Physical Activity as a Predictor of Absence of Frailty in Subjects With Stable COPD and COPD Exacerbation

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BACKGROUND: Frailty is a key issue in the care of elderly patients. Patients with COPD are more likely to be frail, with a prevalence of 57.8%. Frailty is associated with a low level of physical activity. The aim of this study was to analyze the predictive power and identify the cutoffs of physical activity in their different domains (household, leisure time, and sport) for the absence of frailty in subjects with COPD exacerbation and stable COPD. METHODS: A cross-sectional study was conducted. The participants underwent an individual interview, including sociodemographic and clinical aspects. The total physical activity and its domains were assessed by the modified Baecke questionnaire, and frailty was measured according to the modified version of Fried. A total of 212 subjects with COPD (104 stable and 108 with COPD exacerbation) were enrolled, along with 100 healthy subjects. RESULTS: The prevalence of frailty was higher in subjects with COPD compared with the control group. An activity level of 3.54 for COPD exacerbation, 3.88 for stable COPD, and 3.50 for healthy subjects assessed using the Baecke questionnaire were recommended as the cutoff points for frailty. Sensitivity and specificity values were 0.95 and 0.807; 0.95 and 0.815; and 0.95 and 0.947, respectively. CONCLUSIONS: Physical activity level can predict the absence or presence of frailty in subjects with stable and exacerbated COPD. *Key words: COPD; frailty; physical activity; physical impairment; exacerbation; activity levels.* [Respir Care 2016;61(2):212–219.

Introduction

Frailty is a key notion in the care of elderly patients that directs attention away from organ-specific diagnoses and toward a more comprehensive patient-centered approach. Between 25–50% of patients older than 85 y are estimated to be frail, with a consequent increased risk of falls, disability, death rate, and use of long-term care.[1,2]

Based on 21 cohorts involving 61,500 participants, on average, 10.7% of community-dwelling older persons are frail.[2] The incidence of frailty in older adults ranges from 9 to 59.1%.[3] The rate varies, depending the geographical zone,[4] the frailty index used,[5] and age.[2]

Patients with COPD are more likely to be frail,[6,7] as those with other advanced chronic diseases,[8-10] with a prevalence of 57.8%.[6] The strongest predictor of frailty was

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self-reported shortness of breath. In addition, frailty was significantly associated with a reduction in activities of daily living and with balance impairments.[11] Frail community-dwelling elderly individuals are characterized by loss of functionality.[12] Similarly, people with COPD become progressively immobile and physically limited, mainly due to dyspnea and fatigue.[13] According to Fried et al,[1] the loss of muscle mass plays an important etiologic role in the frailty process in elderly subjects. It has been described as a key player of its latent phase and it explains many aspects of the frailty status itself.[14]

COPD has been reported[15] to be related to reduction in peripheral muscle performance and functional capacity on the clinical course of the disease. Impaired functional capacity[16] and physical activity levels[17] have been identified as predictors of hospitalization for COPD patients, and the loss of muscle strength has been related to the increased utilization of health-care resources.[18] Additionally, the natural course of COPD includes frequent exacerbations[19] that are associated with impaired lung function and a reduction in muscle strength, endurance, and physical activity levels.[20,21] An exacerbation of COPD is defined as "a sustained worsening of the patient's condition, from the stable state and beyond normal day-to-day variations that is acute in onset and may warrant additional treatment in a patient with underlying COPD."[22] Exacerbations of COPD contribute to disease progression.[23] Although this clearly suggests that patients with COPD can show significantly higher frailty scores than healthy individuals and that COPD exacerbation can also significantly increase frailty scores after an exacerbation, no previous studies have focused on this.

Frailty is associated with a decrease in the value of low peak oxygen consumption and with a low level of physical activity.[24] Sedentary behavior and moderate-to-vigorous physical activity have been shown to be independently associated with frailty and adverse health outcomes in middle to older age adults.[25] Although the level of physical activity is commonly included as one of the components of frailty in older adults, it is essential to establish cutoff points for different domains of physical activity to enhance the prediction of frailty in patients with COPD in different clinical situations: exacerbation of COPD and stable COPD.

