Disability in Moderate Chronic Obstructive Pulmonary Disease: Prevalence, Burden and Assessment – Results from a Real-Life Study

Fulvio Braidò^a Ilaria Baiardini^a Nicola Scichilone^b Claudio Sorino^{b, c}
Fabiano Di Marco^d Angelo Corsico^f Pierachille Santus^e
Giuseppe Girbino^g Giuseppe Di Maria^h Carlo Mereuⁱ Eugenio Sabato^j
Maria Pia Foschino Barbaro^k Giuseppina Cuttitta^l Alberto Zolezzi^m
Caterina Buccaⁿ Sara Balestracci^a Giorgio Walter Canonica^a

^aAllergy and Respiratory Diseases Clinic, DIMI, University of Genoa, IRCCS AOU San Martino-IST, Genoa,

^bDipartimento Biomedico di Medicina Interna e Specialistica, University of Palermo, 'Villa Sofia-Cervello' Hospital, Palermo, ^cPulmonology Unit, AO Sant'Anna, Como, ^dClinica di Malattie Respiratorie, UOC Pneumologia, Ospedale San Paolo, and ^eUniversità degli Studi di Milano, Pneumologia Riabilitativa, Fondazione Salvatore Maugeri, Istituto Scientifico di Riabilitazione di Milano (IRCCS), Milan, ^fDipartimento di Medicina Molecolare, Fondazione IRCCS Policlinico San Matteo, Università di Pavia, Pavia, ^gRespiratory Department, University Hospital, Messina, ^hSchool of Specialization in Respiratory Diseases, University of Catania, Catania, ⁱPulmonology Department, Santa Corona Hospital, Pietra Ligure, Savona, ^jDepartment of Pneumology and Respiratory Rehabilitation 'A. Blasi', Brindisi, ^kInstitute of Respiratory Disease, Medical and Surgical Sciences Department, University of Foggia, Foggia, ^lPulmonary Environmental Epidemiology Unit, CNR Institute of Clinical Physiology, Pisa, ^mPulmonology Unit, AOU Carlo Poma, Mantova, and ⁿDepartment of Medical Sciences, University of Turin, Turin, Italy

Key Words

Chronic obstructive pulmonary disease · Disability · Patient-reported outcomes

Abstract

Background: The role of disability and its association with patient-reported outcomes in the nonsevere forms of chronic obstructive pulmonary disease (COPD) has never been explored. **Objectives:** The aim of this study was to assess, in a cross-sectional real-life study, the prevalence and degree of disability in moderate COPD patients and to assess its association with health status, illness perception, risk of death and well-being. **Methods:** Moderate COPD outpatients attending scheduled visits were involved in a quantitative re-

search program using a questionnaire-based data collection method. **Results:** Out of 694 patients, 17.4% were classified as disabled and 47.6% reported the loss of at least one relevant function of daily living. Disabled patients did not differ from nondisabled patients in terms of working status ($p = 0.06$), smoking habits ($p = 0.134$) and ongoing treatment ($p = 0.823$); however, the former showed a significantly higher disease burden as measured by illness perception, health status and well-being. The stepwise regression analysis showed that the modified Medical Research Council (mMRC) score was the most relevant factor related to COPD disability ($F = 38.248$; $p = 0.001$). Patient stratification was possible according to the forced expiratory volume in 1 s (FEV_1) value and an mMRC score ≥ 2 , which identified disabled patients, whereas the mMRC values were differently associated with

the risk of disability. **Conclusion:** A significant proportion of individuals with moderate COPD reported a limitation of daily life functions, with dyspnea being the most relevant factor inducing disability. Adding the evaluation of patient-reported outcomes to lung function assessment could facilitate the identification of disabled patients. © 2015 S. Karger AG, Basel

Introduction

Chronic obstructive pulmonary disease (COPD) is considered as a heterogeneous disease, and forced expiratory volume in 1 s (FEV₁) does not fully describe its complexity [1]. In 2011, the Global Initiative for Chronic Obstructive Lung Disease (GOLD) recommendations [1] proposed for the first time a multidimensional approach that included both functional parameters and patient-reported outcomes, with the aim to provide a comprehensive assessment of the disease, thus meeting both the needs of the patient and the role of the physician. However, the prognostic and clinical implications of this classification, which integrates patients' and physicians' perspectives, need to be clearly understood.

