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Original Research Article

An Observational Assessment of the Impact of Physical Activity in Individuals with Chronic Obstructive Pulmonary Disease

Vaibhav Shankar[1], Abhigyan Kumar[2]

[1]Consultant, Department of Pulmonary Medicine, Holy Promise Hospital, Patna, Bihar, India

[2]Assistant Professor, Department of General Medicine, Netaji Subhas Medical College and Hospital, Bihta, Patna, Bihar, India

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Corresponding Author: Dr. Abhigyan Kumar
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Abstract

Aim: Physical activity in individuals with chronic obstructive pulmonary disease

Material and Methods: This study was conducted in the Department of Pulmonary Medicine, Holy Promise Hospital, Patna, Bihar, India for 10 months. In brief, COPD patients were enrolled during their first hospitalisation due to COPD exacerbation in nine teaching hospitals in Spain. Patients were evaluated 3 months after discharge, when clinically stable (baseline). The diagnosis of COPD was established according to the American Thoracic Society/European Respiratory Society (ERS) guidelines. Patients were invited to participate in a second visit for follow-up assessment 18–24 months later, while clinically stable. In this second visit, a sample of 177 patients, representative of the PAC-COPD cohort, accepted the monitoring of their physical activity with an accelerometer.

Results: We enrolled 177 COPD patients (94% male, mean ±SD 71±8 years, FEV1 52±16% predicted). Mean 6663±4675 steps·day-1 and were physically active (>5000 steps·day-1) a median 4 days per week. During follow-up, 67 (38%) patients suffered at least one COPD hospitalisation. All physical activity variables decreased according to increased severity of airflow limitation in a statistically significant linear pattern (online supplementary table E2). When patients were stratified above or below the median of the average intensity of physical activity (⩾2.7 METs), we observed that the relationship between variables describing the quantity of physical activity and risk of COPD hospitalisations was restricted to those with low average intensity of physical activity (online supplementary table E3). After stratification according to airflow limitation, in patients with severe to very severe airflow limitation (FEV1 <50% pred) high quantity of activity at high average intensity was associated with a higher risk of COPD hospitalisation (online supplementary table E4).

Conclusion: In conclusion, a greater quantity of low-intensity physical activity reduces the risk of COPD hospitalisation. The observation that high-intensity daily-life physical activity does not generate additional protective effects in the most severe COPD patients will require replication.

Keywords: Physical activity, chronic obstructive pulmonary disease

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality worldwide, characterized by persistent respiratory symptoms and airflow limitation. COPD's burden extends beyond the lungs, contributing to systemic inflammation, muscle wasting, and cardiovascular complications. [1-4] Physical activity is a critical component in the management of COPD, as it has been shown to improve overall health outcomes, enhance quality of life, and reduce the risk of exacerbations and hospitalizations. Physical inactivity is prevalent among individuals with COPD, often due to dyspnoea, fatigue, and muscle dysfunction. These factors contribute to a cycle of deconditioning, where reduced activity levels lead to further physical deterioration and increased breathlessness during exertion. Encouraging physical activity in this population is essential for breaking this cycle and enhancing physical and mental well-being. Pulmonary rehabilitation programs, which include structured exercise training, education, and behavioural interventions, are highly effective in promoting physical activity among COPD patients. These programs improve exercise capacity, muscle strength, and endurance, and have been associated with decreased symptoms of dyspnoea and fatigue. Moreover, regular physical activity has been linked to better cardiovascular health, reduced inflammation, and improved metabolic function in COPD patients. Despite the benefits, maintaining long-term physical activity remains challenging for many COPD patients.

Barriers such as lack of motivation, fear of breathlessness, and limited access to rehabilitation programs hinder sustained engagement in physical activity . Strategies to overcome these barriers include personalized exercise plans, tele-rehabilitation, and community-based exercise programs, which have shown promise in supporting continued physical activity. [5-10]

Material and Methods

This study was conducted in the Department of Pulmonary Medicine, Holy Promise Hospital, Patna, Bihar, India for 10 months. In brief, COPD patients were enrolled during their first hospitalisation due to COPD exacerbation in nine teaching hospitals in Spain. Patients were evaluated 3 months after discharge, when clinically stable (baseline). The diagnosis of COPD was established according to the American Thoracic Society/European Respiratory Society (ERS) guidelines. Patients were invited to participate in a second visit for follow-up assessment 18–24 months later, while clinically stable. In this second visit, a sample of 177 patients, representative of the PAC-COPD cohort [11], accepted the monitoring of their physical activity with an accelerometer (see later).

