



Early View

Original research article

Improving the well-being in caregivers of patients with COPD using a home-based pulmonary rehabilitation programme

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Title

Improving the well-being in caregivers of patients with COPD using a home-based pulmonary rehabilitation programme.

Take home message

Integrating the caregivers of patients with COPD in a personalized home-based pulmonary rehabilitation programme was effective for improving their burden, anxiety and depressive symptoms and general fatigue.

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Author contribution

JMG: funding acquisition, conceptualization, execution, acquisition of data, data interpretation, writing the original draft. **SG**: acquisition of data, formal analysis and interpretation, writing the original draft. **MK**: formal analysis and interpretation. **OLR, CC**: writing – review and editing. All authors gave final approval of the version to be published.

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Abstract (249/250 words)

Objectives. To evaluate the effects of a home-based pulmonary rehabilitation (PR) programme on anxiety and depressive symptoms, general fatigue and burden in informal caregivers of patients with COPD. We also evaluated the baseline characteristics of both patients and caregivers that contributed to the change in caregiver's outcomes after PR.

Methods. In this retrospective study, patients with COPD were referred to an 8-week home-based PR programme consisting of a weekly supervised 90-minute session. Informal caregivers, according to the patient's preference and its availability, were invited to participate in PR. Caregivers received educational supports, behavioral therapies and self-management strategies using the same methods as for patients. Burden, anxiety and depressive symptoms and general fatigue of caregivers were assessed at baseline and at the end of PR.

Results. 241 patients with COPD and 138 (57.3%) caregivers were included. The majority of the caregivers were women (70.5%), spouses (90.3%) and with at least three comorbidities (57.3%). A large proportion of caregivers showed baseline high burden, anxiety symptoms, and abnormal fatigue (40%, 40%, 45%, respectively). Burden, anxiety and depressive symptoms and general fatigue of informal caregivers were all improved after PR ($p < 0.05$). Long-term oxygen therapy and/or non-invasive ventilation, coronaropathy and/or peripheral arterial disease and a higher baseline mMRC score in patients with COPD were associated with a decrease in caregiver's burden after PR.

Conclusion. A large proportion of caregivers of patients with COPD showed anxiety symptoms, fatigue and a high burden. These outcomes were improved by integrating the caregiver into a home-based PR programme.

Introduction

In addition to dyspnea, patients with chronic obstructive pulmonary disease (COPD) commonly show exercise intolerance, kinesophobia and anxiety and depressive symptoms, compromising daily physical activity, quality of life and even survival [1-3]. As the severity of the symptoms and the number of comorbidities increase, patients with COPD become care dependant with difficulties in fulfilling their daily life activities and experience social isolation [4].

Informal caregiver refers to an individual (commonly a spouse or a child), who provides unpaid care to persons with one or more disabilities to perform daily life activities and provide support for medical care and symptom management [5, 6]. Informal caregivers are of major importance for patients with COPD, since they can facilitate and enhance adherence to COPD management behaviors, such as treatment adherence or increasing daily physical activity, possibly leading to a reduction in exacerbations and hospitalisations [7-9]. However, providing informal care to a patient with COPD can take a considerable toll on the caregiver's physical, psychological and social well-being [5, 10]. A large survey conducted in Spain reported that 35, 83 and 38% of the informal caregivers caring for patients with COPD, experienced health, social/leisure time and occupational problems, respectively [10]. Additionally, they may experience helplessness, powerlessness, anxiety, depression, vulnerability to fatigue, disability and/or burnout when trying to cope with the symptoms related to COPD [11-13]. The situation may even be worse for caregivers of patients with advanced COPD with higher risks of exacerbations, hospitalisations and even death compared to the less severe forms of the disease [14, 15].

Pulmonary rehabilitation (PR) is a cornerstone of treatment for patients with chronic respiratory disease [16, 17]. PR is effective at reducing symptom burden and improving exercise tolerance in patients with COPD [18]. Despite the undeniable burden placed on the informal caregiver, formal support for caregivers is lacking [19]. Few studies have included the patient-carer dyad in education and self-management sessions during pulmonary rehabilitation, with conflicting results across studies [19-21]. These interventions focused on improving the caregiver's understanding of the disease and on coping strategies to adequately equip caregivers for effectively supporting patients with COPD. Nevertheless, the informal caregiver should be also seen as a person to treat using a personalized intervention leading to improving their physical and psychological well-being. Relieving the caregiver's burden is critical to sustain and support the home-care network and might have a positive long-term impact on the economic burden of COPD by reducing the yearly number of exacerbations and hospitalisations [7, 8].

