# Female and male chronic obstructive pulmonary disease patients with severe dyspnea do not profit less from pulmonary rehabilitation

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**Abstract: Introduction.** Pulmonary rehabilitation (PR) is an established component of COPD management. The lack of exercise performance improvement (EPI) in severely dyspnoeic patients (Medical Research Council [MRC] score 5) has been questioned. The data on the gender impact on EPI after PR remain scarce. **Objectives.** The impact of dyspnea severity on PR outcomes was investigated and a question was raised whether severe dyspnea at training onset limits the profit from PR in COPD patients. Additionally, the impact of gender on PR results was analyzed. **Patients and methods.** 263 consecutive COPD patients underwent outpatient PR. Exercise capacity was assessed by the incremental shuttle walking test (SWT) and dyspnea with the MRC dyspnea score at inclusion (preSWT, preMRC) and at the end of PR (postSWT, postMRC). The data were analyzed in groups according to preMRC. The grade of improvement (ΔSWT, ΔSWT% and ΔMRC) was compared between groups. The influence of gender was analyzed in 138 men and 125 women. **Results.** A significant absolute increase in SWT and a decrease in MRC score were shown in all groups and for both sexes ($p < 0.05$) with no significant intergroup differences ($p > 0.05$). ΔSWT% rose significantly with preMRC score and exceeded the values of a clinically important increase (exception: group 2 with preMRC score 2). No significant differences between men and women were observed (ΔMRC: –0.6 vs. –0.7, ΔSWT: 66.7 vs. 56.0 m, ΔSWT%: 63.7 vs. 58.1%, $p > 0.05$, respectively). **Conclusions.** Patients with severe dyspnea did not benefit less from PR. Gender did not influence PR outcome in this study.

**Key words**: chronic obstructive pulmonary disease, dyspnea, exercise tolerance, Medical Research Council, pulmonary rehabilitation

## INTRODUCTION

The importance of pulmonary rehabilitation (PR) in the management of chronic obstructive pulmonary disease (COPD) has been proven in numerous papers. The impact of dyspnea severity on the results of PR in COPD has been continuously evaluated. The use of Medical Research Council (MRC) dyspnea scale as a stratification measure [1] allows to compare results between studies. The data regarding the impact of the MRC score on rehabilitation outcomes remain inconclusive and their usefulness as a predictor of PR improvement is under discussion.

Experts have stated that referral for rehabilitation of patients with COPD becomes appropriate when these patients become aware of their disability (e.g. usually grade 3 to 5 on the MRC dyspnea scale) [2-4]. However, in a paper from 1998, Wedzicha et al. [5] reported that exercise performance of severely dyspneic (MRC score 5) COPD patients receiving exercise did not improve. This observation was subsequently confirmed by Garrod et al. [6]. The Maugeri Study [7] shed new light on pulmonary rehabilitation showing equivalent effectiveness of an inpatient PR program in the more severe COPD patients with chronic respiratory failure (CRF) supporting PR prescription also in this group. Both patients with MRC score 1/2 [8] and 5 [7] seem to benefit from PR focused on the extrapulmonary features of COPD.

The data concerning gender impact on physical efficiency improvement after PR remain scarce and address mostly the Canadian population [9].

This study tested the hypothesis that the severity of dyspnea at the training onset or COPD patients' gender may affect the outcome of a 6-week course of pulmonary rehabilitation.

