ORIGINAL ARTICLE

Female sexual dysfunction in chronic obstructive pulmonary disease

Disfunción sexual femenina en la enfermedad pulmonar obstructiva crónica

Müfide Arzu Özkarafakılı[1] **Cemil Kutsal** [2]

1 University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital, Department of Chest Diseases, Istanbul, Turkey , **2** University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital, Department of Urology, Istanbul Turkey

Abstract

Background:

The sexual life of women with chronic obstructive pulmonary disease (COPD) can be affected by breathing difficulties, decreased in functional status, depressive mood and fatigue.

Objective:

To evaluate the sexual dysfunction in female COPD patients and the possible explanatory mechanisms or correlations between these conditions.

Methods:

The study included 70 female patients with COPD aged between 36-65 and 70 age-matched controls. All the subjects completed questionnaires for the Female Sexual Functional Index (FSFI), BECK depression inventory and, spirometry.

Results:

Statistically significant sexual dysfunction was noted in COPD patients compared to the non-COPD group ($p<0.001$). BECK depression inventory scores of the COPD patients were also significantly lower ($p<0.001$). no correlation between FSFI and BECK depression scores in 'patients' characteristics (r=-0.055, p=0.651). No significant difference was found in age, forced expiratory volume (FEV)1%, and exacerbation history of the previous year according to severity of depression ($p>0.005$). In linear regression analysis determining depression, no statistically significant factor was found among age, number of comorbidities, and FEV1/ forced vital capacity (FVC) % predicted ($p>0.05$). In multivariable analysis, only fatigue during intercourse was found to be a statistically significant factor in predicting sexual dysfunction among factors like age, presence of comorbidities, duration of the disease, smoking status, FEV1%, m MRCpoints, 6-minutes walk test, BECK depression scores (p=0.008).

Corresponding author:

Müfide Arzu Özkarafakılı. University of Health Sciences, Sisli Hamidiye Etfal Training and Research Hospital, Department of Chest Diseases, Istanbul, Turkey. **Email: aaarzup@yahoo.com**

Conclusions:

Sexual dysfunction is reported in many COPD females and seems to be related not to spirometric measures or exercise capacity but to fatigue. Depression is also a common comorbidity, of which both disorders are often neglected.

Resumen

Antecedentes:

La vida sexual en mujeres con enfermedad pulmonar obstructiva crónica (EPOC) es afectada por dificultades respiratorias, disminución del estado funcional, estado de ánimo depresivo y fatiga.

Objetivo:

Evaluar la disfunción sexual en mujeres con EPOC y posibles mecanismos explicativos de esas dos condiciones.

Métodos:

Participaron 70 pacientes mujeres con EPOC, rango edad 36-65 años y 70 controles emparejados por edad. Todos los sujetos respondieron un cuestionario para el índice funcional sexual femenino e inventario de depresión de BECK, mas una espirometría.

Resultados:

Se observó disfunción sexual significativa en las pacientes con EPOC comparado con el grupo sin EPOC. Las puntuaciones del inventario de depresión BECK fueron significativamente inferiores a las del grupo control. No hubo correlación entre las puntuaciones del FSFI y la depresión BECK con las características de las "mujeres" (r=-0.055). No se encontraron diferencias significativas en edad, FEV1% y antecedentes de exacerbación del año anterior según la gravedad de la depresión. En la regresión lineal para determinar la depresión, no hubo ningún factor estadísticamente significativo entre edad, número de comorbilidades y FEV1/FVC% predicho. En el multivariado, sólo la fatiga durante el coito resultó ser un factor significativo para predecir la disfunción sexual entre factores como edad, presencia de comorbilidades, duración de la enfermedad, hábito tabáquico, FEV1%, m MRCpoints, prueba de la marcha de 6 minutos y puntuaciones de depresión de BECK.

Conclusiones:

La disfunción sexual parece no estar relacionada con las medidas espirométricas o la capacidad de ejercicio, pero si con la fatiga. La depresión es una comorbilidad frecuente, de la que a menudo se descuidan ambos trastornos.

Remark

1) ¿Why was this study conducted?

To examine the sexual dysfunction in female patients with COPD.