Furthermore, the main objective of this retrospective study was to evaluate the effectiveness of a home-based PR programme on the burden, anxiety and depressive symptoms and general fatigue in caregivers of patients with COPD. We also evaluated the baseline characteristics of both patients and caregivers that may have contributed to the change in caregiver's well-being after PR. Our hypothesis was that in addition to improve the physical and psychological well-being of the patients with COPD, the home-based PR programme will be effective for improving the burden, anxiety and depressive symptoms and general fatigue of the informal caregivers. We also assumed that the baseline severity of the patient's disease (requiring long-term oxygen therapy, spirometry data, dyspnea, comorbidities) will affect the changes in caregiver's well-being after PR.

Methods

Study design and participants.

This was a retrospective study conducted on prospectively collected data. Data was collected from January 2018 to December 2019. Details regarding the referral and criteria selection of the patients with COPD, and the home-based PR programme can be found elsewhere [22, 23]. Briefly, patients with COPD performed an 8-week home-based PR programme, consisting of a weekly supervised 90-minute home session, during which supervised physical training, education and self-management strategies were implemented. Prior to starting the programme, an evaluation of the patient's needs and expectations was performed for designing a personalized intervention. Personalized exercise and daily physical activity training, educational, motivational and self-management plans were implemented through a collaborative process between the PR team, the patient and their caregiver. Apart from the weekly visit of the team member, participants were expected to perform, on their own, personalized physical training and self-management plan the rest of the week. A cycle ergometer (Domyos essential 2, Decathlon, Villeneuve-d'Ascq, France) and/or or a stepper (Go Sport, Grenoble, France) were available at home to perform physical exercise during the 8-week training component of the programme.

The caregiver, according to the patient's preference and its availability, helped in the design of the personalized patient's action plan and could expressed what he/she was expected from the home-based PR for the patient with COPD but also for him/herself. Caregivers who attended the weekly visits of the PR team member, could react and share their difficulties regarding helping the patient during daily life activities, but also their own feelings and emotions. Since caregivers (a person) experienced a similar burden to that of patients (a person) with COPD [11, 12], the same educational supports, behavioral therapies and self-

management strategies were also applied to caregivers to meet their own needs and expectations by using personalised interventions. To reduce the burden and anxiety symptoms of the caregivers when caring for their loved-one, cognitive behavioural therapy, counselling, motivational support, mindfulness meditation and cardiac coherence techniques were specifically offered to the caregivers. Motivational communication was used at each home sessions and was frequently re-evaluating and readjusting [24]. PR team members received training in the principles of behaviour change and motivational communication skills.

Regarding the education, the following topics were systematically discussed with the patients and their caregiver: management of dyspnea, exacerbations, medication, exercise training and daily physical activities. End of life and fear of dying was also addressed according to the needs of the patient-carer dyad. Smoking cessation or cessation of other unhealthy behaviours (alcoholism, drug addiction, nutritional issues), were discussed with both the patient and the caregiver if necessary. When the caregivers also presented these issues, the same support was offered to him/her. During the 8-week programme, these topics were discussed in order of the patients and caregivers needs and goals as certain supports were more required depending on how the participants were progressing on a week-to-week basis. In the absence of medical contraindications, caregivers could also perform the physical exercises training with the patients. They were also encouraged to increase independent leisure activities outside the family home and to not hesitated to seek additional assistance in caring for the patient.

The study was approved by the observational research protocol evaluation committee of the French Language Society of Pulmonology (CEPRO, number: 2021-054). All participants (patients with COPD and their caregiver) signed a written informed consent prior to the start of the programme which included their approval to use the collected data for research purposes. The study was conducted according to the principles of the Declaration of Helsinki.

