

# Health-related quality of life of COPD patients aged over 40 years

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## ABSTRACT

**Background:** Chronic obstructive pulmonary disease (COPD) is the fourth most frequent disease globally, and its worldwide prevalence is projected to increase in the following decades. Health-related quality of life (HRQOL) of COPD patients depends on multiple factors. **Objective:** The aim of this study was to identify the most important risk factors affecting HRQOL of COPD patients and to measure how specific clinical parameters can predict HRQOL. **Methods:** A questionnaire-based cross-sectional study combined with clinical data was conducted among patients diagnosed with COPD ( $n = 321$ , 52.6% females, mean age  $66.4 \pm 9.5$ ) at the National Koranyi Institute for Pulmonology, Budapest in 2019–2020. The inclusion criteria were age  $\geq 40$  years and existing COPD. Multivariate linear regression analyses were conducted on three components of the COPD-specific Saint George's Respiratory Questionnaire (SGRQ-C) and on the physical (PCS) and mental component scales (MCS) of the 36-Item Short Form Health Survey (SF-36). Multiple linear regression analysis was performed to evaluate the effects of patient and disease characteristics on COPD Assessment Test (CAT) scores. **Results:** We found that frequent exacerbations, multiple comorbidities and tobacco smoking were associated with worse HRQOL. Engaging in more frequent physical activity and better 6-minute walking distance results were associated with better HRQOL. **Conclusions:** Our

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results indicate that the complex therapy of COPD should focus not only on improving lung functions and preventing exacerbation, but also on treating comorbidities, encouraging increased physical activity, and supporting smoking cessation to assure better HRQOL for patients.

## KEYWORDS

chronic obstructive pulmonary disease, quality of life, SF-36, SGRQ-C, CAT

## INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a progressive inflammatory condition of the lungs characterized by pulmonary symptoms, such as shortness of breath and/or cough, and extra-pulmonary manifestations, such as cachexia and/or systemic inflammation [1–3]. As of 2016, a total of 251 million people were affected by COPD worldwide, and the disease accounts for approximately 5% of global deaths yearly [4]. According to projections for future disease burden, COPD will be the 3<sup>rd</sup> leading cause of death by 2030 [4], which may be partially linked to the growing proportion of elderly citizens in aging populations, as the risk of developing COPD increases with age [5]. The health-related quality of life (HRQOL) of COPD patients often depends on multiple factors. Thus, patients are usually affected by more than one comorbidity, such as cardiovascular diseases, diabetes, and osteoporosis [6]. Furthermore, the concurrent presence of certain other risk factors, like tobacco smoking, lower body weight, or lack of physical activity further worsen their HRQOL [7–9].

HRQOL measures the impact of a disease on the day-to-day functioning of patients [10]. According to recent protocols, the treatment model of COPD patients should focus not only on the evaluation of symptoms, but also on the improvement of patients' HRQOL [11]. Better quality life can be achieved by reducing the frequency of exacerbations, improving lung functions, and encouraging smoking cessation, body weight control, and regular physical activity [6, 7, 12–14].

Studies indicate that the forced expiratory volume in one second (FEV<sub>1</sub>) often correlates poorly with HRQOL, thus it doesn't account for extra-pulmonary manifestations of COPD, such as depression, anxiety, or the patients' ability to fulfil their daily duties [15]. As a result, instruments measuring HRQOL are often included in the assessment of COPD patients completing the classical clinical parameters. Thus, several general and disease-specific instruments can be used to quantify the HRQOL. For instance, the generic 36-Item Short Form Health Survey (SF-36) includes questions for eight separate HRQOL components [16]. Among the COPD-specific questionnaires, one of the most frequently used is the COPD-specific Saint George Respiratory Questionnaire (SGRQ-C) [17]. This instrument measures not only the severity of COPD symptoms but also the impact of the disease on the activity and everyday life of the patients. On the other hand, the COPD Assessment Test (CAT) focuses more on the effect of symptoms (e.g. cough, sputum, dyspnea, chest tightness) [18]. Even though both general and disease-specific indices are widely used to assess HRQOL among COPD patients, the SGRQ-C is more reliable in differentiating among patients concerning changes in COPD disease severity over time compared to other instruments [19].

