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Sex-related differences in COPD Assessment Test scores of COPD populations with or without significant anxiety and/or depression

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Background/aim: Sex-related differences have not been thoroughly explored in chronic obstructive pulmonary disease (COPD). We aimed to evaluate possible sex-related differences in COPD Assessment Test (CAT) scores of COPD patients with or without significant anxiety and/or depression.

Materials and methods: Stable COPD patients were prospectively enrolled in the study between July 2013 and April 2014. Levels of anxiety, depression, dyspnea, and health-related quality of life parameters were assessed using specific questionnaires, including the CAT and others. Demographic and clinical data were recorded and physiological tests were performed. All the data were compared to determine any sex-related differences.

Results: A total of 128 COPD patients (86 men, 42 women, mean age: 60.5 ± 9.3 years) were included. The women were significantly younger and had lower pack-years of cigarette smoking, and higher biomass smoke exposure, but displayed similarly severe COPD as compared to men. Beck anxiety (13.5–11) and Beck depression (15–11) inventory results were significantly higher in women than men ($P = 0.04$, $P = 0.01$). No statistically significant difference was found between the sexes in terms of CAT score, Modified Medical Research Council score, or COPD stage parameters ($P > 0.05$).

Conclusion: Female patients have higher levels of depression and anxiety scores but present the same CAT scores related to COPD severity as compared to men.

Key words: Sex, chronic obstructive pulmonary disease, COPD Assessment Test, depression, anxiety

1. Introduction

Sex-related differences have not been thoroughly explored in chronic obstructive pulmonary disease (COPD). The available data on symptom differences in female patients with COPD are quite limited. Most of the studies have not included a sufficient number of women within their scope to allow for accurate comparisons. Recent studies have suggested that while the overall prevalence and incidence of COPD are higher in men (1–3), the incidence of COPD in younger age groups (i.e. age 55–59) is now much higher in women (3). Women may be more susceptible to develop COPD and display more severe symptoms and activity intolerance (4). In addition, there are inadequate data available on the COPD Assessment Test (CAT) in female patients with COPD.

Psychiatric disorders are highly prevalent in patients with COPD (5). In general, psychiatric disorders are more common in women than in men (6,7). The extent to which women with COPD suffer from greater psychiatric and psychological morbidity remains unknown. Furthermore, there are limited data available about the impact of psychiatric disorders on the quality of life (QoL) and COPD severity in female patients in comparison to male patients (8).

The CAT is a short, simple questionnaire for assessing and monitoring COPD. It has good measurement properties, is sensitive to differences in state, and provides a valid, reliable, and standardized measure of COPD health status with worldwide relevance (9). This study primarily aimed to evaluate the possible CAT differences between male and female patients with or without a significantly high level of anxiety and/or depression by employing the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011 strategy (10), and finally to establish a correlation between psychological aspects, symptoms, functional parameters, and QoL.

2. Materials and methods

This was a prospective observational study carried out between July 2013 and April 2014. The study was approved

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by the relevant ethics and review boards, and written informed consent from all participants was obtained upon the commencement of their assessment. Stable COPD patients attending the respiratory outpatient clinic of the Chest Diseases Education and Training Hospital were included in the study based on the following criteria: documented COPD according to the GOLD guideline definitions as a forced expiratory volume in 1 s (FEV_1) of less than 80% of the predicted value after bronchodilator use and a ratio of FEV_1 to forced vital capacity (FVC) of 0.7 or less after bronchodilator use (10), as confirmed by a chest physician; cumulative current or past cigarette smoking of at least 10 pack-years (obtained by multiplying the average number of packs smoked per day by the number of years smoked) or biomass smoke exposure (exposure to household air pollution from biomass burning); and age <85 years. The clinical status of all the patients was stable on the day of their interview (no acute exacerbation in the last 4 weeks).

Exclusion criteria were as follows: documented and potentially confounding conditions posing greater risk for morbidity than COPD (e.g., symptomatic cancer), receiving treatment for anxiety and depression at the time of the assessment, acute coronary event (e.g., myocardial infarction) or invasive surgery within the past 6 months, apparent cognitive deficits, hospitalization in long-term health care centers that treat more severe and disabled patients, or physical inability to complete the 6-min walking test or pulmonary function tests.

