



## Early View

Research letter

### **Tailored exercise is safe and beneficial for acutely hospitalised older adults with chronic obstructive pulmonary disease**

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**Tailored exercise is safe and beneficial for acutely hospitalized older adults  
with chronic obstructive pulmonary disease**

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Contributions: NMV FZF, MLSA, MI designed the study. All authors undertook study related procedures. NMV FZF, MLSA, MI collected the data. NMV, PLV, FZF, MLSA,RRV, AFH, AL and MI analyzed and interpreted the data. NMV, PLV, AL and MI, wrote the paper and all authors reviewed and revised the paper. All authors approved the final version.

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## **Abstract**

Exercise rehabilitation programs have proven to increase exercise capacity and quality of life (QoL) in hospitalized patients with COPD. However, controversy exists as to the actual safety and effectiveness of this type of intervention. We assessed the effects of an individualized exercise program on the functional capacity of acutely hospitalized older adults with COPD (as assessed with Barthel index and physical performance (Short Physical Performance Battery [SPPB])). Depression and QoL indicators, as well as serum C-reactive protein [CRP] and red blood cell distribution width [RDW] were also determined. Exercise-related side effects and incidence of readmission and mortality at 3 and 12-month follow-up were also reported. We used the intention-to-treat approach. Of the 370 patients initially included in the RCT (11), 86 with COPD were identified (40 and 46 for the control and intervention group, respectively). The median length of stay was 8d (interquartile range, 4) for both groups. The exercise intervention improved all functional and physical performance-related outcomes (Barthel index, SPPB, 1RM leg strength) as well as depression and QoL scores, but no significant changes were found for CRP or RDW. No side effects associated were noted with the exercise sessions. No between-group differences were found for the incidence of readmission at 3 or 12-month follow-up; or for the incidence of mortality at 3 or 12-month follow-up. Our findings add to the existing limited literature supporting the benefits and safety of early rehabilitation programs in acutely hospitalized, older patients with COPD. Of note, the fact that our results were found in very older people (87yrs on average) strengthens the potential safety of this type of interventions.

Chronic obstructive pulmonary disease (COPD) is predicted to affect approximately half of the older population in the next decade. The incidence of hospitalizations associated with this condition is also likely to rise, even surpassing those caused by major conditions (notably, ischemic cardiomyopathy) (1). In this context, the collateral effects of hospitalization—even for a few days—must not be overlooked, especially in the oldest segment (>80yrs). Nearly one third of older adults, indeed, lose their ability to independently perform 1+ activities of daily living from hospital admission to discharge even if successfully treated from the condition that caused hospitalization—the so-called ‘hospital induced-disability’. This condition has major short- and long-term consequences, notably an increased risk of re-admission and mortality. Moreover, hospitalized patients with COPD present with a proinflammatory profile (*i.e.*, elevated serum C-reactive protein [CRP]) and high range of variation in red blood cell volume (*i.e.*, elevated red blood cell distribution width [RDW]), both features associated with poorer outcomes (2).

The inverse relationship between physical activity levels and functional decline in hospitalized patients with COPD (3) and the benefits of exercise intervention on inflammation (4) and RDW (5) provide rationale to the hypothesis that in-hospital exercise might be beneficial for them. However, controversy exists as to the actual safety and effectiveness of this type of intervention (6). Exercise rehabilitation programs have proven to increase exercise capacity and quality of life (QoL) in hospitalized patients with COPD (7). Yet, recent joined guidelines from the European Respiratory Society (ERS) and American Thoracic Society (ATS) discourage implementation of these programs in hospitalized patients with COPD (9). This recommendation was based, at least partly, on previous results showing an increased long-term mortality in patients with COPD (45–93yrs) who had participated in an exercise program (10).

We assessed the effects of an individualized exercise program on the functional capacity of acutely hospitalized older adults with COPD. Depression and QoL indicators, as well as CRP and RDW were also determined.