2) ¿What were the most relevant results of the study?

Female sexual dysfunction in patients with COPD seems to be related not to spirometric measures or exercise capacity but to fatigue.

3) ¿What do these results contribute?

In contrary to the published literature data, female sexually dysfunction in COPD is not related only with the spirometric measurements.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a well-known cause of chronic morbidity and mortality worldwide [1]. It is a common, preventable and treatable disease but a significant public health problem with its increasing burden on the population because of the continuing exposure to COPD risk factors [2]. There is limited data explaining the heterogeneous clinical features of COPD which makes it not taken seriously enough among communities [3]. A growing body of research suggests that young people may develop COPD due to environmental factors or predisposing circumstances other than tobacco smoking [4]. From this aspect, the increasing rates of female patients with COPD and the impact of the disease on their quality of life draw particular attention. That opens new windows for realizing COPD as a clinical context far beyond a lung disease. Airflow obstruction is the characteristic of this progressive disease, demonstrated in the spirometry test [1]. Dyspnea, chronic cough with or without sputum production, wheezing and fatigue are the major complaints of COPD patients [5]. Shortness of breath inevitably limits physical activity and leads to health status impairment [1]. Global Initiative for Chronic Obstructive Lung Disease (GOLD) states in its latest report that not only spirometric grading or symptom burden reflect the severity of COPD, but fatigue, exacerbation history of the previous year, and the co-existing diseases constitute the clinical aspect of this complex disease [1]. World Health Organization (WHO) defines sexual health as a state of mental, social and physical well-being about sexuality and sexual relationships [6]. Sexual function is a part of the quality of life, and breathlessness, fatigue, and physical incompetence have adverse effects on the sexual activity of both COPD patients and their partners [7]. However, patients often do not prefer talking about their sexual life with doctors, and the physicians do not ask about these issues, which extend to unawareness of these problems. Since female sexual dysfunction is usually reported confidentially, it is not widely known and underestimated. Patients with COPD frequently have other comorbidities which influence their clinical condition as well [1]. Anxiety and depression often accompany COPD, which contributes to disability in sexual functions[8]. The study's aims were to evaluate the sexual dysfunction in female COPD patients and the possible explanatory mechanisms or correlations between this condition and the particular context of COPD.

Material and Methods

This study comprised female patients with an established diagnosis of COPD according to GOLD guidelines which were followed up by Chest Diseases Outpatient clinic for at least two years and age matched non-COPD females as a comparison group [1]. The G*Power Version 3.1.6 program calculated the sample size with the assumptions: effect size = 0.5, power 90%, sample size for the case group =70 and sample size for the control group =70.

Women over 18 ages, sexually active and voluntarily accepted to participate in the study were included. In line with the previous studies, the conditions that might affect sexual life were the exclusion criteria of the study: age of 65, pregnancy or lactation period, having gynecological disorders (in whom hormone therapy were administered), mastectomy or total hysterectomy, diagnosis of psychiatric or neurological diseases, malignancies, uncontrolled cardiovascular or renal diseases [8-11]. Patients with multiple comorbidities were included.

The study was conducted in a single center between December 2022 and February 2023, after the ethics committee's approval and in compliance with the criteria of the Declaration of Helsinki. All the participants were informed that their information would be kept confidential and provided consent.

The detailed medical examination of the COPD patients, which includes demographic data, co-existing diseases, partnership status, smoking habits, education, marital status, employment, residence area, duration of COPD, exacerbation history of the previous year, treatment details of inhalation therapy, requirement of noninvasive mechanical ventilation or long-term oxygen treatment at home are all recorded.

Spirometry was performed by a spirometry technician using the MIR Spirolab II device. The forced expiratory volume in the first second (FEV_1), the forced vital capacity (FVC) and FEV_1/FVC ratio were measured. We followed the American Thoracic Society (ATS) criteria and used the lower limit of normal (LLN) as the cutoff for the adults [12]. After the initial assessment, we classified the severity of airflow obstruction, which was based on post-bronchodilator FEV_1% predicted as follows: GOLD 1 (mild) FEV_1 >80%, GOLD 2 (moderate) 50% <FEV_1<80%, GOLD 3 (severe) 30%<FEV_1<50%, GOLD 4 (very severe) FEV_1<30%.

