

#### Abstract

Introduction. Anxiety and depression are frequently associated conditions in COPD patients, and have also significant impact on their quality of life (QoL) and on the course of the disease. Pulmonary rehabilitation (PR) is an adjuvant, non-pharmacological method used in symptomatic COPD patients. The study aimed to evaluate the impact of COPD on QoL depending on disease severity, and to assess the supposedly positive effects of a pulmonary rehabilitation program (PRP) for COPD patients. Material and method. This research included patients with COPD GOLD stages II-IV undergoing bronchodilator therapy. QoL was assessed with the self-administered St George's Respiratory Questionnaire (SGRQ), and depression with the Beck Depression Inventory (BDI). PRP included 3-5 weekly physical training sessions for an average period of 12 weeks, but not less than 3 weeks. Results. The degree of QoL impairment was moderate in stage II (41.07) and severe in stages III (70.28) and IV (81.02). The most severe depression (score 26.6 vs 2.5 in healthy subjects) was also recorded in this group. After the patients underwent all PRP, QoL reassessment at 6 months revealed statistically significant improvements in all 3 groups (p <0.05). In the GOLD COPD stage II group the average reduction was -4.38 units, in the group GOLD COPD stage III -5.37 units, and in the GOLD COPD stage IV -6.75 units. The depression score correlated with the SGRQ score, both of them being higher in the severe stages of disease. BDI administered again 6 months after PRP revealed a significant improvement in average score in all groups, respectively a decrease of -2.17 units in the COPD II group, -2.03 units in the COPD III group and -1.88 units in group COPD IV B group. Conclusion. The results of this study demonstrate a favorable impact of PRP on improving COPD associated symptoms, depression, and OoL in all the 3 monitored COPD patient groups, with statistically significant and persistent positive results over time (6 months after completion of PRP).

Key words: COPD, pulmonary rehabilitation program, Quality of life (QoL), depression,

#### Introduction

Patients diagnosed with chronic obstructive pulmonary disease (COPD) present with different symptoms that significantly impair health-related quality of life (QoL). Anxiety and depression are frequently associated conditions in COPD patients, and have also significant impact on their QoL and on the course of the disease. Pulmonary rehabilitation (PR) is an adjuvant, non-pharmacological method used in symptomatic patients with chronic lung disease. Chronic obstructive pulmonary disease (COPD) is the first indication for referral to a pulmonary rehabilitation program (1). Given the chronic and disabling nature of this disease, the quality of life (QoL) of these patients is profoundly altered. COPD patients have chronic symptoms, especially dyspnea, cough and asthenia. The course of disease is characterized by exacerbations mainly

due to respiratory tract infections, noxious exposure, non-adherence to chronic inhaled medication or long-term oxygen therapy, or decompensation of associated diseases (2-7). Systemic inflammatory changes, weakness and muscle atrophy (8) occur in advanced stages of disease. All of these result in limited exercise capacity, restriction in activities of daily living (ADL) and occurrence of depression (9). The reported frequency of depression in COPD patients differs between studies (10-55%), but is higher than in other chronic diseases and worsens in severe or exacerbated forms (10-86%) (10,11).

The study aimed to evaluate the impact of COPD on QoL depending on disease severity, and to assess the supposedly positive effects of a pulmonary rehabilitation program for COPD patients.

#### Materials and methods

This research is part of a study conducted at the Pulmonology Department of the Timisoara "Victor Babes" Hospital, aimed to determine the effectiveness of PR on lung function, exercise tolerance and QoL in patients with COPD GOLD stages II-IV undergoing bronchodilator therapy. The inclusion and exclusion criteria had been described in a previous publication (12). QoL was assessed with the self-administered St George's Respiratory Questionnaire (SGRQ), and depression with the Beck Depression Inventory (BDI).

SGRO, developed by PW Jones et al., is one of the most frequently used questionnaires for assessing QoL in chronic respiratory diseases (13). The questionnaire is structured as follows: Part I addresses the symptoms: presence of cough, expectoration, dyspnea, wheezing; frequency, duration and time of occurrence of dyspnea episodes, number of good days/week; Part II assesses activity (16 items about activities limited by dyspnea) and impacts (26 items), gradually following the impact of the disease on ADL, psychosocial, professional, material status and treatment options. Patients are asked to tick a box for each question, and three domain scores and a total score are obtained. The highest score is 100 units, a higher score indicating poorer quality of life (14). A minimal decrease in time or an over4-unit difference between groups is considered clinically significant (15).

