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Symptom burden and functional performance in patients with chronic obstructive pulmonary disease

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Symptom Burden and Functional Performance in Patients with Chronic Obstructive Pulmonary Disease

ABSTRACT

*Background***:** The burden of COPD is growing, and it is one of the leading disease burdens worldwide. Studies on symptom burden as a multidimensional concept in COPD and functional performance are lacking, and little is known about the effect of multiple symptoms and symptom burden on functional performance.

Methods: A descriptive, cross-sectional correlational survey design was used. The Memorial Symptom Assessment Scale (MSAS) and the Functional Performance Inventory-Short Form (FPI-SF) were used to measure the symptom burden and functional performance. Data were analyzed using descriptive and inferential statistics. Participants (n=214) were recruited from the respiratory outpatient clinic in one of the teaching hospitals in Ireland.

Results: Patients with COPD, regardless of classification, experienced significant physical and psychological symptom burden. A total of 20 symptoms were negatively correlated with overall functional performance, indicating a high symptom burden for those symptoms was associated with low overall functional performance. A statistically significant negative correlation between physical symptom burden, psychological symptom burden, total symptom burden, and functional performance was found.

Conclusion: Patients with COPD experience a significant symptom burden and low functional performance. Decreased functional performance was not related only to a single burdensome symptom, but may also be related to the contribution of several physical/psychological burdensome symptoms, or both. Assessment and management of these symptoms are essential and imply that alleviating these symptoms' burden may promote improved functional performance. This study supported the growing body of evidence of the need for patients with advanced COPD to receive palliative care.

Keywords: Chronic Obstructive Pulmonary Disease (COPD), symptoms, symptom burden, Activity of daily living, ADLS, function, functional performance

1. **Introduction**

Chronic obstructive pulmonary disease (COPD) is the condition with most prevalent among lung diseases. It is a progressive disease that presents a substantial clinical and economic burden worldwide and one of the most causes of mortality and morbidity (GOLD, 2019). Researchers suggested that patients with COPD may experience their symptoms as a burden similar to other chronic conditions such as chronic kidney disease (Brown et al., 2017) and bowel disease (Farrell et al., 2016). The symptoms that patients with COPD might experience can cause a negative impact on their health and well-being. Shortness of breath and coughing for example, may limit their physical mobility and abilities, especially during exacerbations (Williams et al., 2014). Furthermore, psychological symptoms such as worrying and feeling irritable have been found predictive of poor quality of life (Blinderman et al., 2009). The effect of such symptoms can be referred to as a symptom burden. Symptom burden (SB) is defined as an individual experience that incorporates physical and psychological symptoms of a condition taking into consideration the severity, frequency, and distress (Farrell and Savage, 2012).

Research on SB in patients with COPD is essential as it will inform the clinical practice and provide a guidance to decease the burden on patients' health and their fiscal status. Research on SB, can help in adding clinical strategies to assess and manage individual who have multiple symptoms. Furthermore, the prevention and management of SB are important to offsetting patients' adverse consequences (Miravitlles & Ribera, 2017). For instance, increased risk of COPD symptoms exacerbations, disease progression, poor prognosis and reduced survival rates (May & James, 2015; Miravitlles & Ribera, 2017). The research on SB in patients with COPD may help in identifying the medical cost and its related burden on patients, increased health service utilization such as emergency department admissions, or increased frequency of hospitalizations (Ding et al., 2017; Gapstur 2007). It is important to understand how much SB may affect the functional performance of patients with COPD.

Functional performance is an outcome of SB, and is defined as the physical, psychological, social, occupational or spiritual activities that people actually do in the normal course of their lives to meet basic needs, fulfil usual roles, and maintain their health and well-being (Leidy & Knebel 2010; Leidy 1994). Reduction in functional performance such as physical activity was found to be a predictor of mortality and exacerbations of COPD symptoms (Gimeno et al., 2014). Moreover, decrease physical activity was found to be associated with dyspnea and cough. Poor quality of life is another concern that derives from worrying and irritability among patient with COPD (Miravitlles & Ribera, 2017). For that, helping the patients to improve their debilitating symptoms became evident.

Improvement of symptoms and activities is one of the primary treatment goals for patients with COPD (GOLD 2021). However, the Global initiative for Chronic Obstructive Lung Disease (GOLD) guidelines and other COPD guidelines, such as the American Thoracic Society (ATS), British Thoracic Society (BTS), and European Respiratory Society (ERS), lack the proper identification of "functional performance". Besides, the GOLD guidelines recognize the need to address the disease's effect on the patient's daily life and reduce the risk of future exacerbations. From the research conducted to date, a piecemeal picture of knowledge about SB in patients with COPD and its relation to functional performance is apparent.

To date, most studies have investigated the effects of a single symptom or the effects of the disease-specific symptoms, treatment regimen, or lung function, in reducing the functional performance in patients with COPD (Ozosy et al. 2019, Ding et al. 2018, Lee et al. 2018), or the relationship between a limited number of symptoms and the patients' level of functional performance (Johansson et al., 2019, Lee et al., 2018, Van et al., 2017). besides; the COPD guidelines lacked the proper identification of SB and its' consequences on the functional performance of the patients. Moreover, with the lack of literature; this study helped in providing knowledge about the assessment of the SB and its' related effect on the functional performance for patients with COPD. Therefore, the purpose of this study was to investigate symptom burden and its relationship to functional performance in patients with COPD.