COPD assessment test (CAT) is questioning COPD patients about the symptoms; "cough, sputum production, chest tightness, fatigue and feeling confident in leaving home" with a score from 0 to 40, in which a high score indicates high severity of COPD. We used the study's validated Turkish form of the CAT scale [13].

Modified Medical Research Council (mMRC) is a dyspnea scale which is in the form that rates between 0 to 4. mMRC is assessing the perception of dyspnea on the basis of questioning several physical activities in which grade 4 indicates very severe dyspnea of the COPD patient [1].

Afterwards, combining the spirometric grading system by levels of symptoms and exacerbation history, we categorized the COPD patients according to groups as GOLD A, B, E; GOLD A; symptom score mMRC 0-1, CAT <10 and exacerbation history 0 or 1 which requires no hospital admission, GOLD B; symptom score mMRC >2, CAT >10 and exacerbation history 0 or 1which requires no hospital admission, GOLD E; any symptom score with an exacerbation history >2 moderate exacerbations or >1exacerbations which requires hospitalization (1). Six-minute walk test (6MWT) is associated with the daily physical activity of the individuals which is a standardized and an objective test for evaluating cardiopulmonary and musculoskeletal functions [14]. A physician supervised 6MWT, by walking along a 30 meters flat corridor as quick as the patient could successfully manage. The distance walked by the patient within 6 minutes was recorded and respiratory rate, arterial blood pressure, heart beats are checked before and after the 6MWT has been done. The 6MWT was performed as it was described by ATS criteria also [14].

BODE is a multidimensional scoring system (B; body mass index O; airflow obstruction measured by FEV_1 D; dyspnea evaluated by mMRC E; exercise capacity measured by 6MWT) which is used as a predictor of severity in COPD patients [15]. We calculated BODE index with the points given from 0 to 3 for the abovementioned parameters. O is the lowest and 3 is the maximal value and the score of 7-10 indicates reduced functional capacity and a worse prognosis [13].

Since depression is a frequent and disabling manifestation of COPD, it is essential to conduct proper screening for diagnosing depression. BECK Depression Inventory is a self-report questionnaire which is consisted of 21-items that evaluates the severity of 'subjects' depression [16]. The participants select the answer which reflects their mood in the last two weeks. They are measured on a 0 to 3 on 4 points scale, with higher scores indicate more severe depression (10-16 mild, 17-29 moderate, 30-63 severe).

Female Sexual Function Index (FSFI) is a standardized, widely used self-evaluation tool, questioning and assessing the female sexual functions quantitatively [17]. We used the validated form of the Turkish version of FSFI in our study for the participants. The physician from the Department of Urology supervised the subjects while answering the survey. It comprises 6 domains: desire, arousal, lubrication, orgasm, sexual satisfaction, pain. In FSFI scoring system while score of zero means that the patient had no sexual activity in the past four weeks, score 2 corresponds to positive sexual activity in the previous four weeks. For sexual dysfunction, a cutoff score on the FSFI is 26.55.

The participants of the study, outcome analyzers and the supervising physicians who were administering the tests and questionnaires were all blind to each other throughout the study. The spirometry measures, BECK Depression Inventory and FSFI scores were compared between females with COPD and age matched comparison group of individuals without COPD.

Statistical analysis

The data were evaluated using Statistical Package for Social Sciences software (SPSS 15.0 for Windows). Descriptive statistics, numbers and percentages were given for categoric variables and numerical variables were given as mean, standard deviation, minimum, maximum, and median. Chi-square test was used to compare categorical data between groups. Since continuous variables were not normally distributed, comparison of two independent groups were made with Mann Whitney U test and comparison of more than two independent groups were made with Kruskal Wallis test. The relations between numerical variables were analyzed by Spearman correlation analysis since the parametric test condition was not met. Multivariate logistic regression analysis was performed for determining factors analysis. $P<0.05$ was accepted statistically significant.