Assessments

Comorbidity data of the patients with COPD were collected from the individual's medical record provided by the pulmonologist. Comorbidities data of the caregivers were only collected from those who participated in the study using a questionnaire completed with the PR team member during the first visit. Patients with COPD and their caregivers were evaluated at home at the beginning (M0) and at the end of the PR program (M2).

The burden of the informal caregivers was self-assessed using the Zarit Burden Interview (ZBI) (22 items with a test score ranging from 0 to 88; lower is better) [25]. The ZBI measures subjective burden in terms of the degree (from 'never = 0' to 'almost always = 4') to which the caregiver experiences physical, psychological, emotional, social and financial problems as a result of their care-giving role [25]. A ZBI score >24 was considered a high burden [26]. The anxiety and depressive symptoms and the general fatigue of the informal caregivers were self-assessed with the Hospital Anxiety and Depression (HAD) scale (14 items: seven each for anxiety and depression with minimum and maximum subscores of 0 and 21; lower is better; an anxiety or depressive symptoms score ≥ 11 indicates a probable clinical diagnosis of anxiety or depression) [27], and the Fatigue Assessment Scale (FAS) (10 items: five reflecting physical fatigue and 5 reflecting mental fatigue with a test score ranging from 10 to 50; lower is better; a score ≥ 22 suggests abnormal fatigue) [28], respectively. The minimal clinically important difference (MCID) of the ZBI, HAD scale and FAS has never been documented in informal caregivers.

In patients with COPD, in addition to anxiety and depressive symptoms and general fatigue, dyspnea, health related quality of life and exercise tolerance were also assessed using the modified Medical Research Council Dyspnea scale (mMRC) [29], the Clinical COPD Questionnaire (CCQ) [30], and the 6-minute stepper test (6MST) [31], respectively. In COPD,

the minimal clinically important difference (MCID) of the HAD-anxiety and - depression scores, the CCQ and the 6MST is considered to be a change of 1.5 units [32], 0.4 unit [33] and 40 strokes [34], respectively. The MCID of the FAS has not been documented in COPD but is considered to be a change of 4 points in patients with sarcoidosis [35].

Statistical analyses

Statistical analyses were performed using SAS V9.4 (SAS Institute, Cary NC, USA) and significance threshold was considered at 0.05. Quantitative variables are expressed as means (standard deviation, SD) in the case of normal distribution or medians (interquartile range, IQR) otherwise. Categorical variables are expressed as numbers (percentage). Normality of distributions was assessed using histograms and the Shapiro-Wilk test. Non-normally distributed data were log-transformed before analysis.

Changes between M0 and M2 in the study assessments of the patients with COPD and their informal caregivers were analyzed using paired student t test. A linear regression model adjusted on baseline value of each score was performed to evaluate the baseline characteristics of both patients with COPD and caregivers that contributed to the change in caregiver's burden, anxiety and depressive symptoms and general fatigue after PR. To evaluate whether the number of sessions attended by the caregivers impacted their improvements after PR, a one-way ANOVA with anxiety symptoms, depression symptoms, FAS and ZBI scores as dependent variables was performed. Baseline characteristics of the caregivers who attended more than a half of the home visits (8 to 5 visits) were compared to those of caregivers who attended 4 or fewer visits using a one-way ANOVA.

Baseline characteristics of the patients with COPD who dropped-out during PR were compared to those who finish PR using standardized difference analysis (SDA). A standardized difference greater than 20% was considered important [36].

Results

Baseline characteristics

From January 2018 to December 2019, 241 patients with COPD were included in the PR programme. The majority were males (61.8%), former smoker (75.1%), had severe airway obstruction (FEV_1 , 39.0 ± 18.5 % predicted value) and at least three COPD-associated comorbidities (87.2%), and 59.3% patients required long-term oxygen therapy (Table 1).