The original trial is registered at ClinicalTrials.gov (NCT02300896) and its full details are published (10). Patients admitted to an Acute Care for Elders unit (February 1<sup>st</sup> 2015–August 30<sup>th</sup> 2017) who provided written informed consent were eligible for inclusion. Participants were randomized to receive usual care alone

(controls); or combined with an in-hospital supervised exercise intervention lasting 5-7d/wk and including two sessions/d of 15-20min-duration where participants performed moderate-intensity resistance (uprising from a chair, leg press, knee extension/extension, hip abduction, seated bench press [2-3 sets, 8-10 repetitions, 30-60% of one-repetition maximum [1RM]]) and walking exercises (11). Patients diagnosed with COPD in their primary care clinical record, and presenting with COPD-exacerbation related symptoms (increased dyspnea or increased sputum volume/purulence) with a duration range of 24h-21d were included in the present analysis.

The primary endpoint was pre-post change in functional ability (as assessed with Barthel index and physical performance (Short Physical Performance Battery [SPPB])). Secondary endpoints included changes in CRP, RDW, 1RM leg strength, mood status (15-item Yesavage Geriatric Depression Scale [GDS]; Spanish version), and visual analog scale of the EuroQol-5 Dimension (ED-5D) for QoL. Exercise-related side effects and incidence of readmission and mortality at 3 and 12-month-follow-up were also reported. We used the intention-to-treat approach. Between-group comparisons of continuous variables were conducted using linear mixed models. Time was treated as a categorical variable.

Of the 370 patients initially included in the RCT (11), 86 with COPD were identified (40 and 46 for the control and intervention group, respectively; **Table 1A**). The median length of stay was 8d (interquartile range, 4) for both groups. All patients in both groups were discharged home. Multicomponent physical exercise program “Vivifrail” ([www.vivifrail.com](http://www.vivifrail.com))(11) to prevent weakness and falls were recommended as post-hospitalization care. The exercise intervention improved all functional and physical performance-related outcomes (Barthel index, SPPB, 1RM leg strength) as well as depression and QoL scores, but no significant changes were found for CRP or RDW (**Table 1B**). No side effects associated were noted with the exercise sessions. No between-group differences were found for the incidence of readmission at 3 (25.0 versus 30.4% for the control and intervention group, respectively; odds ratio [OR]: 1.313 [95% confidence interval 0.506-3.401]) or 12-month follow-up (52.5 versus 56.5%; OR: 1.176 [0.502-2.756]); or for the incidence of mortality at 3 (10.0 versus 17.4%; OR: 1.895 [0.525-6.841]) or 12-month follow-up (37.5 versus 34.8%; OR: 0.889 [0.368-2.147]).

The results of functional/physical performance and depression/QoL-related outcomes are in agreement with previous research. There is, indeed, high-quality meta-analytical evidence supporting a beneficial effect of rehabilitation programs on exercise capacity and QoL in patients with COPD after an exacerbation (8). The ERS/ATS guidelines in fact state that rehabilitation programs initiated during hospitalization are effective for increasing exercise capacity in these patients (8). Of note, it is that even though the SPPB increased following intervention, the patients were still physically frail when they were discharged home. Accordingly, multicomponent individualized physical exercise program “Vivifrail” (11) were prescribed at post-hospitalization. The lack of changes in blood biomarkers is also in line with previous findings in hospitalized patients with COPD (12).

There is, nevertheless, controversy as to whether individuals with COPD exacerbation should exercise during hospitalization. An RCT by Greening et al. (10) found a higher risk of mortality during a 12-month follow-up (OR: 1.74 [1.05–2.88]) in patients hospitalized due to COPD exacerbation who had been involved in an early rehabilitation intervention. Mostly based on this result, an ERS/ATS joined meta-analysis concluded that rehabilitation programs initiated during hospitalization increase exercise capacity but they might also be associated with an increased risk of mortality (8). As such, initiating rehabilitation during hospitalization should be discouraged—even if the quality of the evidence for an actual risk was acknowledged to be ‘very low’(9). It must noted, however, that in the Greening et al. (10) study no between-group differences were found when per-protocol—instead of intention-to-treat—analyses were conducted, suggesting that those who actually received the intervention did not have an increased mortality risk.