The patients' self-reported respiratory symptoms, medications, smoking history, occupational exposure, exacerbation rates over the past 12 months, and coexisting medical conditions were documented at the beginning of the study. Comorbid diagnoses were established using the clinical history and physical examination findings during the visit and were supported by a review of the available medical records.

In this prospective study, levels of anxiety, depression, dyspnea, and health-related QoL were assessed in all cases via a face-to-face interview employing the Turkish versions of specific questionnaires stated specifically below. Moreover, all patients underwent physiological tests (spirometry by Elite DL, Medgraphics, USA), such as a 6-min walking test as defined by American Thoracic Society (ATS) standards (11), and pre- and post-Borg scores were recorded according to the study of Borg (12). The body mass index (BMI, kg/m^2) and carbon monoxide (CO) levels in the exhaled breath (to prove the smoking status) were evaluated. CO breath levels were measured using a Pico Smokerlyzer device (Bedfont Scientific Ltd., UK) following the manufacturer's recommendations. The COPD patients were grouped into 4 severity subgroups according to the GOLD 2011 classification, based on FEV_1 values, individual patient histories of exacerbation rates, and Modified Medical Research Council (mMRC) dyspnea scale/CAT scores (A, B, C, D) (10).

2.1. Psychological measurements and health-related QoL questionnaires

2.1.1. QoL

The CAT is a recently introduced, patient-completed QoL assessment instrument that contains 8 questions that cover the impact of COPD symptoms (9). The scoring scale ranges from 0 to 40 points and indicates the impact of the disease. Scores in the intervals of 0–10, 11–20, 21–30, and 31–40 represent mild, moderate, severe, and very severe clinical impact, respectively. The validity and reliability of the Turkish version of the CAT have already been established (13).

2.1.2. Dyspnea

The Medical Research Council dyspnea scale was developed to help physicians establish clinical grades of breathlessness for their patients with emphysema (14). The modified version of this scale, the mMRC scale, has been in use for many years for grading the effect of breathlessness on daily activities. mMRC scores were well correlated with dyspnea index and lung function. The mMRC dyspnea scale consists of 5 statements about perceived breathlessness: from grade 0 ("only get breathless with strenuous exercise") up to grade 4 ("I am too breathless to leave the house") (14–16). The Turkish version of the scale was used in the study.

2.1.3. Anxiety

The Beck Anxiety Inventory (BAI) consists of 21 questions about how the subject has been feeling in the last week, expressed as common symptoms of anxiety (such as numbness and tingling, sweating independent of heat, and fear of the worst) (17). Validity and reliability of the Turkish version of the BAI have been demonstrated (18). The BAI was designed for an age interval of 17–80 years. Each question contains the same set of 4 possible alternatives: "not at all" (0 points), mildly ("It did not bother me much", 1 point), moderately ("It was very unpleasant, but I could stand it", 2 points), and severely "I could barely stand it", 3 points). The BAI has a maximum score of 63 and scores falling in the intervals of 0–7, 8–15, 16–25, and 26–63 represent minimal, mild, moderate, and severe levels of anxiety, respectively (17).

2.1.4. Depression

The Beck Depression Inventory (BDI) consists of 21 questions. Possible scores range from 0 to 63: the higher the score, the higher the level of depression. This instrument is of particular relevance since it has been widely used for normal persons as well as in various patient groups, including patients suffering from chronic respiratory diseases, making considerable validation of the

data available, as well as in a large number of comparison groups to aid in the interpretation of the results (19,20). Scores falling in the intervals of 0–9, 10–16, 17–29, and 30–63 represent minimal, mild, moderate, and severe levels of depression, respectively. It has been demonstrated that the Turkish version of the BDI is reliable and valid (21,22).

