing GOLD stage; GOLD stage 2 (22.8%) \(-192 (135)\)m, stage 3 (40.4%) 165 (108)m and stage 4 (36.8%) 154 (96)m \(p = 0.081\) by ANOVA and there were no significant intergroup differences.

**Results of pulmonary rehabilitation**

395 patients (88%) completed the seven-week programme. The patients that dropped out of the programme had significantly worse lung function; mean (SD) FEV\(_1\) 0.88 (0.41)L vs 1.05 (0.50)L \((p = 0.025)\), and significantly lower baseline ISWT performance; 120 (108)m vs 173 (112)m \(p = 0.001\). There was no difference in the percentage of dropouts in each group: MRC grade 2: 15.6%, MRC grade 3: 11.6%, MRC grade 4: 8.0% and MRC grade 5: 16.4% \((p = 0.127)\).

The mean improvement in MRC grade was 0.7 \(<p < 0.0005\) with 54% of patients improving by at least one MRC grade. The mean (95% CI) improvement for the ISWT performance was 59 (54–65)m \((p < 0.0005)\). Over 58% of patients achieved at least a 48 m improvement in ISWT distance after pulmonary rehabilitation (the minimum clinically important difference (MCID) of the ISWT).\(^\text{15}\) There was no relationship between baseline ISWT distance and the absolute change in ISWT distance with rehabilitation, Spearman’s correlation coefficient \(-0.018\) \((p = 0.728)\) i.e. a lower baseline ISWT did not predict a lesser improvement in ISWT distance after rehabilitation and vice versa (Fig. 2).

The change in ISWT with pulmonary rehabilitation for the baseline MRC grade and the percentage of patients that achieved the MCID of the ISWT in each MRC grade are shown in **Table 2**. The mean (95% CI) improvement in ISWT performance with pulmonary rehabilitation for each MRC grade was highly statistically significant \((p < 0.0005)\) with moderate effect size and above the threshold of the minimum clinical important difference of the ISWT (48 m) see **Table 2**. There was no statistically significant difference in the mean improvement in ISWT across the MRC grades (Two way ANOVA \(p = 0.52)\). Post hoc analysis confirmed that there were no differences in the change in ISWT distance between any of the grades \((p = 1.0)\). The percentage change in ISWT distance after PR was significantly different between the MRC grades (Two way ANOVA <0.002) Table 2. When expressed as percentage change MRC grade 5 improved significantly more than MRC grade 2 \((p = 0.009)\), but there were no other intergrade differences. There was no significant difference between the grades in the percentage of patients achieving the MCID of 48 m ranging from 50 to 65% \((p = 0.131)\) see **Table 2**. Patients with MRC grade 2 breathlessness achieved similar improvements compared to the other grades and half of the very disabled patients (MRC grade 5) achieved an improvement greater than the MCID of the ISWT.

Univariate analysis showed that age \((-\text{ve } p = 0.021)\), gender (female \(-\text{ve } p = 0.044)\) and FEV\(_1\) \((-\text{ve } p = 0.029)\) influenced the change in ISWT with PR. The baseline ISWT distance had no effect on outcome \((p = 0.370)\). There were small but statistically significant differences between FEV\(_1\) and gender for the MRC grades, but no difference in age. An ANCOVA was performed and confirmed that there was no difference between the change in ISWT with rehabilitation between the MRC grades whilst allowing for the differences in age, FEV\(_1\) and gender.

There was no significant difference in the improvement in mean (95% CI) ISWT distance after pulmonary rehabilitation when stratifying the patients according to GOLD stage; stage 2 \(-56.3 (42.9–69.8)\)m, stage 3 \(-65.4 (55.1–75.6)\)m and stage 4 \(-57.1 (46.8–67.3)\)m \(p = 0.426\) by two way ANOVA.

There were 35/450 patients whose baseline MRC grade was not documented and were therefore excluded from further analysis. 33 of these patients completed pulmonary

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<tr>
<th>Table 1</th>
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<tr>
<td><strong>MRC grade</strong></td>
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<tr>
<td><strong>No. a (% of total)</strong></td>
</tr>
<tr>
<td>Gender (% male)</td>
</tr>
<tr>
<td>Age (yrs)</td>
</tr>
<tr>
<td>FEV(_1) (L)</td>
</tr>
<tr>
<td>FEV(_1) % predicted</td>
</tr>
<tr>
<td>ISWT (m)</td>
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All units described as mean (SD) unless stated.

\[ a \] Total \(n = 414\) – one patient with MRC grade 1 was excluded.
rehabilitation. The improvement in mean (95% CI) ISWT distance for these patients was similar 58 (43–72)m compared to the patients with complete data sets 59 (54–65)m (p = 0.913). There were no differences in age (p = 0.742), gender (p = 0.351) or lung function (p = 0.612) between the group with missing MRC data and the complete data group.

Discussion

This retrospective, observational study of a large cohort of patients with COPD demonstrates that the benefits of outpatient pulmonary rehabilitation apply equally to people with mild (MRC2) and severe (MRC5) disability. Patients with COPD were stratified for disability using the five-point MRC dyspnoea scale. All patients underwent our usual seven-week high intensity endurance training programme. The mean improvement in ISWT distance was similar and statistically significant for all MRC grades. The minimum clinically important difference for the ISWT has been shown to be 48 m and the mean improvement in ISWT was over this level for all the MRC grades.

This is the first time that patients in MRC grade 5 have shown similar benefits in exercise performance to patients in the lower (less disabled) grades. At least 50% of the MRC grade 5 patients gained clinically significant benefits in exercise performance and gained the largest percentage change in the ISWT distance after rehabilitation. The population of COPD patients in the current study were particularly disabled with a mean baseline ISWT of 167 m and a third classifying themselves as MRC grade 5.