Among the 241 patients with COPD, 47 (19.5%) patients did not report a caregiver and 56 (28.9%) caregivers refused to participate in the study (Figure 1). The baseline characteristics of the remaining 138 (57.3%) caregivers are presented in Table 1. The majority of them were women (70.3%), spouses (87.7%) and had at least three comorbidities (57.3%). Among the caregivers, 56 (40.6%) and 16 (11.6%) individuals had a probable clinical diagnosis of anxiety and depression (score ≥ 11) respectively, 63 (45.6%) individuals had an abnormal fatigue (score ≥ 22) and 54 (39.1%) individuals reported a high burden (score > 24). Twenty-three (16.7%) informal caregivers attended the 8 home visits, 34 (24.6%) attended 7 to 4 visits, 44 (31.9%) attended 1 to 3 visits and 37 (26.8%) caregivers did not attend any visit with an exception for the first diagnostic evaluation session. Caregivers who attended more than a half of the home sessions (8 to 5) were younger ($p=0.002$), more often female ($p<0.001$) and with higher baseline anxiety symptoms ($p=0.009$) than caregivers who attended 0 to 4 visits.

PR effectiveness

Among the 241 included patients with COPD, 25 (10.3%) patients did not complete PR (Figure 1). These patients had lower BMI (SDA = 51%), 6MST score (SDA = 76%), and CCQ total score (SDA = 51%), and higher depression symptoms (SDA = 58%) and fatigue score (SDA = 33%) compared to those who completed PR. Caregivers of these 25 patients had higher anxiety symptoms (SDA = 41%), depression symptoms (SDA = 50%) and fatigue score (SDA = 48%) compared to the caregivers of patients who completed PR.

The effects of the home-based PR programme are presented in Table 2. All study assessments were improved at the end of PR in both patients with COPD and informal caregivers ($p < 0.05$) (Table 2). Patients with COPD reporting a caregiver had a higher decrease in anxiety symptoms ($p = 0.015$) and general fatigue score ($p = 0.039$) after PR compared to patients without a caregiver. The number of sessions attended by the caregivers was not associated with their improvements observed in burden questionnaire ($p = 0.915$), anxiety symptom ($p = 0.474$), depressive symptoms ($p = 0.073$) and fatigue questionnaire ($p = 0.317$).

Correlates of the changes in caregiver's burden, anxiety and depression symptoms and general fatigue

Table 3 reports correlation parameters between baseline characteristics of both patients with COPD and their caregivers and changes in the burden, anxiety symptoms, depression symptoms and general fatigue of caregivers, from baseline to M2. Long-term oxygen therapy and/or non-invasive ventilation, coronaropathy and/or peripheral arterial disease and a higher baseline mMRC score in patients with COPD were associated with a decrease in caregiver's burden after PR. A higher baseline Charlson Index in patients with COPD was associated with a diminution in caregiver's depressive symptoms after PR (0.018), while decrease in caregiver's general fatigue was associated with baseline FEV₁ of patients with COPD.

Discussion

This prospective interventional study originally integrated the caregivers of patients with COPD into an 8-week home-based PR programme. Although caregivers are usually poorly involved into traditional PR, with a participation rate of 70%, this study demonstrated the strong interest of the caregivers to be integrated in the patient's care. Almost a half of the caregivers reported an impaired well being (anxiety, fatigue, burden) at the beginning of PR, showing the importance of recognizing their difficulties and needs when caring for their loved one. Integrating the caregivers of patients with COPD in a personalized PR programme was effective for improving at short-term their burden, anxiety and depressive symptoms and general fatigue. Since only 40% of the caregivers attended at least half of the home-based sessions, the present positive results may suggest that only a few sessions were sufficient for improving caregivers' well being when adequately targeting their needs. This is supported by a recent cluster randomized trial showing that only 90-min of a structure nurse-led advance care planning was effective for improving anxiety symptoms of the caregivers of patients with COPD [40]. However, because of the design of the present study and the absence of a control group of caregivers not participating in the PR programme, caution needs to be taken when interpreting the results. Therefore, we cannot conclude whether the benefits observed in the caregivers are a consequence of their participation in the PR programme, or whether they are an indirect consequence of the physical and psychological improvements of the patients with COPD. Moreover, linear regression models showed that the caregivers of patients with severe COPD (requiring long-term oxygen therapy and/or non-invasive ventilation, reporting heart diseases and severe baseline dyspnea) were more likely to better improved their burden after PR. Confirming our previous studies, patients with COPD benefited from the home-based PR by significantly and clinically (reaching the respective minimal clinically important difference of each assessment) improving anxiety and depressive symptoms, general fatigue, health

related quality of life and exercise tolerance. The decrease in anxiety symptoms and general fatigue after PR was even higher in patients with COPD reporting a caregiver compared to those without one. Taken all together, these results support the importance of integrating the caregivers into the patient's care, which should be routinely considered when designing future PR programme.