2.2. Statistical analysis

All analysis was conducted by using SPSS 17.0 (SPSS, Chicago, IL, USA). Normality distribution was tested by the Shapiro–Wilk test for numeric variables. Categorical variables were described by frequencies and percentages, continuous variables with normal distribution were presented with means and standard deviations, and numeric variables without normal distribution were presented by medians and minimum–maximum values. The chi-square test (or Fisher's exact test or exact test) was used to define relationships between two categorical variables and the Jonckheere–Terpstra test was chosen when both categorical variables were ordinal. Two independent means were compared by Student's t-test, two independent medians were compared by Mann–Whitney U test, and more than two independent medians were compared by Kruskal–Wallis test with a post hoc comparison by Dunn's test. Logistic regression analyses were conducted to identify independent factors effecting BAI and BDI scores. $P < 0.05$ was chosen to state statistically significant differences between investigated parameters.

3. Results

A total of 128 patients with COPD (86 men, 67.2%; and 42 women, 32.8%) in stable condition were included in the study. The mean age of the patients was 60.5 ± 9.3 years. The sex-related differences according to demographic data are presented in Table 1. No statistically significant difference was observed between male and female patients with COPD according to the level of education ($P = 0.2$) and accompanying diseases ($P = 0.8$). In comparison to men, the women with COPD were significantly younger (56.3 ± 9.3 years vs. 62.7 ± 8.7 years, $P < 0.001$). The men and women showed a significant history of smoking at 98.8% and 80.9%, respectively ($P < 0.001$). While women had fewer pack-years of cigarette smoking than men (median pack-years 35 (0–90) vs. 48 (0–172), $P < 0.001$), they had similarly severe COPD (GOLD classification D: 57.1% for women and 46.5% for men, $P = 0.051$) and presented higher biomass smoke exposure (14.3% vs. 2.3%, $P = 0.09$). We found that the level of regular medication was less than the level displayed by men (73.8% vs. 88.2%, $P = 0.04$). The distribution of medication was found to be similar between the sexes (Table 1).

Differences between spirometric values and the distribution of the patients according to the new GOLD classification (A, B, C, D) are presented in Table 2. No statistically significant difference was observed between the sexes in terms of CAT score, mMRC score, hospitalization and number of attacks in the last 1 year, and COPD stage parameters ($P > 0.05$), as shown in Table 2. The 6-min walk distance was significantly lower in female patients (411.4 (58–510) m vs. 451.2 (28–598) m, $P = 0.017$). The pre-Borg and post-Borg scale values were observed to be higher at a statistically significant level in women ($P < 0.001$ and $P = 0.005$, respectively), as shown in Table 2. The BAI (13.5–11) and BDI (15–11) results were also significantly higher in women than in men ($P = 0.042$, $P = 0.011$, respectively).

We observed that those with CAT scores of <10 displayed statistically lower BAI scores and BDI scores, respectively ($P < 0.001$ and $P < 0.001$). Furthermore, the number of exacerbations and severity of COPD were significantly higher in the group that displayed high CAT scores ($P = 0.02$, $P < 0.001$) (Table 3). The patients were divided into 4 groups as minimal, mild, medium, and severe, as mentioned in Section 2, according to BAI and BDI scores. In patients with COPD stage B and D, and those with CAT scores of >10, anxiety and depression scores were observed to be severe ($P < 0.001$, $P < 0.001$ for BAI and $P < 0.001$, $P < 0.001$ for BDI, respectively). We also found that BAI scores increased inversely proportionally to age ($P = 0.001$), and BDI scores increased at a statistically significant level as the mMRC score and 6-min walking distance decreased and as the number of exacerbations in the last 1 year increased ($P = 0.04$, $P = 0.004$, $P = 0.007$).

In multivariate analysis we found that sex and COPD stage were independent factors affecting BAI scores ($P = 0.024$, $P = 0.003$). Age, number of hospitalizations, and CAT score were independent factors affecting BDI scores ($P = 0.015$, $P = 0.015$, $P = 0.047$) (Table 4).

