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ORIGINAL RESEARCH

Physical Activity, Depression and Quality of Life in COPD – Results from the CLARA II Study

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Background: Symptoms of depression, pain and limitations in physical activity may affect quality of life in COPD patients independent from their respiratory burden. We aimed to analyze the associations of these factors in outpatients with COPD in Austria in a stable phase of disease.

Methods: We conducted a national, cross-sectional study among patients with COPD. For depression, the Patient Health Questionnaire-9 (PHQ-9) and for respiratory symptoms the St. George's Respiratory Questionnaire for COPD patients (SGRQ-C) were used along with 10-point scales for physical activity and pain.

Results: After exclusion of 211 patients due to non-obstructive spirometry or missing data, 630 patients (62.5% men; mean age 66.8 ± 8.6 (SD) years; mean FEV_1%pred. 54.3 ± 16.5 (SD)) were analyzed. Of these, 47% reported one or more exacerbations in the previous year, 10.4% with hospitalization. A negative depression score was found in 54% and a score suggesting severe depression (PHQ-9 score ≥ 15) in 4.7%. In a multivariate linear regression model, self-reported pain, dyspnea, and number of exacerbations were predictors for higher PHQ-9-scores. A negative pain score was found in 43.8%, and a score suggesting severe pain in 2.9% (8–10 points of 10-point scale). Patients reporting severe pain were more often female, had more exacerbations, and reported more respiratory and depressive symptoms, a lower quality of life, and less physical activity. About 46% of patients rated their physical activity as severely impaired. These patients were significantly older, had more exacerbations, concomitant heart disease, a higher pain and depression score, and a lower quality of life (SGRQ-C – total score and all subscores).

Conclusions: In Austria, nearly half of stable COPD outpatients reported symptoms of depression, which were associated with lower levels of self-reported physical activity, more pain, and respiratory symptoms. The associations were particularly strong for depression with SGRQ-C.

Keywords: chronic obstructive pulmonary disease, depression, PHQ-9, pain, quality of life, St. George's Respiratory Questionnaire, physical activity

Introduction

COPD (chronic obstructive pulmonary disease) is an obstructive airway disease, characterized by chronic respiratory symptoms, as dyspnea, cough, excess sputum production, due to airway abnormalities that cause persistent airflow obstruction.[1] Diagnosis of COPD is confirmed by the presence of not completely reversible obstructive airflow limitation as assessed by spirometry. Apart from preventive measures, especially smoking cessation, treatment of COPD is based on inhaled pharmacotherapy to mitigate the symptoms of this disease.[2]

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Furthermore, COPD is frequently accompanied by comorbidities, such as pulmonary hypertension, malnutrition, venous thromboembolism, anxiety, depression, osteoporosis, obesity, metabolic syndrome, diabetes, sleep disturbance and anemia, some of which being seen as systemic manifestations of this disease.[3–5]

In addition to the mitigation of clinical symptoms, COPD therapy aims to improve QoL (quality of life), whereby disease specific questionnaires for monitoring have been developed. The St. George's Respiratory Questionnaire (SGRQ, with scores 0 – 100, with higher scores indicating lower QoL),[6,7] where a validated COPD-specific version (SGRQ-C) is available,[8] is frequently used to measure health status in COPD.

Integrated health assessment may further include other parameters to describe well-being in chronic diseases. In COPD symptoms of depression and pain are frequently described as related to quality of life[9–12] and may even impact the risk of future exacerbations or death.[13] Hence, monitoring depressive symptoms, using specific questionnaires like the Patient Health Questionnaire (PHQ-9),[14] may be useful. Similarly, there is evidence of impaired physical activity in COPD,[15,16] and it is well known that exercise training is associated with better exercise tolerance, skeletal and respiratory muscle functions, symptoms of dyspnea and fatigue and health-related quality of life.[17]

In 2018, the non-interventional CLARA[18] study investigated the health status of COPD patients in Austria in order to characterize the impact of disease on overall health and perceived well-being. Since the conduct of this study, two major developments may have affected disease progression and QoL in Austrian COPD patients: In 2019, smoking was finally prohibited in restaurants and all public indoor places in Austria, which may have reduced the exposure of COPD patients to smoke and therefore facilitated their treatment. Furthermore, the COVID-19 pandemic influenced the routine care of COPD patients on many levels, whereby social distancing likely increased symptoms of anxiety and depression, and thereby contributed to physical deconditioning.[19,20] Moreover, mental well-being and the prevalence of co-existing pain were not evaluated in CLARA I.

To address these previous findings, CLARA II was conducted, and the original design was expanded to include the PHQ-9 questionnaire to screen for symptoms of depression and a 10-point scale assessing overall intensity of self-reported pain. Furthermore, COVID-19 vaccination status was documented. We aimed to analyze the associations of symptoms of depression, pain, limitations in physical activity and quality of life in outpatients with COPD in Austria in a stable phase of disease.

