

Functionality and caregiver burden in COPD

Title: Severe COPD patient functionality is related to caregiver burden. A cutoff point proposal.

Autors: María Granados Santiago¹, Ramón Romero Fernández², Andrés Calvache Mateo², Alejandro Heredia Ciuro², Javier Martín Nuñez², Laura López López^{*2}, Marie Carmen Valenza².

Affiliation:

- 1. Department of Nursing. Faculty of Health Sciences. University of Granada, Spain.**
- 2. Department of Physiotherapy. Faculty of Health Sciences. University of Granada, Spain.**

Corresponding author

Laura López López.

Department of Physiotherapy. University of Granada. Faculty of Health Sciences. Av.

De la Ilustración, 60

18016 Granada, Spain

Tlf: +34958248035

E-mail: lauralopez@ugr.es

**Title: Relationship between patient functionality impairment and caregiver burden:
is there a cut-off point for the severe COPD patient?**

Abstract

Background: Chronic obstructive pulmonary disease (COPD) patients experience a progressive limitation of their functionality accompanying their clinical evolution. Concretely, severe COPD patients usually require the figure of a caregiver. Caregiver burden have been yet explored in other similar chronic diseases

Objective: To propose a cut-off point in different functional impairment aspects, to predict the presence of caregiver burden.

Methods: Severe COPD patients were divided into two groups according to the caregiver burden, measured with the Zarit Burden Interview (ZBI). The patients were assessed with the London Chest Activity of Daily Living (LCADL) scale, the Functional Independence Measure (FIM), and the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0). **Results:** 70 COPD patients and their caregivers were included in this cross-sectional study. The ROC curve indicated a cutoff point of 19 in the LCADL scale (AUC=0.722). Dependence in daily life activities had a cutoff point of 123 in the FIM (AUC=0.776). Social participation in activities of daily living had a cutoff point of 37 in the WHODAS 2.0 (AUC=0.739).

Conclusion: Dyspnea related to functional status, dependence in daily life activities, and social participation in activities of daily living of severe COPD patients can predict caretaker burden.

Keywords: Pulmonary disease; chronic obstructive; ROC curve; caregivers; global burden of disease; dependence

1. Introduction

Chronic obstructive pulmonary disease (COPD) is the most widespread respiratory disease, with a prevalence of 8-20% worldwide [1]. Progressive airflow limitation in COPD patients is related to the severity of cardinal symptoms, dyspnea [2], and fatigue [3]. As the disease progresses, COPD patients experience progressive functional impairment [4], with a decrease in their quality of life [5].

The majority of caregivers are middle-aged adult children and older spouses who care for a parent or spouse with functional limitations giving emotional support and monitoring disease progression [6]. The role of caregivers is becoming essential in COPD management, due to their potential role in adherence to medical recommendations and pharmacological treatment [7]. More than 70% of COPD patients have one or more caregivers [8]. By some estimates, more than 15 million adults currently provide care to relatives, saving the formal health care system billions of dollars annually [9,10].

Caring for patients, especially disabled ones, demands physical, psychological, and financial resources from caregivers [11]. Although family caregivers perform an important service for society and their relatives, they do so at a considerable cost to themselves.

According to Schulz et al. [12] primary caregiving role, mediated by the caregiver burden, is an independent risk factor for an increased mortality rate (63%).

Recent studies have found that caregivers of individuals with COPD frequently could report pathological stress, such as distress, anxiety, and depression the most common complaints associated with the caring experience [13-16]. According to the model of carer stress and

burden, there is an association between the severity of patient disease, duration of care provided, interference with the carer's life, and the carer's subjective assessment of their role, which may increase the risk for care burden by exacerbating factors [17,18]. Thus, a review about the unmet needs of caregivers observed the urgent need to evaluate the caregiver burden of patients with COPD and to identify strategies to effectively support this neglected group [19].

Therefore, it is important to develop appropriate solutions to screen caregivers at risk for caregiver burden and in need of further assessment and intervention.

Considering this, we hypothesized that caregiver burden could be predicted using COPD patient functional status. Thus, this study aims to propose a cut-off point in different functional impairment aspects, to predict the presence of caregiver burden.

2. Patients and methods

2.1.Study design

This cross-sectional study was conducted from January 2017 to January 2019 with COPD patients and their caregivers. This study was approved by the Biomedical Research Ethical Committee of Granada and was conducted following the ethical guidelines of the Declaration of Helsinki reviewed in 2013. The STROBE guidelines [19] were followed during the research.

2.2.Participants

COPD patients and their respective caregivers were recruited during their routine clinical visits in the pulmonology service of San Cecilio University Hospital in Granada, Spain. All

subjects and their caregivers who agreed to voluntarily participate, signed a written informed consent form after receiving detailed information about the study protocol. The inclusion criteria of COPD patients were: a) stable patients with moderate to very severe COPD as the main diagnosis with Global Initiative for Chronic Obstructive Lung Disease (GOLD) grades III or IV [20]; b) ability to answer and understand the questionnaires; c) having one or more caregivers. All patients had oxygen therapy and sometimes required home ventilatory support according to the severity of COPD [20]. Caregivers who met the following definition were included: “Caregiver is defined as any person including parents and other family members who with or without payment provides care, support, or assistance to a person with disability” [21,22]. COPD patients were asked to nominate one informal caregiver to participate.