The complex management of COPD should focus not only on lung function values, other functional variables, and exacerbation rates but also on the improvement of the patients'



HRQOL. In the next decades, COPD is projected to increasingly affect the HRQOL of the global population. Therefore, the goals of our study were (1) to identify risk factors influencing HRQOL of COPD patients and (2) to measure how specific clinical parameters are associated to HRQOL.

## MATERIALS AND METHODS

### Participants and procedure

A cross-sectional study was performed among COPD patients at an inpatient department of the Hungarian National Koranyi Institute for Pulmonology, Budapest in 2019–2020. Inclusion criteria were age  $\geq 40$  years and recognized COPD (post-bronchodilator  $FEV_1/FVC < 70\%$ ). Exclusion criteria were simultaneous asthma, malignant diseases, and/or autoimmune diseases in terms of ICD-10 definitions. Participation was voluntary, and before signing the consent document, all patients were informed verbally and in writing about the study and its purpose. An appointed coordinator conducted the questionnaire-based interviews and filled out the questionnaires according to the patients' answers in a timeframe of 30 minutes. Clinical examination of patients followed the completion of the questionnaire, generally on the same day. Altogether 321 patients were approached and all of them agreed to participate in the study. The study protocol and the study were approved by the Ethical Committee of the National Koranyi Institute for Pulmonology (25/2017) and the Institutional Review Board of Semmelweis University (TUKÉB 44402-2/2018/EKU) in compliance with the Helsinki Declaration.

### Measurement

Our questionnaire contained items exploring the patients' socio-demographic, lifestyle, and disease-specific characteristics. Specific items included age, gender, COPD exacerbation in the past year (yes/no), body mass index (BMI), current smoking status (yes/no), frequency of physical activity ( $\leq 1$  time a week/ $\geq 2$  times a week), and number of comorbidities. Exacerbation was defined as an acute and significant change of the patient's daily symptoms resulting in change of therapy. As noted by Guo et al., BMI for COPD is more consistent if BMI is categorized as  $\leq 21$ , 21.1–29.99, and  $\geq 30$  compared to the traditional categories of  $< 18.49$ , 18.5–25.0, and  $> 25.1$  [20]. To be able to include BMI in our analysis, we used two separate dummy variables to examine the effect of obesity ( $BMI \geq 30$  vs. reference  $BMI \leq 29.9$ ) and underweight ( $BMI \leq 21$  vs. reference  $BMI \geq 21.1$ ) as risk factors. Regarding comorbidities, cardiovascular diseases, diabetes, immunological diseases, osteoporosis, musculoskeletal diseases, psychiatric diseases, allergies, hypersensitivities, and gastrointestinal diseases were included in the analysis. Data on comorbidities, lung function values, and BMI were collected from the latest medical records from the past month. Presence of exacerbation was examined from medical records dating back one year. All other data were collected with questionnaires.

HRQOL was measured by SGRQ-C, COPD Assessment Test (CAT) and Short Form Health Survey (SF-36) instruments. The SGRQ-C instrument consists of 40 questions divided into three separate components. The symptoms component describes the frequency and severity of symptoms over the past three months, the activity component measures the impact of breathlessness on activities, whereas the impact component describes the effect of the disease on social