2. Methods

2.1 Conceptual Framework

The study was guided by a conceptual framework of symptom burden derived from the concept analysis of symptom burden (Gapstur 2007). In this conceptual framework, symptoms are categorized as physical and psychological. These symptoms are depicted as occurring in multiples because patients with COPD experience more than one symptom at a given time (Figure 1).
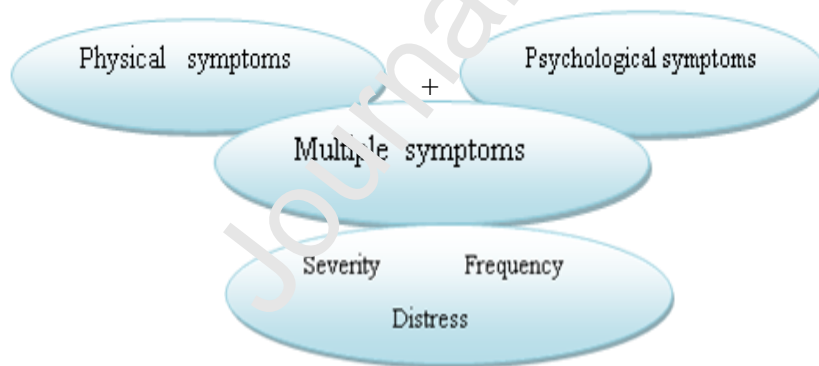

Figure (1) Conceptual Framework of Symptom Burden

2.2 Design and Setting

The study was employed using a descriptive, cross-sectional correlational survey design in one academic teaching hospital in Dublin, Ireland. Participants were recruited from the respiratory outpatient clinic over a three months' period.

2.3 Sample

The targeted population was a convenience sample of all patients with COPD attending the respiratory outpatient clinic. The severity of COPD was defined according to GOLD grading system. Inclusion criteria were patient with mild COPD (FEV1 >=80%), moderate COPD (FEV1 50-80%), severe COPD (FEV1 30-50%), and very severe COPD (FEV1 > 30%), and patients able to speak and read English well enough to complete the questionnaire. Exclusion criteria were hospitalized patients (inpatients) with COPD or patients with COPD who reside in long term care facilities or respite care, and patients with a history of cognitive impairment would prevent their ability to give informed consent to read and answer questions.

2.4 Instruments

The Memorial Symptom Assessment Scale (MSAS) (Portenoy et al., 1994) was used to measure symptom burden. The MSAS is a patient-rated, multidimensional instrument that evaluates the prevalence, severity, frequency, and distress associated with symptoms the patients' experienced in the last week. The MSAS includes a total of 32 physical and psychological symptoms (26 physical and 6 psychological). symptom burden, namely the severity, frequency, and distress of symptoms, was measured using the MSAS (Portenoy *et al*. 1994). Physical and psychological symptom burden experienced over the last week was measured.

Severity is the intensity of symptoms experienced. Severity was measured by asking participants to indicate how severe the symptoms were in the last week. The severity of symptoms was measured through a 4-point Likert scale: 1 (slight), 2 (moderate), 3 (severe), and 4 (very severe). Scores range from 0 to 4 (Portenoy *et al*. 1994). Frequency refers to the occurrence of symptoms over time. Frequency was measured by asking participants to indicate how often they experienced symptoms in the last week. The frequency of each symptom experienced was measured through a 4-point numeric scale: 1 (rarely), 2 (occasionally), 3 (frequently), and 4 (almost constantly). Scores range from 0 to 4 (Portenoy *et al*. 1994). Distress is the degree to which symptoms bother individuals. Distress was measured by asking participants to indicate how much the symptom experienced distressed or bothered them in the last week. The distress of symptoms experienced was measured through a 5-point numeric scale: 0.8 (not at all), 1.6 (a little bit), 2.4 (somewhat), 3.2 (quite a bit), and 4 (very much). Scores range from 0 to 4 (Portenoy *et al*. 1994).

The Likert scale scoring for each of the dimensions (frequency, severity, distress) ranges from 0 to 4. A score of 0 is given to a symptom if it is not experienced in the last week. Cronbach's

alpha for the Total MSAS in this study was 0.86, demonstrating that the overall scale has good internal reliability

Functional performance was measured using the Functional Performance Inventory-Short Form (FPI-SF). The FPI-SF is a 32-item instrument with six subscales: body care (5 items), household maintenance (8 items), physical exercise (5 items), recreation (5 items), spiritual activities (4 items) and social activities (5 items). Participants score 0 points for activities they do not perform in the last week. If the participants can do an activity in the last week, they were asked to indicate how strenuous the activity is for them to perform on a scale of 3 "no difficulty", 2 "some difficulty", to 1 "much difficulty". If respondents do not perform an activity, they were asked if this is an activity they do not do because of "health reasons" or "choose not to". The total score was computed by taking the mean across all subscale scores. The total FPI is 0 to 3, with higher scores reflecting higher functional performance levels (Leidy & Knebel, 2010). Cronbach's alpha for the overall FPI was 0.95, demonstrating that the overall scale has good internal reliability.

2.5 Data Collection

Data were collected daily (except weekends) at the respiratory outpatients' clinic over a three-month period. Prior to each clinic, the Respiratory Nurse Specialist (RNS) reviewed the scheduled patient's medical notes to identify those who met the inclusion and exclusion criteria. Potentially eligible participants were informed by the RNS about the study and invited them to meet the researcher. Patients, who agreed, met with the researcher in a separate room at the outpatient's department. The researcher gave an overview of the study and once a patient showed interest, the researcher gave the patient a study information leaflet. After reading the study information leaflet, patients willing to participate in the study were asked to sign a consent form and were then given a copy of the MSAS and FPI-SF to complete. Participants were asked to return the completed questionnaire to the researcher or the RNS. A stamped return envelope with the researcher's address was provided for participants who were not able to complete the questionnaire at the clinic but willing to complete the questionnaire at a different time in their homes.

2.6 Ethical Approval

The Institutional Review Board of the participating hospital approved the study. Oral and written information were given to participants before giving written informed consent.