4. Discussion

COPD is one of the most common chronic conditions worldwide and is now the third-leading cause of death in the United States (23). Although COPD is known to be a predominantly male disease, over the past 20 years, COPD prevalence and mortality have increased more rapidly among women than men (24). Recent evidence suggests that men and women differ in their susceptibility to COPD risk factors, which is possibly related to biologic and hormonal mechanisms (25). In addition, the clinical presentation of COPD, comorbidities, and other factors vary between the sexes. For this reason, we investigated available data to determine the effect of sex in association with smoking habits, symptoms, spirometry differences, quality of life (CAT and mMRC), and the prevalence of anxiety and depression in a COPD population divided into subgroups according to combined assessment.

Table 1. Patient characteristics according to sex.

	Total n = 128	Female n = 42 (33%)	Male n = 86 (67%)	P
Age (years, mean ± SD)	60.5 ± 9.3	56.3 ± 9.3	62.7 ± 8.7	<0.001[1]
Literacy (n, (%))				
Illiterate	11 (8.6)	4 (9.5)	7 (8.1)	0.750[4]
Literate	117 (91.4)	38 (90.5)	79 (91.9)	
Education (n, (%))				
Primary school	44 (37.6)	16 (42.1)	28 (35.4)	0.200[3]
Secondary school	19 (16.2)	8 (21.1)	11 (13.9)	
High school	46 (39.3)	10 (26.3)	36 (45.6)	
University	8 (6.9)	4 (10.5)	4 (5.1)	
BMI (mean ± SD)	25.7 ± 4.2	26.6 ± 4.5	25.3 ± 3.9	0.081[1]
Smoking (n, (%))				
Nonsmoker	9 (7.0)	8 (19.1)	1 (1.2)	<0.001[3]
Ex-smoker	82 (64.1)	19 (45.2)	63 (73.2)	
Current smoker	37 (28.9)	15 (35.7)	22 (25.6)	
Smoking quantity (packs/year) (median, min–max)	41 (0–172)	35 (0–90)	48 (0–172)	<0.001[2]
Biomass smoke exposure (n, (%))				
Absent	120 (93.7)	36 (85.7)	84 (97.7)	0.015[4]
Present	8 (6.3)	6 (14.3)	2 (2.3)	
Comorbid disease (n, (%))				
Absent	87 (68.0)	29 (69.0)	58 (67.4)	0.855[3]
Present	41 (32.0)	13 (31.0)	28 (32.6)	
Drug usage (n, (%))				
Irregular	21 (16.5)	11 (26.2)	10 (11.8)	0.040[3]
Regular	106 (83.5)	31 (73.8)	75 (88.2)	
Medication (n, (%))				
ICS + LABA	15 (11.7)	5 (11.9)	10 (11.6)	0.057[5]
LAMA	14 (10.9)	3 (7.1)	11 (12.8)	
SABA/SAMA	8 (6.3)	6 (14.3)	2 (2.3)	
Multiple drugs	91 (71.1)	28 (66.7)	63 (73.3)	
1: Student's t-test; 2: Mann–Whitney U test; 3: chi-square test; 4: Fisher's exact test; 5: exact test.				

BMI: Body mass index, ICS: inhaled steroids, LABA: long-acting β2 agonists, LAMA: long-acting antimuscarinic agents, SABA: short-acting β2 agonists, SAMA: short-acting antimuscarinic agents.

Cigarette smoking is the most important risk factor for COPD across the developed world. In the National Emphysema Treatment Trial study, women had fewer pack-years of cigarette smoking than men, but displayed similarly severe COPD (26). In this study, we have demonstrated that although women smoked fewer cigarettes than men, they displayed similar COPD severity. A possible reason for this could be that women might have higher dose-dependent tobacco susceptibility. Women have smaller lungs and airways than men; therefore, the same amount of tobacco smoke results in a greater exposure. In addition, we found that women were diagnosed with COPD at a

Table 2. Sex-related differences according to pulmonary function tests, exacerbations, COPD stage, and quality of life parameters.

