Effects of an Exercise Intervention in Frail Older Patients with Chronic Obstructive Pulmonary Disease Hospitalized due to an Exacerbation: A Randomized Controlled Trial

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ORIGINAL RESEARCH

Effects of an Exercise Intervention in Frail Older Patients with Chronic Obstructive Pulmonary Disease Hospitalized due to an Exacerbation: A Randomized Controlled Trial

Irene Torres-Sánchez, Marie Carmen Valenza, Irene Cabrera-Martos, Isabel López-Torres, Ángela Benítez-Feliponi, and Alicia Conde-Valero

Department of Physical Therapy, School of Health Sciences, University of Granada, Granada, Spain; Pulmonary Medicine Service, San Cecilio University Hospital, Granada, Andalusian Health Service, Spain

ABSTRACT

The objective of this study was to determine whether an exercise intervention using a pedal exerciser is able to reduce disability in frail older patients with chronic obstructive pulmonary disease (COPD) during hospitalization due to an acute exacerbation.

This study was a randomized, single-blind clinical trial. Fifty-eight frail older patients admitted to hospital due to an acute exacerbation of COPD (AECOPD) were included in this study. All patients received standard medical and pharmacological care. Patients assigned to the intervention group also received an exercise intervention. The main outcome measures were balance, muscle strength, and exercise capacity. Significant between-group differences were found in muscle strength (p = 0.028) and balance (p = 0.013) after the intervention. All the variables improved significantly (p < 0.05) in the exercise intervention group. In the intervention group, the mean difference in muscle strength between baseline and discharge was 10.47 N. Balance also improved, showing a mean difference of 7.56 seconds on the right leg and 6.57 seconds on the left leg. Exercise capacity improved as well, with a difference of 4.97 stands between baseline and discharge. All the variables showed impairment in the control group.

In conclusion, an exercise intervention using a pedal exerciser during the hospital stay of frail elderly patients with an AECOPD improves muscle strength, balance, and exercise capacity.

List of abbreviations

ATS American Thoracic Society
COPD Chronic obstructive pulmonary disease
FEV1 Forced expiratory volume in the first second
FVC Forced vital capacity
GOLD Global initiative for chronic Obstructive Lung Disease
OLS one leg stance
SO2 resting oxygen saturation
STS sit-to-stand

Introduction

Elderly patients with chronic obstructive pulmonary disease (COPD) generally have a larger burden of disease and higher potential morbidity and mortality than the general population despite the considerable progress made in pharmacotherapy and therapeutic management (1). Over half of patients with COPD (57.8%) are frail (2). Frailty is an emerging concept in clinical medicine and it has been demonstrated that frail patients are predisposed to falls, hospitalization, and institutionalization (3). Additionally, the presence of frailty has been shown to substantially increase mortality (4).

The strongest predictor of frailty is self-reported shortness of breath (5), although frailty has also been associated with a reduction in activities of daily living. In patients with COPD, frailty can increase dramatically due to hospitalizations and the impact of exacerbations on patients’ physical status and disability (6). In fact, impairment in lower-extremity strength has been associated with functional limitation and disability.

Interventions to counteract these impairments are indicated (7). Several systematic reviews (8,9) have provided evidence that exercise interventions have a positive impact on frail older adults. There is good evidence (8,9) that exercise improves cardiorespiratory function, muscle function, balance, performance of activities of daily living, and functional ability in frail older adults. In a review, Weening-Dijksterhuis et al. (8) concluded that there is firm evidence to compose an effective training program to increase physical fitness outcomes, functional performance, and quality of life in institutionalized frail older adults.

Exercise seems to be more beneficial in frail elderly people living in long-term care facilities compared to those living in the community (8). However, the evidence to support exercise interventions in hospitals and retirement homes is currently insufficient.

The objective of this study was to determine whether an exercise intervention using a pedal exerciser was able to reduce...
disability in frail older patients with COPD during hospitalization due to an acute exacerbation.

