

Age does not hamper the response to pulmonary rehabilitation of COPD patients

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Abstract

Background: pulmonary rehabilitation (PR) improves health status and exercise tolerance, but not respiratory function in patients with chronic obstructive pulmonary disease (COPD). Our objective was to identify predictors of improvement in the 6-min walked distance (6'WD) in elderly COPD patients after PR.

Methods: this was a prospective observational study performed in an ambulatory rehabilitation setting. We enrolled 74 patients aged 65–83 years (mean: 74.2, SD: 4.4) with stable COPD in GOLD stage 3–4. About half (45.6%) of them had a basal O₂ saturation of 90% or less. After a baseline multi-dimensional assessment, patients underwent a 20-session rehabilitation cycle including training of the upper and lower extremities, and respiratory exercises, along with education sessions. The difference between final and basal 6'WD was expressed as a per cent of the basal value (6'WD gain). Patients were divided into two groups according to whether the 6'WD gain was above or under the 75th percentile, corresponding to 33% gain.

Results: patients whose 6'WD improved more had lower baseline forced expiratory volume in the first second (FEV₁)/forced vital capacity (FVC) (46.0 versus 52.2%, $P = 0.03$) and baseline 6'WD, both as an absolute value (329.5 versus 408.9 m, $P = 0.01$) and as a per cent of the predicted (71.1 versus 93.5%, $P = 0.002$). After correction for potential confounders, baseline 6'WD was the only variable associated with the outcome (OR for 5% increments: 0.79; 95% CI 0.65–0.95).

Conclusions: among elderly patients with COPD, a comprehensive rehabilitation programme can significantly improve the 6'WD even in the presence of chronic hypoxemia. The most physically impaired patients achieve the greatest benefit from rehabilitation, but we could not develop a model accurately predicting the response to rehabilitation.

Keywords: pulmonary rehabilitation, aged, chronic obstructive pulmonary disease

Introduction

Pulmonary rehabilitation (PR) has been shown to improve health status and exercise tolerance in patients with chronic obstructive pulmonary disease (COPD) [1, 2]. These effects seem to be independent of age [3, 4], and even patients older than 80 years can benefit from a PR programme [5]. PR improved health status and performance indexes in an older population after an acute exacerbation of COPD [6], as well as in patients on oxygen therapy [7]. While the evidence on positive effects of PR in elderly COPD patients is convincing, data on the characteristics of patients who are more likely to benefit from PR are conflicting. Neither demographic nor respiratory function parameters seem to predict the effects of rehabilitation on dyspnoea, anxiety and depression [8, 9]. Garrod *et al.* could not find any predictor of improvement in health status or physical performance, and only severe dyspnoea was associated with poorer

outcome [10]. On the other hand, in a sample of 28 patients with COPD with a mean age of 70 years undergoing a simple home rehabilitation, health status improvement was inversely related to age and baseline forced expiratory volume in the first second (FEV₁), and directly to the residual volume/total lung capacity ratio (RV/TLC), body weight and cognitive performance [11]. Finally, age was found to be inversely related to the improvement in the maximal consumption of oxygen induced by PR [12].

We designed this study to verify whether the response to rehabilitation can be predicted on the basis of easily measurable baseline variables.

Methods

We recruited patients attending a day hospital facility specialised in pulmonary diseases. The study was based upon routine diagnostic and rehabilitation procedures. The

study was approved by the local Ethical Committee, and patients gave their informed consent to participate in the study.

Patients

We studied 83 patients diagnosed with COPD according to American Thoracic Society guidelines, all in stable clinical and functional conditions [13]. Criteria of exclusion were:

- Age <65 years.
- COPD severity (GOLD stage) <3.
- Co-morbid diseases able to limit exercise capacity: severe conditions (neurological deficit or anaemia) or minor problems potentially affecting the adaptation to exercise (rhinitis).
- Cognitive decline that would impair the quality of spirometry or adherence to rehabilitation [14, 15].