Measurements

Patients were instructed to wear an accelerometer (Sense Wear Pro 2 Armband; Body Media, Pittsburgh, PA, USA) placed on the right arm during waking hours (08:00–10:00 h) over eight consecutive days. On average, they wore the accelerometer for 6 days and recorded a mean 95% of daytime hours (13.5 h of a maximum 14 h).[11] The quantity of physical activity was assessed using 1) the number of steps per day; 2) the number of days per week that the patient could be considered physically active, operationally defined by ⩾5000 steps per day [12]; and 3) time (minutes) per day spent in physical activity (defined as any minute with ⩾1.5 metabolic equivalent tasks (METs)). The intensity of physical activity was assessed by the average METs over the time spent in physical activity. The information about COPD hospitalisations (dates and diagnoses at discharge) during the 12 months prior to enrolment and during follow-up was obtained from a national administrative database (online supplementary material). Other measurements included sociodemographic factors, pharmacological and nonpharmacological treatment, smoking habit, dietary habits, comorbidities, health-related quality of life, dyspnoea, complete lung function (including forced spirometry, body plethysmography, diffusing capacity and arterial blood gases), nutritional status, exercise capacity, lung density and structure and systemic inflammation (online supplementary material).

Results

We enrolled 177 COPD patients (94% male, mean ±SD 71±8 years, FEV1 52±16% predicted). Table 1 shows their main anthropometric, clinical and functional characteristics. Table 2 shows that patients walked a mean ± SD 6663±4675 steps·day-1 and were physically active (>5000 steps·day-1) a median 4 days per week. During follow-up, 67 (38%) patients suffered at least one COPD hospitalisation. Additionally, 10 patients died during follow-up without having had any hospitalisation; they exhibited lower physical activity levels in all variables than survivors (online supplementary table E1). The number of daily steps and physically active days at baseline was lower in patients who were hospitalised during follow-up than in those who were not, while no differences were observed with regard to time in activity or intensity of physical activity (table 2). All physical activity variables decreased according to increased severity of airflow limitation in a statistically significant linear pattern (online supplementary table E2). When patients were stratified above or below the median of the average intensity of physical activity (⩾2.7 METs), we observed that the relationship between variables describing the quantity of physical activity and risk of COPD hospitalisations was restricted to those with low average intensity of physical activity (online supplementary table E3). Consequently, physical activity intensity was included as an interaction term in all subsequent analyses. The multivariate Cox model, adjusted both for potential confounders and the interaction term between intensity and daily steps, showed that for every additional 1000 daily steps at low average intensity, the risk of COPD hospitalisation was reduced by ~20% (hazard ratio (HR) 0.79, 95% CI 0.67–0.93; p=0.005) (table 3). However, increasing the number of daily steps when average intensity of physical activity was high did not result in any reduction in risk of COPD hospitalisation (table 3). Similar results were observed for the other two variables describing the quantity of physical activity (number of physically active days and time in activity) (table 3). After stratification according to airflow limitation, in patients with severe to very severe airflow limitation (FEV1 <50% pred) high quantity of activity at high average intensity was associated with a higher risk of COPD hospitalisation (online supplementary table E4). Stratification of patients by hospitalisation for COPD in the previous year (online supplementary table E5), additional analysis using volume of physical activity as the exposure (online supplementary table E6), as well as the sensitivity analyses (online supplementary tables E7, E8, E9 and E10) all yielded similar results.

TABLE 1 Sociodemographic, clinical and functional characteristics of participants