Materials and Methods

Study Setting and Population

The population-based, non-interventional observational CLARA II study was conducted as a multicenter study and aimed to include at least 800 patients from all over Austria. In order to ensure comparability with the previous CLARA study,[18] a similar sampling design was used. Data was captured by two questionnaires and review of the patients' medical records. Subjects were not exposed to any diagnostic or therapeutic measures besides routine care. Ethical approval was obtained from the ethics committee of the Johannes Kepler University, Linz (vote 1129/2021). Study centers were selected based on previous experience with observational studies and to achieve an even distribution across Austria. Each study site was allowed to enroll up to a maximum of 20 patients.

Main inclusion criteria were selected to allow for a broad population of outpatients and consisted of (1) age $\geq$ 40 years and older, and (2) diagnosis of COPD according to GOLD criteria.[1] Main exclusion criteria were (1) having undergone major lung surgery (eg, lung volume reduction, lung transplant), (2) reported moderate or severe exacerbation within the last four weeks, (3) lung cancer and (4) physical or cognitive impairment resulting in an inability to walk or to complete the questionnaires. No specific treatment was studied or required for participation.

Study Conduct and Endpoints

Eligible patients were offered to participate in CLARA during routine clinical visits. After providing informed consent and collecting relevant data, the treating physician completed the case report forms (CRF). Thereafter, the patients were asked to complete the questionnaires, which were united, sealed, collected by the study staff, and analyzed centrally. Data collection was performed between 09/2021 and 01/2022.

Questionnaire

The treating physicians provided spirometry data (FEV_1%pred, FEV_1/FVC, FVC), as well as data about the number of exacerbations during the last year and how often the patient was hospitalized for COPD exacerbations. Additionally, documentation of inhaled therapy and information on any previous COVID-19-infections and vaccinations were provided. Inhaled therapy was categorized as mono therapy (LABA or LAMA), dual therapy (LABA+ICS or LABA +LAMA) or triple therapy (LABA+LAMA+ICS). Furthermore, the last absolute blood eosinophil count was documented (if available in the patient`s medical record).

The patient provided information on demographics (age, sex, weight, height, smoking status) and comorbidities (arterial hypertension, diabetes mellitus, osteoporosis, and cardiac diseases).

Furthermore, the patient answered the SGRQ-C according to the current manual.[21] The SGRQ–C is a well characterized, widely used tool to describe patient reported health status specific for COPD.[8] It consists of a total score and the domains activity, symptoms, and impact on daily life. Each domain is given a score between 0 and 100, and higher scores indicate worse health status.

The PHQ-9 questionnaire was used to screen for depressive symptoms.[22] As a self-administered tool it was filled by the patient. According to the questionnaire manual and current literature,[14,23] we used the scores of the PHQ-9 to discriminate between no symptoms of depression (< 5), mild to moderate depression (5–14) and severe depression (≥ 15).

A 10-point scale for pain (ranging from 1 to 10, no pain to very severe pain) was used to capture the patient`s current general pain condition. Mild pain was defined as 2–7, severe pain as ≥ 8 points.

Two different items were used to assess the physical activity of patient. Firstly, out of the SGRQ-C two groups were constructed, using the following two questions asking how the chest trouble affects daily life activities: "Exercise is not safe for me." and "I cannot play sports or games.". Group 1 ("Impaired physical activity") were all patients who answered affirmatively to both of the two questions of the SGRQ-C. Group 2 ("Preserved physical activity") were all patients who answered in the negative to both questions from above.

Secondly, a 10-point scale answering the question "How much physical activity do you perform during a typical week?" and ranging from 1 (no physical activity) to 10 (a lot of physical activity) was used.

Data Management and Statistics

CLARA II did not test a predefined hypothesis; therefore, estimation of sample size was neither necessary nor possible. A minimum of 800 COPD patients recruited all over Austria was considered adequate to draw meaningful conclusions with acceptable precision.

Categorical data were reported as absolute number and percentage, metric data by arithmetic mean, median, minimum, maximum, and standard deviation. Univariate and multivariate linear regression was used to study the relationships between PHQ-9 scores and demographic and disease specific characteristics. Fisher's exact test and chi-square test were used to test for statistically significant relationships in categorical variables, *T*-test, Kruskal–Wallis test and Mann–Whitney-*U*-Test were used in metric variables. Statistical significance was defined as $p \leq 0.05$. Data analysis was conducted in R (R: A Language and Environment for Statistical Computing; Version 4.3.0; https://www.R-project.org).

Results

A total of 89 pulmonologists contributed to this study and enrolled a total of 841 COPD patients. We excluded 28 patients because of missing data (eg, sex, age or FEV_1). Furthermore, 183 patients were excluded because the spirometric criterion of airways obstruction was not met (FEV_1/FVC <0.7).

Finally, 630 patients (62.5% men; mean age 66.8 ± 8.6 (SD) years; mean FEV_1%pred. 54.3 ± 16.5 (SD)) were included in this study (see also Table 1). 89.0% were current or former smokers, and mean BMI was 26.6 kg/m² ± 5.5 (SD). Arterial hypertension, diabetes mellitus, heart disease or osteoporosis was reported in 46.0%, 16.0%, 16.7% and 11.6%, respectively.