All patients underwent baseline assessment, but 10% did not complete the rehabilitation programme and were excluded. The final sample size was 74.

Assessment

Lung volumes (FEV₁, forced vital capacity: FVC, RV, TLC) were measured before and after administration of salbutamol 200 µg using a Jaeger Master Screen-PFT system (Höchberg, Germany), using the He-dilution technique for the measurement of RV. Predicted normal values were those by the European Community for Coal and Steel [16].

Maximal inspiratory mouth pressure (MIP) from RV and maximum expiratory mouth pressure (MEP) from TLC were measured with a standard mouthpiece and a transducer (Spirovis-Cosmed, Pavona di Albano, Rome, Italy).

Arterial blood gases and pH were measured by an ABL equipment (Radiometer, Copenhagen, Denmark) while the patient was at rest and had been breathing room air for at least an hour. The 6-min walking test (6'WT) was performed according to American Thoracic Society recommendations [17] to measure the 6-min walked distance (6'WD), which was expressed also as per cent of the predicted [18], and the time with a transcutaneous oxygen saturation (ScO₂) <90%. Briefly, patients were instructed to walk back and forth along a 30-m hospital corridor to cover as much ground as they could during the 6'WD, without running. An assistant gave encouragement every minute. Patients were allowed to stop and rest, but they were encouraged to resume walking as soon as possible. No supplemental oxygen was given during the test. The ScO₂ and the heart rate were continuously recorded throughout the test using a model 9500 finger pulse oximeter (Nonin Medical, Plymouth MN, USA).

The assessment was performed both at baseline (pre-rehabilitation) and after the completion (post-rehabilitation) of the PR programme.

PR programme

Patients attended the outpatient rehabilitation sessions for 1.5 h, 5 times a week for 4 weeks. This was the first phase of a PR programme, which was continued at home twice a week for a further 6 weeks by a respiratory physical therapist. We measured the effect of rehabilitation after the completion of the 4-week ambulatory training. The target duration for each exercise was 20 min, with a warm-up and a cool-down 3-min period. The initial duration of each exercise varied depending upon the individual response.

- (1) Upper arm exercises started with a series of low-intensity contractions of isolate muscle groups to prevent the onset or worsening of dyspnoea. After a time, that changed according to the individual response to the training, lifting weights in the 1–5-kg range and stretching elastic bands were added to the baseline exercise.
- (2) Exercise training consisted initially of unloaded cycling using a Bikerace HC600 (Technogym, Gambettola, Forlì, Italy). As the patient became more accustomed to the exercise, the therapist adjusted the intensity of the training by imposing a load of 20 W and, then, increased the load up to 70% of the W_{max} measured at baseline or, if the patient could not reach this goal, up to the maximal tolerated load. For patients who did not tolerate loaded cycling, the length of the unloaded cycling session was increased to 30 min.
- (3) Inspiratory muscle training: the threshold-loading method was started at very low intensity, i.e. at a load corresponding to the generation of 10% of the MIP. The load was progressively increased to achieve 60% of the MIP or, for patients unable to reach this goal, 30% of the MIP, which corresponds to the minimal load proved to have a training effect [19].

The PR programme also included sessions of general education for groups of 2–4 patients aimed at improving the patient's knowledge of the disease and self-management strategies.

Analytic approach

Our conceptual outcome was the response to the rehabilitation therapy. We chose the 6'WD to measure the outcome because its changes are correlated with changes in personal abilities, dyspnoea and health status [20–22], more than any other walk test [23]. Operationally, we considered the 6'WD at the end of intervention relative to the 6'WD at baseline, computed as $[(6'WD-Post) - (6'WD-Pre)] / (6'WD-Pre)$. We evaluated the presence of a relationship between this outcome and continuous demographic and clinical variables using scatterplots and calculating Pearson's rho; then we used a linear regression model to identify variables independently associated with the outcome, using diagnostic plots of the residual to check model adequacy.

