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Determinants of Physical Activity in Patients with Chronic Obstructive Pulmonary Disease: A 5-Year Prospective Follow-Up Study

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Key Words

Chronic obstructive pulmonary disease · Physical activity · Determinant · Longitudinal study

Abstract

Background: Although many studies examined determinants of physical activity in patients with chronic obstructive pulmonary disease (COPD), most were cross-sectional and focused on single determinants only. ***Objectives:*** The aim of this study was to determine how COPD patients' physical activity changes over time and to identify the determinants of physical activity using multivariable and longitudinal methods. ***Methods:*** In a prospective cohort study, 409 primary care patients with COPD in the Netherlands and Switzerland were followed for up to 5 years. Physical activity was assessed at baseline and every 6 months using the Longitudinal Aging Study Amsterdam Physical Activity Questionnaire (LAPAQ) adapted to a 0- to 23-point scale. We studied the associations between determinants at baseline and patients' long-term physical activity levels using linear mixed models. ***Results:*** Unadjusted analysis showed an overall gradual decline in physical activity (0.22 points of the LAPAQ scale every 6 months, 95% CI: 0.17–0.28; $p < 0.001$). In multivariable analyses, baseline determinants that were independently associated ($p \leq 0.05$) with lower long-term physical activity levels included (starting from coefficients with the smallest p value) lower exercise capacity, older age, working, more smoking pack-years, more fatigued, male sex, lower educational levels, previously not in fitness programs, more depressed, lower lung function, lower overall health status, and more prescription drug use. ***Conclusions:*** We found that physical activity of COPD patients may decline more than reported in the healthy elderly. Longitudinal analysis identified independent determinants of physical activity, which allows the identification of patients having low physical activity levels and who may benefit from physical activity interventions.

Introduction

Diminishing physical activity is considered an important characteristic of many chronic diseases and in particular of chronic obstructive pulmonary disease (COPD). In COPD patients, even if airflow limitation is mild, levels of physical activity are considerably lower than those of age-matched healthy controls [1–4]. Qualitative studies conducted with COPD patients suggested that the amount

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of physical activity, the symptoms experienced during physical activity, as well as adaptations made to facilitate physical activity are important aspects of their health status [5]. Besides, in patients with COPD, low levels of physical activity have been shown to be a strong predictor for severe exacerbations and mortality [6–8].

Given that low levels of physical activity are associated with exacerbations and mortality, the management of COPD may benefit from a better understanding of the factors that determine physical activity. For example, identifying patients at risk of having low levels of physical activity may facilitate the initiation of effective treatments which can target those who need them most [9–11]. The majority of studies that have examined determinants of physical activity in patients with COPD were cross-sectional and focused on single determinants only, although many determinants may exist, and their relative impact on physical activity was seldom examined [8, 11]. Thus, these studies were often inconclusive about the directionality of the associations between determinants and physical activity and, taken together, showed inconsistent results [8, 11].

In the present study, we followed a cohort of COPD patients and measured their levels of physical activity for up to 5 years. Using a longitudinal design, we aimed to (1) determine how COPD patients' levels of physical activity change over time and (2) identify the baseline determinants of long-term physical activity levels.

Materials and Methods

Study Sample

We used the participants from the International Collaborative Effort on Chronic Obstructive Lung Disease: Exacerbation Risk Index Cohorts (ICE COLD ERIC), a prospective study of primary care COPD patients from Switzerland and the Netherlands [12, 13]. A total of 409 patients who were ≥40 years of age with Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages II–IV were recruited between April 2008 and April 2009. The baseline assessment included medical history, lung function, exercise capacity, and blood sample, and patients were also asked to complete questionnaires regarding their health-related quality of life, self-efficacy, symptoms of anxiety and depression, and physical activity. We excluded patients if their life expectancy was deemed less than 12 months by their general practitioners or patients with psychiatric disorders. Patients were contacted every 6 months (up to 5 years of follow-up) to update their risk profiles and to complete the questionnaires. Our analysis was based on data from the baseline visit and the follow-up visits (up to 10).