Several studies analyzed existing cohorts of COPD subjects to explore different aspects of the GOLD 2011 [1] assessment proposal. Han et al. [2] used the COPDGene cohort [3] to investigate the influence of choosing different tools on severity group assignment and the risk of exacerbations during the follow-up period, showing that the choice of a specific measurement of the respiratory symptoms, that is, dyspnea [modified Medical Research Council (mMRC)] versus health status [St. George's Respiratory Questionnaire (SGRQ) as a surrogate for the COPD Assessment Test (CAT)], can significantly change the category assignment. Lange et al. [4] investigated the ability of the GOLD 2011 proposal [1] to predict the clinical course of the disease, showing that both prebronchodilator spirometric GOLD grades and the ABCD GOLD 2011 [1] classification predicted mortality in the general population, however, without exploring which approach best applied to it. Similar findings were obtained by Soriano et al. [5], who analyzed pooled data from eleven Spanish cohorts followed for at least 10 years, and by the GenKOLS cohort study in which COPD patients were followed for 8 years [6]. Both studies failed to demonstrate any difference between the GOLD lung function classification and the ABCD classification in predicting mortality. In contrast, Leivseth et al. [7] showed that the ABCD classification was less sen-

sitive in predicting mortality compared to the lung function classification.

Besides mortality, other relevant outcomes such as disability need to be fully evaluated in COPD patients. This is what emerges from a recent editorial by Yohannes [8] that underlines the necessity to properly assess the limitations in daily activities in order to help physicians to design tailored interventions for patients with COPD. It has been previously shown that a significant percentage of disabled patients can be identified in each disease stage, with dyspnea serving as the most relevant factor inducing disability [9]. A systematic review of 65 studies shows that patients with a moderate disease severity are the most frequent in the whole population of COPD [10]. In this respect, the assessment of the prevalence of disability and its association with patient-reported outcomes in less severe COPD patients is a prerequisite for planning specific behavioral, educational and therapeutic interventions. If deterioration is not detected early, besides increasing the burden of the disease in the early stages, it may lead the patient to require assistance to maintain independence at home [8]. It is possible to evaluate the limitations of physical activity in moderate COPD patients [11] in order to monitor the impact of disease and therapeutic interventions. The aim of the present study was to assess the prevalence and degree of disability in moderate COPD patients according to the GOLD 2007 [12] classification of severity and to assess its association with health status, illness perception, risk of death and well-being. Furthermore, we evaluated whether the addition of an mMRC cutoff (≥ 2 or < 2) to spirometric parameters provides additional advantages for discriminating different populations in terms of disease impact on patients' life.

Materials and Methods

Study Design and Patients

A quantitative research program using a questionnaire data collection method was performed. The study population included adult patients with physician-diagnosed moderate COPD according to the GOLD 2007 guidelines (stage II: $50\% < \text{FEV}_1 \leq 80\%$) [12], attending 18 academic and/or hospital centers for follow-up visits from April to December 2011. While waiting for the visit, patients were invited to fill in questionnaires regarding their illness perception, health status and well-being. The inclusion criteria were the comprehension of written and spoken Italian language and the availability for participation in the study. Exclusion criteria were lack of knowledge of the Italian language, presence of impaired cognitive functions and visual-auditory defects, physical inability to autonomously complete the questionnaire, presence of asthma or respiratory diseases other than COPD. This study was performed according to Good Clinical Practice standards and the