Finally, a considerable heterogeneity of response for muscle function, physical performance, cognitive function and QoL-related outcomes could be also detected after usual care or physical exercise. Thus, as previously reported (13), response rate for functional capacity could not predict similar changes in other clinical characteristics, such as muscle strength and cognition. These findings support the need for a individualized tailored exercise and cognitive training program as a leading treatment strategy to prevent functional and cognitive decline usually associated with prolonged bed-rest during hospitalization in older population with COPD.

In summary, our findings add to the existing limited literature supporting the benefits and safety of early rehabilitation programs in acutely hospitalized, older patients with COPD. Of note, the fact that our results were found in very older people (87yrs on average) strengthens the potential safety of this type of interventions. Further evidence is needed to confirm our findings.

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**Table 1.** Baseline characteristics of study participants (A) and results of primary and secondary end points (B).

A)				B)											
Outcomes	Control		Intervention		Endpoints	Control		Intervention		Between-Group Difference (95% CI)					
	(n = 40)		(n = 46)			Pre	Post	Pre	Post						
Age (years)	87	(5)	87	(5)	<b>Primary</b>										
Women (%)	18		19		SPPB (score) <sup>a</sup>	4.7	(2.7)	4.7	(2.9)	4.7	(2.2)	6.8	(3.0)	-2.1	(-2.9 to -1.3)
Weight (kg)	69	(11)	68	(17)	Barthel Index (score) <sup>b</sup>	83.2	(16.1)	75.9	(20.5)	83.6	(18.2)	86.0	(15.3)	-9.3	(-14.2 to -4.5)
BMI (kg/m <sup>2</sup> )	28	(4)	27	(6)	<b>Secondary</b>										
CIRS (score)	14	(5)	14	(5)	1RM leg press (kg)	59.8	(26.8)	57.8	(27.5)	59.1	(24.7)	76.1	(32.7)	-19.0	(-26.2 to -11.9)
FEV1 (%)	71	(26)	68	(26.)	GDS (score) <sup>c</sup>	4	(3)	5	(3)	4	(2)	2	(2)	2	(2 to 3)
FVC (%)	76	(21)	74	(20)	EQ5D (score) <sup>d</sup>	58	(21)	57	(20)	58	(20)	67	(18)	-11	(-21 to -1)
FEV1/FVC (%)	65	(11)	64.	(15)	RDW (%)	15.0	(2.5)	15.2	(2.6)	13.8	(1.6)	14.1	(1.9)	0.1	(-0.3 to 0.4)
					CRP (mg/L)	95.1	(27.0)	93.8	(47.6)	78.5	(37.7)	72.7	(55.3)	-22.2	(-52.9 to 8.4)

Data are mean (standard deviation) except for % of women. FEV1, FVC and FEV1/FVC are expressed as % of normal age-predicted values. Abbreviations: BMI, body mass index; CIRS, Cumulative Illness Rating Scale-Geriatric; FEV1, forced expiratory volume; FVC, forced vital capacity; 1RM, one-repetition maximum; CI, confidence interval; CRP, C-reactive protein; EQ5D, EuroQol Questionnaire–5 Dimensions; RDW, red blood cell distribution width; SPPB, short physical performance battery.

<sup>a</sup> SPPB ranges from 0 (worst) to 12 (best).

<sup>b</sup> Barthel Index ranges from 0 (severe functional dependence) to 100 (functional independence).

<sup>c</sup> GDS ranges from 0 (best) to 15 (worst).

<sup>d</sup> EQ5D ranges from 0 (worst health status) to 100 (best health status).