Characteristics of the included caregivers are consistent with previous studies in patients with chronic lung disease: they are mainly spouses with a significant proportion having health issues including anxiety symptoms and general fatigue [11, 12, 21]. Anxiety and depressive symptoms are common in both patients with COPD and their caregivers, and often result from the difficulty in managing dyspnea and the fear of the future [12, 13]. With a cut-off score > 8 in the Hospital Anxiety and Depression subscores, the prevalence of anxiety and depressive symptoms in people with COPD and their caregivers was 46.4% and 42.9% and 46.0% and 23.0%, respectively [37]. Using the same cut-off, we confirmed the previous results (patients with COPD: 54.4% and 44.9% respectively; caregivers: 54.5% and 20.9%, respectively), highlighting the importance of providing personalized psychological and physical care for both the patient and their caregiver. Additionally, more than a third of the caregivers reported that caring for their sick beloved one was a high burden (ZBI score > 24 points). Nevertheless, the mean ZBI score of 21.6 ± 15.1 points was relatively low compared to a recent study reporting a mean ZBI score of 52.4 ± 14.6 points in 201 caregivers of hospitalized patients with COPD [38]. However, since patients with COPD were hospitalised, we can assume that they had a more severe disease compared to the patients in the present study which could explain the higher caregiver burden score. Moreover, in Yi and al study, caregivers were mostly the patient's children (66%). It could be more difficult for the spouse (87% in the present study) to admit that their husband/wife is a burden. Nevertheless,

whether they are spouses or children, the burden of the caregiver will take a considerable toll on their physical (fatigue), psychological (anxiety and depression symptoms) and social/financial (isolation, difficulty in communication, loss of employment) well-being [10, 12, 39]. A recent interesting study reported that patients with COPD living with a physically active caregiver had higher levels of physical activity and a higher likelihood of being physically active compared to patients living with a physically inactive caregiver [9]. This result highlighted the importance of engaging the caregiver as part of the PR programme as they can help their sick loved one to engage in healthy behaviours.

Both patients with COPD and their caregivers benefited significantly from PR. The anxiety symptoms and general fatigue improvement after PR was even higher in patients reporting a caregiver compared to those without one. This result highlights the importance of considering the caregiver as part of the intervention to improve outcomes in patients with COPD. However, despite that caregivers might play a crucial role in patient's adherence to new health behaviours (smoking cessation, physical activity training, symptom management including dyspnea, medications adherence) [7], the literature regarding this topic is scarce [19] and clinically relevant changes are not documented in caregivers. Marques et al [21] reported that 12 weeks of a family-based PR was effective in enhancing the coping strategies of both the patients and their family members. The experimental group performed one session a week in a primary care center, during which psychological support and education were given to both the patients and their caregivers [21]. An overall adherence rate of 92% was found, but details regarding caregivers' attendance were not provided. In a pragmatic randomized control design, Jonsdottir et al [20] showed that a 6-month partnership-based self-management programme had benefits on the intrusiveness of the disease and its treatment in patients with mild to moderate COPD. Nevertheless, the impact of the caregiver in these positive results is

questionable as only one quarter of the patients were accompanied by a family member during the intervention [20]. Although the clinical relevance of the caregiver's improvements after PR is questionable, the decrease of -0.9 and -0.6 in the anxiety and depressive symptoms score, respectively, are similar to those reported by Houben and al [40] offering one home-based session of structured advance care planning to patients with COPD and their loved one. Comparison regarding the improvement of the burden and fatigue of the caregivers after PR is impossible since no study has ever investigated it. A few literature reviews have highlighted the importance of educating the informal caregivers for managing the patient's disease but also highlighted the need to provide them specific physical and psychological support [13, 41-43]. By evaluating the burden, anxiety and depressive symptoms and general fatigue of the caregivers, the present study is a first step towards assessing the abilities and needs of caregivers leading to an appropriate support.