Declaration of Helsinki and was approved by the local ethics committee, and all patients gave their written informed consent. During the visit, patients underwent postbronchodilator spirometry (European Respiratory Society – American Thoracic Society guidelines) [13]. Each patient was invited to complete the following questionnaires:

- The Barthel activities of daily living (ADL) index [14], which evaluates the self-sufficiency of the patient by means of 10 items describing the ADL and the ability to move. The score of each item may be 0, 5, 10 or 15; higher scores are associated with a greater likelihood of being able to live at home.
- The Lawton instrumental ADL (IADL) scale [15], which assesses a person's ability to perform different tasks (using a telephone, doing laundry, handling finances, preparing meals, home management, using transportation, shopping and adhere to therapy). It provides a global score ranging from 0 (low function) to 8 (high function).
- The Charlson comorbidity index [16], which is used to estimate the risk of mortality at 1 year in patients affected by different comorbidities that may influence the long-term survival. It includes 19 medical conditions weighted from 1 to 6 with a total score ranging from 0 to 37. From the weighted conditions, a sum score can be tallied to yield the total comorbidity score.
- The mMRC dyspnea scale [17], which is used to evaluate dyspnea and its effect on the daily activities. This is a simple, standardized scale consisting of 5 statements that describe the range of respiratory disability, from no disability at all (stage 1: 'I only get breathless with strenuous exertion') to almost complete incapacity (stage 5: 'I am too breathless to leave the house').
- The Illness Perception Questionnaire (IPQ-R) [18], which is used to evaluate patients' opinion and understanding of the disease. It is divided into two parts: the first one describes the presence of symptoms and the identification by the patient of the potential relationship between each symptom and the disease; the second part investigates the following factors: consequences, timeline acute/chronic, timeline cyclical, illness coherence, personal control, treatment control and emotional representation.
- The Psychological General Well-Being Index (PGWBI) [19], which measures the subjective perception of well-being. This self-administered index is rated on a 6-point scale and consists of 22 items assessing the psychological and general well-being in 6 domains: anxiety, depressed mood, positive well-being, self-control, general health and vitality. Adding the scores of the 6 dimensions investigated, a summery distress index (0–60 points = severe distress; 61–72 points = moderate distress; 73–97 points = no distress; >98 points = positive well-being; 110 points = best-achievable well-being) can be obtained.
- The SF-12 Health Survey [20], which is used to assess health status. It consists of 12 items (obtained by 36 items of questionnaire SF-36) that provide two measures: Physical Component Summary and Mental Component Summary. The scores range from 0 to 100, where a zero score indicates the lowest level of health measured by the scales and 100 indicates the highest level of health.

Sample Size and Statistical Analysis

A total of 18 centers, homogeneously distributed across Italy, were asked to recruit the first 50 consecutive moderate COPD patients attending their clinic for a routine visit in a 6-month pre-

Fig. 1. Procedure of patient enrollment.

defined period. The recruitment of a minimum of 650 patients was considered sufficient to explore the aim of the study. The sample size was estimated considering a 20% data failure due to patients and physicians failing to fill in the questionnaire and the prevalence of moderate COPD in patients attending hospital clinics. Analyses were conducted in the overall population and in two sub-populations defined according to the mMRC score (≥ 2 or < 2).

For the purpose of the study, patients were classified on the basis of their Barthel score into self-sufficient (ADL score = 100) and disabled (ADL score < 100). The latter were stratified into 4 degrees of disability: mild (score 91–99), moderate (61–90), severe (21–60) and very severe (0–20).

The results are shown as means (standard deviations; SD), unless otherwise stated. Student's *t* test was used to detect significant differences of quantitative variables, while the χ^2 test was used to detect significant differences of qualitative variables. Spearman's ρ was applied to test the relationship between variables or rank scores. Linear regression was used to estimate the coefficients of the equation that provided the best value of the dependent variables.