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**Table 1. Medical Research Council (MRC) Dyspnea score**

| MRC Dyspnea score | Definition – ticked by the patient in the questionnaire |
|---|---|
| 1 | I only get breathless with strenous exercise. |
| 2 | I get short of breath when hurrying on the level or walking up a slight hill. |
| 3 | I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking at my own pace on the level. |
| 4 | I stop for breath after walking about 100 yards (91 metres) or after a few minutes on the level. |
| 5 | I am too breathless to leave the house or I am breathless when dressing or undressing. |

**Table 2. Baseline physiological parameters and exercise tolerance (preSWT) in groups with mild, moderate and severe dyspnea according to MRC Dyspnea score at inclusion (preMRC) (n = 262)**

| Group | 2 (n = 40) | 3 (n = 62) | 4 (n = 81) | 5 (n = 79) | p |
|---|---|---|---|---|---|
| preMRC score | 2 | 3 | 4 | 5 | |
| Age (years) | 52–90<br>69.8 (8.7) | 48–81<br>68.8 (7.7) | 52–87<br>70.2 (8.0) | 49–88<br>70.0 (9.0) | NS |
| $FEV_1$ (l) | 1.19 (0.48) | 1.22 (0.58) | 0.99 (0.42) | 0.87 (0.38) | <0.05<br>2 vs. 5, 3 vs. 5 |
| FVC (l) | 2.34 (0.75) | 2.26 (0.76) | 2.06 (0.72) | 1.8 (0.69) | <0.05<br>2 vs. 5, 3 vs. 5 |
| $FEV_1$/FVC (%) | 51.6 (16.2) | 55.2 (18.8) | 49.3 (15.0) | 50.8 (19.1) | NS |
| preSWT (m) | 283.3 (108.4) | 208.7 (84.1) | 149.3 (99.2) | 102.7 (75.2) | <0.05<br>2 vs. 4, 2 vs. 5, 3 vs. 4, 3 vs. 5, 4 vs. 5 |

Values are mean (SD).

Abbreviations: $FEV_1$ – forced expiratory volume in one second, FVC – forced vital capacity, NS – not significant, preSWT – shuttle walking distance at inclusion, SD – standard deviation

## PATIENTS AND METHODS

In this prospective observational study 263 consecutive COPD-patients in stable clinical condition receiving optimal medical treatment were scheduled for a 6-week course of pulmonary rehabilitation. COPD was diagnosed according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria. Spirometry measurements were performed (Vitalograph Pneumotrac, UK) according to the current guidelines [10]. Exclusion criteria were as follows: current significant cardiac complaints and/or cerebrovascular symptoms making training impossible, unsafe, or life-threatening, musculoskeletal abnormalities severely limiting mobility or malignancy. Supervised sessions were held twice a week in an outpatient setting at the Department of Cardiac and Pulmonary Rehabilitation in Glenfield Hospital, Leicester, and consisted of middle-intensity exercises for upper and lower limbs and interactive lectures on COPD. Training intensity was set at 60% of the peak exercise capacity assesed by the incremental Shuttle Walking Test (SWT) at inclusion. Rest periods and self-limitation of exercise intensity by dyspnea were used if needed. Pursed lips breathing, breathing in forward leaning position, active expiration, inspiratory muscle training and diaphragmatic breathing were part of warm-up and cool-down. Patients were strongly encouraged to exercise at home without supervision.

The outcome measures were exercise capacity assessed by the incremental SWT and dyspnea reflected by the MRC dyspnea score (Table 1). The patients performed testing at inclusion (preSWT, preMRC) and at the end of the PR program (postSWT, postMRC). The better of 2 reproducible SWT at inclusion was used to avoid learning curve effects. In case of an exacerbation during the PR course, patients completed the number of sessions before undergoing the post tests.

The patients data were stratified in five groups according to their MRC dyspnea score at inclusion (preMRC): group 1 – preMRC score 1 (1 patient), group 2 – preMRC score 2 (40), group 3 – preMRC score 3 (62), group 4 – preMRC score 4 (81) and group 5 – preMRC score 5 (79 patients) (Table 2). Treatment effect sizes were calculated by subtracting the measurements at PR onset from the measurements after PR (absolute values in natural units: $\Delta SWT$ = postSWT – preSWT, and $\Delta MRC$ = postMRC – preMRC). The differences in SWT after PR were also expressed as percentages of the inclusion value ($\Delta SWT\%$ = $\Delta SWT$/preSWT). The results were compared between groups. Group 1 was excluded from analysis due to scanty data.