2.7 Data Analysis

Data collected were stored and analyzed using Predictive Analytics Software (PASW). A data – coding framework was developed before data collection. All variables were given names and labelled with number and code.

Descriptive statistics were used to describe the demographic characteristics, symptom burden and functional performance of patients overall and by COPD stages. Inferential statistics were conducted to compare symptom burden and functional performance between COPD stages and to examine the relationships between patients' symptom burden and functional performance.

Inferential statistics were conducted to compare symptom burden and functional performance between COPD stages and to examine the relationships between patients' symptom burden and functional performance. For comparisons between COPD stages, Fisher's exact test was used for categorical variables (e.g. symptom prevalence) and if a statistically significant difference was found, pairwise comparisons were performed using Fisher's exact test, with Bonferroni correction for multiple testing. The Kruskal-Wallis test was used for the comparison of continuous variables between COPD stages and if statistically significant differences were found, pairwise comparisons were performed using the Mann-Whitney test, with Bonferroni correction for multiple testing. The non-parametric Kruskal-Wallis test was used as the assumptions required for the parametric one-way ANOVA (i.e. normally distributed data within each COPD stage and equal variance across COPD stages) did not hold. The paired t-test was used to compare physical and psychological symptom burden. The strength and direction of the relationships between total, physical and psychological symptom burden scores and functional performance overall and subscale scores were assessed using Pearson's correlation coefficient (r) while the strength and direction of the relationships between individual symptom burden scores and overall functional performance were assessed using Spearman's correlation coefficient (r_s). Spearman's correlation was used instead of Pearson's correlation to assess the strength and direction of the relationships between individual symptom burden scores and overall functional performance as many of the individual symptoms had non-normal distributions. Statistical analysis was performed using Stata 13 0. All tests were two-sided and a p-value <0.05 was considered to be statistically significant. To investigate the relationships between total symptom burden, physical symptom burden, psychological symptom burden and overall functional performance and subscale scores, Pearson's correlation coefficients were employed.

3. Results

The sample comprised a cross-section of patients (n=214): 20.1% (n=43) had mild COPD, 26.2% (n=56) had moderate COPD, 33.2% (n=71) had severe COPD, and 20.5% (n=44) had very severe COPD. The mean FEV1 for the overall sample was 52% (SD= 21.9). Socio-demographic characteristics including age, gender, marital status, employment status, and living arrangement (Table 1)

Table 1 Sociodemographic and clinical characteristics

Characteristic	Overall	COPD Stages			
		Mild (n=43)	Moderate (n=56)	Severe (n=71)	Very severe(n=44)
Age (years): Mean(SD)	68.1 (8.1)	61.5 (8.1)	69.2 (8.4)	70.7 (6.4)	68.9 (6.7)
Range	49 to 90	49 to 85	49 to 90	56 to 81	60 to 87
	% (n)	% (n)	% (n)	% (n)	% (n)

Gender

Male	43.9 (94)	34.9 (15)	32.1 (18)	64.8 (46)	34.1 (15)
Female	56.1 (120)	65.1 (28)	67.9 (38)	35.2 (25)	65.9 (29)
Marital status					
Single	4.2 (9)	0.0 (0)	3.6 (2)	9.9 (7)	0.0 (0)
Married	37.4 (80)	41.9 (18)	28.6 (16)	38.0 (27)	43.2 (19)
Separated	23.8 (51)	34.9 (15)	46.4 (26)	11.3 (8)	4.5 (2)
Divorced	11.7 (25)	2.3 (1)	8.9 (5)	2.8 (2)	38.6 (17)
Widowed	22.9 (49)	20.9 (9)	12.5 (7)	38.0 (27)	13.6 (6)
Employment status					
Employed with wages	5.1 (11)	23.3 (10)	1.8 (1)	0.0 (0)	0.0 (0)
Self-employed	3.3 (7)	2.3 (1)	1.8 (1)	7.0 (5)	0.0 (0)
Unemployed	6.1 (13)	20.9 (9)	5.4 (3)	1.4 (1)	0.0 (0)
Retired	29.4 (63)	11.6 (5)	32.1 (18)	25.4 (18)	50.0 (22)
Unable to work	56.1 (120)	41.9 (18)	58.9 (33)	66.2 (47)	50.0 (22)
Living arrangements					
Alone	22.9 (49)	14.0 (6)	3.6 (2)	42.3 (30)	25.0 (11)
With family member	57.9 (124)	79.1 (34)	66.1 (37)	38.0 (27)	59.1 (26)
Shared accommodation	19.2 (41)	7.0 (3)	30.4 (17)	19.7 (14)	15.9 (7)
Currently using oxygen therapy					
No	52.8 (113)	79.1 (34)	62.5 (35)	26.8 (19)	56.8 (25)
Intermittent oxygen	31.3 (67)	20.9 (9)	19.6 (11)	40.8 (29)	40.9 (18)
Permanent oxygen	15.9 (34)	0.0 (0)	17.9 (10)	32.4 (23)	2.3 (1)
Current medication use					
Inhalers	39.7 (85)	53.5 (23)	42.9 (24)	35.2 (25)	29.5 (13)
Nebulizers	16.4 (35)	23.3 (10)	21.4 (12)	16.9 (12)	2.3 (1)
Both inhalers and nebulizers	43.9 (94)	23.3 (10)	35.7 (20)	47.9 (34)	68.2 (30)
Smoking status					
Currently not smoking	84.1 -180	76.7 -33	80.4 -45	88.7 -63	88.6 -39
Currently smoking	15.9 (34)	23.3 (10)	19.6 (11)	11.3 (8)	11.4 (5)
Smoked in the past	68.7 (147)	69.8 (30)	62.5 (35)	78.9 (56)	59.1 (26)
Never smoked	3.3 (7)	0.0 (0)	3.6 (2)	7.0 (5)	0.0 (0)
Hospital admission in the last six months					
None	21.0 (45)	51.2 (22)	28.6 (16)	9.9 (7)	0.0 (0)
Once	39.3 (84)	48.8 (21)	50.0 (28)	29.6 (21)	31.8 (14)
Two times	23.8 (51)	0.0 (0)	12.5 (7)	31.0 (22)	50.0 (22)
Three times or more	15.9 (34)	0.0 (0)	8.9 (5)	29.6 (21)	18.2 (8)