	Total n = 128	Female n = 42 (33%)	Male n = 86 (67%)	P
FEV_1% (mean, SD)	47.1 ± 14.9	45.2 ± 13.7	48.0 ± 15.5	0.319[1]
FVC% (mean, SD)	63.7 ± 16.5	62.2 ± 15.7	64.4 ± 17.0	0.483[1]
FEV_1/FVC% (median, min–max)	63 (27–74)	63 (36–70)	63 (27–74)	0.998[2]
6-MWT (median, min–max)	437.4 (28–598)	411.4 (58–510)	451.2 (28–598)	0.017[2]
Number of exacerbations (median, min–max)	0 (0–9)	1 (0–9)	0 (0–4)	0.114[2]
Number of hospitalizations (median, min–max)	0 (0–3)	0 (0–3)	0 (0–3)	0.753[2]
Pre-BORG score (median, min–max)	1 (0–3)	1 (0–3)	0 (0–3)	<0.001[2]
Post-BORG score (median, min–max)	2 (0–10)	3 (0–10)	1 (0–10)	0.005[2]
Presaturation (median, min–max)	96 (84–99)	96 (84–98)	96 (84–99)	0.099[2]
Postsaturation (median, min–max)	95 (80–99)	95 (85–99)	95 (80–99)	0.675[2]
COPD stage (n, (%))				
A	18 (14.0)	1 (2.4)	17 (19.8)	0.051[3]
B	33 (25.8)	11 (26.2)	22 (25.6)	
C	13 (10.2)	6 (14.3)	7 (8.1)	
D	64 (50.0)	24 (57.1)	40 (46.5)	
mMRC score (n, (%))				
0	4 (3.1)	0 (0)	4 (4.7)	0.098[4]
1	45 (35.2)	11 (26.2)	34 (39.5)	
2	53 (41.4)	23 (54.8)	30 (34.9)	
3	26 (20.3)	8 (19.0)	18 (20.9)	
4	0 (0)	0 (0)	0 (0)	
CAT score (median, min–max)	14 (0–90)	15 (8–40)	13.5 (0–90)	0.050[2]
BAI score (median, min–max)	12 (0–50)	13.5 (0–50)	11 (0–41)	0.042[2]
BDI score (median, min–max)	13 (0–43)	15 (2–43)	11 (0–43)	0.011[2]
1: Student's t-test; 2: Mann–Whitney U test; 3: chi-square test; 4: exact test.				

6-MWT: Six-minute walk test distance, CAT: COPD Assessment Test, mMRC: modified Medical Research Council dyspnea scale, BAI: Beck Anxiety Inventory, BDI: Beck Depression Inventory.

younger age in comparison to men and displayed higher levels of biomass smoke exposure than men. This was generally an indoor biomass smoke exposure because 76% of the women were housewives (never worked).

The CAT is a COPD-specific questionnaire that assesses health-related QoL. It has been demonstrated to be reliable and valid. However, there are limited data available on the CAT regarding how it varies between the sexes. Recent studies have shown that women have poorer QoL than men and face higher levels of depression and anxiety (27,28). In this study, female patients had higher levels of depression and anxiety scores compared to men. However, when we considered other QoL parameters such as CAT and mMRC scores, we found that these were related to disease severity but were not related to sex. We used both CAT and mMRC scores in order to compare these 2 QoL tests in female patients with COPD. No significant difference was determined between sexes in terms of CAT score, mMRC score, and COPD stage parameters. Therefore, we can suggest that female patients with the same level of COPD severity compared to men have higher anxiety and depression scores than men; however, these scores did not seem to have an effect on the CAT score.

It was observed that anxiety and depression scores were lower in patients with CAT scores <10. Moreover, the number of exacerbations and the severity of COPD

Table 3. Comparison of parameters between low and high CAT scores.

