Usefulness of the LCOPD, CAFS and CASIS Scales in Understanding the Impact of COPD on Patients

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Key Words

Chronic obstructive pulmonary disease • Quality of life • Fatigue • Sleep • Patient-reported outcomes

Abstract

Background: The Living with COPD (LCOPD), COPD and Asthma Fatigue Scale (CAFS), and COPD and Asthma Sleep Impact Scale (CASIS) are instruments developed to assess the overall impact of chronic obstructive pulmonary disease (COPD) on daily life, fatigue, and sleep impairment, respectively. **Objectives:** To assess the usefulness of these instruments and to identify factors associated with the concepts they measure. **Method:** The questionnaires were administered to patients with moderate to severe COPD. Descriptive analyses of sociodemographic and clinical data were performed, and bivariate and multivariate analyses were used to identify factors associated with the overall impact of COPD on patients' lives, fatigue, and sleep impairment. **Results:** A total of 408 patients was included (mostly males, 91.2%), with an average age of 68 years (SD = 9.3). Statistically significant differences were observed in the scores of the three questionnaires with regard to level of education, presence of chronic cough or expectoration, level of dyspnea, number of exacerbations, physical activity level, pres-

ence of depression and anxiety, and number of treatments indicated for COPD. The LCOPD and CAFS questionnaires also discriminated between different levels of airflow obstruction and, in the case of CAFS, age and gender. Linear regression showed that level of dyspnea, physical activity, and presence of anxiety were significantly related to the LCOPD, CAFS and CASIS scores. The presence of depression was significant in the LCOPD and CAFS questionnaires and chronic cough was significant in the CAFS questionnaire. **Conclusions:** The LCOPD, CAFS, and CASIS instruments are valid and useful in understanding the overall impact of COPD on daily life, fatigue, and sleep impairment in patients with moderate to severe COPD.

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Introduction

Chronic obstructive pulmonary disease (COPD) is one of the main causes of morbidity and mortality worldwide [1] and has a very significant impact on patients' quality of life [2]. This is one of the main reasons why interest in outcomes centered on the patients and their experience with COPD has grown exponentially in recent years [3, 4].

Table 1. Sociodemographic and clinical characteristics of the study sample

<i>Sociodemographic data</i>	
Age, years	68 ± 9.3
Males, n (%)	372 (91.2)
Level of education, n (%)	
Unfinished primary studies	81 (20.1)
Primary studies	241 (59.8)
Secondary studies	59 (14.6)
University studies or similar	22 (5.5)
<i>Clinical data</i>	
Time since diagnosis, years	11 ± 6.2
Spirometry values pre-bronchodilation	
FVC, ml	2,636.5 ± 787.1
FVC, %	70.1 ± 15
FEV ₁ , ml	1,331.9 ± 490.7
FEV ₁ , %	47.6 ± 13.5
FEV ₁ /FVC	50.4 ± 10.8
Spirometry values post-bronchodilation	
FVC, ml	2,776.1 ± 831.6
FVC, %	72.4 ± 15.1
FEV ₁ , ml	1,407.2 ± 490.8
FEV ₁ , %	50.3 ± 14.1
FEV ₁ /FVC	50.8 ± 11.2
Positive bronchodilator test, n (%)	63 (15.4)
Smoking habits, n (%)	
Nonsmoker	6 (1.5)
Ex-smoker	335 (82.5)
Smoker	65 (16)
Pack-years	51.9 ± 33
Degree of dyspnea	2.7 ± 0.89
Exacerbations in the last 12 months, n (%)	
None	132 (35.7)
Between 1 and 2	161 (43.5)
Between 3 and 4	49 (13.2)
More than 4	28 (7.6)
Medication treatment, n (%)	
Short-acting β ₂ -agonists	207 (50.7)
Long-acting β ₂ -agonists	358 (87.7)
Inhaled corticosteroids	348 (85.3)
Oral corticosteroids	14 (3.4)
Anticholinergics	363 (89)
Theophylline	42 (10.3)
Treatments indicated, n	3.26 ± 1.01
Valus are means ± SD unless otherwise indicated.	