functioning and mental health of patients [17]. Scores range from 0 to 100 with higher scores indicating more severe symptoms/limitations [17]. CAT is a unidimensional tool, consisting of eight items with six response options for each question [18]. Scores range from 0 (best) to 40 (worst) [18]. Finally, SF-36 contains 36 questions measuring eight separate components related to quality of life (physical functioning, role limitation–physical, role limitation–emotional, vitality, mental health, social functioning, pain, and general health) [16]. Results range from 0 (worst) to 100 (best) [16]. We decided to calculate two subscales derived from the SF-36 scale, namely the physical (PCS) and mental (MCS) component scales to decrease the number of concurrent comparisons. Therefore, we standardized each of the eight components of SF-36 with a Z-score transformation. Individual Z-scores were calculated by subtracting the population mean from the respondents' score and dividing it by the standard deviation. For both the PCS and MCS scales, scores were multiplied by weighting coefficients calculated from a USA population and standardized to a T-score with means set at 50 and standard deviation set at 10 [21].

Patients were assigned to one of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages based on their FEV<sub>1</sub> results, as measured after the completion of the questionnaire according to the following specifications: FEV<sub>1</sub> ≥ 80% as stage 1, 50–80% as stage 2, 30–50% as stage 3, and ≤ 30% as stage 4 [22]. The FEV<sub>1</sub>, FVC (forced vital capacity), and FEV<sub>1</sub>/FVC values were measured by spirometry [23]. Exercise capacity was assessed by the 6-minute walking distance (6MWD) test [24, 25]. We requested patients to walk up and down a hallway with predefined turning points for a total of 6 minutes. Results were measured in meters.

## Statistical analysis

Socio-demographic characteristics and HRQOL scores by gender were analyzed with Pearson's Chi-square test, independent samples t-tests, and Mann-Whitney U-test. Normality was assessed by Shapiro-Wilk's normality test. Bivariate correlational analyses were performed for the three components (symptoms, activity, and impact) and for the total score of SGRQ-C, CAT, and the PCS and MCS scales of SF-36 by including individual variables in our models one at a time. This was followed by multivariate linear regression analyses for different components of the SGRQ-C and SF-36 questionnaires and multiple linear regression analysis for the unidimensional CAT questionnaire by including all variables in each respective model. Multivariate regression analysis was used for SGRQ-C and SF-36 as both are multidimensional tools and are comprised of more than one dependent variable, whereas multiple linear regression analysis was used for CAT as it is a unidimensional instrument with a single dependent variable. Maximum likelihood estimation with robust standard error was used to calculate regression coefficients. Results of the correlation matrices of each analysis were presented as well. We evaluated the effect of gender, age, smoking, physical activity, BMI, exacerbations, comorbidities, FEV<sub>1</sub>/FVC, and 6MWD results on HRQOL scores in our linear regression analyses. For each model,  $R^2$  values were calculated to describe the proportion of explained variance. Significance was set at  $P < 0.05$ . All analyses were conducted in R statistics (lavaan package).

## RESULTS

Table 1 shows the descriptive characteristics of the sample. Compared to males (47.4%), females (52.6%) had significantly higher BMI, greater number of comorbidities, and lower 6MWD



Table 1. Sociodemographic, disease-specific, and quality of life characteristics of the sample by gender ( $n = 321$ )