It was proposed that by using receiver operating characteristic (ROC) analysis, optimal physical activity for clinically relevant outcomes could be derived. This can help to generate objectives and to develop clinical guidelines. The aim of this study was to analyze the predictive power and identify the cutoffs of physical activity in their different domains (household, leisure time, and sport) for the absence of frailty in subjects with exacerbated and stable COPD.

QUICK LOOK

Current knowledge

Frailty is an important issue in the care of elderly patients that directs treatment toward a more comprehensive patient-centered approach. Up to half of patients older than 85 y are estimated to be frail, with an increased risk of falls, disability, death, and use of long-term care.

What this paper contributes to our knowledge

Subjects with COPD are more likely to be frail, with a prevalence of 58%. The strongest predictor of frailty in this group is self-reported shortness of breath. There was a close link between frailty and physical status in COPD, suggesting that the physical activity level might predict the absence or presence of frailty in COPD subjects.

Methods

Study Design

In this cross-sectional study, participants underwent an individual interview, including sociodemographic and clinical aspects. The Ethical Committee of the San Cecilio and Virgen de las Nieves University Hospital, Granada, approved this study. Before participation, all subjects signed a written informed consent form.

Participants

A total of 212 subjects with COPD (104 stable and 108 with COPD exacerbation) were enrolled, along with 100 healthy subjects. Subjects with stable and exacerbated COPD were selected from those admitted to the Pulmonary Medicine Service, San Cecilio and Virgen de las Nieves University Hospitals in a population-based consecutive enrollment process. The subjects with COPD exacerbation were included and evaluated during the hospitalization period. The control group was composed of healthy volunteers recruited from the community.

The inclusion criteria for people with COPD were diagnosis with COPD according to the American Thoracic Society guidelines[26] and age ≥60 y old. The inclusion criteria for the volunteers included in the control group were the absence of COPD and age ≥60 y. The exclusion criteria for all of the participants were inability to provide informed consent, presence of psychiatric or cognitive disorders, progressive neurological or severe musculoskeletal disorders, severe orthopedic problems, organ failure, cancer, or inability to cooperate. Subjects with stable COPD had to be free of exacerbations for at least 2 months prior to testing.

Measurements

Sociodemographic and anthropometric data were collected during the interview of the subjects. The clinical profile included the independence level in functional activities assessed with the Barthel index,[27] the cognitive status evaluated by the mini-mental state examination,[28] comorbidities evaluated by the Charlson score,[29] exacerbations in the previous year, and the quality of life reported by the EuroQol-5D questionnaire.[30,31] Additionally, the severity of COPD was recorded using the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification. Balance with the one-leg stance test,[32-34] functional capacity with the 2-min step in place,[35-37] and fatigue with the Piper fatigue scale[38-40] were also assessed due to the association of these measurements with frailty.

Frailty. Frailty was measured according to the frailty index as modified by Fried et al.[1] Previous studies used this measure to assess frailty in COPD subjects,[41,42] being identified by the presence of ≥3 of the 5 following components: decreased handgrip strength, unintentional self-reported weight loss, reports of exhaustion, functional limitation at the chair rise, and low level of physical activity. 1) Decreased handgrip strength in the dominant hand was measured by a dynamometer and adjusted for sex and body mass index (BMI) (weakness was defined as an adjusted handgrip strength in the lowest 20th percentile of a community-dwelling population of adults ≥65 y old). Men met the criteria for weakness if their BMI and handgrip strength were ≤24 and ≤29 kg; 24.1–26 and ≤30 kg; 26.1–28 and ≤31 kg; or >28 and ≤32 kg, respectively. Women met the criteria for weakness if their BMI and handgrip strength were ≤23 and ≤17 kg; 23.1–26 and ≤17.3 kg; 26.1–29 and ≤18 kg; or >29 and ≤21 kg, respectively.). 2) Unintentional self-reported weight loss was considered >5% of body weight in the previous year. 3) Reports of exhaustion were evaluated by the question, "Do you feel full of energy?" from the Geriatric Depression Scale developed by Sheik and Yesavage.[43] 4) Functional limitation at the chair rise was evaluated by the elderly individual's incapacity to rise 5 consecutive times from the chair without using the arms. Subjects were asked to rise from a standard height chair without armrests 5 times, as fast as possible, with their arms folded. Subjects undertook the test barefoot, and performance was measured in seconds, as the time from the initial seated position to the final seated position after completing 5 stands. The cutoff point for this test is ≥12 s with sensitivity 0.66 and specificity 0.55.[44] Subject with an inability to perform the test in <12 s were considered to have functional limitation. 5) A low level of physical activity was considered <150 min/week.