Results

Seventy female patients with COPD and 70 age-matched female individuals without COPD have been included in the study. The demographic and disease characteristics of the patient group were demonstrated in Table 1. The average age of the COPD patients was 53.51 ±6.99. Ischemic heart disease and diabetes mellitus (25.7%) were the most common comorbidities, and 12.9% of the patients had multiple comorbidities. 42.9% were current smokers whereas 18.6% quit smoking. 57.4±12.2 was the mean % predicted value for FEV_1 in pulmonary function test. The mean score assessing the severity of dyspnea in the mMRC scale was 1.87±0.98 units, and 96,3±1,2 % was the average for oxygen saturation.

The mean distance 378.8 ±27.5 meters in 6MWT were covered as are showed the exercise capacity of COPD patients and 65.7% of the patient group were in moderate stages according to spirometric grading. The mean value for the duration of the disease was 10.74 ± 5.66 years. 42.9% of the COPD patients were categorized as GOLD E and 40% were as GOLD B in COPD combined assessment, which comprised symptom scores and exacerbation history of the previous year of the patients as defined in GOLD 2023 strategy report [1]. 80% of them were on inhalation therapy, 18.6% had long-term oxygen treatment (LTOT) and 14.3% had noninvasive positive pressure ventilation (NPPV) at home (Table 1).

There was no statistically significant difference in terms of age, BMI and number of comorbidities among the females with COPD and the control group ($p= 0.973$, $p= 0.846$, $p= 0.482$, respectively). Hypertension was more frequent in the control group, and diabetes

Table 1. Demographic and clinical characteristics of the patient group

Variables		n (%)
Smoking status n (%)	Never	27 (38.6)
	Current	30 (42.9)
	Ex-smoker	13 (18.6)
		Mean ±SD
Duration of disease (years)		10.74 ± 5.66
mMRC points		1.87±0.98
SO2%		96.3±1.2
CAT score		23.7±6.4
6 Minute Walk Test (meters)		378.8±27.5
BODE points		2.33±1.23
COPD combined assessment n (%)	GOLD A	12 (17.1)
	GOLD B	28 (40.0)
	GOLD E	30 (42.9)
Sprirometric grading (FEV1 %) n (%)	Mild	2 (2.9)
	Moderate	46 (65.7)
	Severe	22 (31.4)
Inhalation therapy n (%)		56 (80)
Long-term oxygen treatment n (%) (LTOT)		13 (18.6)
Noninvasive Positive Pressure Ventilation (NPPV) n (%)		10 (14.3)
β-2 mimetic use before intercourse n (%)		42 (60)
Living as a couple n (%)	+	59 (84.3)
Occupation status n (%)	+	22 (31.4)
Education level n (%)	High (University Degree)	23 (32.9)
	Low	47 (67.1)
Residence area n (%)	Urban	46 (65.7)
	Suburban	24 (34.3)
Fatigue during intercourse n (%)	+	42 (60)
Dyspnea during intercourse n (%)	+	39 (55.7)
Fatigue + dyspnea during intercourse n (%)		12 (17.1)

Data presented as means± standard deviation, or as frequency (percentage). COPD: Chronic Obstructive Pulmonary Disease, CAT score: Chronic Obstructive Pulmonary Disease assessment test, FEV1%: predicted value of forced expiratory volume in 1st second, mMRC: Modified Medical Research Council scale, SO2%: Oxygen saturation.

was more common in the patient group (p <0.05). The mean predicted values of pulmonary function test parameters such as $FEV_1\%$, FVC%, FEV_1/FVC% of the patient group were statistically significantly lower and BECK depression inventory scores were higher than the control group (p <0.001). Besides, moderate and severe depression rates were found to be higher among the patient group (p <0.001). The FSFI scores of the females with COPD were statistically significantly lower than the ones without COPD (p<0.001) (Table 2).

Age, number of comorbidities, BMI, the predicted % values of FEV_1, FVC, FEV_1/FVC ratio, BODE index, oxygen saturation %, mMRC scores, 6MWT and the exacerbation history of the previous year in females with COPD were not found to be correlated with the FSFI scores in Spearman analysis (p>0.05). There was only a statistically significant reverse correlation between BECK depression inventory scores and FEV_1/FVC % values of the patient group (p= 0.049) (Table 3). We regrouped the patients according to age, as 36-51 and 52-65, to determine the association between the sexual function scores and the patient characteristics. Only body mass index was found to be inversely correlated with FSFI in the group of ages between 52 to 65 (p= 0.008) (Table 4).