Variables	Participants			P-value
	Total ( $n = 321$ )	Male ( $n = 152$ )	Female ( $n = 169$ )	
Age (years), mean (SD)	66.4 (9.5)	65.8 (9.4)	67.0 (9.7)	0.363
BMI ( $\text{kg}/\text{m}^2$ ), mean (SD)	26.0 (7.0)	24.7 (6.3)	27.2 (7.4)	0.003
BMI, n (%)				0.036
$\leq 21$	82 (26)	47 (31)	35 (21)	
21.1–29.99	140 (45)	69 (46)	71 (44)	
$\geq 30$	92 (29)	35 (23)	57 (35)	
Physical activity $\geq 2$ times/week, n (%)	65 (20)	34 (22)	31 (18)	0.405
Current smoker, n (%)	137 (44)	70 (47)	67 (41)	0.306
Exacerbation in the past year, n (%)	165 (51)	82 (54)	83 (49)	0.434
Comorbidities (n), mean (SD)	2.14 (1.7)	1.91 (1.7)	2.35 (1.7)	0.009
GOLD stages, n (%)				0.200
Stage 1	26 (9)	8 (6)	18 (12)	
Stage 2	98 (34)	49 (36)	49 (31)	
Stage 3	120 (41)	52 (39)	68 (43)	
Stage 4	48 (16)	26 (19)	22 (14)	
FEV <sub>1</sub> /FVC (%), mean (SD)	53.4 (13.1)	51.7 (12.7)	55.0 (13.4)	0.054
6MWD (m), mean (SD)	265 (133)	307 (136)	226 (118)	<0.001
SGRQ-C, mean (SD)				
Symptom	67.1 (20.2)	66.3 (21.4)	67.7 (19.1)	0.747
Activity	65.9 (24.2)	60.8 (25.3)	70.6 (22.2)	<0.001
Impact	53.9 (24.9)	48.2 (26.5)	59.0 (22.2)	<0.001
Total	59.9 (21.4)	55.3 (23.0)	64.1 (18.9)	<0.001
CAT, mean (SD)	24.8 (8.8)	23.8 (8.7)	25.7 (8.7)	0.036
SF-36, mean (SD)				
PCS	33.1 (8.5)	35.0 (8.3)	31.4 (8.2)	<0.001
MCS	42.8 (11.3)	43.3 (11.4)	42.2 (11.1)	0.395

Note: Pearson Chi-Square test or independent samples t test or Mann-Whitney test  $P$ -values were used to examine the differences between males and females.

BMI: body mass index; CAT: COPD Assessment Test; COPD: chronic obstructive pulmonary disease; FEV<sub>1</sub>: forced expiratory volume in the first second; FVC: forced vital capacity; GOLD: Global Initiative for Chronic Obstructive Lung Disease; MCS: mental component scale; 6MWD: 6-minute walking distance; PCS: physical component scale; SD: standard deviation; SF-36: 36-Item Short Form Survey; SGRQ-C: COPD-specific Saint George Respiratory Questionnaire.

results. Regarding HRQOL, females reported poorer HRQOL according to the activity and impact components, and total scores of SGRQ-C. Furthermore, the mean score of the PCS of SF-36 was also significantly lower among them than among males, whereas their mean score of CAT was significantly higher.

In the multivariate analysis of SGRQ-C (Table 2), we found that current smokers had higher scores on the symptom subscale ( $\beta = 0.11$ ,  $P < 0.05$ ), more comorbidities correlated with higher activity scores ( $\beta = 0.13$ ,  $P < 0.01$ ) and total scores ( $\beta = 0.09$ ,  $P < 0.05$ ). The occurrence of exacerbations in the past year was associated with an increased score on the symptoms



Table 2. Predictors of the COPD-specific Saint George Respiratory Questionnaire's (SGRQ-C) three domains and total score ( $n = 280$ )

	Bivariate correlations				Multivariate regression analysis			
	Symptoms $r$	Activity $r$	Impact $r$	Total $r$	Symptoms $\beta$	Activity $\beta$	Impact $\beta$	Total $\beta$
Gender	0.05	0.21***	0.20***	0.20***	-0.00	0.06	0.09	0.07
Age	0.02	0.19**	0.06	0.10	-0.03	0.04	-0.05	-0.02
Smoking	0.14*	-0.02	0.07	0.06	0.11*	-0.02	0.04	0.04
Physical activity	-0.16**	-0.34***	-0.29***	-0.32***	-0.11*	-0.28***	-0.24***	-0.26***
Underweight	0.14*	0.06	0.09	0.10	0.06	0.02	0.04	0.04
Obesity	-0.09	0.01	-0.01	-0.02	-0.08	-0.03	-0.06	-0.06
Comorbidities	0.18**	0.23***	0.15*	0.20***	0.10	0.13**	0.05	0.09*
Exacerbation	0.42***	0.33***	0.37***	0.41***	0.35***	0.20***	0.28***	0.29***
FEV <sub>1</sub> /FVC	-0.10	-0.16**	-0.08	-0.12*	0.05	-0.01	0.08	0.05
6MWD	-0.28***	-0.50***	-0.43***	-0.48***	-0.19**	-0.37***	-0.34***	-0.36***
$R^2$	N/A	N/A	N/A	N/A	26.0%	39.7%	34.2%	41.0%