Assessment of Physical Activity

Patients completed the Longitudinal Aging Study Amsterdam Physical Activity Questionnaire (LAPAQ) [14] that covered six types of activities, namely walking outside, bicycling, gardening, sport activities, light and heavy household activities, to indicate the type, frequency, and duration of their physical activity during the previous 2 weeks. For this study, we decided to generate a modified LAPAQ score that was indicative of the types of physical activity patients had done, and we assigned weights to each activity according to the metabolic equivalent tasks [15]. Detailed justification and the calculation of the modified LAPAQ score can be found in the online supplementary S-Appendix (for all online suppl. material, see www.karger.com/doi/10.1159/000447975).

Measurement of Potential Determinants

Online supplementary table S1 lists the 24 potential determinants of physical activity that we assessed at baseline. This selection was based on availability, common sense (prior knowledge), and the published literature, including a recent systematic review of the determinants and outcomes of physical activity in patients with COPD [11].

Statistical Analysis

To investigate how a single determinant of interest was associated with (1) the level of physical activity and (2) change in physical activity over time, we built 24 longitudinal models, one for each determinant that was assessed at baseline. We used mixed-effect models with a random intercept and a random time slope for each patient to account for clustering due to repeated measurements of physical activity within each patient (*xtmixed* command in STATA 13; Stata Statistical Software, StataCorp LP, College Station, Tex., USA). Each model had the following independent variables: the determinant, time (a continuous variable for follow-up visits ranging from 0 to 10), and an interaction term of the determinant and time.

We built multivariable models that included all determinants and time (follow-up visit) to assess the strength of determinants that were independently associated with physical activity. Then, we extended this model by adding interaction terms of some determinants with time (whose interaction terms with time had a p value <0.2 in the previous analysis with only one determinant in each model) to additionally identify the determinants that were associated with the rate of change in physical activity.

We applied multiple imputation using the *ice* command in STATA [16] to deal with missing values of the determinants at baseline. For physical activity measurements, we included all available data at each follow-up visit [17]. Since we were concerned that the missing data in physical activity that were due to death could be potentially informative dropouts, we conducted sensitivity analyses using the joint multivariable random-effects approach (*jmre1* command in STATA) [18], which jointly modeled measurements of physical activity and time to death (log-normal survival time model), to investigate their impacts on our study findings. All STATA codes for data analysis are available upon request.

Statement of Ethics

The ethics committees (EK-1519 and EKSG 08/065/1B for Switzerland and NL22118_018_08 for the Netherlands) approved the study, and all patients provided written informed consent.

Table 1. Patients' responses to the LAPAQ at each follow-up visit

	Baseline	Follow-up visit									
		year 1		year 2		year 3		year 4		year 5	
		V1	V2	V3	V4	V5	V6	V7	V8	V9	V10
Patients under follow-up, n	409	389	374	354	346	329	317	270	258	241	230
Responders, n	409	353	331	313	336	294	299	246	236	215	207
Responses (n = 409), %	100	86	81	77	82	72	73	60	58	53	51
Responses to the LAPAQ by type of physical activity, n (%)											
Walking outside	360 (88)	292 (83)	269 (81)	249 (80)	265 (79)	230 (78)	237 (79)	200 (81)	179 (76)	158 (73)	158 (76)
Bicycling	102 (25)	95 (27)	86 (26)	82 (26)	76 (23)	65 (22)	72 (24)	63 (26)	59 (25)	50 (23)	52 (25)
Gardening	124 (30)	134 (38)	99 (30)	123 (39)	89 (26)	100 (34)	82 (27)	85 (35)	66 (28)	59 (27)	57 (28)
Sport activities	172 (42)	153 (43)	138 (42)	131 (42)	148 (44)	123 (42)	126 (42)	109 (44)	114 (48)	100 (47)	100 (49)
Light household activities	367 (90)	310 (88)	286 (86)	270 (86)	291 (87)	252 (86)	252 (84)	208 (85)	202 (86)	178 (83)	174 (84)
Heavy household activities	238 (58)	205 (58)	198 (60)	179 (57)	186 (55)	148 (50)	168 (56)	142 (58)	133 (56)	119 (55)	110 (53)
Summary score, median (IQR)	11 (8.5–15)	12.5 (8.5–16.5)	11 (6.5–15)	12.5 (8.5–15)	11 (6–15)	10.75 (5–15)	11 (5–15)	11 (6.5–16.5)	11 (6.5–15)	11 (6.5–15)	11 (5–15)