Materials and methods

Design

The study was a randomized, single-blind clinical trial. The research assistant who collected the data was blinded to the hypothesis of the study and to the patient’s allocation. The study protocol was approved by the Research Ethics Committees of San Cecilio University Hospital and Virgen de las Nieves Hospital; the procedures followed were in accordance with the 1975 Declaration of Helsinki, as revised in 2013.

The Consolidated Standards of Reporting Trials (CONSORT) statement (10) was followed during the course of the research. The aim of the study was fully explained to the participants, who all gave written informed consent. This study has been registered in clinicaltrials.gov with the reference number NCT01826682.

Participants

Older patients admitted to the respiratory ward of San Cecilio and Virgen de las Nieves hospitals (Granada, Spain) due to an exacerbation of COPD were recruited during an eight-month period (from December 2013 to July 2014). Inclusion criteria were being clinically diagnosed with an acute exacerbation of COPD (AECOPD) according to the criteria of the American Thoracic Society (ATS) and being aged 65 years or older. Frailty was evaluated with the Brief Frailty Index (11), which includes five items scored 0 or 1: Balance assessment, Body mass index, Trail Making Test Part B, Geriatric Depression Scale, and Living alone. The index score ranges from 0—the highest score—to 5, indicating high risk. It consists of four categories: 0, 1, 2, and ≥3. Patients with COPD who scored over 3 in the Brief Frailty Index were included in this study.

Exclusion criteria were inability to provide informed consent, presence of psychiatric or cognitive disorders, progressive neurological or musculoskeletal disorders, severe orthopedic problems, organ failure, cancer, or inability to cooperate. Patients who had experienced another exacerbation of COPD in the previous month were also excluded. Patients who did not complete at least four days of intervention were excluded.

Randomization

An independent nurse assigned participants to the intervention or control groups by opening opaque pre-sealed envelopes that randomly allocated participants to either group following a computer-generated list. The nurse informed the physiotherapist of patients’ group assignment once participants had given their approval to participate in the study. Data were collected by an independent researcher who was blinded to patients’ assignment. The assessments were performed on the second day of hospitalization and the day of discharge.

Measures

For descriptive purposes, anthropometric measures, functionality (assessed with the Barthel Index) (12), quality of life (assessed with St. George’s Respiratory Questionnaire) (13), and physical activity levels (measured with the modified Baecke physical activity questionnaire) (14) were recorded.

Respiratory function was assessed with spirometry (CareFusion, Micro Spirometer, Basingstoke, UK) in all patients following the criteria of the ATS (15). Participants’ resting oxygen saturation (SpO2) was assessed using a pulse oximeter (Konica Minolta Pulsox-1, Pulse oximeter, Japan) and percentages of forced vital capacity (%FVC) and forced expiratory volume in the first second (%FEV1) were assessed and compared to predicted values.

Dyspnea perception at rest was recorded using the modified Borg scale (16).

The outcome measures used to assess patients’ disability were lower-limb strength, balance, and exercise capacity. These measures were evaluated at baseline and at discharge.

Lower-limb strength was evaluated in the quadriceps using a portable handheld dynamometer (17) (Lafayette Manual Muscle Testing System, model 01163, Lafayette, IN, USA). The highest value of three repetitions allowing patients to rest between the measurements was used in the statistical analysis. Quadriceps weakness contributes to reduced functional performance. In COPD patients, reduced maximal muscle strength is a significant contributor to work capacity limitation.

Balance was assessed in a static position with the one-leg stance (OLS) test (18). Exercise capacity was assessed with the 30-second sit-to-stand (STS) test, a field exercise test, which has been accepted as an indicator of functional status for elderly people. It is able to identify peripheral muscle weakness in patients with COPD (19). Participants were asked to stand up and sit down landing firmly, as fast as possible, without using the arms during 30 seconds. The number of times that the patient STS was recorded was the participant’s score.