Patients and caregivers were excluded if there were: a) the presence of psychiatric or cognitive disorders, progressive neurological disorders, organ failure, cancer, or inability to cooperate; or b) inability to provide informed consent.

2.3. Outcome measures

After verifying the inclusion and exclusion criteria, data that had been per-protocol routinely collected by the health team were recorded. Anthropometric and sociodemographic data were collected through patients’ history medical records and with an interview of patients and their caregivers. All the variables were measured in the patients and their respective caregivers.

To evaluate caregiver-related aspects, the relevant severity of the patient disease, the carer’s psychoemotional well-being and the characteristics of care provided related to the functional impairment of the patient were evaluated as follows.

The severity of patient disease was explored including the dyspnea perception, assessed with the modified Borg scale [23], the degree of disability that dyspnea causes in day-to-day activities, measured with modified Medical Research Council (mMRC) [24], and comorbidities were evaluated with the Charlson score [25].

The carer's psychoemotional well-being was evaluated by psychoemotional distress and care burden. Anxiety and depression were assessed with the Hospital Anxiety and Depression (HAD) scale [26]. Caregiver burden was measured with the Zarit Burden Interview (ZBI). The questionnaire consists of 22 items on the psychological, physical, emotional, financial, and social problems caregivers experience. Each item is evaluated with a Likert scale from 0 (never) to 4 (nearly always), and includes questions such as "Do you feel that your relative asks for more help than he/she needs?", or "Do you feel angry when you are around your relative?" A maximum score of 88 indicated the highest level of burden in caregivers [27]. When psychometric testing of the ZBI was conducted with caregivers of COPD patients, construct validity and adequate internal consistency (Cronbach's alpha 0.92) were determined [28].

To describe the characteristics of the care provided, we evaluate all the functional demanding aspects by care recipients. In this line, we evaluate the symptomatic related functionality, the functional dependence and the restrictions in daily life activities and social participation.

Symptomatic-related functionality was measured with the London Chest Activity of Daily Living (LCADL) scale measured dyspnea levels related to functionality. This scale is used to analyze dyspnea limitation during activities of daily living in COPD patients. The

LCADL scale is composed of 15 questions on four domains: domestic activities, personal care, physical activity, and leisure, such as “dressing upper body, “bending” or “going out socially”. Higher scores indicate lower levels of functional status.. Patients score from 0: “I wouldn’t do anyway”, to 5: “Someone else does this for me (or helps)”, being a total score ranges from 0 to 75 points. The instrument is valid and reliable among patients with respiratory disease conditions [29]. The internal consistency reliability of the questionnaire was evidenced by a cronbach’s alpha of 0.98 in COPD patients [30].

The Functional Independence Measure (FIM) assesses patient dependence or independence in activities of daily living. It measures 2 dimensions – motor and cognitive which include motor items as “eating”, “stairs” or “toilet”, and cognitive items such as “comprehension”, “social interaction” or “memory”. There are 7 response levels, where there are 2 functionally independent, 3 partial assistance, and 2 total assistance levels. The total score ranges between 18 points (total dependence) and 126 points (complete independence) [31]. The FIM is a valid measure correlated with functionality during acute exacerbation of COPD [32].

Restrictions in daily life activities and social participation in patients were assessed with the World Health Organization Disability Assessment Schedule 2.0 (WHODAS 2.0). This test is composed of 36 items on six domains: cognition, mobility, self-care, getting along with people, living activities, work, and participation in society. “Standing for long periods such as 30 minutes?”, “concentrating on doing something for 10 minutes?” or “washing your whole body?” are included in this questionnaire. Each domain score ranges from 1 “no difficulty” to 5 “extreme difficulty/can’t do”. Higher scores indicate greater levels of functional impairment. The internal consistency reliability of the WHODAS 2.0 was a cronbach’s alpha standard of 0.7 in the four domains related to chronic diseases [33].

Numerous studies have used WHODAS 2.0 to assess functionality in COPD patients [34, 35].

2.4. Statistical analysis

Statistical analysis was performed using SPSS 20.0 (SPSS, Chicago, Illinois). $P < 0.05$ was considered statistically significant. The characterization of the variables was expressed as mean \pm SD, minimum and maximum values, and frequencies. We correlated the carer's psychoemotional well-being against the characteristics of care provided related to the functional impairment of patients using Pearson correlation coefficients. Correlation coefficients were statistically significant when the p -value < 0.05 , being a value of -1 meaning a total negative linear correlation, 0 being no correlation, and + 1 meaning a total positive correlation. The predictive power and cutoff points of various patterns and domains of functionality were identified by a receiver operating characteristic curve (ROC curve), which is often used to determine cutoff points for diagnostic or triage tests. The cutoff points were determined by the point of convergence of sensitivity and specificity, which produce the area under the curve (AUC). AUC ranges in value from 0 to 1, being an AUC < 0.7 considered as low, ≥ 0.7 to < 0.8 as moderate and ≥ 0.8 as high predictive accuracy. The Youden's index was used to assess the best cut-off point between the sensitivity and specificity of a test.

