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Predicting Health-Related Quality of Life in Patients with Chronic Obstructive Pulmonary Disease: The Impact of Age

Alexandru Corlateanu[a] Victor Botnaru[a] Serghei Covantev[a] Silvia Dumitru[b] Nikolaos Siafakas[c]

[a]Department of Respiratory Medicine, State University of Medicine and Pharmacy 'Nicolae Testemitanu', Chisinau, Republic of Moldova; [b]Respiratory Department, Metropolitan Hospital, Athens, and [c]Department of Thoracic Medicine, University General Hospital, Heraklion, Greece

Key Words
Chronic obstructive pulmonary disease · Quality of life · St. George's Respiratory Questionnaire · Clinical COPD Questionnaire

Abstract
Background: Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity in the elderly population. COPD leads to a reduced health-related quality of life (HRQL), but the factors which contribute to this are not well understood. A better understanding of the factors which determine HRQL should lead to an improved care for such patients. ***Objectives:*** The purpose of this study was to investigate possible age-related differences in HRQL in a population of patients with a similar severity of obstruction. ***Methods:*** A total of 180 consecutive COPD patients were enrolled into the study. We analyzed spirometric data, BODE index and its components, and comorbidities were assessed by the Charlson index. HRQL was assessed by the Clinical COPD Questionnaire (CCQ) and St. George's Respiratory Questionnaire (SGRQ). ***Results:*** The cohort consisted of 93 'younger' patients (mean age 54.8 ± 3.1 years) and 87 older patients (mean age 73.1 ± 5.5 years). Patients in both groups had a similar severity of obstruction: FEV_1 (% from predicted) was 39.9 ± 13.2% in the elderly group compared to 41.7 ± 11.7% in the younger group ($p > 0.05$). The forward stepwise regression analysis shows that the BODE index, the Charlson index, and the rate of exacerbations are important predictors of deterioration of HRQL in elderly COPD patients, which explains 29% of the total SGRQ score. In the younger COPD patients, the coefficient of determination R^2 was 0.27, but the predictors were the BODE index and the rate of exacerbations. ***Conclusions:*** The BODE index, the Charlson index, and the rate of exacerbations were found to be the major determinants of HRQL in elderly COPD patients, while in younger COPD patients, the BODE index and the rate of exacerbations were influential factors.

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Introduction

Chronic obstructive pulmonary disease (COPD) is a major problem for public health at the global level and an important cause of morbidity and mortality worldwide. Pharmacological and nonpharmacological treatment should be guided by COPD severity and aim to control symptoms, decrease exacerbations, and improve patient function and quality of life [1, 2].

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Alexandru Corlateanu, MD, PhD
State University of Medicine and Pharmacy 'Nicolae Testemitanu'
Stefan cel Mare Street 165
MD–2004 Chisinau (Republic of Moldova)
E-Mail alexandru_corlateanu@yahoo.com

The assessment of the quality of life has become a significant research issue in COPD. Since COPD is a debilitating disease, several methods have been developed to accurately assess the health-related quality of life (HRQL) of patients: St. George's Respiratory Questionnaire (SGRQ) [3] and the Clinical COPD Questionnaire (CCQ) were specially designed for COPD patients [4]. With the help of these questionnaires it is possible to assess the current impact of the disease on the life of patients as well as the effect of therapy (pharmacological and nonpharmacological, long-term oxygen therapy, pulmonary rehabilitation, and pulmonary transplant) [5, 6]. This is precisely why these questionnaires represent important instruments which can be used by health-care providers along with classical methods (for example FEV_1) to determine the severity of the disease. Still, patients' HRQL is affected by many factors, such as age, gender, socioeconomic status, smoking, region in which the patient lives, etc.

The SGRQ is a reliable, valid, and sensitive instrument for quality of life evaluation in COPD patients of different age groups, nationalities, and disease severity [7, 8]. The SGRQ can show a modification of HRQL in the absence of a FEV_1 modification. This questionnaire allows a more accurate assessment of the severity of the disease when other data remain inconclusive. Patients with frequent hospitalizations have been found to have an increase in the total SGRQ score [9].