**Table 3. Baseline physiological parameters, exercise tolerance (preSWT) and dyspnea severity (preMRC) in groups according to patients' gender (n = 262)**

| Group | Women (n = 125) | Men (n = 138) | p |
|---|---|---|---|
| Age (years) | 48–88<br>69.6 (8.2) | 50–90<br>69.8 (8.4) | NS |
| $FEV_1$ (l) | 0.88 (0.4) | 1.14 (0.52) | <0.005 |
| FVC (l) | 1.67 (0.57) | 2.32 (0.75) | <0.005 |
| $FEV_1$/FVC (%) | 53.4 (16.0) | 50.2 (18.0) | NS |
| preSWT (m) | 143.2 (94.2) | 186.8 (117.9) | <0.005 |
| preMRC score | 3.9 (1.0) | 3.6 (1.1) | <0.05 |

Values are mean (SD).
Abbreviations – see Table 2

**Table 4. Pulmonary rehabilitation effects for groups with mild, moderate and severe dyspnoea according to MRC score at inclusion (preMRC) for measure of exercise performance assessedby shuttle distance (SWT) and dyspnoea mirrored in MRC Dyspnoea score (postMRC) (n = 262)**

| Group<br>preMRC score | 2 (n = 40)<br>2 | 3 (n = 62)<br>3 | 4 (n = 81)<br>4 | 5 (n = 79)<br>5 | p |
|---|---|---|---|---|---|
| postMRC score | 2.3 (0.8) | 2.6 (0.9) | 3.2 (1.0) | 3.7 (1.0) | <0.005<br>2 vs. 4, 2 vs. 5, 3 vs. 4, 3 vs. 5 |
| ΔMRC | 0.3 (0.8) | –0.4 (0.9) | –0.8 (1.0) | –1.3 (1.0) | <0.01<br>2 vs. 3, 2 vs. 4, 2 vs. 5, 3 vs. 5 |
| postSWT (m) | 348.2 (119.3) | 274.2 (106.0) | 208.4 (101.9) | 170.4 (97.1) | <0.005<br>2 vs. 4, 2 vs. 5, 3 vs. 4, 3 vs. 5 |
| ΔSWT (m) | 59.2 (64.2) | 65.5 (59.5) | 59.1 (53.3) | 64.4 (60.0) | NS |
| Δ%SWT (%) | 23.9 (25.1) | 36.8 (37.1) | 74.5 (161.4) | 86.7 (97.4) | <0.02<br>2 vs. 4, 2 vs. 5, 3 vs.5 |

Values are mean (SD).
Abbreviations: ΔMRC – absolute difference between postMRC and preMRC, ΔSWT – absolute difference between postSWT and preSWT in natural units, Δ%SWT – rate of difference between ΔSWT and preSWT in percent, others – see Table 2

The influence of patients' gender on the rehabilitation results (ΔSWT, ΔSWT% and ΔMRC) was analyzed in 138 men and 125 women (Table 3).

The distributions of variables were analyzed by means of the Shapiro-Wilk test. Student t-test or One Way Analysis of Variance (ANOVA) with post-hoc Tukey tests were used for indexes with normal distribution, depending on the group size. Mann-Whitney U test or a Kruskal Wallis ANOVA rang test were performed for indexes of nonnormal distribution. The threshold for statistical significance was set at 0.05 for all analyses. For all tests, STATISTICA 7.1 (StatSoft) was used.

## RESULTS

A significant improvement understood as an increase in the incremental SWT and a decrease in the MRC-score were shown in all groups and for both sexes (preSWT vs. postSWT and preMRC vs. postMRC, $p < 0.05$). ΔSWT did not differ statistically between all groups ($p > 0.05$), however, the percentage improvement (ΔSWT%) did not reach statistical significance only between the neighbouring groups (2 vs. 3, 3 vs. 4, 4 vs. 5, $p > 0.05$) and its value rose with preMRC score. The average distance of 64.4-metre ΔSWT for group 5 did not differ significantly from the results obtained in the other groups. However, it was equal to a 86.7% increment of the baseline (preSWT) value (Table 4).