Table 1 Characteristics of Participants

	Female n = 236	Male n = 394	All n = 630	p-value
Characteristics				
Age (mean, SD)	66.1 (8.3)	67.2 (8.7)	66.8 (8.6)	0.050
40–59 years (n, %)	48 (20.3)	71 (18.0)	119 (18.9)	0.217
60–69 years (n, %)	104 (44.1)	155 (39.3)	259 (41.1)	
70+ years (n, %)	84 (35.6)	168 (42.7)	252 (40.0)	
BMI (mean, SD)	25.2 (5.8)	27.4 (5.2)	26.6 (5.5)	< 0.001
Smoking				
Current smoker (n, %)	89 (39.2)	120 (31.3)	209 (34.2)	0.134
Former smoker (n, %)	121 (53.3)	231 (60.2)	352 (57.6)	
Never smoker (n, %)	17 (7.5)	33 (8.5)	50 (8.2)	
GOLD groups (exacerbation history)				
A and B (n, %)	185 (78.4)	309 (78.4)	494 (78.4)	0.991
E (previously C and D) (n,%)	51 (21.6)	85 (21.6)	136 (21.6)	
GOLD – grades (FEV_1)				
1 (n, %)	14 (5.9)	21 (5.3)	35 (5.6)	0.809
2 (n, %)	132 (55.9)	213 (54.1)	345 (54.8)	
3 (n, %)	72 (30.5)	134 (34.0)	206 (32.7)	
4 (n, %)	18 (7.7)	26 (6.6)	44 (7.0)	
FEV_1%-predicted (mean, SD)	55.3 (17.1)	53.7 (16.1)	54.3 (16.5)	0.247
Exacerbations during last year				
0 (n, %)	113 (50.2)	210 (54.7)	323 (53.0)	0.558
1 (n, %)	69 (30.7)	109 (28.4)	178 (29.2)	
≥ 2 (n, %)	43 (19.1)	65 (16.9)	108 (17.7)	
Exacerbations with hospitalization during last year				
0 (n, %)	199 (89.6)	336 (89.6)	535 (89.6)	0.988
≥ 1 (n, %)	23 (10.4)	39 (10.4)	62 (10.4)	
Comorbidities				
Arterial hypertension (n, %)	104 (44.1)	186 (47.2)	290 (46.0)	0.440
Diabetes mellitus (n, %)	27 (11.4)	74 (18.8)	101 (16.0)	0.015
Heart disease (n, %)	30 (12.7)	75 (19.0)	105 (16.7)	0.039
Osteoporosis (n, %)	53 (22.5)	20 (5.1)	73 (11.6)	< 0.001
SGRQ-C				
Total (mean, SD)	40.0 (22.6)	38.1 (20.9)	38.8 (21.5)	0.149
Impact (mean, SD)	28.2 (23.7)	26.4 (21.7)	27.0 (22.4)	0.572
Symptoms (mean, SD)	49.6 (22.4)	51.7 (23.8)	50.9 (23.3)	0.158
Activity (mean, SD)	51.5 (26.1)	48.0 (24.9)	49.3 (25.4)	0.149
PHQ-9				
Total (mean, SD)	5.5 (4.7)	5.3 (4.6)	5.4 (4.7)	0.447
Symptoms				
Cough – several days a week (n, %)	110 (47.0)	204 (52.3)	314 (50.3)	0.200
Phlegm – several days a week (n, %)	88 (37.6)	197 (50.4)	285 (45.6)	0.002
Dyspnea – several days a week (n, %)	92 (81.7)	302 (77.6)	494 (79.2)	0.226
Pain (10-point scale 1–10) (mean, SD)	2.8 (2.1)	2.5 (1.8)	2.6 (1.9)	0.194

Severe airflow limitation (FEV_1pred < 50%, GOLD grades 3 and 4) was seen in 39.7% of patients. Exacerbations in the previous year were reported by 46.9% of participants, 10.4% were therefore hospitalized. More than one exacerbation or a hospitalization due to an exacerbation was stated by 21.6% of patients (GOLD group E, previously C and D).

Female COPD patients were slightly younger, had lower BMIs, and better lung function (FEV_1%pred). Compared to male patients, female COPD patients also reported less phlegm and were less likely to report diabetes mellitus and heart disease, but more frequently osteoporosis.

Inhaled triple therapy (LABA/LAMA/ICS) was used by 49.1% of all patients, while a combination therapy of LABA/LAMA or LABA/ICS was seen in 40.1% and 4.7%, respectively.

A previous COVID-19 infection was reported by 53 patients (6.6%) and 33 patients (5.2%) were not vaccinated against COVID-19. Unvaccinated patients tended to be younger (mean age 65.6 vs 66.8 years), more likely male, and had a numerically higher mean PHQ-9 score (mean total score 7.1 vs 5.3). No difference was seen in the SGRQ-C scores. Multivariate regression analysis confirmed that unvaccinated patients had significantly higher total PHQ-9 scores (OR 1.08 (1.1–1.2 CI, p = 0.029) compared to vaccinated patients.