For the variables associated with the ZBI score, the ROC analysis was used to determine the cutoff points related to a decrease in functional and quality of life in patients. The ZBI cutoff score to measure the caregiver burden of patients with chronic diseases was 46, that is, no burden < 46 , and burden ≥ 46 [36]. We used the ZBI to divide the sample between COPD patients with a caregiver burden and COPD patients without a caregiver burden

[37].

Initially, the total area under the ROC curve was identified among the functional status and quality of life for the absence of caregiver burden. The larger the area under the ROC curve, the greater the discriminatory power of functional status and quality of life for the absence of caregiver burden.

3. Results

184 participants had been admitted in the study, including COPD patients and their respective caregivers. Finally, 140 participants gave written consent to participate. The flowchart of participants is shown in Figure 1.

PLEASE INSERT FIGURE 1

In table 1, the baseline characteristics of COPD patients and the caregivers are presented

PLEASE, INSERT TABLE 1

3.1. Baseline characteristics of COPD patients according to caregiver burden

After grouping COPD patients according to caregiver burden, the division was as follows:

Group with caregiver burden (n=70) and group without burden (n=70), being 35 COPD patients and 35 caregivers in each group. All patients were male in both groups and the mean average duration of COPD was 15 years. In the group without caregiver burden, the mean of age was 71.86 years old. However, group with caregiver burden were for the most part elderly (mean of age 79.20 years old). COPD patients showed significant differences between groups in age ($p=0.006$), the degree of disability that dyspnea causes

($p=0.046$), and dyspnea perception ($p=0.022$). No statistically significant differences were found between sex, comorbidities, or body mass index.

3.2.Characteristics observed in the caregivers of COPD patients

Caregivers were predominately females in both groups. The age of caregivers showed significant differences between groups ($p=0.019$). Among caregivers without burden, 71.4% were aged 65-74 years old; caregivers with burden were younger, that is, 46.1% were under 64 years old. The relationship with COPD patients was spousal in most cases: 94.7% in caregivers without burden, and 76% in caregivers with burden. The anxiety and depression of caregivers showed statistical differences between groups ($p<0.005$), with an increase in the caregiver with burden group. Finally, caregiver burden showed significant differences between groups ($p<0.001$), with greater overload in the caregiver with burden group.

3.3.Functionality characteristic in patients with COPD

Results of main outcome values of COPD patients are explained in Table 2.

PLEASE INSERT TABLE 2

Dyspnea levels related to functionality showed no significant differences between groups. However, self-care and the leisure domains of the LCADL scale exhibited significant differences between groups ($p<0.05$). Besides, COPD patients with caregiver burden showed a decrease in dyspnea levels related to functionality compared to the other group ($p=0.111$).

No significant differences were found in dependence in daily life activities ($p=0.096$).

Nevertheless, COPD patients with caregiver burden reported less functionality than the COPD patients without caregiver burden.

Moreover, significant differences were reported in both groups in measures of social participation in activities of daily living ($p=0.041$). No statistically significant differences were found in any domains of the WHODAS 2.0 questionnaire. COPD patients without caregiver burden showed more social participation in activities of daily living than COPD patients with caregiver burden.

3.4. Correlational and receiver operating characteristic curve analysis

The Pearson correlation coefficients of LCADL, WHODAS, and FIM obtained against HAD were $r = 0.405$ ($p = 0.003$), $r = 0.307$ ($p = 0.043$) and $r = -0.493$ ($p < 0.001$) for patients' functionality and anxiety and depression of caregivers, respectively.

Additionally, LCADL, WHODAS, and FIM related to Zarit were $r = 0.335$ ($p = 0.001$), $r = 0.389$ ($p < 0.001$) and $r = -0.425$ ($p < 0.001$) for patients' functionality and caregiver burden, respectively.

ROC curve analyses were used to determine the optimal cutoff points to predict the caregiver burden of COPD patients. For each functionality outcome, we determined sensitivity, specificity, and AUC. The cutoff points with their respective sensitivity and specificity values are shown in Figure 2.

PLEASE INSERT FIGURE 2

In COPD patients, the cutoff point for dyspnea levels related to functionality was ≥ 19 with an AUC of 0.722 (sensitivity of 0.83 and specificity of 0.93). The cutoff point for

dependence in daily life activities was ≤ 123 , with an AUC of 0.776 (sensitivity of 0.94 and specificity of 0.76). The AUC of social participation in activities of daily living was 0.739 (sensitivity of 0.92 and specificity of 0.80) and the cutoff point was ≥ 37 to predict caregiver burden. Youden's index for caregiver burden was > 0.70 using patients' functionality including LCADL, FIM and WHODAS.

4. Discussion

The present study aimed to analyze the predictive power and identify the cutoff point of caregiver burden and COPD patient functional impairment in care recipients. Our results showed that dependence on daily life activities and dyspnea levels related to functionality in COPD patients were able to predict the presence of burden in caregivers, with an AUC of 0.776 and 0.722 respectively. Patient scores of ≤ 123 in the FIM and ≥ 19 in the LCADL scale were considered a predictor of caregiver burden. In addition, we included the value of social participation in activities of daily living with a cutoff score of ≥ 23 in the WHODAS 2.0 and an AUC of 0.739.