V = Visit; IQR = interquartile range.

Results

Sample Description

The detailed baseline characteristics of the patients in the ICE COLD ERIC study were reported previously [13]. In brief, 57% (233/409) of the patients were male, and the median age of the patients was 67 years (range 41–91). Most patients reported that they were former smokers (55%, 223/409) or current smokers (38%, 156/409), with 5% (19/409) reporting that they were never-smokers. According to the GOLD classification, 66% (268/409) of the patients were classified as stage II, 25% (103/409) as stage III, and 9% (38/409) as stage IV.

Table 1 shows the number and proportion of the patients who provided complete responses to the LAPAQ at each follow-up visit. We tabulated patients' responses by the type of physical activity they reported. At baseline, most patients reported doing light household activities (90%) and outside walking (88%), while 25% of the patients reported doing bicycling. For each physical activity, the proportion of the patients who reported doing the activity remained similar or slightly decreased over time. Table 1 also shows the summary scores (on a 0- to 23-point scale) for physical activity at each follow-up visit.

Change in Physical Activity over Time

Univariable analysis by including only the follow-up visit as an independent variable in the longitudinal model shows that the mean summary score for physical activity decreased over time (coefficient: –0.22 per 6 months; 95% CI: –0.28, –0.17; $p < 0.001$; see online suppl. table S2, model A1). We conducted the effect size calculation to determine if the change in physical activity over 5 years reached the minimal clinically important difference [19, 20]. We divided the mean change in the LAPAQ summary scores over 5 years (–2.2) by the standard deviation of the scores at baseline (5.7) and obtained a value of –0.4. An effect size of ±0.4 is considered a small clinically important difference [19, 20].

Determinants Associated with Physical Activity Levels

We constructed 24 mixed models that each focused on one determinant (adjusted for time and its interaction with time), and the results can be found in online supplementary table S2, model A2–A25. Musculoskeletal disease was not associated with physical activity levels ($p = 0.66$), so it was not considered in the multivariable analyses afterwards.

Table 2 shows the results of one multivariable analysis (model B1) that accounted for all determinants and time

Table 2. Multivariable analysis assessing the determinants of physical activity levels (model B1)