	CAT score <10 n = 30 (23.4%)	CAT score ≥10 n = 98 (76.6%)	P
Age (years, mean ± SD)	60.0 ± 8.6	60.8 ± 9.6	0.684[1]
Smoking (n, (%))			
Nonsmoker	0 (0)	9 (9.2)	0.029[3]
Ex-smoker	25 (83.3)	57 (58.2)	
Current smoker	5 (16.7)	32 (32.6)	
Smoking quantity (packs/year) (median, min–max)	42.5 (10–104)	41 (0–172)	0.166[2]
Biomass smoke exposure (n, (%))			
Absent	30 (100)	90 (91.8)	0.197[4]
Present	0 (0)	8 (8.2)	
FEV_1% (median, min–max)	51.5 (26–73)	46 (17–76)	0.078[2]
FVC% (median, min–max)	64 (33–85)	61 (33–112)	0.426[2]
FEV_1/FVC% (median, min–max)	63.5 (51–74)	63 (27–74)	0.055[2]
6-MWT (median, min–max)	469 (210–598)	434.5 (28–582.4)	0.003[2]
Number of exacerbations (median, min–max)	0 (0–3)	1 (0–9)	0.025[2]
Number of hospitalizations (median, min–max)	0 (0–2)	0 (0–3)	0.555[2]
COPD stage (n, (%))			
A	16 (53.3)	2 (2.1)	<0.001[5]
B	2 (6.7)	31 (31.6)	
C	9 (30.0)	4 (4.1)	
D	3 (10.0)	61 (62.2)	
mMRC score (n, (%))			
0	3 (10.0)	1 (1.0)	<0.001[5]
1	16 (53.3)	29 (29.6)	
2	11 (36.7)	42 (42.9)	
3	0 (0)	26 (26.5)	
4	0 (0)	0 (0)	
BAI score (median, min–max)	8 (0–20)	12 (0–50)	<0.001[2]
BDI score (median, min–max)	7 (0–22)	15 (2–43)	<0.001[2]
1: Student's t-test; 2: Mann–Whitney U test; 3 chi-square test; 4: Fisher's exact test; 5: Jonckheere–Terpstra test.			

6-MWT: Six-minute walk test distance, CAT: COPD Assessment Test, mMRC: modified Medical Research Council dyspnea scale, BAI: Beck Anxiety Inventory, BDI: Beck Depression Inventory.

were significantly higher in the high CAT score group, but this significant difference was not observed in terms of mMRC score groups. Although men and women differ in the outcomes of acute exacerbations and hospitalizations due to COPD, similar rates for acute exacerbations and hospitalizations were found (29).

When we categorized anxiety and depression scores as minimal, mild, moderate, and severe, more symptomatic patients with GOLD stage B and D showed higher levels of depression and anxiety compared to GOLD stage A and C. With the new GOLD classification, we think that it will be easier to predict psychiatric comorbidities according to

Table 4. Independent risk factors affecting anxiety and depression scores.

		OR	95% CI		P
			Lower	Upper	
BAI	Female	4.588	1.227	17.151	0.024
	Education				0.002
	Secondary school	57.290	6.787	483.565	<0.001
	High school	13.427	2.519	71.568	0.002
	University	1.317	0.047	37.086	0.872
	FVC	1.135	1.060	1.216	<0.001
	Presaturation	1.481	1.091	2.011	0.012
	COPD stage C + D	20.835	2.862	151.668	0.003
BDI	Age	0.929	0.875	0.985	0.015
	BMI	0.874	0.771	0.990	0.035
	Regular drug usage	0.226	0.062	0.825	0.024
	FEV_1%/FVC%	0.927	0.878	0.979	0.006
	Number of hospitalizations	2.622	1.210	5.682	0.015
	Post-Borg score	1.241	1.024	1.503	0.027
	CAT score ≥10	5.348	1.019	28.063	0.047

BAI: Beck Anxiety Inventory, BDI: Beck Depression Inventory, BMI: body mass index.

symptom-based groups. We demonstrated that younger patients have higher levels of anxiety compared to older ones. This is quite predictable because young patients have more difficulties in dealing with the symptoms. It was also observed that the patients with higher depression scores have poorer mMRC scores and 6-min walk distances, and experienced frequent exacerbations. We can say that symptomatic COPD patients have difficulty in dealing with the disease and experience more depressing symptoms.

In conclusion, since the CAT displays good performance and is a simple and quick tool to assess the health-related QoL in patients with COPD, there is a growing interest in its use in clinical practice. We attempted to evaluate the use of this questionnaire for female patients with COPD and also aimed to compare sex-related differences in terms of QoL, psychiatric, and psychological parameters. The female patients compared to the males had higher levels of depression and anxiety levels but displayed the same CAT scores in relation to COPD severity.

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