Activity monitoring while awake was evaluated with the SenseWear Armband (BodyMedia, Inc. Pittsburgh, USA). Subjects wore the device during 24 hours in order to count the number of steps walked. The assessments of physical activity levels were performed three consecutive days from the second to the fourth day of hospitalization and the last three days of hospitalization. The SenseWear Armband was placed on the back of patients’ upper left arm (i.e., the triceps) (20).

Intervention

All patients received standard medical and pharmacological care (i.e., systemic steroids, inhaled bronchodilators, and oxygen), a regimen of oral prednisone or its equivalent in doses of 40–60 mg per day for the duration of therapy, taking into account the criteria of the doctor who follows each patient, which could change the medication according to the symptoms of the patients. The patients required antibiotic therapy during the exacerbation. The intervention group additionally received an exercise intervention using a pedal exerciser. The intervention was performed from the second day of admission to discharge. The duration depended on the length of hospital stay of each patient.

The intervention consisted of a cycling exercise using a pedal exerciser (Figure 1) in addition to standard care. The patients were sitting on a chair in a comfortable position during the biking. In the first treatment session we evaluated the status of the
patient; the activity performed during the session was considered basal level. In the next sessions, the exercise was administered with an incremental design of time, velocity, and resistance, taking into account the basal level. Cycling time, velocity, and intensity were adapted to the patients’ levels of dyspnea and fatigue. The activity was stopped if the patient reached level 6 of dyspnea or fatigue in the Borg scale, exercise prescription based on rate of perceived exertion shown to be valid (21). Patients dyspnea or fatigue in the Borg scale, exercise prescription based on rate of perceived exertion shown to be valid (21). Patients were encouraged to increase the velocity during each session of the program. They were instructed in order to maintain a constant velocity during the higher time possible. The resistance of the pedal exerciser was increased each day if the patients tolerated the session and the dyspnea and fatigue levels did not reach 6 points in a Borg scale. A physical therapist instructed the patient during the performance of the program.

During the exercise training, oxygen therapy was administered as required to maintain oxygen saturation above 88%. It was measured with a pulse oximeter. Patients were examined for adverse signs and symptoms such as increased pain, severe dyspnea, desaturation, and/or increased skin temperature during each session. If any soreness lasted more than a few hours after the intervention, the regimen was decreased and adapted to the patient. No supervised or progressive exercise was provided during the hospital stay to patients allocated to the control group.

**Statistical analyses**

Sample size was calculated according to the primary outcome measure of quadriceps muscle strength. On the basis of previous study (22), a small positive effect (10 Nm) was anticipated in the intervention group. Hence, in order to have 90% power using a two-sided $\alpha = 0.05$, with a hypothetical dropout rate of 20%, 29 patients in each group would be needed to show statistically significant differences in quadriceps strength between both groups.

The data were analyzed using SPSS software version 20.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to determine participants’ characteristics. The Kolmogorov–Smirnov test was performed to assess the normality of continuous data prior to the statistical analysis. Normally distributed demographic variables (i.e., age and body mass index) were compared using Student’s t-test. Non-normally distributed variables were compared using the Kruskal–Wallis test. A 2 (baseline vs. discharge) × 2 (exercise + standard care vs. standard care group) two-way mixed analysis of variance (ANOVA) was performed for each measure. If the two-way ANOVA showed a significant interaction, Scheffe’s post hoc test was used to identify the specific mean differences. Statistical significance was accepted at a $p$ value of 0.05.

**Results**

A total of 130 patients with AECOPD were recruited. Of these, 72 patients were excluded, 53 of them did not meet the inclusion criteria (due to the presence of psychiatric or cognitive disorders, progressive neurological or musculoskeletal disorders, severe orthopedic problems, organ failure, cancer, or inability to cooperate. Patients who had experienced another exacerbation of COPD in the previous month were also excluded. Patients who did not complete at least four days of intervention were excluded) and 19 of them decided not to participate in this study. Finally, 58 patients were randomly allocated to one of the two groups (Figure 2). Twenty-nine patients were allocated to the intervention group; the other 29 were allocated to the control group (10).