	Physical activity score			
	mean difference	95% CI	t statistic	p value
Visit	−0.23	−0.28, −0.17	−7.96	<0.001
Sit-to-stand test score	0.14	0.07, 0.20	4.33	<0.001
Age (per year)	−0.10	−0.15, −0.05	−3.60	<0.001
Working	−2.09	−3.26, −0.92	−3.50	<0.001
Smoking pack-year	−0.03	−0.04, −0.01	−3.04	0.002
CRQ (fatigue) score	0.63	0.18, 1.08	2.75	0.006
Sex (ref.: male)				
Female	1.38	0.39, 2.37	2.72	0.007
Education (ref.: primary/secondary school)				
Intermediate vocational or higher	1.33	0.36, 2.29	2.70	0.007
Fitness program	1.34	0.33, 2.35	2.60	0.009
HADS depression score	−0.22	−0.39, −0.05	−2.54	0.01
FEV_1 (liters)	1.15	0.22, 2.08	2.43	0.02
Feeling thermometer score	0.04	0.01, 0.07	2.28	0.02
Number of prescription drugs	−0.27	−0.52, −0.02	−2.11	0.04
CRP	−0.03	−0.06, 0.00	−1.85	0.06
CRQ (mastery) score	−0.40	−0.86, 0.05	−1.74	0.08
BMI (ref.: ≥18.5 and <30)				
<18.5	−1.92	−4.43, 0.60	−1.50	0.14
≥30	0.51	−0.56, 1.58	0.94	0.35
Smoking habits (ref.: nonsmoker)				
Former smoker	−0.79	−2.88, 1.29	−0.75	0.46
Current smoker	−1.60	−3.82, 0.62	−1.42	0.16
History of exacerbations (ref.: 0)				
1–2	−0.60	−1.54, 0.34	−1.25	0.21
≥3	−1.25	−3.46, 0.96	−1.11	0.27
Cardiovascular disease	0.56	−0.48, 1.61	1.06	0.29
HADS anxiety score	0.07	−0.06, 0.20	1.01	0.31
Diabetes	−0.33	−1.63, 0.97	−0.50	0.62
Country (ref.: the Netherlands)				
Switzerland	−0.24	−1.36, 0.88	−0.42	0.68
Living alone	−0.09	−0.96, 0.79	−0.20	0.85
CRQ (dyspnea) score	0.03	−0.34, 0.40	0.15	0.88

BMI = Body mass index; CRP = C-reactive protein.

(follow-up visit). We showed (fig. 1) and listed the coefficient for each determinant of physical activity in the order of the level of significance. In multivariable analysis, determinants that are independently ($p < 0.05$) associated with lower levels of physical activity are (from the strongest to the weakest level of significance): lower sit-to-stand test scores ($p < 0.001$), older age ($p < 0.001$), patients who were working ($p < 0.001$), more smoking pack-years ($p = 0.002$), lower Chronic Respiratory Questionnaire (CRQ) scores (indicating more impairment) for fatigue ($p = 0.006$), male sex ($p = 0.007$), lower educational levels ($p = 0.007$), previously not in a fitness program ($p = 0.009$), higher Hospital Anxiety and Depression Scale (HADS) scores for depression ($p = 0.01$), lower values of forced expiratory volume in one second (FEV_1) ($p = 0.02$), lower scores for feeling thermometer scale ($p = 0.02$), and higher number of prescription drugs ($p = 0.04$).

Determinants Associated with the Rate of Change in Physical Activity

To investigate which determinants are associated with the rate of change in physical activity, we extended the multivariable model to include interaction terms of determinants and time (follow-up visit), and the results are shown in table 3. The interaction terms 'age × visit' (coef-

Table 3. Multivariable analysis assessing the determinants of rate of change in physical activity

	Physical activity score					
	model B1[a]			model B2[a]		
	mean difference	95% CI	p value	mean difference	95% CI	p value
Visit	–0.23	–0.28, –0.17	<0.001	0.14	–0.40, 0.67	0.62
Age × visit				–0.01	–0.02, 0.00	0.02
Living alone × visit				–0.03	–0.15, 0.09	0.59
Working × visit				0.07	–0.09, 0.23	0.39
Fitness program × visit				–0.12	–0.25, 0.01	0.08
Cardiovascular disease × visit				0.03	–0.11, 0.18	0.64
Number of prescription drugs × visit				–0.01	–0.04, 0.02	0.66
FEV_1 (liters) × visit				0.02	–0.09, 0.14	0.68
Sit-to-stand test score × visit				0.01	0.00, 0.01	0.09
CRQ (dyspnea) score × visit				0.02	–0.02, 0.06	0.33

[a] Both models were adjusted for all determinants listed in online supplementary table S1 (except for musculoskeletal disease).