Using the PHQ-9 questionnaire, no evidence of depressive symptoms was found in 53.8% (331 of 615 patients). Symptoms for severe depression (PHQ-9 score ≥ 15) were reported in 4.7%. Higher scores in the PHQ-9 questionnaire, indicating more severe depressive symptoms, were associated with lower quality of life (using the SGRQ-C), worse lung function (FEV_1), more exacerbations, a higher pain score and more respiratory symptoms in crude analysis. Further details are presented in Table 2 and Figure 1. In a multivariate linear regression model, self-reported pain, dyspnea, and number of exacerbations were predictors of higher PHQ-9-scores, hence more depressive symptoms (Table 3).

Table 2 Characteristics of Participants According to Their PHQ-9 Scores (Symptoms of Depression)

PHQ-9 Score	**< 5 No Symptoms of Depression n = 331**	**5–14 Mild to Moderate Depression n = 255**	**≥ 15 Severe Depression n = 29**	**p-value**
Characteristics				
Age (mean, SD)	66.9 (8.4)	66.5 (8.8)	65.4 (8.9)	0.455
40–59 years (n, %)	49 (14.8)	61 (23.9)	8 (27.6)	0.031
60–69 years (n, %)	150 (45.3)	92 (36.1)	11 (37.9)	
70+ years (n, %)	132 (39.9)	102 (40.0)	10 (34.5)	
Sex, female (n, %)	119 (36.0)	101 (39.6)	13 (44.8)	0.486
BMI (mean, SD)	26.4 (5.1)	26.9 (6.0)	29.0 (5.7)	0.616
Smoking				
Current smoker (n, %)	103 (32.1)	91 (36.7)	9 (31.0)	0.810
Former smoker (n, %)	190 (59.2)	138 (55.7)	17 (58.6)	
Never smoker (n, %)	28 (8.7)	19 (7.6)	3 (10.4)	
GOLD groups (exacerbation history)				
A and B (n, %)	283 (85.5)	186 (72.9)	14 (48.3)	< 0.001
E (n, %)	48 (14.5)	69 (27.1)	15 (51.7)	
GOLD grades (FEV_1)				
1 (n, %)	25 (7.6)	9 (3.5)	0 (0.0)	< 0.001
2 (n, %)	194 (58.6)	129 (50.6)	14 (48.3)	
3 (n, %)	100 (30.2)	93 (36.5)	7 (24.1)	
4 (n, %)	12 (3.6)	24 (9.4)	8 (27.6)	
FEV_1%-predicted (mean, SD)	56.9 (16.0)	51.5 (16.5)	46.7 (16.8)	< 0.001
Exacerbations				
0 (n, %)	189 (59.8)	118 (47.2)	8 (28.6)	< 0.001
1 (n, %)	94 (29.8)	72 (28.8.)	9 (32.1)	
≥ 2 (n, %)	33 (10.4)	60 (24.0)	11 (39.3)	

(*Continued*)

Table 2 (Continued).

PHQ-9 Score	< 5 No Symptoms of Depression n = 331	5–14 Mild to Moderate Depression n = 255	≥ 15 Severe Depression n = 29	p-value
Comorbidities				
Arterial hypertension (n, %)	145 (43.8)	121 (47.5)	16 (55.2)	0.400
Diabetes mellitus (n, %)	48 (14.5)	46 (18.0)	6 (20.7)	0.414
Heart disease (n, %)	45 (13.6)	54 (21.2)	6 (20.7)	0.047
Osteoporosis (n, %)	37 (11.2)	29 (11.4)	5 (17.2)	0.615
SGRQ-C				
Total (mean, SD)	29.3 (16.2)	48.4 (20.6)	68.3 (19.3)	< 0.001
Impact (mean, SD)	16.7 (14.6)	37.7 (22.7)	61.5 (20.6)	< 0.001
Symptoms (mean, SD)	43.1 (21.7)	59.1 (21.7)	69.1 (17.1)	< 0.001
Activity (mean, SD)	40.3 (22.5)	58.2 (23.4)	77.0 (25.9)	< 0.001
Symptoms				
Cough – several days a week (n, %)	147 (44.6)	143 (57.0)	15 (54.6)	0.011
Phlegm – several days a week (n, %)	127 (38.5)	134 (53.2)	16 (57.1)	< 0.001
Dyspnea – several days a week (n, %)	234 (71.3)	223 (88.1)	27 (93.1)	< 0.001
Pain (10-point scale 1–10) (mean, SD)	2.1 (1.7)	3.1 (1.9)	4.0 (2.6)	< 0.001

No pain was reported by 43.8% (269 of 630) of patients, whereas 2.9% indicated to suffer from severe pain (8–10 points; 10-point scale). Characteristics according to the current pain status are presented in Table 4. Percent distribution of the pain score is presented in Figure 2A. Patients reporting severe pain were more often female, reported more respiratory and depressive symptoms, were less physical active (self-reported) and had more exacerbations and a lower quality of life (using the SGRQ-C).