There is an abundance of research on describing and gathering knowledge about the impact of COPD on daily life, and also on the impact of different therapeutic approaches [5, 6]. Specific instruments for COPD have been used, such as the St. George's Respiratory Questionnaire [7], as well as generic instruments such as the EuroQoL

5D [8, 9] or a combination of both [10]. Other research has explored the relationship between COPD and mood, quantifying the presence of symptoms of anxiety or depression in specific populations of patients with COPD and/or perceiving how mood can influence tolerance to physical exercise, social isolation, or the likelihood of re-hospitalization [11, 12] by employing instruments such as the Hospital Anxiety and Depression Scale [13, 14]. The relationship between COPD and physical and functional capacity has also been a focus of research [15, 16] with the recent availability of the London Chest Activity of Daily Living scale [17], the validated Spanish version of which was published lately [18].

However, although there is evidence that fatigue and sleep impairment are frequent problems in patients with COPD [19–21], there is little available to help quantify these important aspects. Until very recently there were no suitable instruments considered validated for use within the COPD population. For this reason, two specific instruments have recently been developed and validated for patients with COPD: the COPD and Asthma Fatigue Scale (CAFS) [22] and the COPD and Asthma Sleep Impact Scale (CASIS) [23]. The Living with COPD (LCOPD) questionnaire is a new instrument that measures the overall impact of COPD on daily life [24]. The objectives of the current study were to assess the usefulness of these new instruments and to identify factors associated with the concepts they measure.

Method

Study Design

This was an observational cross-sectional, descriptive, and multicenter study carried out in pneumology departments of 21 hospitals in Spain.

Included patients had to meet the following criteria: (a) diagnosis of moderate or severe COPD (determined by spirometry after a bronchodilator test with an FEV₁/FVC <0.70 and FEV₁ <80%, undergone within 6 months prior to inclusion into the study); (b) age ≥40 years; (c) smokers or ex-smokers of at least 10 pack-years; (d) with COPD for at least 5 years; (e) attended a scheduled follow-up appointment according to usual clinical practice; (f) had signed the informed consent form, and (g) were capable of understanding and completing the questionnaires that would be administered.

Patients not included in the study were those who: (a) presented with an acute exacerbation of COPD at the time of inclusion or had presented with an exacerbation within 8 weeks prior to inclusion; (b) presented with an exacerbation of other concomitant diseases; (c) had a diagnosis of asthma or pneumonia; (d) were already participating in a clinical trial or research study, or (e) were on home oxygen therapy.

The study sample size was calculated for each of the LCPD, CASIS, and CAFS scales, with a statistical significance level of 5%, a power of 90%, an accuracy of ± 2 points, and assuming that 10% of the information gathered from patients would not be valid or analyzable. The greatest necessary sample size was determined by the CASIS scale, estimated at 419 cases, with a typical deviation of 19.8, obtained according to the scale validation [23].

The study was approved by the Ethics Committee of the Hospital Clínic of Barcelona and all patients signed an informed consent form to participate.

Data Collection

Sociodemographic data (age, gender, and level of education), clinical data related to COPD: time elapsed since diagnosis, smoking habits, pulmonary function, clinical symptoms of COPD, treatment(s) received, and exacerbations suffered in the previous 12 months were gathered for each patient. The degree of dyspnea was assessed by means of the Medical Research Council scale [25].

The overall impact of COPD on daily life was assessed using the validated Spanish version of the LCPD [26]. The LCPD consists of 22 items that identify a wide range of situations where COPD could negatively impact daily life. An overall score is obtained ranging from 0 to 22, where high scores indicate a major impact of COPD on daily life [24].

Fatigue associated with COPD was assessed by means of the validated Spanish version of the CAFS [27]. The CAFS is a questionnaire created to assess fatigue associated with COPD and asthma. The questionnaire consists of 12 items that explore the frequency with which certain situations and symptoms associated with tiredness and fatigue arise. A global score is obtained ranging from 0 to 100, where high scores indicate a major impact of COPD on the patient's fatigue [22].

The impact of COPD on sleep was assessed by means of the validated Spanish version of the CASIS [28]. The CASIS is a questionnaire developed to assess sleep-related problems and disorders associated with COPD and asthma. The questionnaire consists of 13 items that explore the frequency with which certain situations and symptoms associated with sleep-related problems arise. An overall score is obtained ranging from 0 to 100, where high scores indicate a major impact of the COPD on the patient's sleep [23].