Note: \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . Multivariate regression.  $\beta$ : standardized regression coefficient; FEV<sub>1</sub>: forced expiratory volume in the first second, FVC: forced vital capacity; 6MWD: 6-minute walking distance;  $R^2$ : proportion of explained variance;  $r$ : Pearson's correlation.

Table 3. Predictors of the COPD Assessment Test (CAT) ( $n = 280$ )

Variables	COPD Assessment Test	
	$r$	$\beta^{\#}$
Gender	0.13*	0.05
Age	0.01	-0.06
Smoking	0.11	0.08
Physical activity	-0.18*	-0.14*
Underweight	0.11	0.07
Obesity	-0.02	-0.03
Comorbidities	0.23***	0.16*
Exacerbation	0.31***	0.23***
FEV <sub>1</sub> /FVC	-0.11	0.01
6MWD	-0.30***	-0.21**
$R^2$	N/A	21.8%

Note: \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . #: Multiple regression analysis.  $\beta$ : standardized regression coefficient; FEV<sub>1</sub>: forced expiratory volume in the first second, FVC: forced vital capacity, 6MWD: 6-minute walking distance;  $R^2$ : proportion of explained variance;  $r$ : Pearson's correlation.

( $\beta = 0.35$ ,  $P < 0.001$ ), activity ( $\beta = 0.20$ ,  $P < 0.001$ ), impact ( $\beta = 0.28$ ,  $P < 0.001$ ) subscales and total scale ( $\beta = 0.29$ ,  $P < 0.001$ ). Conversely, more frequent physical activity and better 6MWD correlated with lower scores on the symptoms ( $\beta = -0.11$ ,  $P < 0.05$  and  $\beta = -0.19$ ,  $P < 0.01$ , respectively), activity ( $\beta = -0.28$ ,  $P < 0.001$  and  $\beta = -0.37$ ,  $P < 0.001$ , respectively), impact

Table 4. Predictors of the 36-Item Short Form Survey (SF-36) of COPD patients ( $n = 257$ )

Variables	Bivariate correlations		Multivariate regression analysis	
	PCS	MCS	PCS	MCS
	$r$	$r$	$\beta$	$\beta$
Gender	-0.20**	-0.03	-0.12	0.04
Age	-0.14*	0.07	-0.04	0.10
Smoking	0.06	-0.15*	0.06	-0.09
Physical activity	0.19**	0.16**	0.12*	0.13*
Underweight	-0.06	-0.11	-0.05	-0.08
Obesity	-0.05	0.00	-0.03	0.01
Comorbidities	-0.09	-0.13*	0.01	-0.09
Exacerbation	-0.28***	-0.23***	-0.21***	-0.16*
FEV <sub>1</sub> /FVC	0.13*	0.03	0.03	-0.08
6MWD	0.38***	0.22***	0.26***	0.20**
$R^2$	N/A	N/A	22.1%	13.7%

Note: \* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . Multivariate regression.  $\beta$ : standardized regression; FEV<sub>1</sub>: forced expiratory volume in the first second, FVC: forced vital capacity; MCS: mental component scale; 6MWD: 6-minute walking distance; PCS: physical component scale;  $R^2$ : proportion of explained variance;  $r$ : Pearson's correlation.