Although both asthma and COPD cause airflow limitation similarly, COPD is associated with a more significant deterioration of lung function, a greater degree of airway obstruction, and more overall health problems [10, 11]. Besides, COPD tends to cause psychiatric disorders and sleep disturbances further deteriorating patients' quality of life [12]. Patients with COPD often suffer from other comorbidities which in combination further affect their HRQL. Frequent exacerbations of COPD also present a risk, since they are linked to sudden cardiac death, which shows that COPD is no longer a disease that affects only the respiratory system [13].

The impact of age on the clinical expression of COPD is not well characterized. The purpose of this study was to investigate possible age-related differences in HRQL in a population of patients with a similar severity of obstruction.

Subjects and Methods

A total of 180 consecutive patients with stable COPD who attended the Hospital 'Sfantul Arhanghel Mihail', Republic of Moldova, from December 2008 to December 2011 were recruited into the study: 117 (65%) were males and 63 (35%) were females; they were between 44 and 80 years old, with a mean age of 63.7 ± 8.1 years. COPD was diagnosed according to the GOLD classification (2011) [14]. All assessments were performed by the lead researcher. The single assessor was not blinded to the age of the patients.

A positive diagnosis was based on the presence of risk factors and airway obstruction which was partially reversible or irreversible, with or without symptoms. We analyzed spirometry, the BODE index, the 6-min walking distance (6MWD) test, and quality of life. The BODE index is a multidimensional index of disease severity in COPD that incorporates 4 factors known to be independent predictors of survival in this disease: body mass index, degree of airflow obstruction assessed by FEV_1, functional dyspnea assessed by the modified Medical Research Council (mMRC) questionnaire, and exercise capacity assessed by the 6MWD test [15]. The 6MWD was performed according to American Thoracic Society guidelines [16]. To quantify the degree of comorbidities, we used the Charlson index [17].

For the assessment of HRQL, we used two original questionnaires validated in Romanian and Russian: the SGRQ and the CCQ (http://ccq.nl/?page_id=4). The SGRQ is a disease-specific HRQL questionnaire divided into 3 subscales, i.e. symptoms (8 items), activity (16 items), and impact (26 items), and 1 overall score. Each score ranges from 0 to 100 points (0 = no impairment).

The CCQ consists of 10 items with an overall score and 3 domains: symptoms (4 items), functional state (4 items), and mental state (2 items). All scores range from 0 to 6 (0 = no impairment).

Statistical Analysis

Data processing was done using Microsoft Excel 2010, Statistica 6.0 (Statsoft Inc.), and SPSS 16.0 (SPSS Inc.). The results were expressed as means ± standard deviations or as absolute numbers (percentages). The correlation analysis of the variables was performed with the use of Pearson's correlation coefficient (when the variables were normally distributed). The t test was used to analyze the parameters resulting from the estimation of the linear regression model; the statistical model was validated using the coefficient of determination (R^2). In all the analyses, p values below the 5% level, two tailed, were regarded as significant.

Statement of Ethics

This study was conducted according to the principles of the Declaration of Helsinki. The protocol of this study was approved by our institutional review boards (State University of Medicine and Pharmacy 'Nicolae Testemitanu', December 12, 2011), and written informed consent was obtained from all patients before enrollment.

Results

The patients were divided into two groups according to their age: elderly patients were ≥65 years old, and 'younger' COPD patients were <65 years old [18]. The first group consisted of 87 patients with a mean age of 73.1 ± 5.5 years; 57 were males (65.5%) and 30 were females (34.5%). The second group consisted of 93 patients with

a mean age of 54.8 ± 3.1 years; 60 were males (64.5%) and 33 were females (35.5%).

The demographical and general data of the patients are shown in table 1. Weight, height, and body mass index were similar in both groups. FEV_1 was similar in both groups: in the younger group, FEV_1 (% from predicted) was 41.7 ± 11.7%, and in the elderly group, FEV_1 was 39.9 ± 13.2% ($p > 0.05$). The rate of COPD exacerbations was assessed retrospectively and was similar in both groups: 4.1 ± 0.7 versus 4.5 ± 0.6, respectively ($p > 0.05$). The Charlson index was higher in elderly COPD patients (2.8 ± 0.7 points), and their most frequent comorbidities were heart failure (67%), systemic hypertension (53%), and coronary heart disease (30%). The Charlson index in younger COPD patients was 1.5 ± 0.7 points, and their most frequent comorbidities were systemic hypertension (38%), heart failure (25%), and anemia (23%).