To express in a more clinically meaningful way the association between patient's characteristics and the changes in the WD, we dichotomised our outcome using the 75th percentile of gain (33% relative to the baseline) as a cut-off value. We used means and contingency tables to compare the demographic and clinical characteristics of the two groups. Student's *t*-test and Pearson's chi-square were used to calculate the *P* values relative to the differences in means and proportions, respectively. We used continuity correction to calculate the *P*-value in tables with cell counts <5, while we used the Wilcoxon rank test with continuous variables that were not normally distributed.

We used logistic regression to obtain a summary description of the relationship between individual characteristics and 6'WD gain. Variable selection was based on clinical relevance and on the association found with the univariable analysis. We used the log likelihood to identify the best-fitting model while minimising the number of covariates, and the Hosmer and Lemeshow goodness-of-fit test to assess the final goodness of fit.

All analyses were performed using SAS V9.0 (SAS Inc, Cary NC, USA).

Results

We studied 74 persons (mean age 74.2 years, SD: 4.4, range: 65–83). Most of them were men (85.1%) and 47.3% had a basal oxygen saturation of 90% or less. Nineteen patients had oxygen saturation below 90 or 80% for most of the time of the 6'WT.

On average, the 6'WD increased by 23.2% (SD: 26%, range: –13.3 to 140%), corresponding to an absolute average increase of 76.2 m (SD: 65.0, range: –45 to 270 m). Among the demographic and clinical characteristics considered, only body mass index (BMI), FEV1, FVC, MIP, and baseline performance showed a relationship with change in 6'WD. A multi-variable linear regression, in which all the above-mentioned variables were included, showed an average increase of 0.6% of the follow-up 6'WD relative to the baseline value for each 1% increment of the 6'WD at baseline.

We found no difference in the demographic and clinical characteristics of people with low and high 6'WD gain (Table 1). People in the high-gain group had a lower BMI (24.1 kg/m² versus 27.0 kg/m², *P* = 0.01) and a lower, albeit non-statistically significant, prevalence of diabetes mellitus (10.5 versus 25.5%, *P* = 0.173).

Table 2 compares functional variables at baseline of high and low 6'WD-gain patients. People with high 6'WD gain had a lower FEV1 per cent predicted (35.6 versus 42.6%, *P* = 0.024), MIP (50.0 versus 60.3 mmHg, *P* = 0.034). The 6'WD at baseline was lower in the 6'WD high-gain people either as absolute value (329.5 versus 408.9 m, *P* = 0.012) or as per cent of predicted (71.1 versus 93.5%, *P* = 0.002). We found no differences between the two groups in baseline PaO₂ or PaCO₂, FVC, RV/TLC ratio, MEP and proportion of participants with partially reversible obstruction.

Table 1. Demographic and clinical characteristics of participants with and without increase in the 6'WD \geq 75th percentile

	Gain in 6'WD \geq 75th percentile		<i>P</i>
	No (<i>n</i> = 55)	Yes (<i>n</i> = 19)	
Age [mean (SD)]	74.4 (4.4)	73.5 (4.3)	0.420
Gender (male), %	85.5	84.2	0.999
Body mass index [mean (SD)]	27.0 (3.5)	24.1 (4.3)	0.013
Charlson's co-morbidity index [mean (SD)]	2.3 (1.2)	2.3 (1.2)	0.886
Heart failure, %	3.6	0.0	0.982
Ischemic heart disease, %	9.1	5.3	0.968
Diabetes mellitus, %	25.5	10.5	0.299

Table 2. Baseline functional characteristics of participants with and without increase in the 6'WD \geq 75th percentile