Subjects were asked to describe their levels of physical activity in the previous week. They were asked about how many hours of moderate physical activity they perform daily and how many times per week. In 1995, the American College of Sports Medicine and the Centers for Disease Control and Prevention published national guidelines on physical activity and public health. The guidelines defined a sedentary lifestyle as those values of physical activity <30 min 5 days/week or <150 min/week. Additionally, 150 min of moderate-intensity aerobic activity per week have been reported to reduce the risk of chronic diseases and other adverse health outcomes.[45]

Physical Activity. The physical activity level was assessed with the modified Baecke physical activity questionnaire, which is a frequently used questionnaire to measure habitual physical activity in the elderly. The questionnaire includes items about household activities, sport, and leisure time activities. The Spanish version of this questionnaire has been shown to be valid in COPD patients.[46] The theoretical total score ranges between 0 and 47.56. It reflects the degree of sedentary lifestyle. Subjects with values of <9 are considered sedentary, between 9 and 16 moderately sedentary, and >16 active.[46]

Statistical Analysis

Sample Size Determination. When determining the sample size, the procedures proposed by Luiz and Magnanini[47] for finite populations were used. In this calculation, a significance level of 5% (corresponding to a CI of 95%, z[a]/2 = 1.96) and tolerable sampling error of 3% were adopted, resulting in a required sample of 80 subjects to estimate the prevalence of frailty in 57%. This first estimate of sample size was increased by 20% to explore the adjusted associations between frailty and the domains of physical activity. In addition, it was increased 10% to compensate for any loss, resulting in 104 participants/group.

Statistics. Statistical analysis was performed using SPSS 20.0 (SPSS, Chicago, Illinois). P <.05 was considered to be statistically significant. The characterization of the variables was expressed as mean, SD, minimum and maximum values, and frequencies. To compare the distribution of variables between groups (stable COPD, COPD exacerbation, and healthy subjects), an analysis of variance (continuous data) and the chi-square test (categorical data) were used. Post hoc comparisons (Bonferroni test) were then used when the analysis of variance was significant. The predictive power and the cutoffs of different patterns and domains of physical activity for the absence of frailty

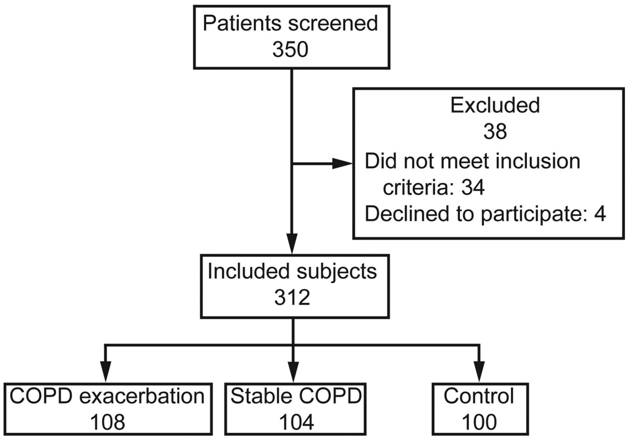

Fig. 1. Flow chart.

were identified by ROC curves, frequently used to determine cutoffs for diagnostic or triage tests.[48]

Initially, the total area under the ROC curve was identified among the physical activity patterns in their different domains (work, transportation, housework, leisure) and total physical activity (the 4 domains analyzed together) for the absence of frailty. The larger the area under the ROC curve, the greater the discriminatory power of physical activity for the absence of frailty.

Results

Three hundred fifty participants were screened for the study, and 346 gave written consent to participate. The flow diagram of participants is shown in Figure 1.