A review [38] suggested that FIM is a generic measure developed for multiple pathologies that include the evaluation of dependence in daily life activities. On the other hand, the LCADL scale is more important for COPD patients because it includes an evaluation of dyspnea related to functionality in activities of daily living [30]. Thus, the LCADL scale showed a high predictive power of caregiver burden according to the Youden index in our study.

Various authors [39, 40] have predicted multiple cutoff points for COPD patients with small sample sizes similar to our study. Belo et al. [41] proposed a cutoff point of 37% in the LCADL score with an AUC of 0.70 (sensitivity of 0.56 and specificity of 0.74) to discriminate the worst prognosis in COPD patients mainly with GOLD stage II disease. Additionally, Almeida Goulart et al. [42] identified a cut-off point of >28% in LCDL to enable discrimination of the functional impairment of patients with COPD. Our study predicted the presence of caregiver burden with a cutoff point ≥ 19 and an AUC of 0.722 (sensitivity of 0.83 and specificity of 0.93) only in severe COPD patients with GOLD stage III-IV disease.

Patients with COPD experience a progressive worsening of dyspnea that leads to a progressive reduction in the ability to perform activities of daily living during their disease [43]. Patients who are dissatisfied with the ability to perform daily activities often report greater reliance on others [44], which in turn leads to functional deterioration derived from dyspnea related to functionality [45], and a reduction of social participation in activities of daily living [46]. In the present study, the clinical application of cutoff values based on the functional impairment of COPD patients may predict caregiver burden with great accuracy.

The prevalence of COPD patients is almost three times higher in men than in women and increases with age [47]. Thus, long-term healthcare implies a large burden for families and ultimately for caregivers [48]. Studies suggest that caregiving is associated with psychological complaints and poor physical activities in multiple pathologies [49, 50]. Thus, the caregiver's health decline should be balanced by the healthy caregiver hypothesis [51]. In addition, the present study can contribute to the early detection and treatment of

caregiver burden in clinical practice, improving the physical and psychological quality of life of caregivers.

Several studies [52, 53] have used physical aspects and clinical profiles to predict complications during the progression of COPD. However, a few studies [54] have explored various psychological aspects of patients with chronic diseases as predictors of caregiver burden. Katsavos et al. [55] predicted the presence of caregiver burden related to the disability of patients with multiple sclerosis. A score of 4.5 in the Expanded Disability Status Scale (sensitivity of 0.32 and specificity of 0.82) indicated the presence of caregiver burden. By contrast, this study assessed social participation in activities of daily living with the WHODAS 2.0. The sensitivity of 0.92 and specificity of 0.80 levels showed the greatest predictive power. Moreover, our results indicated the presence of caregiver burden in relation with progress in the physical status of COPD patients.

Several limitations of this study should be considered. First, the cross-sectional design did not allow for any progress in the temporary analysis of predictor studies due to the reverse causality bias, so no relation of causality could be identified. Second, the use of questionnaires to evaluate functional impairment may have underestimated or overestimated some information. In addition, European male sample with limited diversity and the small sample size may limit to generalize our findings. Additionally, the course of COPD is clinically characterized by a worsening of dyspnea, cough, sputum production, and airflow obstruction, which were not analyzed in this study. Besides, the prediction of cut-off points may have several limitations by the ROC curve analysis, although multiples studies used this analyses type. Moreover, COPD patients was only male and had a

moderate to very severe profile of COPD. Further studies are needed to determine other aspects of COPD symptomatology that can influence caregiver burden in the different stages of COPD.

5. Conclusion

This study showed that mainly dyspnea associated with functionality, dependence in daily life activities, and social participation in activities of daily living in COPD patients may predict caregiver burden. The study findings highlighted the presence of burden on the informal caregivers according to the dyspnea level, functional impairment, and participation in activities of daily living of severe COPD patients. Our results may help in the early identification of the caregiver burden, who may need physical and physiological treatment, and social support to prevent a decrease in quality of life or a reduction of the healthcare provide to their care recipients with severe COPD. Future research should focus on prevention interventions and analyze the impact of caregiver burden development, highlighting the role of caregivers in COPD patients.

6. Funding details

The author Andrés Calvache Mateo and Alejandro Heredia Ciuró have a FPU (“Formación del Profesorado Universitario”) grant to the Spanish Ministry of Education (FPU: 19/02609 and FPU: 20/01670).

7. Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials

discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants, or patents received or pending, or royalties.

8. Author contributions

MGS had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, especially including any adverse effects. ACM contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript. AHC had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. LLL contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript. MCV contributed substantially to the study design, data analysis and interpretation, and the writing of the manuscript. RRF and JMN had full access to all of the data in the study and takes responsibility for the integrity.

9. Data availability statement

The data that support the findings of this study are available from the corresponding author, LLL, upon reasonable request.