3.1 Number of Symptoms Experienced

Participants were asked to identify which 32 symptoms (26 physical symptoms and 6 psychological symptoms) they experienced in the past weeks. Of the 32 symptoms, participants reported a median number of 13 symptoms. Of the 26 physical symptoms included, participants

reported a median number of 9. The number of physical symptoms reported differed by COPD stage (p<0.001). Participants with very severe and severe COPD reported a median number of 10 symptoms, while the median was 8 for patients with moderate COPD and 6 for patients with mild COPD. Post-hoc pairwise comparisons, adjusted for multiple comparisons, indicated significant differences in the number of physical symptoms between participants with mild COPD and participants with severe or very severe COPD and between participants with moderate COPD and participants with very severe COPD (Table 2). Of the six psychological symptoms included, participants reported a median number of 4. The number of psychological symptoms reported differed by COPD stage (p=0.003). Participants with mild and very severe COPD reported a median number of 5 symptoms, while the median was 4 for patients with severe COPD and 3 for participants with moderate COPD. Post-hoc pairwise comparisons, adjusted for multiple comparisons, indicated that the only significant difference was between participants with moderate COPD and participants with very severe COPD (Table 2).

Table 2: Number of symptoms reported by patients, overall and by COPD stage

	Overall (n=214)	COPD stages				
		Mild	Moderate	Severe	Very severe	P-value
All Symptoms (Possible range 0 to 32)						
Median (IQR)	13(10 to 15)	10(0 to 15)	10 (8 to 15)	14(12 to 15)	15(12 to 18)	**<0.001**
Range	3 to 26	3 to 18	3 to 24	4 to 23	11 to 26	
Physical Symptoms (Possible range 0 to 26)						
Median (IQR)	9(7 to 11)	6 (4 to 10)	8 (6 to 11)	10(8 to 11)	10(9 to 14)	**<0.001**
Range	3 to 20	3 to 12	3 to 18	4 to 17	8 to 20	
Psychological Symptoms (Possible range 0 to 6)						
Median (IQR)	4(2 to 15)	5 (0 to 6)	3(2 to 5)	4(2 to 5)	5(3 to 5)	**<0.003**
Range	0 to 6	0 to 6	0 to 6	0 to 6	3 to 6	

3.2 Symptom Burden for Individual Symptom

Overall, the mean symptom scores ranged from 0.1 to 2.6. Of the thirty-two symptoms experienced, shortness of breath (M =2.6, SD=1.0) was the most burdensome symptom, followed by lack of energy (M=2.4, SD=1.0), cough (M=2.3, SD=1.3), difficulty sleeping (M=2.2, SD=1.3), dry mouth (mean=1.9, SD=1.4), worrying (M=1.8, SD=1.3), feeling nervous (M=1.6, SD=1.4)), feeling irritable (M=1.5, SD=1.3), and feeling sad (M =1.4, SD=1.3) (Figure 2).

Symptom burden scores were compared between the COPD stages. For participants with mild COPD, the most burdensome of these symptoms were cough (M=2.4, SD=1.2), shortness of breath (M=2.3, SD=0.4), difficulty sleeping (M=2.41, SD=1.3), lack of energy (M=1.8, SD=0.8), feeling nervous (M=1.8, SD=1.3), feeling sad (M=1.6, SD=1.5), and feeling irritable (M=1.6, SD=1.3). In contrast, the most burdensome symptom experienced by participants with moderate COPD was lack of energy (M=1.9, SD=1.2), followed by shortness of breath (M=1.8, SD=1.3), cough (M=1.8, SD=1.4), dry mouth (M=1.7, SD=1.1), difficulty sleeping (M=1.6, SD=1.5), and worrying [1.5 (1.2). Participants with severe COPD reported shortness of breath (M=3.1, SD=0.6) as the most burdensome symptom in the last week, followed by lack of energy (M=2.8, SD=0.8), difficulty sleeping (M=2.4, SD=0.9), feeling nervous (M=2.2, SD=1.0), cough (M=2.1, SD=1.3), and dry mouth (M=2.0, SD=1.1). Findings revealed that shortness of breath (M=3.3, SD=0.5) was also the most burdensome symptom in patients with very severe COPD, followed by cough (M=3.2, SD=0.5), lack of energy (M=3.1, SD=0.3), difficulty sleeping (M=2.9, SD=1.0), and worrying (M=2.7, SD=0.3).
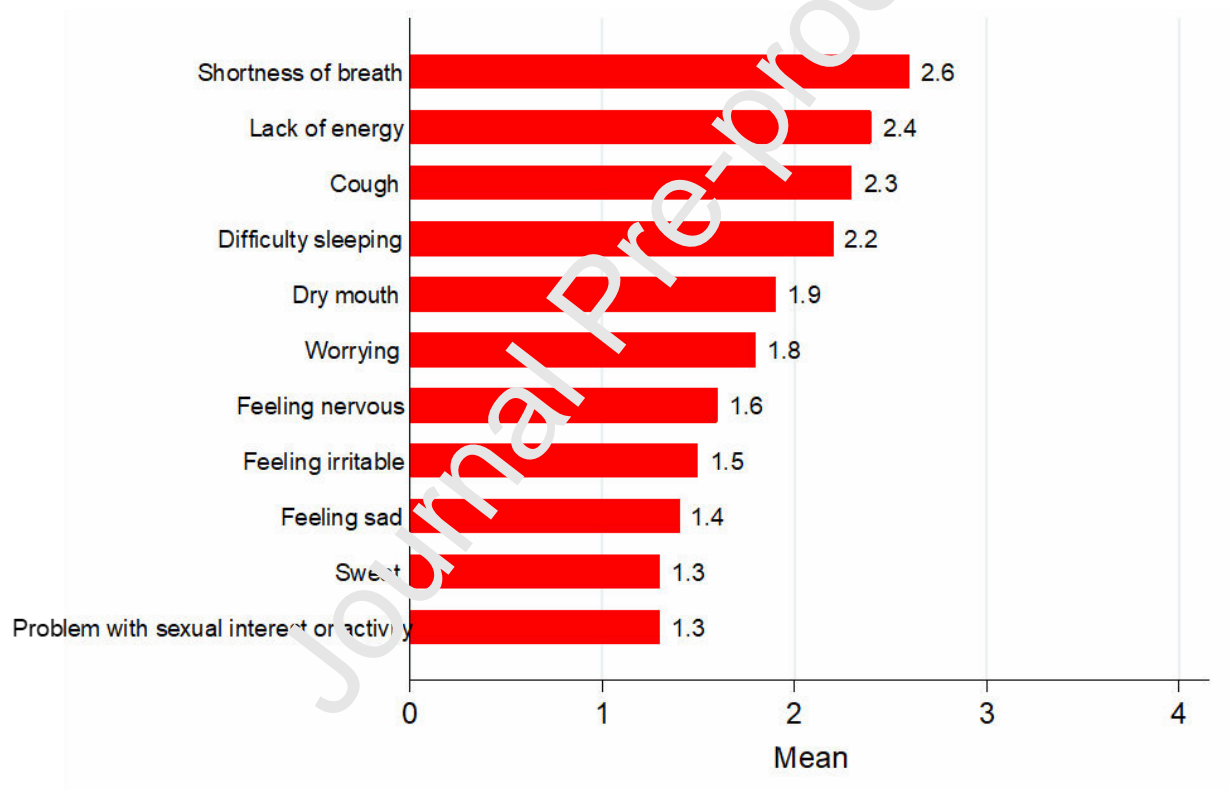