The analysis of PR results depending on the patient's gender did not show significant differences between groups (men vs. women: ΔMRC: –0.6 vs. –0.7, ΔSWT: 66.7 vs. 56.0 m, ΔSWT%: 63.7 vs. 58.1%, $p > 0.05$), but PR led to a significant improvement in exercise capacity and dyspnea in each group (Table 5).

**Table 5. Pulmonary rehabilitation effects for groups according to gender for measure of exercise performance assessedby shuttle walking test (SWT) and dyspnea mirrored in MRC dyspnea score (postMRC) (n = 262)**

| Group | Women (n = 125) | Men (n = 138) | p |
|---|---|---|---|
| postMRC score | 3.2 (1.0) | 3.0 (1.1) | NS |
| ΔMRC | –0.7 (0.9) | –0.6 (1.2) | NS |
| postSWT (m) | 200.2 (101.7) | 256.1 (129.3) | <0.005 |
| ΔSWT (m) | 56.0 (50.7) | 66.7 (60.5) | NS |
| Δ%SWT (%) | 58.1 (78.6) | 63.7 (121.5) | NS |

Values are mean (SD).
Abbreviations – see Tables 2 and 4

## DISCUSSION

Until 2008 there were no studies addressing the value of a minimal clinically important difference (MCID) for the incremental SWT. Recently, the MCID (improvement felt as being "slightly better") for the incremental SWT was found at 47.5 m for a subject [11]. Mean ΔSWT values obtained in each group in this paper were higher, although they did not exceed 78.7 m – the level of increase declared as feeling "better".

The MCID for the 6-minute walking distance (6MWD), a test comparable with SWT [12], was estimated at 54–80 meters (86 meters for an individual patient) [4,13]. This compartment contains the mean ΔSWT values obtained in each group in this paper.

In groups 3 to 5, the increase in walking distance exceeded 25% – the value suggested by Troosters et al. [14] to distinguish responders to PR in exercise capacity from nonresponders. The British Thoracic Society (BTS) reports changes in incremental SWT at the level of 30–55% as resulting from PR [4]. The values obtained in group 4 and 5 were even higher (Figure).

A reduction of muscle mass and strength, together with its metabolic quality impairment are what is seen as "skeletal muscle deconditioning" – a component of the COPD course. It is arguable whether it results from extreme, long-term inactivity, a systemic myopatic effect of COPD or a combination of both, but certainly PR addresses them and enables muscle function normalization [15].

Despite patients with MRC score 2 being reported to have a higher prevalence of muscle mass depletion [8], a session of PR led to a similar absolute improvement in SWT in each group. This made a better percentage result in more dyspneic patients due to a shorter SWT distance at enrollment.

The level of motivation could be suggested as one of possible explanations – a difference of a few meters more would be easier to be notice in more limited patients encouraging them to participate even more intensively [16].