Severely impaired physical activity was reported by 45.9% (225 of 490) of patients. They were older, had more exacerbations, comorbidities (heart disease), pain, depressive symptoms, and a lower FEV_1%pred.

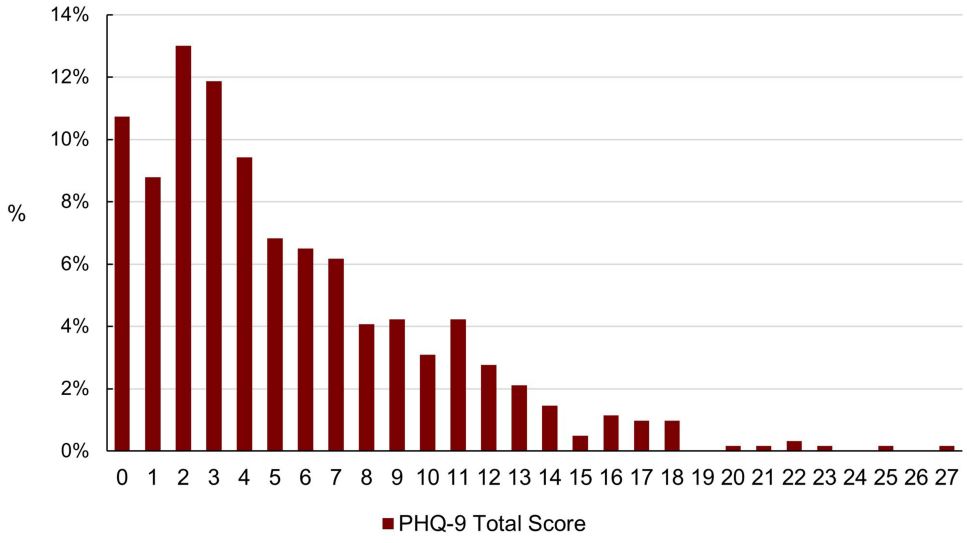

Figure 1 Percent distribution of PHQ-9 total scores (symptoms of depression).

Table 3 Clinical Parameters and Their Associations with Symptoms of Depression - A Linear Regression Model with PHQ-9 as Dependent Variable (Range 0–27)

Dependent Variable: PHQ-9 Score (Range 1–27)	**Univariate**		**Multivariate**	
Independent Variables	**Regression Coefficient (SE)**	**p-value**	**Regression Coefficient (SE)**	**p-value**
Age	−0.01 (0.02)	0.521		
Sex (female vs male)	0.20 (0.39)	0.610		
BMI	0.02 (0.03)	0.517		
FEV_1% predicted	−0.06 (0.01)	< 0.001		
Exacerbations last 12 months	1.35 (0.19)	< 0.001	1.00 (0.17)	< 0.001
Arterial hypertension	0.53 (0.38)	0.158		
Diabetes mellitus	0.70 (0.51)	0.169		
Heart disease	1.71 (0.50)	< 0.001		
Osteoporosis	0.54 (0.59)	0.356		
SGRQ-C - total	0.14 (0.01)	< 0.001		
SGRQ-C - impact	0.14 (0.01)	< 0.001		
SGRQ-C - symptoms	0.09 (0.01)	< 0.001		
SGRQ-C - Activity	0.08 (0.01)	< 0.001		
Cough	1.36 (0.37)	< 0.001		
Phlegm	1.65 (0.37)	< 0.001		
Dyspnea	3.12 (0.45)	< 0.001	2.17 (0.45)	< 0.001
Pain (1–10)	0.80 (0.10)	< 0.001	0.61 (0.10)	< 0.001
Activity per week (1–10)	−0.73 (0.10)	< 0.001		

Table 4 Characteristics of Participants According to General Pain (10-Point Scale - No Pain (1) vs Mild (2–7) to Severe Pain (8–10)

	No Pain n = 276	**Mild Pain n = 336**	**Severe Pain n = 18**	**p-value**
Characteristics				
Age (mean, SD)	66.7 (8.3)	66.8 (8.8)	68.1 (9.2)	0.718
40–59 years (n, %)	48 (17.4)	67 (19.9)	4 (22.2)	0.731
60–69 years (n, %)	117 (42.4)	137 (40.8)	5 (27.8)	
70+ years (n, %)	111 (40.2)	132 (39.3)	9 (50.0)	
Sex, female (n, %)	101 (36.6)	122 (36.3)	13 (72.2)	0.008
BMI (mean, SD)	26.4 (5.5)	26.6 (5.4)	28.3 (5.5)	0.334
Smoking				
Current smoker (n, %)	81 (30.6)	123 (37.4)	5 (29.4)	0.231
Former smoker (n, %)	164 (61.9)	179 (54.4)	9 (52.9)	
Never smoker (n, %)	20 (7.6)	27 (8.2)	3 (17.6)	

(*Continued*)

Table 4 (Continued).