The physical activity level was gathered by means of the validated Spanish version of the London Chest Activity of Daily Living scale (LCADL) questionnaire [18]. The LCADL is a questionnaire developed to assess the physical activity level and functional autonomy of respiratory care patients. It consists of 15 items distributed in 4 dimensions ('basic self-care tasks', 'domestic tasks', 'physical activities', and 'leisure/free time') as well as an additional independent item concerning the limitations associated with the patient's breathing. An overall score and a summary score are obtained for each dimension, where high scores indicate a major impact of COPD on the patient's physical activity [17].

Detection of anxiety states and depression was performed using the Spanish version of the Hospital Anxiety and Depression Scale (HADS) questionnaire [29]. The theoretical intervals of both dimensions (anxiety and depression) range from 0 to 21, where high scores indicate major levels of anxiety and depression. A score of 8 or higher identifies the probable presence of anxiety or depression [30].

Table 2. Mean scores for the patient-reported outcomes in the sample study

<i>Health status</i>	
LCPD	8.8 $\pm$ 5.9
CASIS	29.7 $\pm$ 22.1
CAFS	35.8 $\pm$ 24.7
LCADL overall score	21 $\pm$ 12.8
LCADL self-care	6.2 $\pm$ 3.6
LCADL domestic tasks	6.2 $\pm$ 7.9
LCADL physical activities	4.6 $\pm$ 2
LCADL leisure/free time	4.1 $\pm$ 2.4
HADS anxiety	5.5 $\pm$ 4.4
Prevalence of anxiety symptoms ^a , n (%)	111 (27.2)
HADS depression	4.7 $\pm$ 4.3
Prevalence of depression symptoms ^a , n (%)	93 (22.8)

Values are means $\pm$ SD unless otherwise indicated.

^a The presence of anxiety or depression is determined if the patient obtains a score greater than 7 on the HADS anxiety/depression questionnaire.

Statistical Analysis

The categorical variables were described as the number and percentage of subjects in each category and the continuous variables as means and SD. Nonparametric tests were performed (Kolmogorov-Smirnov bilaterally with a confidence level of 95%) to assess the normal distribution of the questionnaire scores. Bivariate analysis was performed using nonparametric Mann-Whitney tests (for two samples) and the Kruskal-Wallis test (for n samples), both bilaterally with a confidence level of 95%, and Spearman's rho for continuous variables, as appropriate in each case.

Multivariate analysis was performed using a simple linear regression model. The purpose of this analysis was to explore and, to the greatest extent possible, identify variables associated with the impact on daily life, fatigue, and sleep impairment. $p < 0.05$ was considered statistically significant. Statistical analysis was performed with SPSS software, version 13.0.

Results

A total of 431 patients were screened, 23 of whom were excluded for noncompliance with one or more of the inclusion criteria. The study population was composed of 408 patients. Table 1 presents sociodemographic and clinical characteristics. Patients were, for the most part, males (91.2%) with an average age of 68 years (SD = 9.3) and a low or very low education level (80%). The average time elapsed since the diagnosis of COPD was 11 years (SD = 6.2). The mean FEV₁ (%) post-bronchodilator was 50.3% (SD = 14.1%). Sixteen percent of the population

Table 3. Bivariate analysis of variables that affect daily life (LCOPD), sleep impairment (CASIS), and fatigue (CAFS)