Figure (2) Individual symptom burden scores for most burdensome symptoms overall

3.2 Symptom Burden

For overall symptom burden, participants with very severe COPD had the greatest symptom burden (median (IQR): 1.26(0.93 to 1.43)), followed by those with severe COPD (median(IQR): 1.06(0.88 to 1.27)), moderate COPD (median (IQR): 0.73(0.58 to 1.11)), and mild COPD (median (IQR): 0.68(0.38 to 1.02)). The difference between groups was statistically significant

(p<0.001). Post-hoc pairwise comparisons using Bonferroni correction indicated significant differences in total symptom burden between participants with very severe COPD and those with moderate or mild COPD and between participants with severe COPD and those with moderate or mild COPD.

The distribution of physical and psychological symptom scores also differed between the COPD stages (p<0.001). Physical symptom scores were highest for participants with very severe COPD (median (IQR): 1.07(0.87 to 1.34)), followed by those with severe COPD (median(IQR): 0.88(0.77 to 1.13)), moderate COPD (median(IQR): 0.67(0.46 to 1.06)), and mild COPD (median(IQR): 0.52(0.36 to 0.74)). Psychological symptom scores were highest for participants with very severe COPD (median (IQR): 2.04(1.25 to 2.28)), followed by those with mild COPD (median(IQR): 1.77(0.00 to 2.58), severe COPD (median(IQR):1.47(1.02 to 2.47)), and moderate COPD (median(IQR): 1.09(0.73 to 1.78) (Table 3).

Table 3: Total, physical and psychological symptom burden scores by COPD stage

	n	observed range	mean (SD)	median (IQR)	p-value[1]	groups having difference (pairwise test)
Total symptom burden (TMSAS)					**<0.001**	a-c, a-d, b-c, b-d
Mild COPD	43	0.18 to 1.55	0.79 (0.4..)	0.68 (0.38 to 1.02)		
Moderate COPD	56	0.21 to 2.33	0.88 (0.50)	0.73 (0.58 to 1.11)		
Severe COPD	71	0.23 to 1.85	1.05 (0.30)	1.06 (0.88 to 1.27)		
Very severe COPD	44	0.83 to 2.27	1.31 (0.44)	1.26 (0.93 to 1.43)		
Subscales						
Physical symptom burden (MSAS-PHYS)					**<0.001**	a-c, a-d, b-c, b-d
Mild COPD	43	0.22 to 1.10	0.59 (0.29)	0.52 (0.36 to 0.74)		
Moderate COPD	56	0.._ to 2.02	0.78 (0.44)	0.67 (0.46 to 1.06)		
Severe COPD	71	.._9 to 1.73	0.91 (0.27)	0.88 (0.77 to 1.13)		
Very severe COPD	44	0.7' to 2.07	1.17 (0.40)	1.07 (0.87 to 1.34)		
Psychological symptom burden (MSAS-PSYCH)					**0.001**	b-c, b-d
Mild COPD	43	0 to 3.40	1.61 (1.22)	1.77 (0.00 to 2.58)		
Moderate COPD	56	0 to 3.72	1.28 (0.98)	1.09 (0.73 to 1.78)		
Severe COPD	71	0 to 3.18	1.66 (0.79)	1.47 (1.02 to 2.47)		
Very severe COPD	44	1.19 to 3.29	1.90 (0.67)	2.04 (1.25 to 2.28)		