	No Pain n = 276	Mild Pain n = 336	Severe Pain n = 18	p-value
GOLD groups				
A and B (n, %)	220 (79.7)	264 (78.6)	10 (55.6)	0.054
E (n, %)	56 (20.3)	72 (21.4)	8 (44.4)	
FEV_1%-predicted (mean, SD)	54.7 (16.9)	53.9 (16.2)	56.0 (14.7)	0.846
Exacerbations				
0 (n, %)	153 (57.7)	164 (50.3)	6 (33.3)	0.053
1 (n, %)	70 (26.4)	103 (31.6)	5 (27.8)	
≥ 2 (n, %)	42 (15.9)	59 (18.1)	7 (38.9)	
Comorbidities				
Arterial hypertension (n, %)	123 (44.6)	156 (46.4)	11 (61.1)	0.385
Diabetes mellitus (n, %)	35 (12.7)	60 (17.9)	6 (33.3)	0.028
Heart disease (n, %)	38 (13.8)	61 (18.2)	6 (33.3)	0.055
Osteoporosis (n, %)	17 (6.2)	48 (14.3)	8 (44.4)	< 0.001
SGRQ-C				
Total (mean, SD)	33.1 (20.3)	42.8 (21.2)	54.4 (24.8)	< 0.001
Impact (mean, SD)	20.9 (19.7)	31.5 (23.1)	41.8 (25.9)	< 0.001
Symptoms (mean, SD)	45.4 (22.8)	55.0 (22.7)	61.4 (24.3)	< 0.001
Activity (mean, SD)	44.2 (25.3)	52.5 (24.6)	68.1 (25.6)	< 0.001
PHQ-9				
Total (mean, SD)	3.4 (4.1)	6.3 (4.6)	9.4 (7.1)	< 0.001
Symptoms				
Cough – several days a week (n, %)	124 (45.1)	178 (53.6)	12 (70.6)	0.027
Phlegm – several days a week (n, %)	111 (40.4)	165 (49.6)	9 (52.9)	0.064
Dyspnea – several days a week (n, %)	197 (72.2)	281 (84.1)	16 (94.1)	< 0.001
Physical activity (10-point scale, self-reported – 1 bis 10) (mean, SD)	5.5 (2.3)	4.8 (2.0)	4.2 (1.8)	< 0.001

Furthermore, they reported less quality of life using the SGRQ-C (total score and all subscores). Further details are presented in Table 5. Percent distribution of the results of self-reported physical activity using a 10-point scale is presented in Figure 2B.

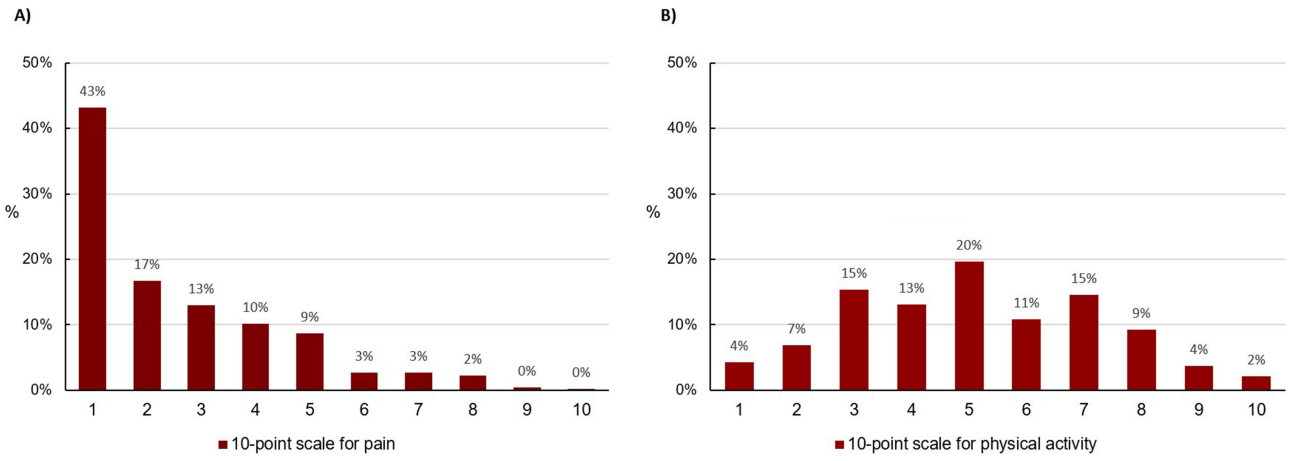

Figure 2 Percent distribution of a self-reported pain (A) and physical activity (B); data from 10-point scales.