The degree of depression was assessed using a specific questionnaire, namely the BDI, the most popular depression screening tool (14). The assessment consisted of a 21-question interview aimed at measuring the depressive symptoms and irritability, guilt, fatigability, weight loss, and sexual dysfunction. For each question there are 4 answers, rated 0-3, and the total score reflects the degree of depression.

The pulmonary rehabilitation program (PRP) included 3-5 weekly physical training sessions (25 to 45 minutes each) for an average period of 12 weeks, but not less than 3 weeks, according with previous published data (16). After warming-up and stretching. patients proceeded to endurance exercises, such as treadmill walking or cycling. Later on, the patients continued with aerobic exercises for respiratory muscle, arm, and lower limb training. Strength training included weight lifting exercises or the use of multifunctional machines. Patients received education about diaphragmatic breathing exercises. Intensity of exertion was established so that the patients to have a dyspnea score between 4 and 8 on the Borg scale. Joint educational meetings of the multidisciplinary team with the patient groups were organized.

# Results

The pre-rehabilitation assessment included 141 patients and 32 healthy subjects. QoL was visibly impaired in patients with severe COPD forms (Table 1).

<b>D</b> (	Heathy	COPD GOLD stage			
Parameters	subjects	GOLD II	GOLD III	GOLD IV	
No. subjects	32	43	45	53	
No. of subjects who completed the PRP		12	29	33	
Mean age, years	55.6	62.9	63.1	64.2	
FEV1%	96.2±9.8	64.21±9.5	39.50±5.86	24.49±7.54	
SGRQ score	17.8±5.09	41.07±29.11	70.28±24.37	81.02±6.86	
BDI score	2.5±2.0	17.5±4.22	23.33±8.07	26.6±4.49	
Patients with comorbidities (no, %)	9 (28.12)	18 (41.8)	23 (51.1)	38 (71.6)	

Table 1. General data and initial assessment.Comparison by stages of disease severity

The degree of QoL impairment was moderate in stage II (41.07) and severe in stages III (70.28) and IV (81.02). The most severe depression (score 26.6 vs 2.5 in healthy subjects) was also recorded in this group. We found an average increase of 24.72 units from the GOLD COPD stage II group to GOLD COPD stage III group (the highest increase, equivalent to the most marked alteration in OoL), and an average increase of 5.78 units from the COPD stage III group to COPD stage IV group. Increases in the degrees of OoL impairment were encountered in all the three sections assessed by the SGRO (symptoms, activity, and impacts. respectively). After the patients underwent all PRP phases, QoL reassessment at 6 months revealed statistically significant improvements in all 3 groups (p < 0.05). Thus, significant reductions in the score were obtained in each group. In the GOLD COPD stage II group the average reduction was -4.38 units, in the group GOLD COPD stage III -5.37 units, and in the GOLD COPD stage IV -6.75 units.

The depression score correlated with the SGRQ score, both of them being higher in the severe stages of disease (Table 2).

# Table 2. Comparison of QoL and depression measures according to COPD severity stage

COPD GOLD stages	QoL score			BDI score		
	Baseline	6 months after PRP	Diff	Baseline	6 months after PRP	Diff
GOLD II	42.46 (DS±5.98)	38.08 DS±5.2 0	4.38	17.83 DS±2.98	15.66 DS±2.50	2.17
Outpatient PRP	42.47	38.67	3.8	17.5	16.25	1.25
Inpatient PRP	42.45	36.9	5.55	18.5	17	1.5
GOLD III	68.17 DS±10.52	62.80 DS±9.54	5.37	22.75 DS±4.13	20.72 DS±4.17	2.03
Outpatient PRP	66.04	61.26	4.78	21.6	19.2	2.4
Inpatient PRP	70.45	64.46	5.99	23.9	22.2	1.7
GOLD IV	75.33	68.58	6.75	24.84	22.96	1.88

In the groups receiving PRP we found the same tendency, with the gradual increase of the average score from the COPD stage II group (17.83 units mild depression) to the COPD stage III group (22.75 units - moderate depression), with the highest score recorded in the COPD stage IV group (24.84 units severe depression). BDI administered again 6 months after PRP revealed significant а improvement in average score in all groups, respectively a decrease of -2.17 units in the COPD II group, -2.03 units in the COPD III group and -1.88 units in group COPD IV B group.

Patients who underwent inpatient PRP had a poorer QoL than those on outpatient PRP, both at baseline and at 6 months. The difference between the outcomes of inpatient and outpatient PRP was not statistically significant (p > 0.05). Both groups had a favorable evolution, respectively with a decrease at 6 months (Table 3).