3.3 Individual symptom burden and functional performance

To investigate the relationships between the individual symptom burden scores and overall functional performance, Spearman's rank correlation coefficients was employed. A total of 20 symptoms were negatively correlated with overall functional performance, indicating that high symptom burden for those symptoms was associated with low overall functional performance. Lack of energy had the strongest negative correlation with functional performance (r_s= -0.572, p <0.001), and was the only symptom to show a strong correlation. Six of the symptoms, nausea (r_s=-0.441, p<0.001), shortness of breath (r_s=-0.386, p<0.001), dry mouth (r_s=-0.375, p<0.001), feeling nervous (r_s=-0.346, p<0.001), lack of appetite (r_s=-0.330, p<0.001) and worrying (r_s=-0.327, p<0.001)) had a moderate, negative correlation with overall functional performance. The correlation was negative and weak for the other thirteen symptoms. Only two of the symptoms,

were constipation (r_s=0.166, p=0.022) and changes in skin condition (r_s=0.175, p=0.017) had statistically significant positive correlations with overall functional performance, indicating that high symptom burden for those symptoms was associated with high overall functional performance. However, the strength of these associations was weak (Table 4).

Table 4: Correlations between individual symptom burden scores and functional performance

scores

	Spearman's rank correlation		
	n	r_s	p-value
Lack of energy	189	-0.572	<0.001
Nausea	187	-0.441	<0.001
Shortness of breath	190	-0.386	<0.001
Dry mouth	189	-0.375	<0.001
Feeling nervous	189	-0.346	<0.001
Lack of appetite	190	-0.330	<0.001
Worrying	190	-0.327	<0.001
Diarrhea	187	-0.296	<0.001
Sweat	189	-0.292	<0.001
Vomiting	189	-0.286	<0.001
I don't look/feel like myself	190	-0.230	0.001
Feeling sad	189	-0.219	0.003
Difficulty sleeping	189	-0.210	0.004
Difficulty swallowing	184	-0.209	0.004
Dizziness	184	-0.193	0.009
Swelling of arms or legs	189	-0.192	0.008
Numbness/tingling in hands/feet	186	-0.187	0.010
Cough	190	-0.172	0.017
Problems with urination	187	-0.166	0.023
Difficulty concentrating	187	-0.156	0.033
Feeling irritable	189	-0.125	0.087
Mouth sores	187	-0.125	0.089
Pain sores	188	-0.114	0.120
Feeling drowsy	185	-0.110	0.136
Itching	188	-0.052	0.475
Problem with sexual interest or activity	186	-0.026	0.724
Hair loss	189	0.019	0.793
Weight loss	189	0.028	0.697
Changes in the way food tastes	188	0.053	0.469
Feeling bloated	186	0.081	0.274
Constipation	190	0.166	0.022
Changes in skin condition	188	0.175	0.017

3.4 Total Symptom Burden, Physical and Psychological Symptom Burden and Functional Performance

To investigate the relationships between total symptom burden, physical symptom burden, psychological symptom burden and overall functional performance and subscale scores, Pearson's correlation coefficients were employed. Moderate, negative, statistically significant correlations were found between overall functional performance and total symptom burden, physical symptom burden and psychological symptom burden, indicating that high symptom burden or high burden associated with physical or psychological symptoms were associated with low functional performance. All correlations between overall symptom burden and functional performance subscales were statistically significant, negative in direction and ranged from low (r=-0.145 for Spiritual Activities subscale) to moderate (r=-0.434) for Physical Exercise subscale. Similarly, the correlations between physical symptom burden and all functional performance subscales except Social Activities were statistically significant and negative in direction and ranging from low (r=-0.236) for Spiritual Activities subscale to moderate (r=-0.400) for Physical Exercise subscale. Although there was no evidence of a linear relationship between physical symptom burden and social activities, a curvilinear relationship was found. The correlation between physical symptom burden and the square of social activities was low but statistically significant (r=-0.156, p=0.023). For all functional performance subscales except Spiritual Activities, the linear relationships with psychological symptom burden were negative, and ranged from low (r=-0.140 for Household Maintenance subscale) to moderate (r=-0.418 for Recreation subscale). Although there was no evidence of a linear relationship between psychological symptom burden and spiritual activities, a non-linear relationship was found. The correlation between psychological symptom burden and the log (ln) transformation of spiritual activities was low but statistically significant (r=-0.222, p=0.001) (Table 5).

Table 5: Correlations between functional performance scores and symptom burden scores

	MSAS			MSAS-PHYS			MSAS-PSYCH		
	n	r	p-value	n	r	p-value	n	r	p-value
Overall functional performance	190	-0.417	<0.001	190	-0.418	<0.001	190	-0.317	<0.001
Subscales									
Body Care	214	-0.314	<0.001	214	-0.363	<0.001	214	-0.141	0.039
Household maintenance	214	-0.303	<0.001	214	-0.349	<0.001	214	-0.140	0.040
Physical Exercise	204	-0.434	<0.001	204	-0.400	<0.001	204	-0.395	<0.001
Recreation	213	-0.418	<0.001	213	-0.360	<0.001	213	-0.418	
Spiritual Activities	202	-0.145	0.040	202	-0.236	0.001	202	0.064	0.367
Social Activities	213	-0.160	0.020	213	-0.097	0.159	213	-0.231	0.001

For all stages of COPD, except the moderate stage, there was an evidence of a negative linear relationship between the two variables, indicating that those with high symptom burden had low functional performance. Pearson's correlation coefficient was highest for the very severe group (r=-0.796, p<0.001, n=36), followed by the mild group (r=-0.619, p<0.001, n=36) and the severe group (r=-0.302, p=0.017, n=62). No relationship was found between total symptom burden and overall functional performance for the moderate group (r=0.102, p=0.453, n=56).