The final sample (n = 58) was composed of 27.9% (n = 16) women and 72.1% (n = 44) men. The age was similar in the intervention (75.65 ± 6.25years) and control groups (72.12 ± 8.19years).

The pre-intervention sociodemographic and clinical characteristics of the sample are shown in Table 1. The groups were statistically equivalent in clinical measures, lung function, and, importantly, length of hospital stay. Length of stay (LOS) was 12.47 ± 1.9 and 10.38 ± 2.47 in intervention and control group, respectively ($p = 0.354$), with an overall median LOS of 11 days (interquartile range [IQR] 7 to 14 days) in both groups. No significant between-group differences were found in the outcome measures at baseline.

Pre- to post-intervention outcome measures are shown in Table 2. Mean change from baseline to discharge in muscle strength was an improvement of 10.53 ± 25.07 N and a decrease of 15.2 ± 27.45 N on intervention and control group, respectively. The length of time during which patients maintained balance on one leg improved, showing a mean difference of 7.56 seconds on the right leg and 6.57 seconds on the left leg. Exercise capacity also improved by 4.97 stands from baseline to discharge. The number of steps increased by 1162.5 in the intervention group. Lower-limb strength, balance, and exercise capacity deteriorated in the control group; the number of steps increased by 451 steps. Results show that all the measured variables improved significantly ($p < 0.05$) in the intervention group compared to the within-group $p$ value obtained in the control group. The control group also showed a significant decrease in strength and balance (right leg) ($p < 0.05$). Significant between-group differences ($p < 0.05$) were shown in lower-limb muscle strength, balance, and activity monitoring (number of steps) at discharge. No patients reported any adverse signs or symptoms during the intervention.
Discussion

Patients included in this study were at severe stages of the disease (Global initiative for chronic Obstructive Lung Disease [GOLD] stages II–IV). They showed moderate levels of dependency (61–90) assessed with the Barthel Index when they were included in the study. Patients scored lower than 5 seconds in the balance test, indicating a risk of falls (23). Strength was shown to be reduced, and exercise capacity or functionality was very impaired (24).

Most hospitalized patients with an AECOPD show a progressive deterioration of strength and endurance in both peripheral and respiratory muscles during their hospital stay (25,26). The muscle impairment increases the risk of falls and reduces lower-extremity function, which has a negative impact on the ability of older people to remain independent (27).

The results of this study show that an exercise intervention can reduce disability in frail older patients with an AECOPD.

Table 1. Descriptive characteristics of the sample at baseline.

<table>
<thead>
<tr>
<th></th>
<th>Intervention group (n = 29)</th>
<th>Control group (n = 29)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>75.65 ± 6.25</td>
<td>72.12 ± 8.19</td>
<td>0.744</td>
</tr>
<tr>
<td>Sex n (%women)</td>
<td>7 (24.13)</td>
<td>9 (31.03)</td>
<td>0.684</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>31.32 ± 1.80</td>
<td>29.12 ± 2.54</td>
<td>0.514</td>
</tr>
<tr>
<td>Length of hospital stay (days)</td>
<td>12.47 ± 1.9</td>
<td>10.38 ± 2.47</td>
<td>0.354</td>
</tr>
<tr>
<td>Resting SO₂ (% O₂)</td>
<td>86.31 ± 3.47</td>
<td>89.16 ± 4.71</td>
<td>0.149</td>
</tr>
<tr>
<td>%FVC predicted</td>
<td>48.51 ± 18.65</td>
<td>45.23 ± 20.14</td>
<td>0.256</td>
</tr>
<tr>
<td>%FEV₁ predicted</td>
<td>42.35 ± 10.62</td>
<td>39.12 ± 12.06</td>
<td>0.123</td>
</tr>
<tr>
<td>Dyspnea</td>
<td>6.4 ± 0.98</td>
<td>7.0 ± 1.57</td>
<td>0.563</td>
</tr>
<tr>
<td>Barthel Index</td>
<td>84.56 ± 11.84</td>
<td>85.62 ± 14.85</td>
<td>0.607</td>
</tr>
<tr>
<td>SGRQ total score</td>
<td>52.47 ± 7.41</td>
<td>55.78 ± 9.56</td>
<td>0.368</td>
</tr>
<tr>
<td>Baecke total score</td>
<td>2.41 ± 1.82</td>
<td>2.69 ± 2.06</td>
<td>0.721</td>
</tr>
</tbody>
</table>