		No	Yes	
Baseline				
Subjects n	177	110	67	
Male	166 (94)	103 (94)	63 (94)	1.000
Age years	71±8	70±8	71±8	0.725
Marital status married	146 (83)	94 (86)	52 (78)	0.222
Family >2 members	79 (45)	52 (47)	27 (40)	0.436
Primary education or higher	106 (60)	69 (63)	37 (55)	0.346
Active workers	15 (8)	12 (11)	3 (5)	0.171
Low socioeconomic status (level IV or V)#	130 (80)	82 (80)	48 (80)	1.000
Current smokers	57 (33)	37 (34)	20 (30)	0.765
BMI $kg \cdot m^{-2}$	29±5	29±5	28±5	0.054
FFMI# $kg \cdot m^{-2}$	20±3	20±3	19±3	0.168
Dyspnea m MRC score 0–4	1 (1–2)	1 (0–2)	2 (1–4)	<0.001
Charlson index score 0–30	2 (1–3)	2 (1–3)	2 (1–3)	0.537
Cardiovascular disease	30 (17)	18 (16)	12 (18)	0.838
SGRQ total score 0–100	32±18	26±16	41±18	<0.001
FEV1 % pred	52±16	57±16	43±14	<0.001
COPD grade				
Mild (FEV1 ⩾80% pred)	9 (5)	9 (8)	0 (0)	<0.001
Moderate (FEV1 50–80% pred)	87 (49)	67 (61)	20 (30)	
Severe (FEV1 30–50% pred)	64 (36)	31 (28)	33 (49)	
Very severe (FEV1 <30% pred)	17 (10)	3 (3)	14 (21)	
RV/TLC# %	58±10	56±10	61±9	<0.001
*D*LCO# % pred	63±21	67±20	57±20	0.004
*P*aO # mmHg	74±10	76±9	70±10	<0.001
6-min walking distance# m	407±96	424±91	379±100	0.003
V′O2max#,¶ % pred	16±4	17±4.6	15±3.9	0.028
⩾1 COPD hospitalization in the previous 12 months	29 (16)	6 (6)	23 (34)	<0.001
Previous COPD hospitalizations in the previous 12 months+	1.4 (0.8)	1.0 (0.0)	1.5 (0.9)	<0.001
CRP ⩾3 $mg \cdot L^{-1}$	119 (67)	75 (74)	44 (69)	0.596
Lung density# HU	−842±41	−849±26	−832±55	0.215
Emphysema# % lung tissue <−950 HU	31±14	31±15	30±13	0.681
Bronchial wall thickness extension score# (0–3)	2.0±1.4	1.8±1.4	2.1±1.3	0.295
Follow-up Duration of follow-up years	2.6 (2.0–3.2)			
Participation in any pulmonary rehabilitation programme	19 (11)			
COPD hospitalization during follow-up	67 (38)			
COPD hospitalizations§ n	2 (1–3)			
Time to first COPD hospitalization § years	0.7 (0.3–1.3)			
Mortality	28 (16)			

Data are presented as n, n (%), mean ±SD or median (interquartile range), unless otherwise stated. COPD: chronic obstructive pulmonary disease; BMI: body mass index; FFMI: fat-free mass index; m MRC: modified Medical Research Council; SGRQ: St George's Respiratory Questionnaire; FEV1: forced expiratory volume in 1 s; RV: residual volume; TLC: total lung capacity; DLCO: diffusing capacity of the lung for carbon monoxide; % pred: % predicted; PaO2: arterial oxygen tension; V′O2max: maximal oxygen uptake; CRP: C-reactive protein. #: some variables have missing values: socioeconomic status (n=15), FFMI (n=13), RV/TLC (n=11), DLCO (n=17), PaO2 (n=6), 6-min walking distance (n=10), V′O2max (n=66), CRP (n=11), lung density and emphysema (n=112) and bronchial wall thickness (n=96). Missing values were distributed at random and were mainly due to the hospital logistics and patient
availability, as previously published [10]. during exercise testing using the reference values of NEDER et al. [13]; +: n=29; §: n=67.

TABLE 2 Characteristics of patients' physical activity at baseline and according to hospitalisations for chronic obstructive pulmonary disease (COPD) during follow-up

	All patients	COPD hospitalization		P vale
		No	Yes	
Subjects	177	110	67	
Physical activity steps·day^{-1}	6663±4675	7470±4939	5339±3890	0.003
Physically active days per week$^{\#}$	4 (1–7)	5 (2–7)	2 (0–7)	0.007
Time in physical activity min·day^{-1}	176±123	185±131	160±108	0.272
Average intensity of physical activity METs	2.8±0.5	2.8±0.5	2.8±0.6	0.258

Data are presented as n, mean ±SD or median (interquartile range), unless otherwise stated. METs: metabolic equivalent tasks. #: defined as ⩾5000 steps·day-1. [12]

TABLE 3 Adjusted# association between physical activity variables and hospitalisation for chronic obstructive pulmonary disease (COPD) (multivariate Cox proportional hazards regression)