The total SGRQ score was higher in the elderly patients than in the younger patients (69.7 points vs. 57.4 points, $p < 0.0001$; table 2). The SGRQ 'activity' and SGRQ 'impact' scores were higher in the elderly patients than in the younger patients (65.7 vs. 53.7 points, $p < 0.05$, and 67.1 vs. 55.7 points, $p < 0.05$, respectively), whereas the difference between the SGRQ 'symptoms' score was not statistically significant (82.7 vs. 79.1 points, $p > 0.05$). There is a tendency for the 'symptoms' score to increase in 'younger' adults, which may be explained by the higher impact of COPD on their lives.

The quality of life assessed by the CCQ also proved to be more affected in elderly patients than in younger patients (total CCQ score 3.3 vs. 3, $p < 0.05$). The functional and mental domain scores were more elevated in elderly than in younger patients (2.7 vs. 2.3, $p < 0.05$, and 4.1 vs. 3.5, $p < 0.05$, respectively), but the symptoms domain score was similar in both groups (3.4 in elderly vs. 3.3 in younger patients, $p > 0.05$). It is important to mention that the mental score also tends to be affected, which is usually underestimated in clinical practice.

At the same time, it is crucial to evaluate the HRQL of the patients depending on their COPD stage. It was demonstrated that the HRQL of COPD patients decreases with the progression of the disease. Therefore, each COPD stage can be characterized not only by functional parameters, but also using the HRQL (table 3).

The analysis of the correlations between the HRQL scores and different variables in the 180 patients showed that patients with severe obstruction (GOLD stage IV) had a higher SGRQ score ($p < 0.01$) than those with GOLD stages II and III. The total SGRQ score in elderly COPD patients with GOLD stage IV was 74.7 ± 12.3 points, while it was 57.1 ± 11.1 and 68.5 ± 11.8 points in GOLD stages II and III, respectively. In the younger COPD patients, the highest value of the total SGRQ score was found in patients with GOLD stage IV (66.7 ± 12.3 points).

In elderly COPD patients, Pearson's correlation coefficient demonstrates a significantly positive correlation between the BODE index and the total scores of the CCQ ($r = 0.6$, $p < 0.01$) and of the SGRQ ($r = 0.45$, $p < 0.01$). There were similar findings for the younger group, namely a significantly positive correlation between the BODE index and the total scores of the CCQ ($r = 0.6$, $p < 0.01$) and of the SGRQ ($r = 0.4$, $p < 0.01$).

Table 1. Caracteristics of patients with COPD according to age

Variable	Younger COPD patients (n = 93)	Elderly COPD patients (n = 87)	p
Age, years	54.8±3.1	73.1±5.5	<0.01
Weight, kg	78.3±17.3	73.7±17.7	>0.05
Height, m	1.67±0.07	1.66±0.08	>0.05
BMI	26.7±5.6	25.8±5.8	>0.05
FEV_1, %	41.7±11.7	39.9±13.2	>0.05
FVC, %	49.4±16.5	47.2±20.9	>0.05
FEV_1/FVC ratio	57.5±10.7	59.5±8.5	>0.05
mMRC score	3.2±0.7	3.7±0.63	<0.01
6MWD, m	267.5±87.2	203.7±81.9	<0.01
BODE score	5.3±1.8	6.8±1.5	<0.01
Pack-years	31±15.7	33.5±16.7	>0.05
Rate of exacerbations	4.1±0.7	4.5±0.6	>0.05
Charlson index	1.5±0.7	2.8±0.7	0.0001

Values are means ± SD. BMI = Body mass index.

Table 2. HRQL in the younger and elderly COPD groups

Variable	Younger COPD patients	Elderly COPD patients	p
SGRQ symptoms score	79.1±11.7	82.7±12.9	>0.05
SGRQ activity score	53.7±13.4	65.7±12.5	<0.05
SGRQ impact score	55.7±11.4	67.1±12.4	<0.05
SGRQ total score	57.4±12.7	69.7±11.4	<0.05
CCQ symptoms score	3.3±0.9	3.4±0.8	>0.05
CCQ functional domain score	2.3±0.8	2.7±0.7	<0.05
CCQ mental domain score	3.5±1.1	4.1±0.9	<0.05
CCQ total score	3±0.7	3.3±0.6	<0.05

Values are means ± SD.