10. References

- 1.- Vestbo J, Hurd SS, Agustí AG, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. *Am J Respir Crit Care Med.* 187, 347–65 (2013).
- 2.- Sundh J, Ekström M. Persistent disabling breathlessness in chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis.* 11, 2805-12 (2016).

- 3.- Spruit MA, Vercoulen JH, Sprangers MAG, et al. Fatigue in COPD: an important yet ignored symptom. *Lancet Respir Med.* 5(7), 542-4 (2017).
- 4.- Spruit MA, Singh SJ, Garvey C, et al. An official American thoracic society/European respiratory society statement: Key concepts and advances in pulmonary rehabilitation. *Am J Respir Crit Care Med.* 188(8), e13–e64 (2013).
- 5.-Waschki B, Spruit MA, Watz H, et al. Physical activity monitoring in COPD: Compliance and associations with clinical characteristics in a multicenter study. *Respir Med.* 106(4), 522-30 (2012).
- 6.- Trivedi RB, Bryson CL, Udris E, et al. The influence of informal caregivers on adherence in COPD patients. *Ann Behav Med.* 44(1), 66–72 (2012).
- 7.- Strang S, Fährn J, Strang P, et al. Support to informal caregivers of patients with severe chronic obstructive pulmonary disease: a qualitative study of caregivers' and professionals' experiences in Swedish hospitals. *BMJ open.* 9(8), e028720 (2019).
- 8.- Gautun H, Werner A, Lurås H. Care challenges for informal caregivers of chronically ill lung patients: Results from a questionnaire survey. *Scand J Public Health.* 40(1), 18–24 (2012).
- 9.- Schulz R, Quittner AL. Caregiving for children and adults with chronic conditions: introduction to the special issue. *Health Psychol.* 17, 107-111 (1998).
- 10.- Son J, Erno A, Shea DG, et al. The caregiver stress process and health outcomes. *Journal of aging and health.* 19(6), 871-887 (2007).
- 11.- Göriş S, Kılıç Z, Elmalı F, et al. Care burden and social support levels of caregivers of patients with chronic obstructive pulmonary disease. *Holistic nursing practice.* 30(4), 227-35 (2016).

12.- Schulz R, Beach SR. Caregiving as a Risk Factor for Mortality. *Jama*. 282(23), 2215–9 (2003).

13.- Schulz R, Sherwood P. Physical and mental health effects of family caregiving. *Am J Nurs*. 108(9 Suppl), 23–7 (2008).

14.- Chu HH, Lee KS, Ho Lee K, et al. Association of physical and psychological health status between chronic obstructive pulmonary disease patients and their family caregivers. *Health care for women international*. 40(10), 1019-30 (2019).

15.- Miravittles M, María L, Peña-Longobardo LM, et al. Caregivers' burden in patients with COPD. *Int J COPD*. 10, 347–56 (2015).

16.- Grant M, Cavanagh A, Yorke J. The impact of caring for those with chronic obstructive pulmonary disease (COPD) on carers' psychological well-being: a narrative review. *International journal of nursing studies*. 49(11), 1459-71 (2012).

* This narrative review identified studies of the psychological well-being of informal carers of patients with COPD.

17.- Sörensen S, Duberstein P, Gill D, et al. Dementia care: mental health effects, intervention strategies, and clinical implications. *The Lancet Neurology*. 5(11), 961-73 (2006).

18.- Gérain P, Zech E. Informal caregiver burnout? Development of a theoretical framework to understand the impact of caregiving. *Frontiers in Psychology*. 10, 1748 (2019).

19.- Mansfield E, [Bryant J](#), [Regan T](#), et al. Burden and unmet needs of caregivers of chronic obstructive pulmonary disease patients: a systematic review of the volume and focus of research output. *COPD*. 13(5), 662-667 (2016).

- 20.- von Elm E, Altman DG, Egger M, et al. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: Guidelines for reporting observational studies. *Int J Surg*. 12(12), 1495–1499 (2014).
- 21.- Global Initiative for Chronic Obstructive Lung Disease. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease 2019. [Internet]. [cited 2022 Sep 30] Available: <http://www.goldcopd.org>
- 22.- The Rights of Persons with Disabilities Act; December 28, 2016. [Internet]. [cited 2022 Oct 4]. Available from: <http://lawmin.nic.in/ld/P-ACT/2016/A2016-49.pdf> .
- 23.- Kaur N, Puria A, Kumar A, et al. Caregiver burden among working women and homemakers taking care of psychiatric patients. *Industrial Psychiatry Journal*. 30(Suppl 1), S166 (2021).
- 24.- Borg GAV. Psychophysical bases of perceived exertion. *Med Sci Sports Exerc*. 14, 377–81 (1982).
- 25.- Bestall JC, Paul EA, Garrod R, et al. Usefulness of the medical research council (MRC) dyspnoea scale as a measure of disability in patients with chronic obstructive pulmonary disease. *Thorax*. 54, 581–86 (1999).
- 26.- Kastner C, Armitage J, Kimble A, et al. The Charlson comorbidity score: A superior comorbidity assessment tool for the prostate cancer multidisciplinary meeting. *Prostate Cancer Prostatic Dis*. 9(3), 270–74 (2006).
- 27.- Herrero MJ, Blanch J, Peri JM, et al. A validation study of the hospital anxiety and depression scale (HADS) in a Spanish population. *Gen Hosp Psychiatry*. 25(4), 277–83 (2003).
- 28.- Zarit S, Reever K, Bach-Peterson J. Relatives of the impaired elderly: correlates of feeling of burden. *Gerontologist*. 20, 649-55 (1980).