Results

Overall Population Analysis

Out of the 900 COPD patients who were asked to participate in the study, 740 filled in the questionnaires. Only the questionnaires of patients with a >90% completion rate ($n = 694$) were considered for analysis (fig. 1). The sociodemographic and functional characteristics of the study sample are reported in table 1.

The Barthel index revealed that 17.4% of patients had features of disability at different levels: 12.3% had mild, 2.5% had moderate, 1.9% had severe and 0.7% had very

Table 1. Sociodemographic characteristics of the study COPD population (n = 694)

Characteristics	
Mean age $\pm$ SD, years	70.23 $\pm$ 9.7
Male sex, %	74.9
Mean FEV ₁ $\pm$ SD, %	64.09 $\pm$ 9.07
mMRC score, %	
1	15.6
2	36.7
3	23.7
4	19.4
5	4.6
Mean BMI $\pm$ SD	27.57 $\pm$ 5.06
Smoking habits, %	
Current smokers	27.8
Nonsmokers	9.7
Former smokers	62.5
Education, %	
Primary school	49.6
Secondary school	26.5
High school	19.1
Degree	4.8
Employment status, %	
Workers	15.3
Retired	84.7
Ongoing therapies, %	
Short-acting β_2 agonist	16.6
Long-acting β_2 agonist	15.1
Long-acting muscarinic antagonists	54.4
Inhaled corticosteroids in association with long-acting bronchodilators	58.4
Oral theophylline	5
Oral corticosteroids	0.4
Long-term oxygen therapy	4.5

severe disability. According to the IADL scale responses, no function was lost by 52.4% of patients; 16.2% of patients lost 1 function, 10.5% lost 2 functions, 8.2% lost 3 functions and 13% lost between 4 and 8 functions. According to the mMRC, 15.6, 36.7, 23.7, 19.4 and 4.6% of patients belonged to the 1–5 levels of dyspnea, respectively. The Charlson index mean values were as follows: Charlson weighted index of comorbidity 2.26 ± 1.52 ; Charlson age-related risk 4.83 ± 1.93 ; Charlson combined comorbidity index and age-related risk 36.59 ± 32.49 .

Population Analysis According to Disability

Compared to nondisabled patients, disabled subjects had a statistically significant lower level of education ($\chi^2 = 21.21$; $p < 0.001$) but did not differ for working status ($\chi^2 = 3.47$; $p = 0.06$), smoking habits ($\chi^2 = 4.01$; $p = 0.134$), use

Table 2. Comparison of clinical parameters, illness perception, health status and well-being in disabled and nondisabled patients

	Disabled patients ^a	Nondisabled patients ^b	Significance (two-tailed)
FEV ₁	62.7 (8.6)	64.3 (9.1)	0.072
Charlson index	15.4 (25.3)	41.0 (32.1)	0.001 ^a
mMRC dyspnea	3.6 (0.9)	2.4 (1.0)	0.001 ^a
<i>IPQ-R</i>			
Identity	4.55 (2.4)	3.3 (2.3)	<0.001 ^a
Timeline	22.9 (4.4)	22.6 (4.6)	0.346
Consequences	20.6 (4.4)	17.8 (4.1)	<0.001 ^a
Personal control	18.2 (3.8)	19.7 (3.8)	<0.001 ^a
Treatment control	17.3 (3.1)	18.2 (2.9)	0.005 ^a
Illness coherence	16.0 (3.9)	17.8 (3.9)	<0.001 ^a
Timeline cyclical	13.7 (2.9)	11.8 (3.3)	<0.001 ^a
Emotional representations	18.9 (4.5)	15.9 (4.6)	<0.001 ^a
<i>PGWBI</i>			
Anxiety	14.7 (4.8)	17.8 (4.7)	<0.001 ^a
Depressed mood	9.4 (3.5)	11.8 (3.1)	<0.001 ^a
Positive well-being	8.3 (3.6)	11.3 (3.9)	<0.001 ^a
Self-control	8.6 (3.2)	11.5 (3.2)	<0.001 ^a
General health	7.1 (3.3)	9.7 (3.2)	<0.001 ^a
Vitality	8.2 (3.6)	12.1 (5.9)	<0.001 ^a
Global score	56.4 (18.1)	73.8 (18.8)	<0.001 ^a
<i>SF-12</i>			
Physical component	30.3 (7.8)	38.9 (9.4)	<0.001 ^a
Mental component	39.6 (11.5)	47.2 (11.5)	<0.001 ^a