4. Discussion

Participants reported experiencing up to an average of 13 symptoms per week. However, this number ranged from 10 symptoms per week for patients with mild and moderate COPD, 14 symptoms for patients with severe COPD, and 15 symptoms for those with very severe COPD. The number of symptoms experienced by patients with COPD in this study was higher than those reported in other studies (Jablionski *et al*. 2007; Blinderman et al. 2009; Bausewein *et al*. 2010; Park *et al*. 2012; Eckerblad *et al*. 2014), with the number of symptoms experienced in these studies ranging from 7 to 12.

Regardless of classification, patients with COPD experienced significant symptom burden, signalling an imperative need for early symptom assessment and management. A multidimensional symptom assessment that includes multiple symptoms rather than focusing on COPD's cardinal symptoms is important and should be performed for all COPD stages. Previous research of patients' experiences of care has reported poor service delivery, little help offered by health care professionals for symptom relief (Van Kruijssen et al., 2015), poor symptom control (Chen et al., 2018), and poor quality of life for those with advanced-stage COPD (Merino et al., 2019, Ahmed et al., 2016). However, researchers such as Sigurgeirsdottir et al., (2019) also report that many patients with COPD would not express their needs as they did not know that there are options to improve their situation. Some studies have compared the prevalence of symptom burden between patients with cancer and with COPD. Yi et al., (2018) found that both patients with COPD and cancer have a similar prevalence of symptoms; however, patients with COPD were found to live longer and experience these symptoms for a more extended period of time. Walke et al. (2004) found that symptom burden in patients with COPD was higher than in patients with cancer. Furthermore, a study by Habraken et al., (2009) found that Health-Related Quality of Life (HRQOL) scores for patients with severe COPD were higher than those with advanced non-small cell lung cancer (NSCCLC). However, it is evident that palliative care intervention reduces cancer-related symptoms and improves the quality of life (Halpin 2018), indicating that patients with COPD with a high symptom burden would benefit from a palliative care approach.

The findings of this study provided insights into the relationship between symptom burden and functional performance. Interestingly, the low functional performance was associated with 20 high-burden symptoms. As expected, the lack of energy had the strongest negative correlation with functional performance. The result is consistent with other quantitative studies in which fatigue was significantly correlated with functional performance (Paddison *et al*., 2013, Walke *et al*., 2007). Besides, nausea, shortness of breath, dry mouth, nervousness, lack of appetite, and worrying had a moderate negative correlation with overall functional performance. This study's findings are supported by previous research in which shortness of breath (Walke *et al*. 2007; Park *et al*. 2012) and appetite problems (Walke *et al*. 2007) were strongly associated with low functional performance. However, diarrhoea, sweat, vomiting, not looking like oneself, feeling sad, difficulty sleeping, difficulty swallowing, dizziness, swelling of arms or legs, numbness of hands/feet, cough, problems with urination, and difficulty concentrating had a negative but weak correlation with functional performance. These findings are important, because most prior research has only investigated the relationship between a single symptom or a limited number of

symptoms and functional performance in COPD. This emphasizes the importance of assessment and management of these symptoms and implies that alleviating the burden of these symptoms may promote improved functional performance.

A low level of functional performance was attributed to symptom burden. The study found a statistically significant negative correlation between physical symptom burden, psychological symptom burden, total symptom burden, and functional performance. This finding is important and shows that decreased functional performance in patients with COPD was not related only to a single burdensome symptom; but may also be related to the contribution of several physical/psychological burdensome symptoms, or both. The finding is also consistent with Park *et al*.'s (2012) study in which the total symptom burden was also significantly related to functional performance. This indicates that overall symptom burden, physical or psychological symptom is associated with low overall functional performance in patients with COPD and that attention to both physical and psychological symptoms is necessary for slowing functional decline in patients with COPD.

With regard to the relationship between symptom burden and overall functional performance across each stage of COPD**,** the study indicates that the strongest negative relationship between high symptom burden and low functional performance was for participants with very severe COPD, followed by mild COPD, and severe COPD. Unexpectedly, no relationship was found between total symptom burden and overall functional performance for moderate COPD**.** This may be due to the fact that participants with moderate COPD had the lowest psychological symptom burden and did not report any highly distressing symptoms compared to participants in the other COPD stages. Therefore, low distress from psychological symptoms could have affected the relationship between the total symptom burden and functional performance. This finding indicates that the severity of COPD had no effect on low functional performance.

An important finding of this study is that most participants with COPD experienced a high symptom burden and low functional performance. Although assessing health-related quality of life (HRQOL) was not the focus of this study, symptom burden and functional performance are important components of HRQOL in patients with COPD. Quality of life reflects the impact of symptoms associated with daily activities. Current guidelines for managing COPD, such as GOLD, have focused only on improving pathological and pathophysiological parameters such as inflammation and narrowing airways (GOLD 2019). The present study suggests that assessing symptom burden is important, and may predict improving functional performance among patients with COPD.

Evidence from literature on cancer indicated that a palliative care approach to cancer patients increases life quality. For patients with advanced COPD with high symptom burden and low functional performance, a palliative care approach should be used as there is no cure for COPD. The current study suggests that patients with COPD should be undergoing routine symptom assessment and management. Health care professionals also have a duty to have open communication with patients, especially those with severe and severe COPD, and discuss the palliative care approach. Currently, the absence of specialist palliative care services for the management of symptoms and other physical, psychological, and psychosocial problems in COPD highlights the need for new models of care that take into account the high symptom

burden, unmet needs of symptom management, functional impairment, social support, and quality of life. However, identifying when the terminal stage of COPD actually begins is one of the major problems with providing quality palliative care for patients with COPD. The absence of involvement of palliative care services highlights the need for new models of care for advanced COPD to address the unmet needs of symptom control. This study supports the growing body of evidence of the need for patients with advanced COPD to receive palliative care.