	LCOPD		CAFS		CASIS	
	n	mean $\pm$ SD	n	mean $\pm$ SD	n	mean $\pm$ SD
Age						
<60 years	94	9.1 $\pm$ 6.2	94	39.8 $\pm$ 25.1	94	32.9 $\pm$ 25.4
61–69 years	101	8.5 $\pm$ 5.9	103	30.5 $\pm$ 22.0	103	26.4 $\pm$ 20.2
70–75 years	111	8.8 $\pm$ 5.7	111	35.7 $\pm$ 24.9	111	27.8 $\pm$ 27.8
>75 years	99	8.8 $\pm$ 6.1	98	37.7 $\pm$ 26.1	99	32.1 $\pm$ 23.0
p value ^a	0.803		0.045		0.214	
Gender						
Male	371	8.7 $\pm$ 6.0	371	35.0 $\pm$ 24.9	372	29.5 $\pm$ 22.0
Female	34	9.8 $\pm$ 5.7	35	43.7 $\pm$ 21.6	35	31.2 $\pm$ 23.6
p value ^b	0.238		0.027		0.783	
Level of education						
Unfinished primary school	80	10.7 $\pm$ 6.1	79	40.3 $\pm$ 25.1	80	34.5 $\pm$ 23.9
Primary education	241	8.9 $\pm$ 5.8	241	36.9 $\pm$ 23.8	241	30.4 $\pm$ 21.3
Secondary education	58	6.5 $\pm$ 5.8	59	28.5 $\pm$ 26.5	59	24.3 $\pm$ 22.6
University or similar	21	5.6 $\pm$ 5.1	22	23.3 $\pm$ 20.7	22	16.6 $\pm$ 13.9
p value ^a	<0.0001		0.002		0.001	
Pack-years						
<36	121	8.3 $\pm$ 6.0	120	33.5 $\pm$ 26.0	121	28.2 $\pm$ 24.7
36–59	123	9.4 $\pm$ 6.0	125	38.2 $\pm$ 23.5	125	30.1 $\pm$ 20.0
>59	126	8.9 $\pm$ 6.0	126	35.7 $\pm$ 25.4	126	30.9 $\pm$ 22.0
p value ^a	0.356		0.207		0.336	
Severity of airflow obstruction (GOLD stages)						
Very severe	29	9.6 $\pm$ 5.7	28	40.1 $\pm$ 25.3	29	29.1 $\pm$ 21.8
Severe	149	10.6 $\pm$ 5.8	149	41.2 $\pm$ 24.7	149	31.5 $\pm$ 22.4
Moderate	192	7.1 $\pm$ 5.7	194	30.7 $\pm$ 23.7	194	27.5 $\pm$ 21.1
p value ^a	<0.0001		<0.0001		0.265	
Chronic cough						
Yes	241	9.7 $\pm$ 5.9	243	40.5 $\pm$ 25.4	243	32.9 $\pm$ 23.0
No	164	7.3 $\pm$ 5.7	163	28.7 $\pm$ 21.8	164	24.9 $\pm$ 19.8
p value ^b	<0.0001		<0.0001		0.001	
Expectoration						
Yes	218	9.6 $\pm$ 5.9	219	38.9 $\pm$ 25.1	219	31.9 $\pm$ 21.7
No	185	7.9 $\pm$ 5.9	185	32.3 $\pm$ 23.8	186	27.1 $\pm$ 22.4
p value ^b	0.003		0.006		0.016	
Degree of dyspnea						
Level 0	27	2.5 $\pm$ 3.0	27	8.6 $\pm$ 11.7	27	10.6 $\pm$ 13.6
Level 1	135	6.0 $\pm$ 4.8	136	24.3 $\pm$ 19.7	136	25.8 $\pm$ 21.4
Level 2	166	9.8 $\pm$ 5.4	167	41.2 $\pm$ 22.7	167	31.2 $\pm$ 21.4
Level 3	63	13.6 $\pm$ 4.8	62	54.1 $\pm$ 21.6	63	38.6 $\pm$ 20.5
Level 4	10	16.8 $\pm$ 4.3	10	60.9 $\pm$ 23.7	10	50.7 $\pm$ 24.1
p value ^a	<0.0001		<0.0001		<0.0001	
Exacerbations						
None	130	6.9 $\pm$ 5.7	131	26.9 $\pm$ 21.5	131	23.4 $\pm$ 19.8
1–2	160	8.4 $\pm$ 5.6	160	35.6 $\pm$ 24.6	161	30.0 $\pm$ 22.3
3–4	49	12.6 $\pm$ 5.0	49	49.0 $\pm$ 22.8	49	37.3 $\pm$ 20.8
>4	28	12.6 $\pm$ 5.3	28	56.4 $\pm$ 20.4	28	47.8 $\pm$ 19.0
p value ^a	<0.0001		<0.0001		<0.0001	
LCADL global score						
<15	125	5.4 $\pm$ 4.8	125	20.6 $\pm$ 17.6	125	20.5 $\pm$ 16.7
15–20	112	7.7 $\pm$ 5.6	111	29.7 $\pm$ 21.3	112	24.8 $\pm$ 19.8
>20	121	13.0 $\pm$ 4.8	123	53.8 $\pm$ 21.3	123	41.9 $\pm$ 21.9
p value ^a	<0.0001		<0.0001		<0.0001	