Values are expressed as means (SD). ^a Barthel ADL index <100. ^b Barthel ADL index = 100. * $p \leq 0.01$.

of short-acting β_2 agonists ($\chi^2 = 0.21$; $p = 0.647$) and treatment ($\chi^2 = 0.911$; $p = 0.823$).

The Lawton IADL scores showed that a significantly higher number of disabled patients lost the ability to use the telephone ($\chi^2 = 33.09$; $p < 0.001$), to take care of shopping needs independently ($\chi^2 = 207.53$; $p < 0.001$), to adequately take care of nutrition ($\chi^2 = 106.94$; $p < 0.001$), to manage their house needs ($\chi^2 = 43.509$; $p < 0.001$), to do the laundry ($\chi^2 = 52.286$; $p < 0.001$), to travel independently on public transport or to drive a car ($\chi^2 = 94.299$; $p < 0.001$), to take responsibility for their own medications ($\chi^2 = 138.330$; $p < 0.001$) and to handle finances ($\chi^2 = 29.928$; $p < 0.001$).

As regards clinical findings and IPQ-R, SF-12 and PGWBI questionnaire scores, the comparison between disabled and nondisabled patients showed significant differences between the two groups, as reported in table 2.

Fig. 2. Estimated odds ratio of being disabled according to the mMRC score and the Charlson age-related risk.

However, when the stepwise regression analysis was performed, the mMRC score remained the only factor associated with COPD disability ($F = 38.248$; $p = 0.001$).

Population Analysis According to mMRC Cutoff Score

A vast proportion of the 694 patients that were evaluated showed an mMRC score ≥ 2 (84.4%) and the median mMRC value was 2. Among the patients with an mMRC score ≥ 2 , 20.3% were disabled. The comparison between disabled and nondisabled patients in the group of subjects with an mMRC score ≥ 2 showed that disabled patients were significantly older ($p < 0.001$), had a greater risk of death defined by the Charlson index ($p < 0.001$), showed worse well-being and health status ($p < 0.001$) as well as higher levels of anxiety/depression ($p < 0.001$). No differences between disabled and nondisabled patients were found concerning airway obstruction ($FEV_1\%$ predicted) and BMI.

The stepwise regression analysis showed that in COPD patients with $\geq 50\%$ FEV_1 predicted and $\leq 80\%$ FEV_1 predicted and an mMRC score ≥ 2 , the mMRC value was the most relevant factor for predicting COPD disability ($F = 63.48$; $p = 0.001$). The increase in mMRC score was significantly related to the increase in disability. In particular, the odds ratio of being disabled was 4.6 for an mMRC score of 3, 10.38 for an mMRC score of 4 and 33.13 for an mMRC score of 5 (while the Charlson age-related risk odds ratio was 1.47; fig. 2).

Using a median score of 2 as a cutoff, 330 patients had mMRC scores of 3, 4 or 5. Among them, 20.3% were disabled. Again, the comparison between disabled and nondisabled patients in the group of subjects with an mMRC score of 3, 4 or 5 showed that disabled patients were significantly older ($p < 0.001$), had a greater risk of death

defined by the Charlson index ($p < 0.001$), showed worse well-being and health status ($p < 0.001$) as well as higher levels of anxiety/depression ($p < 0.001$). No differences between disabled and nondisabled patients were found concerning airway obstruction ($FEV_1\%$ predicted) and BMI.