# Table 3. Comparative statistical analysis of QoLevolution after PRP in COPD by disease severitystages

Table Analyzed	QoL COPD II	QoL COPD III	QoL COPD IV	
Column A	baseline	baseline	baseline	
vs	VS	VS	VS	
Column B	6 month	6 month	6 month	
Paired t test				
P value	<0.0001 <0.0001		<0.0001	
P value summary	***	***	***	
Are means significantly different? (P < 0.05)	Yes	Yes	Yes	
One- or two-tailed P value?	Two-tailed	Two-tailed	Two-tailed	
t, df	t=7.846 df=11	t=7.722 df=28	t=15.71 df=32	
Number of pairs	12	29	33	
How big is the difference?				
Mean of differences	4.383	5.366	6.755	
95% confidence interval	3.154 to 5.613	3.943 to 6.788	5.879 to 7.630	
R square	0.8484	0.6805	0.8853	
How effective was the pairing?				
Correlation coefficient (r)	0.9497	0.9350	0.9816	
P value (one tailed)	<0.0001	<0.0001	<0.0001	
P value summary	***	***	***	
Was the pairing significantly effective?	Yes	Yes	Yes	

Of the total of 141 individuals initially assessed, 79 had one associated disease (56%). More than half (64.3%) of the elderly patients ( $\geq$  65 years) had comorbidities, some of them having 3 to 5 associated diseases. The most common chronic diseases associated with COPD were: cardiovascular diseases (ischemic heart disease, high blood pressure, and lower limb arteriopathy), rheumatic diseases, neurological diseases, diabetes, obesity, sleep apnea.

#### Discussion

Assessment of QoL with SGRQ demonstrated that QoL was affected in all COPD groups, and the degree of impairment correlated strongly with disease severity. However, QoL impairment was found even in patients with milder disease stages (17). Symptoms may have an earlier age of onset when associated with other lung tissue diseases besides emphysema (18). The study by Nonato et al. showed a significant correlation between COPD severity, BODE (Body mass index, airflow Obstruction, Dyspnea and Exercise capacity) score and QoL, the results being comparable (SGRO score  $52.3 \pm 19.0$  regardless of COPD severity) (17).Medinas-Amoróset al. also reported that the total SGRQ score of  $48.26 \pm 16.84$  correlated with the GOLD classification and BODE score. The SGRQ score was 44.06 in stage II; 46.68 in stage III and 53.37 in stage IV COPD, slightly lower than in our study, especially in patients in a very severe disease stage (19).

It is increasingly recognized that, although used as a measure of severity in COPD, FEV1 does not describe all disease manifestations. Thus, besides dyspnea index, exercise capacity index, BODE index, Qol assessment is important as it reflects patient health status (20). As in bronchiectasis, in COPD attempts are being made to find biomarkers predictive of unfavorable course, exacerbations and QoL impairment (21-23).

The comorbidities commonly associated with COPD further affect the health-related quality of life (24). Metabolic disorders and the presence of sleep apnea worsen both the respiratory symptoms and the associated diseases such as type II diabetes, high blood pressure, heart failure (25-29). Along with conventional treatment, patients suffering of anxiety and depression associated with these chronic conditions (30-32) occasionally use complementary and alternative therapies and balneal specific rehabilitation (33-37).

Anxiety and depression assessment is important in COPD patients. Several scales can be used in this respect: Anxiety Inventory for Respiratory disease (AIR), COPD Anxiety Questionnaire (CAF), Primary Care Evaluation of Mental Disorders (PRIME-MD), Patient Health Questionnaire (PHQ), Generalized Anxiety Disorder 7-item (GAD-7), Hospital Anxiety and Depression Scale (HADS), Anxiety Inventory (BAI), Beck and Beck Depression Inventory (BDI). In our study, we used the BDI, which confirmed depression as a symptom in COPD, its severity being correlated with disease stages (11). Patients with COPD and depression are at higher risk of continuing smoking, progression of lung function decline, decreased lung function, exacerbations, hospitalizations and death (38). Although the disease prognosis is not as gloomy as in other lung or infectious diseases, COPD remains a condition that carries significant mortality and morbidity rates (39-42).

## Conclusions

The results of this study demonstrate a favorable impact of PRP on improving COPD associated symptoms, depression, and QoL in all the 3 monitored COPD patient groups, with statistically significant and persistent positive results over time (6 months after completion of PRP). QoL assessment and recognition of COPD-induced depression or anxiety and associated diseases are extremely important. Non-pharmacological interventions (cognitive behavioral therapy), psychoemotional therapy sessions, as well as pulmonary rehabilitation programs can improve the QoLof COPD patients.

## Declaration of conflict of interests/Conflict of Interest Statement

The authors declare that there is no conflict of interest regarding the publication of this article.

#### **Informed consent**

Informed consent was obtained from all patients included in this study.

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