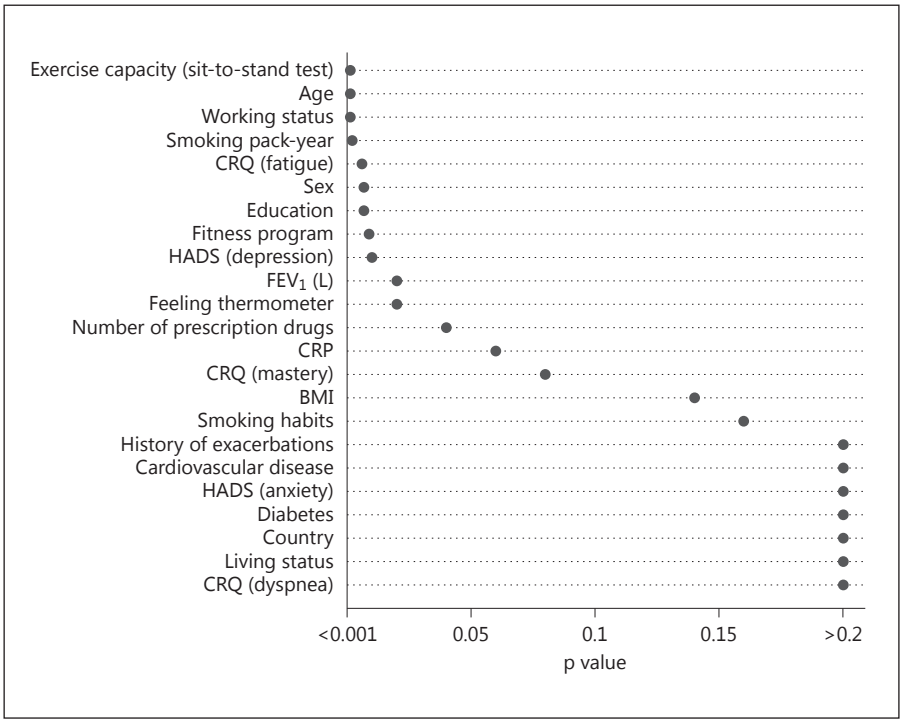

Fig. 1. p values of the coefficients of the determinants in the multivariable model. L = Liters; BMI = body mass index; CRP = C-reactive protein.

ficient: –0.01; 95% CI: –0.02, 0.00; p = 0.02) suggest that the levels of physical activity of older patients deteriorate faster.

We conducted a sensitivity analysis using the joint multivariable random-effects model that combined a linear mixed model for physical activity and a log-normal survival time model for death. Results that were adjusted for death in the joint model are similar to previous findings (see online suppl. table S3, models C1 and C2), suggesting that missing responses due to death may not have a large impact on our primary analysis.

Discussion

The current study shows that patients with COPD experience a decline in physical activity levels over time that may become clinically important after about 5 years on average. In the longitudinal analysis, we identified several determinants of physical activity, either nonmodifiable (age, sex, and education) or modifiable (exercise capacity, patient-reported fatigue and emotional status) and showed the strength of the association in multivariable analysis. These results may help to identify patients with low levels of physical activity, who are likely to benefit particularly from interventions to increase or to maintain their physical activity levels.

There is limited evidence on how levels of physical activity in patients with COPD decline over a long period of time. A recent study done by Waschki et al. [21] in Germany suggested a significant decline in physical activity during a 3-year follow-up in patients with COPD or chronic bronchitis. Using the effect size approach to determine if the difference was clinically important, a value of –0.3 was obtained, which is comparable to our study finding (–0.4 during a 5-year follow-up). The authors objectively measured patients' physical activity levels using the accelerometer, while in our study we measured physical activity based on patients' self-responses on a questionnaire. Interestingly, physical activity data using the objective and patients' subjective measurement tools both suggest a small clinically important change. If we compare this change to the existing data on change in physical activity in the healthy elderly without COPD [22], the effect size is about 2–3 times larger over the same time period. Thus, our results may support the view that as COPD progresses over time, patients' levels of physical activity decline more than expected in healthy subjects and become clinically important.