Table 5. Correlational matrix of quality of life indices ( $n = 296$ )

Index	SGRQ-C				CAT	SF-36	
	Symptoms	Activity	Impact	Total		MCS	PCS
SGRQ-C Symptoms	1.00						
SGRQ-C Activity	0.54*	1.00					
SGRQ-C Impact	0.63*	0.73*	1.00				
SGRQ-C Total	0.73*	0.87*	0.96*	1.00			
CAT	0.55*	0.45*	0.49*	0.54*	1.00		
SF-36 MCS	−0.39*	−0.32*	−0.43*	−0.57*	−0.43*	1.00	
SF-36 PCS	−0.34*	−0.55*	−0.54*	−0.43*	−0.29*	0.02	1.00

Note: Pearson's correlation. \* $P < 0.001$ .

SGRQ-C: COPD-specific Saint George Respiratory Questionnaire; CAT: COPD Assessment Test; SF-36: 36-Item Short Form Survey; MCS: mental component scale; PCS: physical component scale.

( $\beta = -0.24$ ,  $P < 0.001$  and  $\beta = -0.34$ ,  $P < 0.001$ , respectively) subscales and total scale ( $\beta = -0.26$ ,  $P < 0.001$  and  $\beta = -0.36$ ,  $P < 0.001$ , respectively).

Analysis of CAT indicated that increased frequency of physical activity ( $\beta = -0.14$ ,  $P < 0.05$ ) and better results on the 6MWD test ( $\beta = -0.21$ ,  $P < 0.01$ ) were inversely associated with CAT scores, whereas comorbidities ( $\beta = 0.16$ ,  $P < 0.05$ ) and exacerbations ( $\beta = 0.23$ ,  $P < 0.001$ ) were in direct association with CAT scores (Table 3).

In the analysis of PCS and MCS of SF-36 (see Table 4), we found that higher frequency of physical activity ( $\beta = 0.12$ ,  $P < 0.05$  and  $\beta = 0.13$ ,  $P < 0.05$ , respectively) and better results on the 6MWD test ( $\beta = 0.26$ ,  $P < 0.001$  vs.  $\beta = 0.20$ ,  $P < 0.01$ , respectively) were positively correlated with both scores. However, manifest exacerbations in the past year resulted lower scores on PCS ( $\beta = -0.21$ ,  $P < 0.001$ ) and MCS ( $\beta = -0.16$ ,  $P < 0.05$ ).

When we examined the correlations of individual HRQOL indices with each other, they were significant except that between MCS and PCS. In the correlation matrix, SF-36 (PCS, MCS) scores were inversely related to both SGRQ-C and CAT questionnaires because of the opposite scoring methods employed (Table 5).

# DISCUSSION

Our study established that the occurrence of COPD exacerbations, simultaneous comorbidities, and smoking were the most important factors negatively affecting the COPD patients' HRQOL, whereas the frequency of physical activity and better results on the 6MWD test were positively associated with their HRQOL. The correlation between SGRQ-C, CAT and SF-36 questionnaires was fair, indicating that these questionnaires examine slightly different aspects of HRQOL.

Our sample revealed poorer results as measured by the SGRQ-C, CAT, and SF-36 instruments compared to the results of other studies measuring the HRQOL of COPD patients [26–28]. According to the OECD, Hungary ranks in the bottom 20% in health and life satisfaction [29]. Additionally, smoking rates are among the highest in Europe, along with higher rates of alcohol consumption and overweight/obesity, and somewhat poorer performance in





terms of physical activity [30]. These factors, both individually and overall, may affect HRQOL while offering a possible explanation for our results and also explaining why mortality of COPD in Hungary ranks the highest in Europe [31].