Three hundred twelve participants were finally included with a mean age of 72.6 y and a mean BMI of 28 kg/cm^2. Mild cognitive impairment was detected in 91.3% of subjects with COPD exacerbation, 64.3% of subjects with stable COPD, and 16.1% of healthy individuals. The characteristics of participants are presented in Table 1.

The characteristics reported in Table 1 showed similar values for age, independence, comorbidity score, and number of exacerbations in the last year ($P > .05$) between the groups. The severity of the subjects included in the study was severe (GOLD III) and very severe (GOLD IV), showing non significant between-groups differences. BMI and quality of life show significant differences between COPD groups.

The prevalence of frailty was higher in the COPD subjects than in the control group. Significant between-groups differences were found in the variables assessing balance and functional capacity, with the worst values for COPD exacerbation and the best values for healthy subjects. Although frailty was likely to be more frequent in the COPD groups, we found that 52.4% of healthy subjects were frail. The frailty variables by group are presented in Table 2.

Frailty and Activity Levels

Table 3 shows the areas under the ROC curves with their respective confidence intervals for physical activity in the different domains as predictors of the absence of frailty. ROC curves were constructed for all groups. The largest areas were observed in the domain of leisure time. The cutoff points, with their respective sensitivity and specificity values of total physical activity in subjects with COPD exacerbation, subjects with stable COPD, and healthy subjects as predictors of the absence of frailty, are shown in Figure 2.

For COPD exacerbation subjects, the cutoff point determined for total physical activity was 3.54 (sensitivity of 0.95 and specificity of 0.807) for the absence of frailty and less than this value for the presence of frailty. For stable COPD subjects, the cutoff point was 3.88 (sensitivity of 0.95 and specificity of 0.815). For healthy subjects, the cutoff point was 3.50 (sensitivity of 0.95 and specificity of 0.947) for the presence or absence of frailty. The small difference in the cutoffs for the 3 populations reflects the sedentary behavior of elderly people. There is a relationship between frailty and physical activity levels.

Discussion

The aim of this study was to analyze the predictive power and to identify the cutoffs of physical activity in their different domains for the absence of frailty in subjects with COPD exacerbation and subjects with stable COPD. The results show that the physical activity level can predict the presence of frailty in subjects with stable COPD and COPD exacerbation. Subjects with a score of <3.88 and <3.54, respectively, are considered to be frail.

There is a consensus in the literature regarding the role of physical activity in the prevention and the treatment of frailty.[49-51] However, only the study of Tribess et al[52] has attempted to identify the predictive power of physical activity as a discriminator of the presence or absence of frailty in the elderly. As reported by the study of Park et al,[6] the high prevalence of frailty among the COPD population is not surprising, taking into account the clinical characteristics of these individuals. The increase of disease severity and the shortness of breath lead to inactivity,[53-55] which in turn leads to a deterioration of muscle strength,[56-58] independence,[59,60] and finally, frailty. People with COPD experience a loss of muscle strength, primarily in lower limb muscles,[57,61] which is greater when individuals with COPD suffer from an exacerbation. Additionally, our study shows a slightly higher prevalence of frailty in subjects with stable COPD compared with those with COPD exacerbation. This can be explained not only by physical deterioration; cognitive impairment[62] and depression[63] are more severe in COPD exacerbation.