5.1. Strengths and limitations

This study has a number of strengths, and adds to the limited body of knowledge on symptom burden and functional performance in COPD. The strengths relate to consistent data collection with little missing data. The MSAS and FPI-SF used were appropriate to the population under study. The MSAS is the only instrument which measures the multidimensional aspects of both physical and psychological symptoms, namely frequency, severity, and distress. Both instruments were tested for reliability and validity. Cronbach's alpha for the TMSAS in this study was 0.86, and Cronbach's alpha for the overall FPI was 0.95, demonstrating that the overall scales has good internal reliability. Furthermore, Cronbach's alpha for the MSAS and FPI-SF subscales also had good internal reliability.

To the best of the researchers' knowledge, this is the first study exploring symptom burden involving all stages of COPD. Participants with mild, moderate, severe, and very severe COPD were sampled in the study. However, the majority of studies in previous research only explored symptom burden among patients with severe and very severe COPD. This study also provided data on the relationship between both physical and psychological symptom burden and functional performance in COPD. Furthermore, this is the first study to be conducted in Ireland. It therefore adds knowledge to a previously unexplored area, and the results can be used in clinical and education practice to improve symptom burden in COPD. In addition, symptom burden and functional performance had received little research attention in COPD as the majority of studies measured one of a limited number of symptoms and functional performance.

Another strength is that the findings of the study support the conceptual underpinning that symptom burden is a multidimensional phenomenon, with reference to frequency, severity, and distress. However, further studies are required using both quantitative and qualitative data to understand symptom burden from the patient's perspective in terms of the types and dimensions of symptom and their impact on functional performance.

This study provides insight into symptom burden and functional performance in patients with COPD; however, some limitations are acknowledged. The study design was descriptive, cross-sectional and correlational, based on a non-probability convenience sample consisting of patients with COPD. The cross-sectional design allowed the capture of data over an inclusive time period of the past week; the variability of symptom burden and functional performance over this time

was captured. This design does not allow the researcher to determine whether symptom burden and functional performance change over time, particularly as a disease progresses. Therefore, future longitudinal study would be beneficial to understand the pattern of symptom burden and functional performance changes over time. Non probability samples used in this study weaken the generalisability of findings. This study collected data from patients attending only one hospital, which also limits the generalisability. Furthermore, inpatients, or patients without access to health care are not represented. There is a need for a larger national study comparing symptom burden and functional performance across all stages of COPD. Finally, this study addressed the symptom burden in COPD using a quantitative approach only. Qualitative data of symptom burden and functional performance from the perspective of patients with COPD was not captured. More studies using mixed methods approaches are needed to offer in-depth insights into explaining the dimensions of symptoms and their meaning from a patient's perspective.

5.2 Implications for practice

Because of the high symptom burden which was correlated to low functional performance found in the present study, heath care providers have the responsibility to achieve an acceptable level of symptom relief. Conducting a routine assessment for symptoms and symptom burden will lead to better symptom management that will improve their functional performance. Regular visits for patients with COPD are essential to identify the candidate patients for home or personal care support. Findings from this study and previous research revealed that symptom burden, poor functional performance, and palliative care needs in patients with severe and very severe COPD seem to be very similar to patients with cancer. Therefore, there is a need for a palliative care model for patients with advanced COPD. Nurses trained in palliative care are needed to meet the symptom management and functional performance care needs for patients with advanced COPD.

5.2 Implications for Research

This study was a cross-sectional approach to symptom burden and functional performance in COPD, and did not allow the researcher to determine whether symptom burden and functional performance change over time, particularly as the COPD progress. Therefore, there is a need for a future longitudinal study to understand patterns of symptom and functioning change over time, and measure the impact of COPD on a patient's life, and how this changes over time using the COPD assessment test (CAT). This will provide better insights into the symptom burden experience and functional performance in COPD. This study investigated symptom burden and functional performance as a dimension of functional status. Further research is required using both quantitative and qualitative data to understand the symptom burden from the patient's perspective in terms of the types and dimensions of symptom and their impact on functional

performance. The meaning of symptom burden to patients experiencing COPD needs to be better understood.

6. Conclusion

This study was the first to measure symptom burden as a multidimensional concept and functional performance in a sample of patients across all COPD stages. To date, studies on symptom burden in COPD are lacking, giving a piecemeal picture of symptom burden, with most studies presenting descriptive data on percentages of patients reporting frequency, severity, and distress of symptoms. The majority of studies have investigated symptom burden in severe and very severe COPD, with a dearth of studies on symptom burden in mild and moderate COPD. Research has only investigated the relationship between a single symptom or a limited number of symptoms and functional performance in COPD. Little is known about the effect of multiple symptoms and symptom burden on functional performance. It was found that patients with COPD experienced a remarkably high number of symptoms, significant symptom burden, and low functional performance and that patients with COPD experienced a wide range of both physical and psychological symptoms. Total psychological symptom burden was higher than the total physical symptom burden. Given the high prevalence and high-burden physical and psychological symptoms, findings suggest that these symptoms are currently not being adequately managed. There is a need to broaden the clinical and research assessment of both physical and psychological symptoms in COPD. With regard to symptom burden and its relationship to functional performance, a statistically significant negative correlation between physical symptom burden, psychological symptom burden, total symptom burden, and functional performance was found. High symptom burden and low functional performance found in this study supported the growing body of evidence of the need for patients with advanced COPD to receive palliative care.

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Thank you for your consideration of this manuscript

Sincerely,

Dr. Omar Melhem

Highlights

- Patients with COPD experienced a wide range of physical and psychological symptoms. Psychological symptom burden was greater than physical symptom burden.

- Patients with COPD experienced a significant symptom burden, and poor functional performance.

- Managing the symptoms will improve the functional performance of patients with COPD.

- Regular visits and assessment for patients with COPD are essential to identify the candidate patients for home or personal care support.

- There is a need for palliative care model for patients with advanced COPD.