Table 3 (continued)

	LCOPD		CAFS		CASIS	
	n	mean $\pm$ SD	n	mean $\pm$ SD	n	mean $\pm$ SD
Presence of depression symptoms of HADS						
No	312	7.0 $\pm$ 5.1	313	28.4 $\pm$ 20.9	314	24.0 $\pm$ 19.9
Yes	92	14.8 $\pm$ 4.5	92	60.8 $\pm$ 19.4	92	48.5 $\pm$ 18.4
p value ^b	<0.0001		<0.0001		<0.0001	
Presence of anxiety symptoms (HADS)						
No	292	6.9 $\pm$ 5.2	293	27.4 $\pm$ 20.7	294	22.4 $\pm$ 18.6
Yes	110	13.5 $\pm$ 5.2	110	57.1 $\pm$ 20.4	110	48.5 $\pm$ 19.2
p value ^b	<0.0001		<0.0001		<0.0001	
Number of indicated treatments						
0–2	74	5.4 $\pm$ 5.4	74	24.2 $\pm$ 21.1	74	22.1 $\pm$ 19.2
3 treatments	159	8.5 $\pm$ 5.6	160	34.6 $\pm$ 24.0	160	30.4 $\pm$ 22.0
>3	172	10.5 $\pm$ 5.9	172	41.9 $\pm$ 25.0	173	32.3 $\pm$ 22.7
p value ^a	<0.0001		<0.0001		0.002	

^a Kruskal-Wallis test.^b Mann-Whitney test.

still smoked and the average tobacco consumption was 51.9 pack-years (SD = 33). The average dyspnea level was 2.7 (SD = 0.9). The most common medications were anticholinergics (89%), long-acting β_2 -agonists (87.7%), inhaled corticosteroids (85.3%), and short-acting β_2 -agonists (50.7%). Of the patients, 64.3% had suffered at least 1 exacerbation in the 12 months prior to their inclusion into the study, and 20.8% had had 3 or more exacerbations.

The results obtained from the questionnaires are presented in table 2. The mean scores on the LCOPD (interval 0–22) were 8.8 (SD = 5.9) and 21 (SD = 12.8) for the LCADL scale (interval 0–75). The mean scores for the CAFS and CASIS were 35.8 (SD = 24.7) and 29.7 (SD = 22.1), respectively, and both scales had intervals of 0–100. The HADS scale results indicate that 27.2 and 22.8% of the patients had a high likelihood of suffering from anxiety disorders and depression, respectively.

Statistically significant differences were observed in the LCOPD, CAFS, and CASIS scores among patients with different clinical and demographic characteristics (table 3). The patients with worse dyspnea, a greater number of exacerbations in the previous 12 months, less physical activity assessed by means of the LCADL, and more anxiety or depression symptoms had worse scores on all of the scales analyzed ($p < 0.0001$). Statistically significant differences were also observed ($p < 0.0001$) in the LCOPD and CAFS scores depending on the presence or

lack thereof of chronic cough, deterioration of FEV₁ (%), and the number of treatments received for COPD.

The LCOPD and CAFS scores significantly differed depending on the stage of COPD. The scores of the three questionnaires differed according to the degree of dyspnea and the number of exacerbations the previous year (fig. 1–3).

With regard to the correlation analysis between the questionnaire scores and clinical variables, the greatest correlation was observed between the activity score of the LCADL and CAFS ($r = 0.62$), LCOPD ($r = 0.60$), and CASIS ($r = 0.44$). The correlations with the MRC dyspnea scale were also noteworthy ($r = 0.54$, $r = 0.56$, and $r = 0.32$ for CAFS, LCOPD, and CASIS, respectively). The remaining correlations were of a lower intensity (table 4).

The results of the multivariate analysis (table 5) showed that degree of dyspnea, level of physical activity, and presence of anxiety were independently and significantly associated ($p < 0.012$) with the scores of the three LCOPD, CAFS, and CASIS questionnaires. In addition, for both the LCOPD and the CAFS questionnaire independent associations with other clinical variables were observed: the presence of depression in both cases and chronic cough in CAFS. The regression models showed adjustments of 52, 54.5, and 37.1% for the LCOPD, CAFS, and CASIS questionnaires, respectively.