Table 1. Characteristics of the Participants Included in the Study

	COPD Exacerbation Group (*n* = 108)	Stable COPD Group (*n* = 104)	Control Group (*n* = 100)	*P*
Age, mean ± SD y	71.4 ± 9.60	71.6 ± 8.36	74.9 ± 7.32	
Female sex, *n* (%)	34 (42.5)	11 (26.2)	34 (55.4)	<.001
BMI, ± SD kg/m^2*†‡	28.64 ± 5.11	29.07 ± 5	26.27 ± 3.46	
GOLD stage, %§				.49
GOLD 3	47.1	37.7		
GOLD 4	39.1	42.5		
Barthel index, mean ± SD	90.66 ± 12.67	90.15 ± 18.61	90.92 ± 20.45	.02
EQ-5D VAS, mean ± SD‖¶	48.6 ± 20.42	65.56 ± 21.05	70.24 ± 20.07	
Cognitive impairment, *n* (%)§	73 (91.3)	27 (64.3)	9 (16.1)	.001
Charlson score, mean ± SD	4.86 ± 1.58	4.12 ± 2.56	3.89 ± 1.74	
Exacerbations in previous year, mean ± SD	3.06 ± 2.84	2.59 ± 3.16	4.19 ± 2.43	
Frail, %§	62.6	64.8	52.4	<.001
OLS right leg, mean ± SD s*¶‡	5.78 ± 7.88	11.67 ± 8.25	18.47 ± 7.44	
OLS left leg, mean ± SD s‖¶‡	5.05 ± 7.61	13.48 ± 15.69	19.92 ± 6.64	
2MSP, mean ± SD steps‖¶‡	13.67 ± 12.63	53.40 ± 31.55	69.5 ± 17.28	
Fatigue, mean ± SD total score	5.32 ± 1.59	4.22 ± 2.13	3.23 ± 9.88	

* $P < .05$, COPD exacerbation group vs stable COPD group.
† $P < .001$, COPD exacerbation group vs control group.
‡ $P < .05$, stable COPD group vs control group.
§ Chi-square test.
‖ $P < .001$, COPD exacerbation group vs stable COPD group.
¶ $P < .001$, COPD exacerbation group vs control group.
BMI = body mass index
GOLD = Global Initiative for Chronic Obstructive Lung Disease
EQ-5D = EuroQol-5D
VAS = visual analogue scale
OLS = one-leg stance
2MSP = 2-min step in place

Table 2. Variables for Frailty Definition by Group

	COPD Exacerbation Group (*n* = 108)	Stable COPD group (*n* = 104)	Control Group (*n* = 100)	*P*
Handgrip force, mean ± SD newtons	95.37 ± 16.48	102.48 ± 23.54	113.47 ± 22.61	
Self-reported weight loss >5% of body weight, *n* (%)*	21 (19.4)	15 (14.4)	18 (18)	.60
Reported exhaustion, *n* (%)*	75 (69.4)	53 (54)	41 (41)	.003
Functional limitation, *n* (%)*	68 (62.96)	64 (61.53)	38 (38)	.026
Low level of physical activity, *n* (%)*	42 (38.9)	37 (35.57)	39 (39)	.76

* Chi-square test.

It has been previously reported that subjects with COPD experienced marked deficits in mobility,[56,59,60] gait speed,[60] and gait stability,[64] exhibiting balance unsteadiness and limited physical activity when compared with controls.[65,66] This contributes to the high prevalence of frailty in COPD as well as the reduction of physical activity. Our results indicate that, in the same line of previous studies,[56,60,64] subjects with COPD present a significant impairment of balance, functional capacity, and fatigue compared with healthy controls. COPD patients also suffer high levels of impairment after exacerbations. Other studies[67,68] have reported that exacerbations and their frequency could contribute to disease progression and, consequently, can induce an increase in frailty scores.

Subjects >50 y old and especially those who are frail are reported to be highly sedentary.[69] Sedentary behavior has been reported to be independently associated with frailty and adverse health outcomes in middle-age and older adults.[69] Physical activity tends to decrease with age but especially in individuals with COPD compared with sedentary people without COPD. The evaluation of the physical activity level provides additional information on health problems, regarding both func-

Table 3. Area Under the Receiver Operating Characteristic Curve and 95% CI Between the Domains of Physical Activity as Predictors of Presence of Frailty per Group

Domain	COPD Exacerbation Group (n = 108)	Stable COPD Group (n = 104)	Healthy Group (n = 100)
PA household	0.635 (0.522–0.749)	0.602 (0.488–0.716)	0.842 (0.691–0.993)
PA leisure time	0.80 (0.712–0.888)	0.803 (0.717–0.888)	0.737 (0.576–0.898)
PA sport	0.605 (0.492–0.717)	0.637 (0.533–0.741)	0.757 (0.580–0.933)
PA total score	0.907 (0.845–0.970)	0.918 (0.862–0.975)	0.980 (0.942–1.000)