The stepwise regression analysis showed that in COPD patients with $\geq 50\%$ $FEV_1\%$ predicted ≤ 80 and an mMRC score ≥ 2 , the mMRC score was the most relevant factor for predicting COPD disability ($F = 23.03$; $p < 0.001$). Moreover, the Charlson age-related risk odds ratio was 2.5.

Discussion

The present study focused on disability prevalence, burden and assessment in individuals with moderate COPD according to the GOLD 2007 [12] classification. A nontrivial proportion of moderate COPD patients (17.4%) reported a limitation of functions affecting their daily independence. When considering daily life activities, one third of the observed patients lost at least 2 of the 8 explored functions. Interestingly, in our cohort, disabled patients did not differ from nondisabled ones for working status, smoking habit and level of bronchial obstruction, as expressed by the $FEV_1\%$ predicted. This observation is in contrast with previous findings [21] showing that smoking habit strongly predicts disability retirement due to COPD.

Disability impacts the individual perspective of COPD in terms of illness perception, well-being and health status. Disabled patients described more COPD-related symptoms, perceived their illness as more cyclical and ascribed more severe consequences to COPD; moreover, they felt less confident regarding the possibility of controlling COPD and had more difficulties in understanding their disease. Disabled patients reported lower levels of vitality, general health, self-control and positive well-being, and higher levels of depressed mood and anxiety, all of which result in a lower personal well-being. Furthermore, both the physical and mental components of health status resulted in more impairment. These data are in line with those recently published by other researchers [22].

While FEV_1 , ranging from 55 to 73% of the predicted value in our population, did not significantly differ in disabled and nondisabled patients, disability was significantly associated with the risk of death due to comorbidities and dyspnea burden, the latter resulting as the dominant factor. We therefore evaluated whether a patient's classification

according to FEV₁% predicted and mMRC score, with the approach proposed by the GOLD 2011 [1] recommendations, could be useful for identifying disabled patients in daily practice. Our analysis showed that in patients with an mMRC score <2 the proportion of disabled patients is very small (near 2%), while it increases to 20% among those with an mMRC score ≥2. The odds ratio of being disabled grew impressively according to the mMRC score, whereas spirometric and risk-of-death parameters did not.

The cross-sectional nature of this study allowed us to describe a phenomenon (presence and burden of disability) and to assess its association with clinical features (comorbidities, airway obstruction severity and sociodemographic parameters) and patients' subjective experience (illness perception, well-being and health status) without permitting us to explore causal relationships. Moreover, we adopted two widely used generically validated tools to assess disability. A recent review [23] showed that none of the tools available for assessing disability in COPD patients can be considered as a gold standard. A specific questionnaire assessing COPD-related disability has been recently developed and validated [24], although it is not yet available in different languages; this tool could help the enhancement of COPD management by integrating an evaluation of the COPD-related disability into daily practice. After a careful investigation of the available tools, we chose the Barthel index for several reasons: an Italian version is available, it has been used previously with COPD patients and, given the criteria for inclusion in and exclusion from the study, it allowed us to assess

disability in general and not only disability strictly related to COPD.

The present study underlined that the evaluation and classification of COPD patients can benefit from the use of additional, nonfunctional measures. The mMRC score was found to be the most relevant factor related to disability in COPD patients. The determinants of symptoms are various and include physiological, psychological, social and environmental factors that interact, thus affecting both the quality and intensity of symptom perception [25]. The presence of disability appeared to significantly affect different aspects of illness perception; this is expected to worsen patients' quality of life.

The results of this study show that a significant proportion of COPD patients with moderate airflow obstruction report limitations affecting their daily independence, with dyspnea serving as the most relevant factor inducing disability. Patients' stratification according to FEV₁ values and mMRC score (cutoff score ≥2 or median value) was found to be effective in identifying disabled patients, while mMRC values were associated with the risk of disability.

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