Table 5 Characteristics of Participants According to Self-Reported Physical Activity (Impaired vs Preserved)

	Impaired Physical Activity n = 225	Preserved Physical Activity n = 265	p-value
Characteristics			
Age (mean, SD)	68.9 (8.6)	65.0 (8.3)	< 0.001
40–59 years (n, %)	32 (14.2)	58 (21.9)	< 0.001
60–69 years (n, %)	73 (32.4)	132 (49.8)	
70+ years (n, %)	120 (53.4)	75 (28.3)	
Sex, female (n, %)	87 (38.7)	100 (37.7)	0.833
BMI (mean, SD)	26.5 (5.9)	26.5 (5.0)	0.496
Smoking			
Current smoker (n, %)	74 (34.3)	82 (31.9)	0.575
Former smoker (n, %)	120 (55.6)	154 (59.9)	
Never smoker (n, %)	22 (10.2)	21 (8.2)	
GOLD groups			
A and B (n, %)	150 (66.7)	231 (87.2)	< 0.001
E (n, %)	75 (33.3)	34 (12.8)	
FEV_1%-predicted (mean, SD)	49.3 (16.0)	59.5 (15.9)	< 0.001
Exacerbations			
0 (n, %)	87 (39.4)	165 (64.5)	< 0.001
1 (n, %)	73 (33.0)	66 (25.8)	
≥ 2 (n, %)	61 (27.6)	25 (9.9)	
Comorbidities			
Arterial hypertension (n, %)	112 (49.8)	113 (42.6)	0.114
Diabetes mellitus (n, %)	43 (19.1)	34 (12.8)	0.057
Heart disease (n, %)	51 (22.7)	30 (11.3)	< 0.001
Osteoporosis (n, %)	31 (13.8)	24 (9.1)	0.100
SGRQ-C			
Total (mean, SD)	54.9 (18.6)	24.3 (15.5)	< 0.001
Impact (mean, SD)	45.3 (21.3)	12.1 (12.9)	< 0.001
Symptoms (mean, SD)	61.6 (21.5)	39.7 (22.0)	< 0.001
Activity (mean, SD)	64.9 (20.5)	34.7 (22.8)	< 0.001
PHQ-9			
Total (mean, SD)	7.8 (5.0)	3.2 (3.3)	< 0.001
Pain			
Total (mean, SD)	3.1 (2.1)	2.0 (1.6)	< 0.001
Symptoms			
Cough – several days a week (n, %)	130 (58.3)	108 (41.4)	< 0.001
Phlegm – several days a week (n, %)	121 (54.3)	93 (35.5)	< 0.001
Dyspnea – several days a week (n, %)	201 (91.0)	166 (62.9)	< 0.001

In Figure 3 the relationship between self-reported physical activity (10-point scale) and depressive symptoms (total score PHQ-9) is visualized in a box plot. A higher self-reported physical activity was associated with a lower PHQ-9 score suggesting fewer depressive symptoms.

Discussion

In this work, we report real-world data of stable COPD outpatients in Austria, documenting an association of self-reported symptoms of depression and pain.