Table 3. Comparison between grades of COPD severity regarding SGRQ and CCQ scores in younger and elderly COPD patients

	Younger COPD patients				Elderly COPD patients			
	moderate	severe	very severe	p value	moderate	severe	very severe	p value
Patients	25	30	32		23	38	32	
SGRQ symptoms score	69.5±12.3	76.3±10.8	86.7±9.8	≤0.01	74.9±13	82±9.6	86.2±11	≤0.01
SGRQ activity score	47±9.9	48.7±12.1	57.7±16.9	≤0.01	54.5±13	64±14.6	71±14.5	≤0.01
SGRQ impact score	53.7±9.7	55.8±8.9	63±15.1	≤0.01	56.7±12	68.1±11	71.5±14	≤0.01
SGRQ total score	54.3±9	57.1±9.1	66.7±12.3	≤0.01	57.1±11.1	68.5±11.8	74.7±12.3	≤0.01
CCQ symptoms score	2.8±0.6	3.14±0.8	3.99±0.8	≤0.01	2.6±0.5	3.3±0.7	3.8±0.5	≤0.01
CCQ functional domain score	1.78±0.4	2.1±0.8	3.1±0.9	≤0.01	2.2±0.4	2.6±0.6	2.9±0.5	≤0.01
CCQ mental domain score	2.25±0.6	2.7±1.2	3.79±1.3	≤0.01	3.5±0.6	4.1±0.7	4.5±0.6	≤0.01
CCQ total score	2.28±0.5	2.64±0.8	3.6±0.9	≤0.01	2.6±0.4	3.2±0.5	3.6±0.5	≤0.01

Values are means ± SD. Moderate = GOLD stage II; severe = GOLD stage III; very severe = GOLD stage IV.

Table 4. Multiple regression analysis: factors predicting SGRQ total score in elderly COPD patients

	β	SE	B	SE	95% CI	R^2	t	p
Interceptor			35.7	6.0	23.7, 47.78		5.9	0
BODE	0.25	0.11	1.8	0.8	0.24, 3.4	0.18	2.3	0.02
Rate of exacerbations	0.29	0.11	3.7	1.4	1, 6.5	0.06	2.7	0.008
Charlson index	0.23	0.1	2.2	0.9	0.34, 4.1	0.05	2.3	0.02

Total R^2 = 0.29.

Table 5. Multiple regression analysis: factors predicting SGRQ total score in younger COPD patients

	β	SE	B	SE	95% CI	R^2	t	p
Interceptor			37.9	4.4	29.2, 46.8		8.6	0
BODE	0.26	0.12	1.4	0.6	0.1, 2.6	0.19	2.2	0.02
Rate of exacerbations	0.3	0.12	3.3	1.3	0.7, 5.97	0.06	2.5	0.01

Total R^2 = 0.27.

The multivariate logistic regression method (forward stepwise regression) was applied for identifying independent predictors of HRQL deterioration in elderly and younger COPD patients. The results of the statistical analysis for both groups are presented in tables 4–7.

The forward stepwise regression analysis showed that the BODE index, the Charlson index, and the rate of exacerbations are important predictors of deterioration of HRQL in elderly COPD patients, which explains 29% of the total SGRQ score. In the younger COPD patients, the coefficient of determination R^2 was 0.27, while the BODE index and the rate of exacerbations were predictors of HRQL deterioration as assessed by the SGRQ.

The forward stepwise regression analysis showed similar predictors of deterioration of HRQL (BODE index, Charlson index, and rate of exacerbations) in elderly COPD patients, which explains 50% of the total CCQ score. In the younger COPD patients, the coefficient of determination R^2 was 0.39, while the BODE index was a predictor of HRQL deterioration as assessed by the CCQ.

Table 6. Multiple regression analysis: factors predicting CCQ total score in elderly COPD patients

	β	SE	B	SE	R^2	95% CI	t	p
Interceptor			3.5	2.1		−0.68, 7.7	1.66	0.09
BODE	0.4	0.1	0.14	0.04	0.38	0.07, 0.2	3.88	0.0002
Rate of exacerbations	0.33	0.09	0.2	0.06	0.09	0.08, 0.3	3.5	0.0007
Charlson index	0.15	0.08	0.07	0.04	0.02	−0.07, 0.1	1.79	0.05
SaO_2	−0.1	0.1	−0.02	0.02	0.008	−0.06, 0.02	−1.1	0.27