Linear regression models showed that the caregivers of patients with a severe stage of the disease (requiring long-term oxygen therapy and/or non-invasive ventilation, reporting heart diseases and severe baseline dyspnea) were more likely to better improved their burden after PR. On one hand, the improvement in the patient's exercise capacity and general fatigue after PR, making them less dependent on their caregiver could explain this result. On the other hand, we mostly believe that educating both the patients and their caregivers on managing dyspnea, exacerbations, end of life and fear of dying may have positively impacted the burden of the caregivers of the more severe patients. Educating caregivers regarding the management of the patient's dyspnea through increasing caregivers' confidence and/or control and helping patient's better self-manage breathlessness may reduced hospital admissions [44] and anxiety and depressive symptoms of both patients and their caregivers [40].

Strength and limitations

We must recognize that the home-based PR programme was firstly designed for patients with COPD. However, the caregivers were integrating into PR sessions by encouraging them to share their difficulties regarding helping the patient during daily life activities. This real-life study could be the foundation of more robustly designed randomized and controlled studies aiming to better support the caregivers. The monocentric, non-randomized nature of this study and the absence of a control group may limit the scope of the present results. A three-arm randomized controlled trial that compared the effectiveness of an intervention targeted at the patients with COPD only, at the caregivers only, at the patients-caregivers dyad will be an ideal future study. This would provide high-level evidence of the benefit of incorporating caregiver support as a core component of care. Another aspect that should be investigated by future studies is the additional healthcare cost of integrating the caregiver into PR. Since caregivers can facilitate and enhance adherence to COPD management behaviors [7-9], the possible long-term positive economic effect of integrating the caregiver into PR needs to be evaluated. Another limitation of the study was that the specific attendance to each component of PR (physical training, education sessions and self-management strategies) was not documented. Since not all caregivers performed the physical training with their sick loved one, we can only assume that the present positive results are mainly the consequence of the education sessions and self-management strategies. Because of the study design, we did not collect data on the 56 caregivers who refused to participate in the intervention preventing a comparison with the caregivers who participated. Nevertheless, the present data were collected systematically and consistently as an integral part of the home-based PR including a large number of non-selected participants and conducted by the same trained team. By improving external validity and establishment in usual care, real-life studies are useful to complement the results of randomized controlled trial [45].

Conclusion

Completing previous randomized controlled trial, the present real-life study showed that integrating the caregivers of patients with COPD into an 8-week home-based PR programme may be effective for improving the burden, anxiety and depressive symptoms and general fatigue of the caregivers. Although the present results should be taken cautiously, this study could be the foundation of more robustly designed randomized and controlled studies aiming to better support the caregivers. In this context, we believe that integrating the caregiver of patients with chronic respiratory disease into pulmonary rehabilitation programme should be more consistently considered when designing future interventions.

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Table 1. Baseline characteristics of patients with COPD and their caregivers

Characteristics	COPD patients (n=241)	Caregivers (n=138)
Age, years	66.0 (12.1)	60.3 (14.8)
Sex, male	149 (61.8)	41 (29.7)
BMI, kg/m ²	26.5 (7.7)	27.3 (5.8)
Smoker status		
Current	39 (16.2)	30 (21.7)
Former	181 (75.1)	27 (19.6)
Never	17 (7.1)	68 (49.3)
FEV ₁ , % of predicted	39.0 (18.5)	--
FEV ₁ /FVC, % of predicted	56.3 (19.7)	--
LTOT	143 (59.3)	--
NIV	85 (35.3)	--
Marital status		
Married/living as a couple	153 (63.5)	--
Widowed	38 (15.8)	--
Separated/divorced	35 (14.5)	--
Single	15 (6.2)	--
Kin relationship with the patients		
Spouse	--	121 (87.7%)
Son/daughter	--	11 (8.0)
Other	--	6 (4.3)

Data are presented as mean (SD) or n (%). BMI, body mass index; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; LTOT, long-term oxygen therapy; NIV, non-invasive ventilation.

Table 2. Effectiveness of the home-based PR programme in both patients with COPD and their informal caregivers.