Non-categorical variables are expressed as the mean ± SD; SD: Standard deviation; PT group: Physical therapy group; SC group: Standard care group; n: Number of participants per group; BMI: Body mass index; FVC: Forced vital capacity; FEV₁: Forced expiratory volume in 1 second; SGRQ: St. George’s Respiratory Questionnaire.

All the variables measured improved significantly (p < 0.05) in the intervention group. Strength and balance showed significant between-group differences after the intervention. To our knowledge, no previous studies have found a beneficial effect following an exercise program focused on the lower limbs during hospitalization of frail elderly adults due to an AECOPD.

Previous studies (28,29) have investigated the effectiveness of physiotherapy during hospitalization due to AECOPD showing similar results to our study, improving dyspnea, quality of life, strength, and functional status.

In elderly populations, exercise has long been recognized to increase functionality of individuals (8). Exercise seems to be beneficial in older adults, improving physical functions, including STS performance, balance, agility, and ambulation (9).

The recent systematic review and meta-analysis conducted by Giné-Garriga et al. (30) revealed that, compared with a control intervention, exercise improved gait speed and lower-extremity function in the frail elderly. Their results are inconclusive for endurance outcomes, and no consistent effect was observed on balance and functional status. Additionally, the study carried out by Zhang et al. (31) reported that whole-body vibration exercise during eight weeks improved mobility function of the lower extremities and general health status in the frail elderly. Our intervention was shorter and was only conducted during the hospital stay of the patients. It showed similar results, preventing an increase in the impairment and all the adverse consequences of hospitalization in a frail elderly population with a chronic disease. Frailty in older people is recognized as a risk for adverse outcomes (32). The prevention of frailty and the facilitation of recovery from frailty have large benefits for individuals, their families, and society.

Given the importance of balance and strength as measures of independence, it is important to mention that previous studies (33,34) have shown a need for research on the effects of interventions focused on the improvement of physical status in the elderly. Hess et al. (35) showed that change in strength was
significantly correlated with improved balance in older adults. In our intervention, despite the short training period, quadriceps strength increased by 10.47 Newtons and the time patients tolerated in hospitalization period (36,37). However, our intervention was well tolerated in hospitalized patients. No adverse effects were noted during the intervention sessions.

Our data show that lower-limb strength and balance can improve with an exercise program during hospitalization. Other interventions in patients with an AECOPD have proven to be effective at countering the loss of skeletal muscle function in the hospitalization period (36,37). However, our intervention prevented impairment during the hospital stay in frail patients without any negative consequences.

**Study limitations**

This study has different limitations that must be reported. First, it would have been interesting to include a biopsy to assess muscle condition. Motivation could have influenced the test results in the patients submitted to the training program; however, handheld dynamometry has shown to be suitable for monitoring change in muscle strength and to test hypotheses for groups of people with COPD (38). Handheld dynamometry has shown to be a feasible, inexpensive, and portable test of quadriceps muscle strength for use in older people. It is a useful tool for ranking muscle strength of older people in epidemiological studies. It may also be of value for quick and objective assessment of physical function in the clinical setting (39,40).

A second limitation is the absence of a follow-up assessment of participants after discharge in order to explore the possible long-term benefits of the intervention.

Thirdly, differences may have been present in the training intensity and dose of corticosteroids, but these data were not collected.

**Conclusions**

A short exercise intervention focused on the lower limbs in patients hospitalized due to an AECOPD can improve muscle strength, balance, and exercise capacity in frail elderly people.

**Conflict of interest**

The authors report no declarations of interest.
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