- 29.- Del-Pino-Casado R, Frías-Osuna A, Palomino-Moral PA, et al. Social support and subjective burden in caregivers of adults and older adults: A meta-analysis. PLoS ONE. 13(1), e0189874 (2018).
- 30.- Barusso-Grüninger MS, Gianjoppe-Santos J, Sentanin AC, et al. Do London Chest Activity of Daily Living Scale and St George's Respiratory Questionnaire Reflect Limitations During Activities of Daily Living in Patients With COPD?. J Cardiopulm Rehabil Prev. 39(4), 274-80 (2019).
- 31.- Garrod R, Bestall JC, Paul EA, et al. Development and validation of a standardized measure of activity of daily living in patients with severe COPD: The London chest activity of daily living scale (LCADL). Respir Med. 94(6), 589–96 (2000).
- 32.- Hamilton BB, Laughlin JA, Fiedler RC, et al. Interrater reliability of the 7-level functional independence measure (FIM). Scand J Rehabil Med. 26(3), 115–9 (1994).
- 33.- Shih SL, Gerrard P, Goldstein R, et al. Functional status outperforms comorbidities in predicting acute care readmissions in medically complex patients. J Gen Intern Med. 30(11), 1688-95 (2015).
- 34.- Garin O, Ayuso-Mateos JL, Almansa J, et al. Validation of the “World Health Organization Disability Assessment Schedule, WHODAS-2” in patients with chronic diseases. Health Qual Life Outcomes. 19(8), 51 (2010).
- 35.- Da Silva CM, Neto ACP, Júnior BRN, et al. Assessment of patients with functional chronic obstructive pulmonary disease through WHODAS. Acta Fisiatr. 23(3), 125-9 (2016).
- 36.- Athayde FTS, Mancuzo EV, Ferreira LCV, et al. Association between contextual and clinical factors and disability in people with chronic obstructive pulmonary disease. Physiother Theory Pract. 10, 1-8 (2019).

- 37.- Díaz M, Estévez A, Momeñe J, et al. Social support in the relationship between perceived informal caregiver burden and general health of female caregivers. *Ansiedad y Estrés*. 25(1), 20-7 (2019).
- 38.- Martín-Carrasco M, Salvadó I, Nadal-Alava S, et al. Adaptación para nuestro medio de la Escala de Sobrecarga del Cuidador (Caregiver Burden Interview) de Zarit. *Revista de Gerontología*. 6(4), 338-46 (1996).
- 39.- Janaudis-Ferreira T, Beauchamp MK, Robles PG, et al. Measurement of activities of daily living in patients with COPD: A systematic review. *Chest*. 145(2), 253–71 (2014).
- 40.- Soler X, Liao SY, Marin JM, et al. Age, gender, neck circumference, and Epworth sleepiness scale do not predict obstructive sleep apnea (OSA) in moderate to severe chronic obstructive pulmonary disease (COPD): The challenge to predict OSA in advanced COPD. *PLoS One*. 12(5), e0177289 (2017).
- 41.- Ehsani H, Mohler MJ, Golden T, et al. Upper-extremity function prospectively predicts adverse discharge and all-cause COPD readmissions: a pilot study. *Int J Chron Obstruct Pulmon Dis*. 14, 39-49 (2019).
- 42.- Belo LF, Rodrigues A, Paes T, et al. Functional Status of Patients with COPD Assessed by London Chest Activity of Daily Living Scale: Gender Association and Validity of a Cutoff Point. *Lung*. 197(4), 509-16 (2019).
- 43.- Gulart AA, Munari AB, Klein SRV, et al. The London Chest Activity of Daily Living scale cut-off point to discriminate functional status in patients with chronic obstructive pulmonary disease. *Brazilian Journal of Physical Therapy*. 24(3), 264-72 (2020).
- 44.- Troosters T, Sciurba F, Battaglia S, et al. Physical inactivity in patients with COPD, a controlled multi-center pilot-study. *Respir Med*. 104(7), 1005–11 (2010).