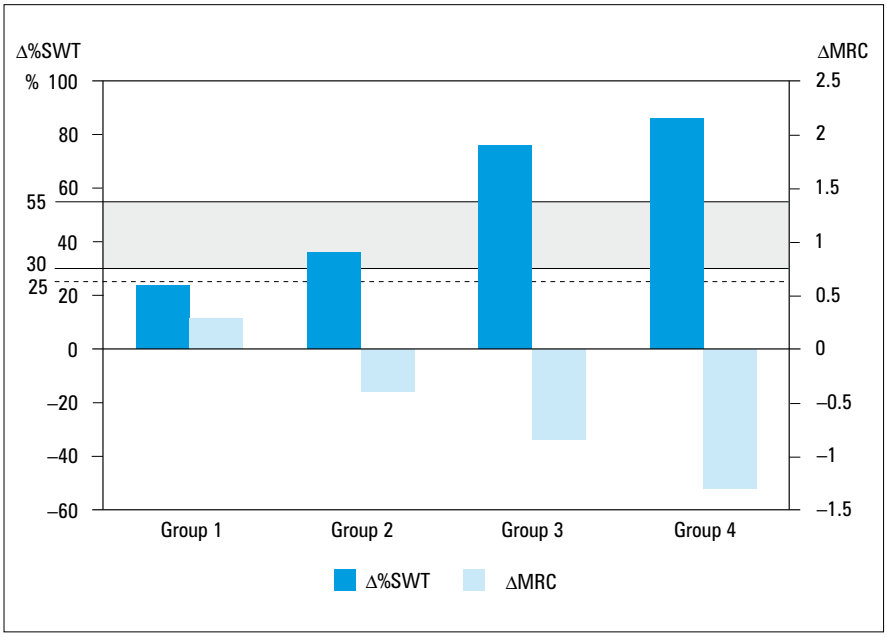


**Fig.** Pulmonary rehabilitation effects for groups with mild, moderate and severe dyspnea according to MRC score at inclusion for measure of exercise performance assessed by shuttle distance (SWT) expressed as percentages of the inclusion value (ΔSWT%) and dyspnea reduction mirrored in MRC dyspnea score (ΔMRC) (n = 262). ΔSWT%: p <0,02 for 2 vs. 4, 2 vs. 5, 3 vs. 5; ΔMRC: p <0,01 for 2 vs. 3, 2 vs. 4, 2 vs. 5, 3 vs. 5. Values are mean. Abbreviations: ΔMRC – absolute difference between postMRC and preMRC, Δ%SWT – rate of difference between ΔSWT and preSWT in percent

A 86.7% increment in SWT distance together with reduced dyspnea (mean ΔMRC of – 1.3 for group 5) may enable severely dyspneic COPD patients to perform activities shown as most important to them including household maintenance, driving or even walking itself [16]. The reason why these findings are not in accordance with the results reported by Wedzicha et al. [5] may be a wider MRC score 5 definition including patients able to participate in an outpatient PR program in this study.

The multidisciplinary PR team addressed other components of COPD, that is mental health and social life. Depression and isolation are more likely to appear in severely dyspneic patients with limited mobility. 6MWD has been shown to correlate directly with the quality of life [17]. Timetabled meetings outside the house with people with similar problems might have worked as additional motivation resulting in improvement similar to less ill patients.

Additionally, patients with lower functional exercise capacity measured with 6MWD were shown to be more likely to experience acute exacerbation of COPD resulting in the reduction in Health Related Quality of Life [18].

The influence of comorbidities (i.e. heart failure) or treatment options (i.e. oral steroids) were not analyzed in the groups. However, systemic steroids administration and their myopathic side effects would be rather expected in more dyspnoeic patients (all patients were on optimal medical treatment) in whom still no limitation of answer to PR was observed.

The importance of inspiratory muscle training and breathing techniques remain questionable.

Gender was not associated with significant differences in PR outcomes in the present study. Both female and male COPD patients seem to benefit to the same extent from a PR program in terms of exercise capacity improvement and dyspnea reduction which confirms earlier findings in the Canadian population [9].

6MWD and MRC score in men and MRC in women were shown to have the highest independent association with quality of life measured by the Saint George's Respiratory Questionnaire in the Spanish COPD population [17]. While no indications occured to develop separate exercise training protocols for each gender, women should be strongly encouraged to start PR on an earlier stage.

To conclude, pulmonary rehabilitation results in a significant improvement in physical efficiency and dyspnea reduction. The improvement measured in natural units is independent of dyspnea severity at program onset, although the rate of efficiency improvement (percent of improvement) increases with higher MRC score at enrolment, which stays in contrary to the previous findings of MRC score 5 patients who had no benefits from PR.

Gender did not influence PR outcome.

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