Gimeno-Santos et al. [11] systematically reviewed the available evidence on determinants and outcomes of physical activity in patients with COPD and proposed a conceptual framework. In their framework, for most of the determinants, the direction of the observed association between determinants and physical activity could not be established due to the cross-sectional design of most studies. In our cohort, we could examine the direction of these associations as we used the baseline measures for determinants and included multiple measurements from baseline and follow-up visits for physical activity. Furthermore, we did multivariable analyses to examine these determinants simultaneously. The results suggest that factors from multiple domains can each play an independent role in long-term physical activity levels in patients with COPD.

Concerning the predictors of the change in physical activity over time, we identified age at baseline to be the determinant that is strongly associated with the rate of change. Older age was associated with a faster decline in physical activity levels. Participating in a fitness/rehabilitation program was associated (marginally significant) with a faster decline in physical activity over time. This may not be surprising, since patients who reported having participated in a fitness/rehabilitation program at baseline started off with higher levels of physical activity, but the effect of a fitness/rehabilitation program is likely to diminish over time once patients discontinue training [23].

These determinants of physical activity, modifiable or not, can provide valuable information for the design and evaluation of interventions for promoting physical activity. A better understanding of the determinants of physical activity behaviors can, firstly, help us properly define the population which the interventions should target [10]. Health-care providers may pay attention to the patient characteristics that indicate a high risk of being physically inactive and, thus, perform a comprehensive assessment of physical activity or implement monitoring of physical activity in such patients. Secondly, a better understanding of the modifiable determinants (e.g. in our study, the health-related quality of life on the fatigue domain and depression symptoms) can help us design the interventions that specifically address these determinants [10]. Pulmonary rehabilitation programs are common interventions recommended to patients with COPD to promote their physical activity [24]. Our study results reemphasize the importance of having the exercise training (to increase the exercise capacity) in a pulmonary rehabilitation program and also suggest several patient symptoms that are associated with physical activity. Such factors are critical to designing and optimizing intervention strategies.

Study Strengths and Limitations

A main strength of our study is the longitudinal design, which allowed patients to be followed intensively for up to 5 years and to report their physical activity every 6 months. Another uniqueness of our study is that patients were recruited in two countries from the primary care setting, so we included a population that mirrors the real-world patients, since most patients with COPD are managed by general practitioners. Many cohorts, how-

ever, have so far recruited patients mainly from the secondary and tertiary care centers, and these patients can have different disease profiles.

The major challenge of our study was the assessment of physical activity. Patient-reported questionnaires are easy and feasible to be implemented in a long-term cohort study to assess levels of physical activity. Although we selected a previously validated questionnaire (LAPAQ), we found that there were many missing responses to the questions on the frequency of and time spent on each type of physical activity and, moreover, more implausible values. Other more objective approaches to physical activity assessment include step pedometers, accelerometers, and the doubly labeled water method [8]. However, based on findings of the PROactive project by the European Union Innovative Medicines Initiative (Physical Activity as a Crucial Patient Reported Outcome in COPD, https://www.imi.europa.eu/content/pro-active) [25], relying solely on activity monitors is not enough, and a comprehensive assessment of physical activity should include both objective measures and patient-reported outcomes. The PROactive project has accordingly developed a comprehensive-outcome instrument that is valid and reliable to capture physical activity levels in COPD patients. We hope that new instruments of this type can be more often applied in future long-term studies.

Conclusions

Our study shows that the levels of physical activity of patients with COPD decline steadily over time and reach a clinically important difference within about 5 years on average. The strongest determinants of being at risk for low physical activity include a lower exercise capacity, older age, working, and a smoking history, while we only identified age to significantly modify the rate of decline. The determinants of physical activity found in this study may help physicians and physiotherapists identify patients with low levels of physical activity who may need a thorough assessment of physical activity with activity monitors as well as effective interventions for promoting physical activity.

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Financial Disclosure and Conflicts of Interest

The authors declare that they have no conflicts of interest.

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