Fig. 1. LCOPD, CAFS, and CASIS scores according to COPD GOLD stage. p values were calculated by means of nonparametric statistics, i.e. the Kruskal-Wallis test for n independent samples with a bilateral confidence level of 95%. **a** LCOPD. $p < 0.0001$. Sample strata: stage II, $n = 192$; stage III, $n = 149$, and stage IV, $n = 29$. **b** CAFS. $p < 0.0001$. Sample strata: stage II, $n = 194$; stage III, $n = 149$, and stage IV, $n = 28$. **c** CASIS. $p = 0.256$. Sample strata: stage II, $n = 194$; stage III, $n = 149$, and stage IV, $n = 29$.

Table 4. Correlations between clinical characteristics and the daily life (LCOPD), sleep impairment (CASIS), and fatigue (CAFS) scales

	LCOPD	CAFS	CASIS
Age	<0.10	<0.10	<0.10
Pack-years	<0.10	<0.10	<0.10
Severity of airflow obstruction (GOLD stages)	0.33	0.26	<0.10
Degree of dyspnea	0.56	0.54	0.32
Number of exacerbations	0.35	0.38	0.31
LCADL global score	0.60	0.62	0.44
Number of indicated treatments	0.34	0.29	0.17

Discussion

The significance of respiratory symptoms and exercise limitation with COPD is well known and can be documented with validated questionnaires or well-established tests [12, 15, 31]. However, when making a complete assessment of the patient with COPD, other relevant aspects affected by the illness must be taken into account. Among these aspects relating to health-related quality of life are: overall impact of COPD, fatigue, and sleep impairment. The current study has shown that patients with moderate to severe COPD are significantly impacted in these areas.

Fig. 2. LCOPD, CAFS, and CASIS scores according to degree of dyspnea. *p* values were calculated by means of nonparametric statistics, i.e. the Kruskal-Wallis test for *n* independent samples with a bilateral confidence level of 95%. **a** LCOPD. *p* < 0.0001. Sample strata: level 0–1, *n* = 162; level 2, *n* = 166, and level 3–4, *n* = 73. **b** CAFS. *p* < 0.0001. Sample strata: level 0–1, *n* = 163; level 2, *n* = 167, and level 3–4, *n* = 72. **c** CASIS. *p* < 0.0001. Sample strata: level 0–1, *n* = 163; level 2, *n* = 167, and level 3–4, *n* = 73.

There are generic [8] and specific questionnaires for chronic respiratory disease [5, 7, 32]. The LCOPD questionnaire which measures the overall impact of COPD as perceived by the patient is a validated instrument consisting of 22 items, which in addition to its good psychometric properties has the advantage of being easy and quick to complete [24]. We have established its discriminating power with respect to the severity of airflow obstruction, degree of dyspnea, presence of respiratory symptoms, and other aspects previously reported using other questionnaires, such as the frequency of exacerbations [33, 34], level of education [35], physical activity [36, 37], and presence of anxiety or depression [38]. The similarity in the direction of the results obtained with the LCOPD

questionnaire and other specific questionnaires for COPD indicates that the LCOPD questionnaire is a simple and useful instrument to assess the impact of COPD on daily life in COPD patients.

One of the most characteristic aspects of COPD is the slow and progressive development of exercise limitation, which in the most severe cases can be disabling [16, 39]. The main manifestation of airflow obstruction is exertional dyspnea, although fatigue can also play an important role. The distinction between dyspnea and fatigue is relevant, since this could imply different or complementary therapeutic approaches. In addition to respiratory causes [40], fatigue in COPD can be the result of comorbidities [41], previous exacerbations or hospitalizations

Fig. 3. LCOPD, CAFS, and CASIS scores according to the number of exacerbations. *p* values were calculated by means of nonparametric statistics, i.e. the Kruskal-Wallis test for *n* independent samples with a bilateral confidence level of 95%. **a** LCOPD. *p* < 0.0001. Sample strata: none, *n* = 130; 1, *n* = 88, and 2 or more, *n* = 149. **b** CAFS. *p* < 0.0001. Sample strata: none, *n* = 131; 1, *n* = 87, and 2 or more, *n* = 150. **c** CASIS. *p* < 0.0001. Sample strata: none, *n* = 131; 1, *n* = 88, and 2 or more, *n* = 150.