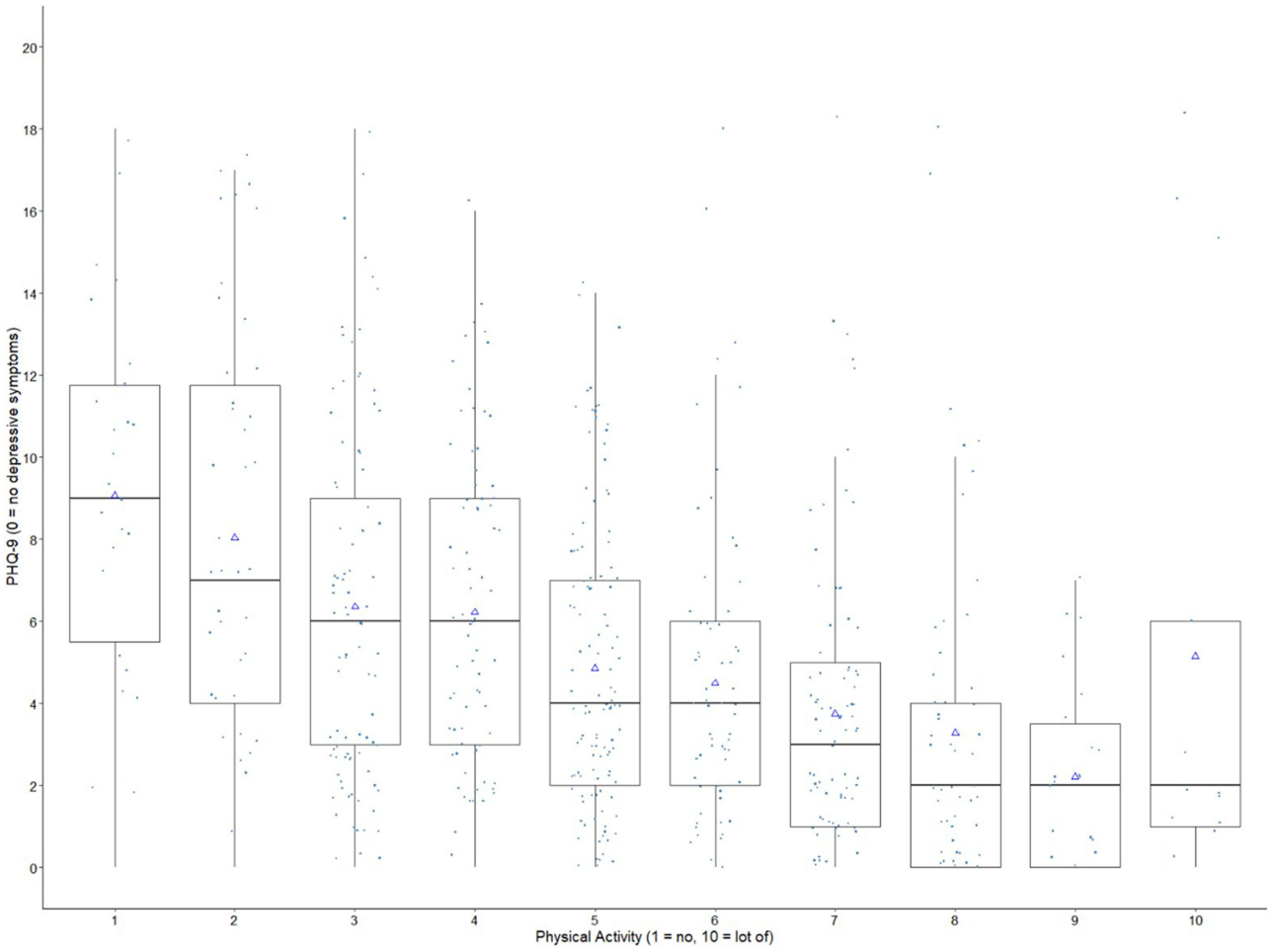

Figure 3 Correlation of symptoms of depression using the total scores of PHQ-9 (0–27) and self-reported physical activity (10-point scale, 1–10); Boxplot: box: 25th percentile, median 75th percentile; triangle: mean; whiskers: 1.5 interquartile range values.

Using the PHQ-9 questionnaire, mild to moderate depressive symptoms were found in 41.5% of COPD patients, symptoms of severe depression in 4.7%. These symptoms were found closely associated with more exacerbations in the previous year, a lower lung function (FEV_1), a higher pain score, and a higher degree of dyspnea (Table 3). In agreement, comparable symptom scores for depression (PHQ-9) were found in other COPD cohorts worldwide, suggesting an increased burden of co-existing depression in COPD patients.[24–27] However, an analysis of the data from the German COPD cohort Cosyconet[24] found an association between total PHQ-9 scores and age, sex and BMI, which we could not observe in our data. Symptoms of anxiety and depression have also been identified as predictors of mortality in the literature.[28–30]

In our cohort only 2.9% of subjects reported severe over-all pain, the remaining patients stated suffering only mild or no pain. Hence, self- reported pain was less likely reported here than other data suggest.[31,32] We speculate that the lower pain scores in our cohort may be due to the selection of patients as only patients with stable disease in an outpatient setting were included. Furthermore, we could not confirm the association between lower FEV_1 and a higher pain score. However, patients who reported more intense pain, tended to present with more exacerbations (Table 4).

Physical activity could be a relevant predictor for exacerbations, quality of life as well as depressive and respiratory symptoms (Table 5). These associations with a lower level of physical activity was also seen in previous publications.[15,33] Moreover, exercise interventions have been effective to improve outcomes in COPD.[34] Furthermore, a similar relationship between depressive symptoms and physical activity (Table 3 and Figure 1) was seen in a meta-analysis by Selzler et al.[9]

Strengths and limitations:

The study used a highly standardized protocol and included COPD patients from all nine Austrian federal states excluding those with a FEV_1/FVC ratio > 0.7. Patient reported outcome included important domains addressing mental and physical well-being as well as disease specific health status (SGRQ-C). Selection of participating study sites was not at random, leaving the possibility of selection bias. The inclusion of COPD patients into the study was left to the investigator's discretion. However, we were not able to address COPD patients, who were either undiagnosed or untreated for their COPD. Population-based random samples indicate that approximately 80% of COPD patients are non-diagnosed with the disease,[35] and these patients experience different burden of disease. Furthermore, due to the cross-sectional design, we were not able to provide any longitudinal data. Due to the ongoing COVID-19 pandemic during the phase of data collection, some variables may have been biased.

Conclusions

In Austria, nearly half of stable COPD outpatients report symptoms indicative of mild to moderate or severe depression, which are associated with older age but not gender or smoking, lower FEV_1, less physical activity, more pain, more respiratory symptoms and exacerbations, and heart disease as the only significant comorbidity. This suggests that depression may be an important therapy target in COPD patients.

Abbreviations

BMI, body mass index; CRF, case report form; COPD, chronic obstructive pulmonary disease; LAMA, long-acting muscarinic antagonist; LABA, long-acting β2-agonist; ICS, inhaled corticosteroid; PHQ-9, Patient Health Questionnaire-9; QoL, quality of life; SGRQ, St. George's Respiratory Questionnaire; SGRQ-C, St. George's Respiratory Questionnaire for COPD patients.

Ethics Approval and Consent to Participate

All participants provided written informed consent to participate in the study. The protocol was approved by the independent ethics committee of the Johannes Kepler University, Linz (vote 1129/2021). This study was conducted in accordance with the Declaration of Helsinki.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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