PA = physical activity

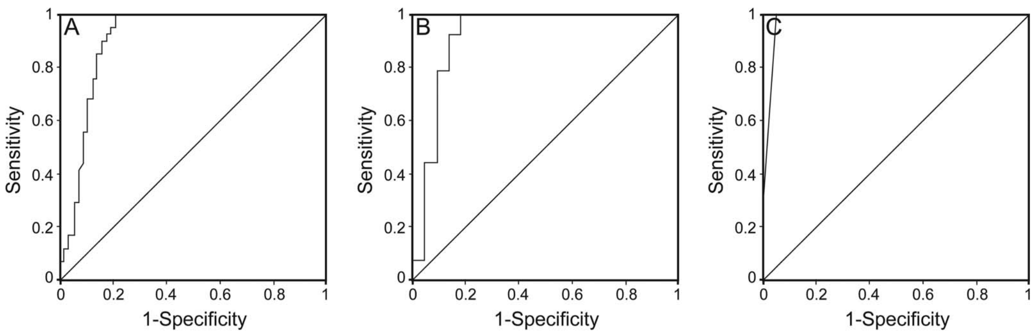

Fig. 2. Cutoffs with respective sensitivities and specificities of physical activity in subjects with COPD exacerbation (A), subjects with stable COPD (B), and control subjects (C) as predictors of the absence of frailty.

tional limitations and incapacity. In this study, the physical activity was shown to be a predictor of frailty. For subjects with COPD exacerbation, the cutoff point determined to be considered frail was 3.54; for stable COPD subjects, the cutoff point was 3.88; and for the healthy subjects, the cutoff point was 3.50. As long as COPD patients have a lower degree of physical activity than healthy adults of the same age,[70] due to their poorer state of health,[71] the questionnaire could contribute to the early detection and treatment of frailty in clinical practice. From the several cutoff points obtained in the analysis of the ROC curve with high sensitivity and specificity, it is proposed to use a cutoff point score of 3.54 points in patients with COPD exacerbation and 3.88 points in patients with stable COPD, in the total of the Baecke questionnaire. Pulmonary function is associated with frailty and may have utility as a straightforward detection test. However, diagnostic accuracy of these assessments has not been confirmed.[72] The increase of symptoms during the exacerbation could explain the difference in the cutoff in subjects with COPD exacerbation compared with those with stable COPD. It is important to consider that physical activity levels are not the only determinate of frailty. Taking into account that specificity is 0.8 for both COPD groups, patients could be missed when clinicians only rely on this measurement. Maybe in some cases, a broader screening should be performed. It is important to highlight the clinical applicability of our results; low physical activity is one of the components of frailty and may be the factor easiest to use in predicting frailty with sufficient predictive capacity.

Some limitations were found in this study: (1) the cross-sectional design hampers advances in temporal analyses of the factor studies, due to the reverse causality bias, so that no relation of causality could be identified; and (2) the use of a questionnaire to measure the physical activity level can underestimate or overestimate some of the information found. However, Cronbach's α coefficient of this questionnaire has been shown to be very high (0.97, $P < .001$). Intraclass correlation coefficients of the test/retest reliability were also very high (0.96). The questionnaire has shown a significant correlation with quality of life (St George Respiratory Questionnaire), dyspnea score (Medical Research Council scale), and exercise capacity (6-min walk test).[46] (3) Another limitation could be that weight loss was based on the recall of subjects; however, previous studies[1,8] have been based on the recall of subjects, using their self-reported unintentional weight loss. Additionally, in the case of COPD patients, weight loss is associated with their disease and the symptoms. Regardless of these limitations, this study has demonstrated the potential usefulness of ROC analysis to derive optimal physical activity for clinically relevant outcomes based on objective surveillance and program evaluation. This study may also provide information to develop clinical and public health guidelines and recommendations.

Conclusions

This study showed the presence of a close link between frailty and physical status in COPD, indicating that the physical activity level can predict the absence or presence of frailty in subjects with stable COPD and COPD exacerbation. Therefore, an increase in physical activity could probably contribute to the prevention of frailty.

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