	6'WD \geq 75th percentile		<i>P</i>
	No (<i>n</i> = 55)	Yes (<i>n</i> = 19)	
FVC [% predicted, mean (SD)]	62.2 (14.9)	59.7 (16.0)	0.568
FEV1 [% predicted, mean (SD)]	42.6 (14.2)	35.6 (10.1)	0.024
RV/TLC (%)	86.0 (38.3)	73.7 (31.7)	0.116
PaO ₂ [mmHg, mean (SD)]	70.3 (7.4)	69.7 (8.7)	0.788
PaCO ₂ [mmHg, mean (SD)]	42.1 (4.3)	41.6 (5.3)	0.735
Maximal inspiratory pressure [mmHg, mean (SD)]	60.3 (19.0)	50.0 (16.7)	0.034
Maximal expiratory pressure [mmHg, mean (SD)]	70.8 (23.0)	62.5 (23.9)	0.202
Participants with partially reversible obstruction (%)	36.4	26.3	0.425
Time with SO ₂ < 90% during the 6'WT (%)	44.0 (39.9)	31.3 (40.0)	0.359
6'WD [mt, mean (SD)]	408.9 (77.7)	329.5 (115.3)	0.010
6'WD [% predicted, mean (SD)]	93.5 (18.2)	71.1 (26.3)	0.002

FEV1 and the 6'WD gain, both expressed as continuous variables, were only weakly correlated (Appendix 1, upper panel; available on the journal's website at <http://www.ageing.oxfordjournals.org/>), with a Pearson's rho of –0.14 (*P* = 0.217), as were variation of FEV1 over the PR programme and 6'WD gain (rho: –0.09, *P* = 0.526). The results were similar for the relationship MIP–6'WD gain (rho: –0.09, *P* = 0.458) (Appendix 1, lower panel; available on the journal's website at <http://www.ageing.oxfordjournals.org/>), while there was a strong linear relationship between baseline 6'WD and 6'WD gain (rho: –0.26; *P* = 0.02) (Appendix 2; available on the journal's website at <http://www.ageing.oxfordjournals.org/>).

In Table 3, panel A, are shown the results of a logistic regression model containing age, gender, BMI, FEV1, MIP

Table 3. Multi-variable logistic regression modelling the probability of having a gain in the 6'WD \geq 75th percentile

Panel A: full model (-2 log likelihood: 60.922; Hosmer and Lemeshow test: $P = 0.225$) ^a		
	OR	95(%) CI
Age	1.02	0.88–1.19
Gender (male versus female)	0.29	0.03–3.24
BMI	0.89	0.73–1.07
Diabetes mellitus	0.17	0.02–1.44
FEV1 per cent of predicted (5% increments)	0.94	0.66–1.33
Maximal inspiratory pressure	0.99	0.94–1.04
6'WD per cent of predicted (5% increments)	0.79	0.65–0.95
Panel B: reduced model (-2 log likelihood: 62.667; Hosmer and Lemeshow test: $P = 0.195$) ^a		
	OR	95(%) CI
Gender (male versus female)	0.31	0.05–1.93
BMI	0.89	0.74–1.07
Diabetes mellitus	0.19	0.02–1.54
6'WD per cent of predicted (5% increments)	0.76	0.64–0.91

^a A high P -value of the Hosmer and Lemeshow goodness-of-fit test is consistent with the logistic model adequately fitting the data.

and baseline 6'WD. To obtain clinically meaningful odds ratios, both FEV1 and 6'WD were rescaled using a factor of 5. In this model, only BMI and baseline 6'WD were associated with the outcome. A 'reduced' model was also produced to predict the outcome using fewer variables (Table 3, panel B). The global fitting of the two models was similar, as expressed by both the -2 log likelihood (60.922 for the full model and 62.667 for the reduced model) and the Hosmer and Lemeshow goodness of fit ($P = 0.225$ and $P = 0.195$, respectively). Of the variables taken into account, only the baseline performance at the 6'WT was associated with the outcome (OR for increments of 5% of predicted: 0.79; 95% CI 0.65–0.95).