- 45.- Dourado VZ, Antunes LC, Tanni SE, et al. Relationship of upper-limb and thoracic muscle strength to 6-min walk distance in COPD patients. *Chest*. 129(3), 551–7 (2006).
- 46.- Mazzarin C, Kovelis D, Biazim S, et al. Physical Inactivity, Functional Status and Exercise Capacity in COPD Patients Receiving Home-Based Oxygen Therapy. *COPD J Chronic Obstr Pulm Dis*. 15(3), 271–6 (2018).
- 47.- Braido F, Baiardini I, Scichilone N, et al. Disability in moderate chronic obstructive pulmonary disease: Prevalence, burden and assessment-results from a real-life study. *Respiration*. 89(2), 100–6 (2015).
- 48.- Miravittles M, Soriano JB, García-Río F, et al. Prevalence of COPD in Spain: impact of undiagnosed COPD on quality of life and daily life activities. *Thorax*. 64(10), 863–8 (2009).
- 49.- Bernabeu-Mora R, García-Guillamón G, Montilla-Herrador J, et al. Rates and predictors of depression status among caregivers of patients with COPD hospitalized for acute exacerbations: a prospective study. *Int J Chron Obstruct Pulmon Dis*. 11, 3199–205 (2016).
- 50.- Pucciarelli G, Vellone E, Savini S, et al. Roles of Changing Physical Function and Caregiver Burden on Quality of Life in Stroke: A Longitudinal Dyadic Analysis. *Stroke*. 48(3), 733–9 (2017).
- 51.- Srivastava G, Tripathi R, Tiwari S, et al. Caregiver burden and quality of life of key caregivers of patients with dementia. *Indian J Psychol Med*. 8(2), 133 (2016).
- 52.- Roth DL, Fredman L, Haley WE. Informal caregiving and its impact on health: A reappraisal from population-based studies. *The Gerontologist*. 55(2), 309-19 (2015).

53.- Tan JY, Molassiotis A, Lloyd-Williams M, et al. Burden, emotional distress and quality of life among informal caregivers of lung cancer patients: An exploratory study. *Eur J Cancer Care (Engl)*. 27(1), 1–11 (2018).

54.- Valenza MC, Torres-Sanchez I, Cabrera-Martos I, et al. Physical Activity as a Predictor of Absence of Frailty in Subjects with Stable COPD and COPD Exacerbation. *Respir Care*. 61(2), 212–9 (2016).

** This cross-sectional study identified the cutoff points of physical activity for the absence of frailty in subjects with exacerbation and stable COPD.

55.- Arthur PB, Gitlin LN, Kairalla JA, et al. Relationship between the number of behavioral symptoms in dementia and caregiver distress: What is the tipping point? *Int Psychogeriatrics*. 30(8), 1099–107 (2018).

56.- Katsavos S, Artemiadis AK, Zacharis M, et al. Predicting caregiving status and caregivers' burden in multiple sclerosis. A short report. *Neurological Research*. 39(1), 13-15 (2017).

** This cross-sectional study assessed the clinical predictors of caregiver burden of patients with multiple sclerosis, related to factors of caregivers' stress.

57.- Chauvin S, Kirkwood R, Brooks D, et al. Which balance subcomponents distinguish between fallers and non-fallers in people with COPD?. *Int J Chron Obstruct Pulmon Dis*. 15, 1557-1564 (2020).

58.- Chen J, Yang Z, Yuan Q, et al. Prediction of gold stage in patients hospitalized with COPD exacerbations using blood neutrophils and demographic parameters as risk factors. *BMC Pulm Med*. 21, 1-9 (2021).

59.- Yang L, Shi M, Situ X, et al. Prediction of exercise-induced desaturation in COPD patients without resting hypoxemia: a retrospective study. BMC Pulm Med. 22(1), 405 (2022).

11.The figures and the tables legends

Figure 1. Flowchart of COPD patients and their caregivers.

Figure 2. Cutoff points with respective sensitivities and specificities of caregiver burden in patient's dyspnea related to functionality (A), dependence in daily life activities (B), and social participation on activities of daily living of COPD patients (C)Table 1. Baseline characteristics of Caregivers and COPD patients.

Table 2. Functionality characteristics of COPD patients.

Table 1. Baseline characteristics of Caregivers and COPD patients.

Variables	Group with caregiver burden	Group without caregiver burden	p-value
COPD patients' data	N=35	N=35	
Age	79.20 ± 4.71	71.86 ± 5.78	0.006*
BMI (kg/cm ²)	29.86 ± 6.95	23.91 ± 0.65	0.133
Modified Borg Scale	7.17 ± 2.03	5.20 ± 2.55	0.022*
mMRC	3.57 ± 0.74	2.91 ± 0.99	0.046*
Charlson Index	5.00 ± 1.00	5.55 ± 2.07	0.672
Caregivers' data	N=35	N=35	
Age	70.00 ± 3.57	47.50 ± 32.90	0.019*
Sex, n (% Male)	5(16.7)	0(0)	0.286
Relationship with patients			
Spouse, n (%)	27(76)	31(94.7)	<0.001**
Sibling, n (%)	0(0)	4(5,3)	
Son/daughter, n (%)	8(24)	0(0)	
Anxiety	13.67 ± 6.62	9.47 ± 5.12	0.134
Depression	11.17 ± 5.95	6.80 ± 5.35	0.117
HAD Scale	24.83 ± 10.11	15.60 ± 8.74	0.005*
Caregiver burden	56.33 ± 4.68	28.73 ± 8.96	<0.001**

Data expressed as mean±SD. *Between-group significant differences, p<0.05. ** Between-group significant differences, p≤0.001. BMI: Body mass index; mMRC: modified Medical Research Council. HAD: Hospital Anxiety and Depression scale.