HR (95% CI)		p-value	*R2*
Subjects n Steps per day (change for each 1000 steps per day)	177 0.79 (0.67–0.93)	 0.005	 0.33
High average intensity of physical activity (⩾2.7 METs)	2.71 (1.27–5.81)	0.010	
Interaction: steps intensity	1.28 (1.06–1.53)	0.009	
⩾1 COPD hospitalization in the previous 12 months	5.17 (2.95–9.06)	<0.001	
FEV1 % pred Physically active days per week (change for 1 day per week)	0.96 (0.95–0.98) 0.79 (0.67–0.93)	<0.001 0.005	 0.32
High average intensity of physical activity (⩾2.7 METs)	2.12 (1.10–4.09)	0.025	
Interaction: days×intensity	1.37 (1.10–1.70)	0.005	
⩾1 COPD hospitalization in the previous 12 months	5.19 (2.97–9.07)	<0.001	
FEV1 % pred Time in physical activity (change for 1 h per day)	0.96 (0.94–0.98) 0.79 (0.63–0.99)	<0.001 0.039	 0.31
High average intensity of physical activity (⩾2.7 METs)	1.64 (0.95–2.85)	0.078	
Interaction: time intensity	1.36 (1.01–1.82)	0.041	
⩾1 COPD hospitalization in the previous 12 months	5.51 (3.16–9.62)	<0.001	
FEV1 % pred	0.96 (0.94–0.98)	<0.001	

Data are presented as n, unless otherwise stated. An increase of 1000 steps per day at low average intensity of physical activity is related to reduced COPD hospitalisation risk (hazard ratio (HR) 0.79); high average intensity of physical activity without increasing the number of steps is related to increased COPD hospitalisation risk (HR 2.71); an increase of 1000 steps per day at high average intensity of physical activity is not related to COPD hospitalisation risk (HR 0.79×1.28=1.01). METs: metabolic equivalent tasks; FEV1: forced expiratory volume in 1 s. #: other potential confounders (sex, age, education, marital status, family members, working status, socioeconomic status, inhaled bronchodilators or corticosteroids, smoking status, smoking duration and intensity, Charlson index, cardiovascular comorbidities, modified Medical Research Council dyspnoea score, health-related quality of life, forced vital capacity, residual volume/total lung capacity, diffusing capacity of the lung for carbon monoxide, arterial oxygen tension, body mass index, fat-free mass index, 6-min walking distance, maximal oxygen uptake, lung density and structure, C-reactive protein, tumour necrosis factor-α, participation in a pulmonary rehabilitation programme and consumption of fruits, vegetables and cured meats) were not finally included in multivariate models because they did not relate to the outcome nor did they modify the coefficient estimate for the exposure >10%.