Assessments	Baseline M0	End of PR M2	$\Delta M2 - M0$	p-value
Informal caregivers				
Anxiety symptoms	9.5 (4.7)	8.5 (4.9)	-0.9 (3.5)	0.006
Depressive symptoms	5.2 (4.1)	4.3 (3.5)	-0.6 (3.1)	0.047
FAS, score	21.9 (7.7)	20.1 (7.2)	-1.4 (6.6)	0.026
ZBI, score	21.6 (15.1)	18.9 (15.0)	-2.5 (11.4)	0.024
Patients				
Anxiety symptoms	9.5 (4.7)	8.0 (4.2)	-1.5 (3.6)	<0.001
Depressive symptoms	8.0 (3.9)	5.8 (4.0)	-2.0 (3.4)	<0.001
FAS, score	27.7 (8.2)	22.7 (7.4)	-4.6 (7.0)	<0.001
mMRC, score	3.0 (1.1)	2.4 (1.2)	-0.5 (0.8)	<0.001
CCQ, total score	3.1 (1.1)	2.3 (1.1)	-0.7 (0.8)	<0.001
6MST, strokes	302 (157)	398 (172)	83 (61)	<0.001

Values are presented as mean (SD). FAS, Fatigue Assessment Scale; mMRC, modified Medical Research Council scale; CCQ, Clinical COPD questionnaire; 6MST, 6-minute stepper test; ZBI, Zarit Burden Interview.

p-values were obtained using paired student t test.

Table 3. Association between baseline characteristics of both patients with COPD and caregivers and changes in caregiver's burden, anxiety and depressive symptoms and general fatigue after PR.

Caregivers	Burden		Anxiety symptoms		Depressive symptoms		General fatigue	
	$\Delta M2 - M0$		$\Delta M2 - M0$		$\Delta M2 - M0$		$\Delta M2 - M0$	
	Estimate (SE)	p-value	Estimate (SE)	p-value	Estimate (SE)	p-value	Estimate (SE)	p-value
<u>Baseline characteristics of patients</u>								
Age > 70	1.63 (2.20)	0.46	0.35 (0.67)	0.61	0.02 (0.55)	0.96	0.79 (1.21)	0.51
FEV ₁ 1% of pred value increase	0.01 (0.06)	0.80	-0.03 (0.02)	0.098	-0.01 (0.01)	0.27	-0.06 (0.03)	0.046
BMI >30	0.66 (2.30)	0.77	-0.66 (0.68)	0.36	-0.46 (0.54)	0.40	-1.49 (1.19)	0.21
LTOT or NIV	-7.51 (2.19)	0.042	0.69 (0.66)	0.30	0.50 (0.53)	0.35	1.18 (1.15)	0.31
Charlson index, 1-point increase	0.62 (0.38)	0.11	-0.14 (0.12)	0.23	-0.22 (0.09)	0.018	-0.19 (0.20)	0.35
Coronaropathy/ peripheral arterial disease	-4.82 (2.33)	0.041	-0.44 (0.72)	0.55	-0.30 (0.58)	0.61	0.38 (1.28)	0.77
Sex, women vs male	0.51 (2.32)	0.83	0.90 (0.69)	0.20	0.51 (0.55)	0.34	0.31 (1.21)	0.80
Anxiety score ≥ 11	0.46 (2.13)	0.83	0.22 (0.65)	0.73	-0.14 (0.53)	0.79	-0.27 (1.15)	0.81
Depression score ≥ 11	4.44 (2.45)	0.073	0.54 (0.77)	0.49	0.99 (0.61)	0.11	-0.71 (1.35)	0.60
FAS score ≥ 22	-0.73 (2.55)	0.77	1.11 (0.74)	0.13	-0.07 (0.60)	0.90	-0.65 (1.32)	0.62
6MST, 50 strokes	0.35 (0.39)	0.36	-0.04 (0.11)	0.73	-0.07 (0.09)	0.46	-0.03 (0.19)	0.89
mMRC, 1-point increase	-2.51 (1.00)	0.014	0.24 (0.32)	0.45	-0.17 (0.25)	0.49	-0.27 (0.55)	0.63
<u>Baseline characteristics of caregivers</u>								
Age > 70	0.85 (2.47)	0.73	0.53 (0.76)	0.48	-0.06 (0.60)	0.92	1.35 (1.33)	0.31
Sex, women vs male	-1.17 (2.41)	0.63	-1.25 (0.72)	0.084	-0.92 (0.56)	0.10	-1.10 (1.27)	0.39
Anxiety score > 11	4.55 (2.61)	0.083	--	--	-0.06 (0.68)	0.94	0.44 (1.48)	0.77
Depression score > 11	6.54 (3.57)	0.094	-1.66 (1.26)	0.19	--	--	-1.12 (2.36)	0.63
FAS score ≥ 22	0.16 (2.30)	0.94	0.42 (0.74)	0.56	0.75 (0.62)	0.23	--	--
ZBI > 24	--	--	2.13 (0.75)	0.005	0.83 (0.60)	0.17	1.78 (1.28)	0.17