[42], or peripheral muscle weakness or atrophy [40]. The need to quantify the sensation of fatigue has led to the development of questionnaires, such as the Manchester fatigue scale, consisting of 27 items distributed in three dimensions. This scale has shown its usefulness in a group of 122 patients with moderate COPD [43]. On the other hand, the CAFS questionnaire consists of only 12 items and has demonstrated excellent psychometric properties in our population of 408 patients with moderate to severe COPD. Also outstanding is its good correlation with the LCADL activity scale, the degree of dyspnea, and a limited correlation with the FEV₁ (%) post-bronchodilator. It is interesting to note how coughing has a significant and direct impact on the CAFS score. Coughing is a signifi-

cant symptom that has been associated with fatigue and deterioration of the quality of life [31, 44, 45].

Lastly, the CASIS questionnaire has allowed us to assess the impact of COPD on sleep impairment. In our study, sleep was impaired as indicated by a mean score of 29.7 out of 100, but with a large dispersion of scores. Poorer sleep quality has been associated with respiratory symptoms, lower activity, more exacerbations, a lower level of education, and higher rates of anxiety and depression. However, it does not seem to be related to age, gender, smoking intensity, or FEV₁ (%). There are scales designed to measure sleep quality, such as the Pittsburgh Sleep Quality Index (PSQI), but they do not take into account the specific aspects of chronic respiratory diseases

Table 5. Multivariate analysis of the characteristics that affect daily life (LCOPD), sleep impairment (CASIS), and fatigue (CAFS) of the studied sample

	LCOPD	CAFS	CASIS
Constant	1.921	11.095	12.131
Level of education			
Regression coefficient	-1.031	-2.552	-2.945
p value	0.004	0.075	0.042
Chronic cough			
Regression coefficient	-	-4.559	-
p value	-	0.041	-
Degree of dyspnea			
Regression coefficient	2.121	6.9219	3.401
p value	<0.0001	<0.0001	0.012
LCADL			
Regression coefficient	0.087	0.5638	0.369
p value	<0.0001	<0.0001	<0.0001
HADS presence of depression			
Regression coefficient	3.221	7.9093	5.657
p value	<0.0001	0.015	0.087
HADS presence of anxiety			
Regression coefficient	2.7806	14.915	14.517
p value	<0.0001	<0.0001	<0.0001
Model R ²	52%	54. 5%	37.1%

The multivariate analysis performed was a simple linear regression by means of the backward stepwise method; the dependent variable in each regression was the LCOPD, CAFS, or CASIS questionnaire score and the independent variables used were common in the three regressions and are described in table 2. The variables concerning age, gender, number of packs of tobacco consumed per year, time elapsed since diagnosis, lung capacity, presence of expectoration, number of exacerbations, and number of indicated treatments are not found to be associated with the LCOPD, CAFS, or CASIS questionnaire scores.

[46]. A high prevalence of sleep quality disturbances in patients with COPD has been observed using this index, similar to those observed in our study with the CASIS questionnaire; moreover, sleep quality has been significantly correlated with general and specific quality of life

[47]. However, the fact that the PSQI is not a questionnaire designed for respiratory patients could be the reason why the incidence of low-quality sleep measured by the PSQI in patients with COPD, although very frequent, would not be different in a group of patients with nocturnal desaturation compared to those having normal desaturation [48]. Perhaps an index gathering more specific respiratory aspects could detect more disorders in patients with COPD, in particular if they are severe. A comparative study of the PSQI and CASIS questionnaires would be necessary to confirm this hypothesis. In any case, the CASIS questionnaire is an easy-to-use instrument which helps in the detection of sleep disorders that significantly affect the quality of life, regardless of the severity of the COPD, and that may require specific treatment.

It must be recognized that self-reported outcomes have methodological limitations [49] and, in particular, one of the limitations of the current study is its cross-sectional design, which does not allow for the establishment of causal relationships or the observation of changes following treatment intervention(s). In the future it would be important to design a study able to assess the efficacy of different interventions on these aspects of COPD, and with which frequency they are relegated to a secondary level in the health care of these patients [50].

In summary, the LCOPD, CAFS, and CASIS questionnaires have demonstrated excellent psychometric properties within a large population of patients with moderate to severe COPD. These instruments can be useful in the comprehensive assessment of patients with COPD.

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