Table 7. Multiple regression analysis: factors predicting CCQ total score in younger COPD patients

	β	SE	B	SE	R^2	95% CI	t	p
Interceptor			6.4	3.1		−0.29, 12.6	2.1	0.04
BODE	0.43	0.12	0.18	0.05	0.36	0.08, 0.27	3.65	0.0005
SaO_2	−0.18	0.11	−0.05	0.03	0.03	−0.1, 0.01	−1.7	0.1
Rate of exacerbations	0.14	0.1	0.12	0.09	0.01	−0.06, 0.32	1.3	0.2

Discussion

One of the main goals of our study was to investigate the impact of COPD on HRQL. Elderly patients with COPD have a deterioration of psychosocial aspects of life as well as a decline in daily physical activity; therefore, it is essential to establish a link between COPD and HRQL in elderly patients.

The previous studies that investigated how an obstructive ventilatory defect affects the HRQL in elderly patients had controversial results. Several authors found a better HRQL in elderly patients with COPD than in younger patients, which may be explained by the restrictions of some of the daily physical activities [19]. Other researchers, on the contrary, found a persistent deterioration of HRQL to be associated with age [20].

In our study, HRQL was more affected in elderly than in younger COPD patients, which confirms that COPD has a huge impact on HRQL in elderly patients. In other studies [21, 22], bronchial obstruction was shown to have an important role, mainly because of the relationship between FEV_1 and the SGRQ scores, and this was confirmed by logistic regression analysis.

Martinez et al. [23] demonstrated that older subjects with COPD report better HRQL than do younger COPD patients and that this age-related difference involves a lower impact of dyspnea with increasing age. Our data suggest that COPD is a major determinant factor for severe deterioration of HRQL leading to limitations of physical activity (good correlation between the 6MWD and FEV_1: $r = 0.6$, $p < 0.01$) and of functional status in elderly patients with COPD, and that this influence largely depends on the severity of airway obstruction. It was demonstrated that, with disease progression, HRQL and physical activity tend to decline; thus, elderly patients with a more severe stage of COPD have a lower HRQL than COPD patients with a moderate stage of the disease.

In one of the previous studies, there were good correlations between the overall scores for the HRQL instruments (CCQ vs. SGRQ: $r = 0.75$, $p < 0.001$) [24]. The authors also found that the CCQ has the advantage of being easier and faster to complete than the SGRQ (578 s for the SGRQ and 134 s for the CCQ). The need for assistance while answering the questionnaire was 86.5% for the SGRQ and 36.0% for the CCQ.

The conducted research revealed that there is a significant correlation between the SGRQ and CCQ domains and the BODE index in elderly and younger adult patients, which is stronger if compared to the correlation with the severity of airway obstruction. In both groups, the BODE index had a good correlation with the total SGRQ score ($r = 0.4–0.45$), but it was not as strong as with the total CCQ score ($r = 0.6$).

Besides, a correlation between HRQL, evaluated by the SGRQ, and the BODE index was pointed out. Ong et al. [25] describe a weak-to-moderate correlation between the SGRQ and the BODE index ($r = 0.27–0.46$), whereas the correlation between COPD stages and some of the SGRQ domains (total, impact, and activity) was weaker ($r = 0.27–0.28$). Higher BODE indexes are associated with

higher total SGRQ scores. Some very strong correlations were found between BODE quartiles and total SGRQ scores ($r = 0.914$, $p < 0.01$). In contrast, GOLD stages showed a moderate correlation with total SGRQ scores [26]. There is an association between HRQL, as assessed by the SGRQ, and the BODE index within the entire spectrum of COPD severity. Even in early disease stages and BODE index zero, HRQL is already impaired [27].

This study has several limitations. First, the number of the subjects included is small. Second, there is a lack of age-matched healthy controls for comparison, although this is complicated by the fact that the elderly often have one or more chronic conditions. Further investigations are needed to analyze the influence of age on the quality of life of COPD patients.

Conclusion

Elderly patients with COPD have a more severe deterioration of the quality of life. The BODE index, the Charlson index, and the rate of exacerbations were found to be the major determinants of quality of life in elderly COPD patients, while the BODE index and the rate of exacerbations serve as the main determinants in younger COPD patients.

Financial Disclosure and Conflicts of Interest

The authors declare no conflicts of interest.

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