Previous studies have suggested that patients who classify their breathlessness as MRC grade 5 to do less well with Pulmonary Rehabilitation. One study showed a mean improvement in ISWT distance of 88 m for grades 3 and 4 compared to only 10 m for MRC grade 5. However, the MRC 5 patients in this study had supervised training at home and the moderately breathless patients received their training at hospital. The intensity was set on an individual basis. A recent detailed prospective study discussed the effect of PR using a three point composite scale based on the MRC grade. The three groups were; 1 = mild (MRC grades 1 and 2), 2 = moderate (MRC grades 3 and 4), 3 = severe (MRC grade 5). Although group three (MRC grade 5) did less well with PR compared to groups two and one, 32.6 (74.8)m improvement in 6 min walk test distance compared to 68.0 (74.2)m and (54.7 45.0)m respectively p < 0.002, the numbers (n = 51) did not allow direct comparison between the five grades. Our data supports the data by Carone et al. who showed in a large cohort that patients with chronic respiratory failure gained similar benefit from PR than those not in respiratory failure.

Patients in the current study with severe disease did equally well with PR whether severe disease was defined by disability (MRC 5) or lung function (GOLD stage 4).

Our programme is individually prescribed at a high intensity (85% VO2 peak) from the outset. This appears to be an efficient use of a short duration programme for all MRC grades with nearly 60% of patients achieving the MCID in ISWT. Intensity can be used to describe the physiological training intensity or the number of training sessions per week. There are only a few studies directly comparing physiological training intensities. Overall these support higher training intensity rather than moderate.

However, there is some evidence that using a smaller muscle mass may delay ventilatory limitation and allow some patients to exercise for longer. Patients with MRC 5 breathlessness had a lower FEV1 percent predicted than the other grades and were therefore more likely to have a ventilatory limitation. However in this study the patients made similar improvements with high intensity endurance training irrespective of MRC grade. Complicated training regimens either require more staff or accommodate less patients. The training prescription in this study is simple, easy to apply and effective for the majority of patients.

Only 15% of patients in this cohort described mild disability (MRC grade 2). This group also made significant and clinically important improvements in ISWT distance; mean 66 m (p < 0.0005), 65% achieving more than 48 m. Patients with MRC grade 2 breathlessness also made significant improvements in the study by Garrod et al. Currently the selection criteria for PR are directed at patients with established disability rather than at preventing future disability. There is a well-described cycle of
decline for the exertional symptoms of COPD; patients avoid their symptoms by becoming less active leading to de-conditioning which in turn worsens the symptoms. It may be possible to interrupt this cycle early in patients with mild disability (MRC grade 2).

Previous work has shown that the MRC scale 3–5 is a good descriptor of exercise capacity measured by the ISWT.22 This study expands this to include MRC grade 2 and shows that the mean ISWT clearly increases with decreasing MRC grade (Fig. 1).

The minimum clinically important improvement of the ISWT is an absolute distance. The percentage change in ISWT that constitutes an important clinical difference is unknown. Fig. 2 demonstrates that the improvement in ISWT distance does not correlate with the baseline ISWT. Although the improvement in distance is absolute, the speed at which this is achieved is different i.e. the mean ISWT distance for MRC grade 2 was 280 m which at level 8 is a walking speed of 1.35 m/s in comparison to a mean ISWT distance of 90 m for MRC grade 5 which at level 3 is a walking speed of 0.84 m/s. This is likely to be why the magnitude of walking distance achieved with PR is not affected by the starting distance and why an absolute improvement for the minimum clinical important difference may be relevant across the spectrum of disability. The conclusions for this paper are therefore based on the absolute improvement in ISWT rather than the percentage change.

This data supports the knowledge that the degree of lung impairment (assessed by spirometry) correlates poorly with exercise capacity.23 There was no statistical difference between the baseline ISWT distance for patients when stratified by the GOLD criteria and there was no difference between the MRC grades in FEV\textsubscript{1} percent predicted. Patients classified by the GOLD criteria into stages 2–4 all improved equally and made clinically significant improvements in ISWT distance. Berry et al. examined the effects of rehabilitation comparing stage 1 to stages 2 and 3 disease stratified by the then current ATS recommendations.24 All three groups made improvements in 6 min walk distance and similar improvements in health status measured by the four domains of the Chronic Respiratory Questionnaire (CRQ). This and the current study support the inclusion of patients with mild disease to rehabilitation programmes whether that’s determined by spirometry (impairment) or MRC dyspnoea scale (disability).

<table>
<thead>
<tr>
<th>MRC grade</th>
<th>Change in ISWT (m)</th>
<th>Effect size</th>
<th>% Achieving</th>
<th>% Change in ISWT</th>
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<tbody>
<tr>
<td>2</td>
<td>66 (50–83)</td>
<td>0.61</td>
<td>65%</td>
<td>26.5 (20.0–33.1)%</td>
</tr>
<tr>
<td>3</td>
<td>63 (50–75)</td>
<td>0.65</td>
<td>58%</td>
<td>37.1 (28.0–46.3)%</td>
</tr>
<tr>
<td>4</td>
<td>59 (49–70)</td>
<td>0.58</td>
<td>63%</td>
<td>68.5 (39.8–97.0)%</td>
</tr>
<tr>
<td>5</td>
<td>54 (43–64)</td>
<td>0.62</td>
<td>50%</td>
<td>78.7 (59.8–97.7)%</td>
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The authors acknowledge the Pulmonary Rehabilitation team at Glenfield Hospital for the provision of Pulmonary Rehabilitation.

Conflict of interest statement
No competing interests.

References