Discussion

The main finding of our study is that increased quantity of physical activity reduces the risk of future COPD hospitalisations when the average intensity of physical activity is low. The finding that high quantity of physical activity at high average intensity of physical activity may be unhelpful in COPD patients with severe to very severe airflow limitation was unexpected and will require replication. The sensitivity analyses showed that our results were very stable in relation to changes in the selection of subjects, variables and the use of different outcome measures. This is the first study that unravels the independent role of the quantity and the intensity of physical activity on the risk of COPD hospitalisations. Previous research consistently demonstrated that higher quantity of physical activity reduces the risk of future COPD exacerbation/hospitalisation.[6] However, some of these previous studies [14–16] measured the quantity of physical activity using variables of energy expenditure (MET-h per week or -kcal per day) that also included intensity in their calculation.[17] In view of the results of the study, this should be taken into account more carefully since it could reduce the beneficial effects of physical activity on COPD hospitalisation risk. It is worth noting that the only study that has used an objective tool (pedometer) to assess the quantity of physical activity found a risk reduction almost identical to that observed in the study (20% for every additional 1000 steps).[18] The modifying effect of intensity of physical activity in the reported associations between its quantity and the risk of future hospitalisation is a novel finding in the COPD literature, although it has been previously reported in healthy elderly people, where health benefits were mainly related to low intensity of physical activity. [8,19, 20] Specifically in the elderly, low-intensity physical activity has been shown to provide wellbeing benefits that were not found with moderate-to-vigorous physical activity.[19] It has been suggested that individuals engaging in more activities in the low intensity range (e.g. leisure-time walking) are more likely to have less stress, increased socialisation and greater quality of life. [19] Furthermore, low-intensity physical activity shows slight advantages over vigorous physical activity in reducing tumour necrosis factor-α and rising insulin-like growth factor binding protein-3 levels in aged people.[20] The interpretation of the results for intensity of physical activity requires prior clarification. First, the intensity of physical activity is usually measured by METs, which express the ratio of energy expenditure during a specific physical activity in relation to the energy expenditure at rest. However, the relative metabolic demand (and, as a result, symptom perception) produced by a specific physical activity does not depend only on its MET value but also on the maximum intensity achievable by each subject. In fact, it is well known that for a given activity, COPD patients use a higher proportion of their metabolic and ventilatory capacities than their healthy peers. [21] Thus, the consideration about what is low- or high- intensity physical activity differs depending on the population under study. [17] Second, it is also important to consider that the intensity was defined in our study as the average of METs during all periods spent in physical activity. This included basic activities of daily living, which represent the greater part of patients' time, and have an intensity of ∼1.5 METs. Thus, to achieve a mean of 3 METs over 1 week, patients need to spend a large proportion of time at very high intensities most days of the week. Third, similarly to the framework that considers physical activity and exercise as different concepts [22], our average intensity of physical activity was conceptually different to an average intensity of exercise. Consequently, our results should not be interpreted as a contradiction of pulmonary rehabilitation programmes, which may include exercise of high intensity, because the impact of the latter on the daily average intensity of physical activity will be very small. In summary, our results support a beneficial effect of physical activity when the average of intensity is low, i.e. if only a small proportion of the daily time in physical activity is spent at high intensity levels. By contrast, when a large proportion of the time in physical activity is spent at higher intensities, physical activity appears no longer beneficial, a finding that will require replication. Several mechanisms have been proposed as responsible for the beneficial effects of physical activity in COPD patients which could ultimately reduce the risk of exacerbations (and subsequent hospitalisations). First, moderate levels of physical activity have been shown to reduce the circulating levels of a number of inflammatory markers, both in experimental and observational studies, as well as in COPD populations. [23–25] Second, the regular practice of physical activity promotes more efficient oxygen delivery to respiratory muscles and improves the oxidative capacity of the muscles in COPD patients. [26] Regular physical activity has also been associated with higher levels of diffusing capacity of the lung for carbon monoxide, maximal expiratory pressure, 6-min walking distance and maximal oxygen uptake in COPD patients. [25] Studies on the effects of physical activity suggest that additional mechanisms may play a role in our observed increased risk of hospitalisation in the inactive patients, including 1) reduced nitric oxide production leading to deleterious vascular effects and loss of its bronchodilator effect [27]; 2) deregulation of gene expression of the β2-adrenergic receptor, therefore possibly inducing a poorer response to therapy [28]; and 3) increased susceptibility to respiratory infections in COPD patients due to a reduction in the number and function of cells mediating cytotoxic activity. [29] Our novel findings of an unhelpful effect of higher quantity of high-intensity physical activity in severe to very severe COPD patients are supported by previous research in COPD patients, healthy subjects, elite athletes and animals. First, strenuous exercise is accompanied by an increase in circulating pro-inflammatory and inflammation-responsive cytokines [30], a response that is exaggerated in specific populations, such as overweight children. [31] In COPD patients, high-intensity exercise alters the nitroso-redox balance, which cannot be balanced by antioxidant mechanisms. [26] Studies in elite athletes have shown an association between high intensity of physical activity and increased airways inflammatory cells, as well as respiratory infections [32] , which has been attributed to exercise-induced immune-suppressive effects of exercise, mostly affecting cell immunity. Finally, studies in animals suggest additional effects of high intensity of physical activity, such as the induction to apoptosis of inflammatory cells, mostly in elderly animals.[33] The complex role of physical activity in the immune system is still a matter of debate, more so in diseases with a high inflammatory component, such as COPD. [29] Several of the observations of our study can have clinical implications for the recommendations about daily physical activity to COPD patients. This is an added value in the management of these patients, since no COPD-specific recommendations are available so far. [1, 2] The linear dose–response relationship between quantity of low-intensity physical activity and the risk of COPD hospitalisations suggests that there is no threshold, either low or high, to achieve clinical benefits. In addition to existing research [6], our results provide evidence to consider in the current COPD guidelines/strategies that COPD patients in general should be encouraged to perform an extra quantity of low-intensity physical activity during their daily life. Furthermore, the data suggest that research aiming to assess the effectiveness of physical activity interventions should consider several physical activity outcomes, including the proportion of individuals meeting certain physical activity goals [34], extra steps per day [35] and the changes, if any, in average intensity.

Conclusion

In conclusion, a greater quantity of low-intensity physical activity reduces the risk of COPD hospitalisation. The observation that high-intensity daily-life physical activity does not generate additional protective effects in the most severe COPD patients will require replication.

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