In our study, the number of exacerbations and comorbidities were strongly related to worse HRQOL. Severe manifestations of COPD are often associated with more frequent exacerbations, which may have a strong impact on the day-to-day functioning of patients [12]. According to Miravittles et al., HRQOL decreases substantially just after an exacerbation, but it tends to improve fairly quickly within days of the event [12]. However, negative effects of exacerbations on HRQOL seem to accumulate over time, explaining why patients with more exacerbations tend to have a lower HRQOL compared to stable patients with fewer events. As for comorbidities, patients with COPD are often aged individuals and are affected by a plethora of other conditions as well, such as cardiovascular diseases, malnutrition, depression, and anxiety, that may also affect their activities and functioning [32]. A previous study identified psychiatric disorders and peripheral artery diseases as the most important comorbidities with negative impact on HRQOL of COPD patients [33]. Our results highlight that effective tertiary prevention along with treatment of any comorbid conditions may be essential for the improvement of HRQOL.

Regarding lifestyle factors, we found that HRQOL was significantly affected by physical activity and smoking. Studies indicate that the improvement of physical fitness during rehabilitation leads to improved functional parameters of COPD patients [34–36]. In our study, physical activity improved all dimensions of HRQOL and also had a positive effect on the mental health of patients. According to the WHO, 150 minutes of moderate-intensity aerobic physical activity or at least 75 minutes of vigorous-intensity aerobic physical activity is advised per week for the maintenance of health between ages 18 and 65 [35, 37]. For patients over 65, counseling should focus more on the importance of leisure time physical activity, transportation, household chores, and gardening for the same amount of time as specified above [37]. Regarding smoking, physicians offering smoking cessation support for COPD patients should emphasize that quitting will positively impact the severity of symptoms, which in turn will also improve their overall HRQOL.

In our study the FEV<sub>1</sub>/FVC index did not correlate with HRQOL, suggesting that it is independent of lung capacity values to a certain extent. This is corroborated by other studies which detected only modest association between FEV<sub>1</sub> or FEV<sub>1</sub>/FVC values and changes in health status and other disease outcomes [15, 38], such as rate of exacerbations [39]. The results are, however, often inconsistent [6]. Namely, in the bivariate model we found that higher FEV<sub>1</sub>/FVC values were associated with improved outcomes on the activity component and total scores of SGRQ-C, although this association disappeared when we controlled for additional factors. The 6MWD results were positively associated with all components of HRQOL. Since physical activity is strongly associated with 6MWD [40], the latter can be used to assess patients' level of fitness and also give an insight for physicians in the HRQOL of their patients [41, 42].

One of the strengths of our study is that we measured HRQOL with three different methods, and we compared them with clinical/diagnostic test outcomes. Having included all variables in the models,  $R^2$  values were relatively high. This indicates that these variables explain the variance in our study population fairly well, suggesting that exacerbations, physical activity, and number of comorbidities affect the HRQOL of COPD patients to a greater extent.

Finally, we must also take into consideration certain limitations of our study, for example the relatively small sample and the single-center involvement. Since we examined hospitalized



in-patients, our study sample may have contained a higher proportion of patients with more severe forms of COPD and thus, worse health-related quality of life. The role of selection bias cannot be ruled out since the participation was voluntary, which explains the better HRQOL outcomes of the sample. It may also have been useful to evaluate comorbidities with a multi-dimensional comorbidity index rather than the total number of comorbidities. An additional limitation was that in the calculation of MCS and PCS scores, weighting coefficients calculated from the Hungarian general population were not available, therefore we had to rely on coefficients calculated from the general USA population. This may have led to biased results for SF-36 even though certain studies suggest that this is a viable option when lacking population-specific estimates, as it produces similar results [43].

COPD is a progressive, multi-organ disease that requires a more complex treatment strategy due to its diverse effects on the body and the health-related quality of life of the patients. In this study, the most important factors negatively affecting HRQOL were frequent exacerbations, number of comorbidities, the lack of physical activity, and current smoking. Regarding clinical parameters, we found a consistent positive effect between 6MWD and all components of HRQOL. The treatment model of patients should focus not only on lung function improvement and the prevention of exacerbations but also on the management of comorbidities, complemented with suggesting physical activity and smoking cessation.

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*Data availability statement:* The data that support the findings of this study are available on request from the corresponding author [JTV].

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