Discussion

We found that neither demographic nor respiratory function indexes were related to the outcome of PR. Thus, older COPD patients should not be excluded from rehabilitation because of age or decreased physical performance.

The finding of an inverse relationship between baseline performance and improvement is in agreement with results by ZuWallack *et al.* obtained using the 12-min walked distance [24]. The fact that 50% of our patients achieved a 6'WD gain greater than 54 m, which is the threshold for the feeling of improved health status [20], confirms that older COPD patients are good candidates for PR. Nonetheless, our results might be due, at least in part, to regression towards the mean. The correlation between the difference in the 6'WD and its baseline value, however, is low (ρ 0.26) compared to what would be expected in cases when regression to the mean plays a major role.

The lack of association between indexes of pulmonary function and gain in the 6'WD extends to an older

population the findings of previous studies on younger populations [2]. We also found that arterial blood gas levels were not significant predictors of the rehabilitation response, suggesting that arterial hypoxemia should not be a barrier to PR. This adds further evidence to the assumption that patients with severe COPD should be considered good candidates for PR [9, 25–27]. Such a conclusion is clinically important because hypoxemic patients are severely limited in personal independence and, then, according to the present findings, are expected to improve the most with rehabilitation [28].

O'Donnell *et al.* found that a PR programme similar to ours improved both respiratory and peripheral muscle function of patients with COPD, but such an improvement was unrelated to the gain in the exercise capacity [29]. Inter-individual variability in the ventilatory response to exercise is a further determinant of the response to rehabilitation [29]. These data suggest that the final effect of PR is the result of complex physiopathological responses to exercise and, as such, is difficult to predict.

The same 6'WD gain can have a very different clinical meaning depending upon the baseline performance: a 70-m gain likely is a negligible or a noticeable effect of the rehabilitation depending upon whether baseline 6'WD was 420 or 100 m. Indeed, there is a strong association between the 6'WD and the level of independence in basic and instrumental activities of daily living (ADL)s. A comprehensive 12-week outpatient PR programme has been shown to increase both 6'WD and ADL score [22]. Accordingly, a seemingly small gain in 6'WD could be a marker of a dramatic improvement in personal independence. Thus, a severe limitation in physical capabilities should not be a reason for excluding elderly COPD patients from a PR

programme; rather these patients may achieve the greatest benefit.

This study has some limitations. First, our PR programme was shorter than recommended [30, 31]. It is possible that the effect of some measures associated with improvement in the 6'WD gain do not appear until after 4 weeks of rehabilitation in this study. However, a patient's early response to PR has been shown to be predictive of their final rehabilitation outcome [32]. Furthermore, we focussed on the induced change in physical performance and not on changes in life style, which would have required a much longer PR programme [33]. Second, our outcome measure, which was based on the distribution of the gain in the 6'WD in this sample, could limit the generalisability of our study. However, our findings are similar to others reported in the literature, and therefore the use of this sample-based outcome measure is not likely to have had a sizeable effect on the results. Third, we did not measure a number of characteristics, such as free fat mass or peripheral muscle strength that may be important in a patient's response to PR. Finally, because patients were required to attend rehabilitation sessions outside their home 5 times a week for 4 weeks, this study excluded homebound patients and selected patients who were willing to comply for such an intense programme.

In conclusion, the present study shows that elderly COPD patients with severely impaired exercise capacity can benefit from PR and, thus, should not be excluded from PR referrals. However, further research is needed to improve the identification of patients most likely to benefit from rehabilitation. Research is also needed to verify whether the addition of occupational therapy or non-conventional forms of rehabilitation, e.g. cognitive enhancement, to PR can be of further benefit in elderly COPD patients.

Key points

- Elderly people with COPD can benefit from PR even when significant hypoxemia is present.
- Those with the worst performance at baseline are most likely to improve after rehabilitation.

Conflicts of interest

None

Supplementary data

Supplementary data for this article are available online at <http://ageing.oxfordjournals.org>.

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