Estimate (SE) and p-values were obtained using linear regression model adjusted on baseline score values of caregivers. SE, standard error; BMI, body mass index; FEV₁, Forced expiratory volume in 1 second; LTOT, long term oxygen therapy; NIV, non-invasive ventilation; FAS, Fatigue Assessment Scale; ZBI, Zarit Burden Interview

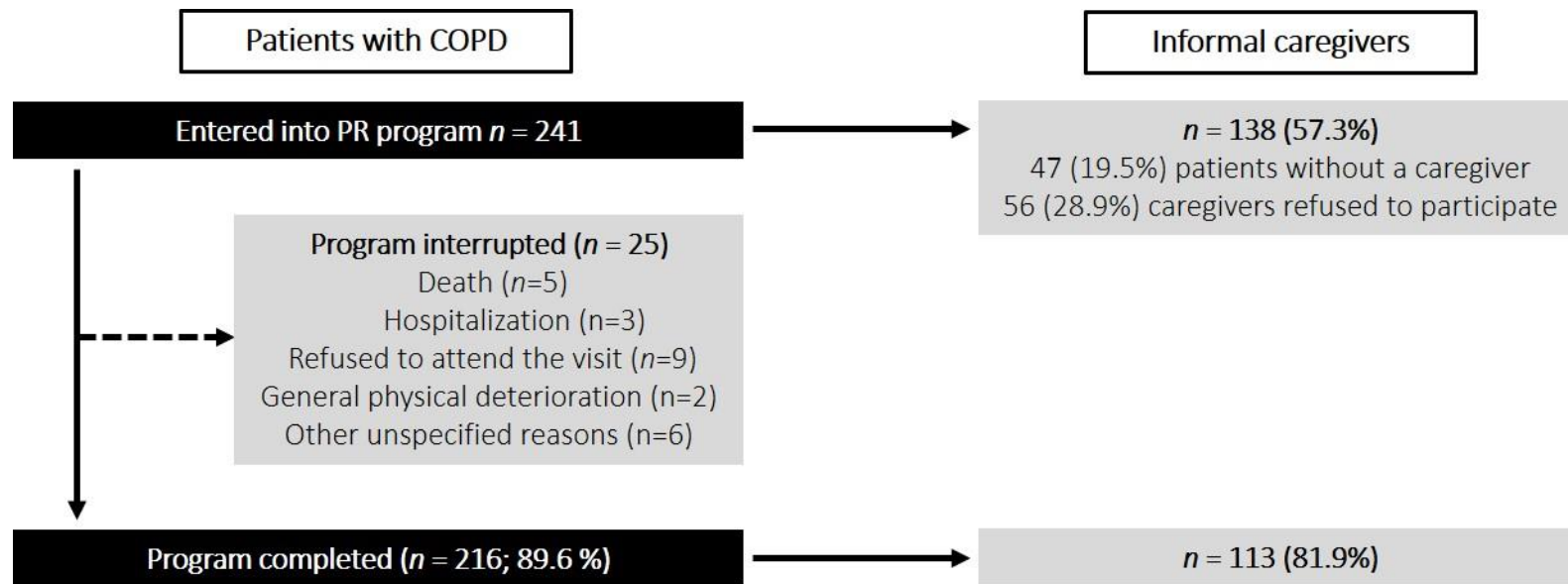


Figure 1. Flow chart of the patients with COPD and their informal caregivers. PR, pulmonary rehabilitation