Table 2. Functionality characteristics of COPD patients.

	COPD group with caregiver burden (n=48)	COPD group without caregiver burden (n=37)	p-value
Dyspnea levels related to functionality			
Self-care	13.00 ± 6.19	8.73 ± 3.04	0.045*
Domestic	11.50 ± 2.78	8.80 ± 3.81	0.583
Physical	8.17 ± 2.23	6.60 ± 2.92	0.254
Leisure	8.83 ± 3.18	6.20 ± 1.93	0.030*
LCALD scale	41.50 ± 6.58	30.00 ± 7.29	0.111
Dependence in daily life activities			
Motor score	81.75 ± 6.02	83.00 ± 7.78	0.777
Cognitive score	33.33 ± 4.08	34.54 ± 0.97	0.315
FIM Scale	104.33 ± 8.03	119.36 ± 7.45	0.096
Social participation in activities of daily living			
Cognition	7.50 ± 3.67	6.46 ± 0.97	0.342
Mobility	10.50 ± 4.17	7.69 ± 2.98	0.236
Self-care	9.17 ± 3.46	6.38 ± 1.94	0.113
Getting along	6.17 ± 2.85	5.77 ± 1.69	0.706
Life activities	9.67 ± 6.47	8.08 ± 5.11	0.569
Social participation	23.00 ± 7.69	15.47 ± 6.91	0.058
WHODAS 2.0	41.25 ± 6.70	28.29 ± 5.15	0.041*

Data expressed in mean±SD. *Between-group significant differences, $p<0.05$. ** Between-group significant differences, $p\leq0.001$. LCALD: London Chest Activity of Daily Living scale; WHODAS 2.0: World Health Organization Disability Assessment Schedule 2.0; FIM: Functional Independence Measure Scale.

Figure 1. Flowchart of COPD patients and their caregivers

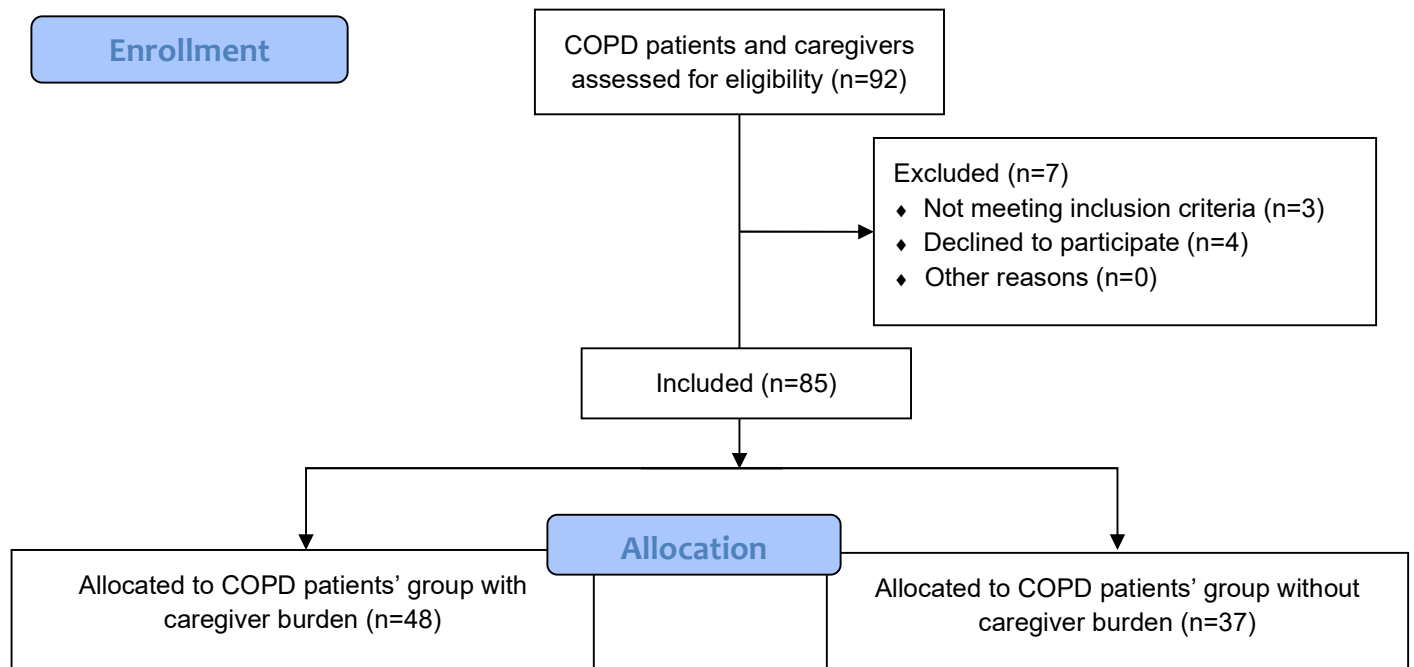


Figure 2. Cutoff points with respective sensitivities and specificities of caregiver burden in patient's dyspnea related to functionality (A), dependence in daily life activities (B), and social participation on activities of daily living of COPD patients (C).