No statistically significant difference was observed in the mean values of age, predicted $FEV_1\%$, mMRC points, BODE index, oxygen saturation %, CAT scores, or BECK depression inventory scores among the groups when we categorized the COPD patients according to the presence of female sexual dysfunction using the cutoff score of FSFI <26.55 (p >0.005) (Table 5).

The FSFI scores were statistically significantly lower only in the patients who had stated fatigue during intercourse compared with those who had not (p= 0.027). No statistical difference was demonstrated in the FSFI scores of the patients who had expressed only dyspnea or both fatigue and dyspnea during intercourse (p >0.05). The presence of comorbidities, smoking status, the severity of COPD according to spirometry, inhalation therapy, having LTOT or NPPV at home, living with a couple, the status of occupation or education were not associated

Table 2. Comparison of groups according to age, BMI, comorbidities, FEV1%, FVC%, FEV1/FVC%, BECK Depression Inventory Scale and FSFI (Female Sexual Function Index)

		COPD Group n= 70	Control Group n= 70	p
Age (years)		53.51±6.99	53.55±7.9	0.973
		36-65 (56)	40-65 (54.5)	
Body Mass Index (kg/m2)		28.2±5.8	26.7±2.3	0.846
		20.1-51 (27.1)	22.4-30.8 (26.6)	
Number of comorbidities n (%)	-	29 (41.4%)	33 (47.1%)	0.482
	1	32 (45.7%)	28 (40%)	
	2	7 (10%)	4 (5.7%)	
	3	2 (2.9%)	5 (7.1%)	
Comorbidities	Hypertension	13 (18.6)	24 (34.3)	0.035*
	Ischaemic Heart Disease	18 (25.7)	11 (15.7)	0.144
	Diabetus Mellitus	18 (25.7)	8 (11.4)	0.030*
FEV_1 (% predicted)		57.4 ±12.2	88.3 ±6.7	<0.001*
		35-88 (59)	74-99 (88)	
FVC (% predicted)		79.2 ±13.1	93.9 ±9	<0.001*
		55-110 (80)	75-120 (90)	
FEV_1/FVC (%)		72.5 ±6.8	94.3 ±5.2	<0.001*
		55-84 (72)	82-106 (96.5)	
BECK Depression Inventory scores		20.2±5.9	14.5±6.9	<0.001*
		11-35 (20)	1-30 (12)	
Depression according to BECK Depression Inventory scale (n (%))	Minimal	0 (0)	11 (15.7)	<0.001*
	Mild	18 (25.7)	33 (47.1)	
	Moderate	45 (64.3)	22 (31.4)	
	Severe	7 (10)	4 (5.7)	
Female Sexual Function Index (FSFI)		22.6 ±3.5	29.15 ±4.99	<0.001*
		13.5-34.1 (22.4)	20.5-34.1(26.2)	
Sexual dysfunction (n (%))		58 (82.9)	17 (24.2)	<0.001*

Mann Whitney U Test, Chi square Test
Data presented as means ±standard deviation, min-max(median) or as frequency (percentage). FEV1%: predicted value of forced expiratory volume in 1st second, FVC%: predicted value of forced vital capacity.

with the FSFI scores of the patients (p>0.05). The BECK depression inventory scores were statistically significantly higher in the patients who had NPPV treatment at home (*p*= 0.031) and, in patients who had comorbidities (p=0.039) compared to those who had not (Table 6).

Only the symptom "fatigue during intercourse" was found to be a statistically significant factor with higher odds of 10.216 (95% CI: 1.822-57.277) in multivariable analysis, which was composed of variables thought to be predictive of sexual dysfunction (*p*= 0.008). Age,

Table 3. Correlation of patient characteristics with FSFI and BECK Depression Inventory scores

	BECK Depression Inventory scores (r)	FSFI (r)
FSFI	-0.055	
Age (years)	-0.150	0.027
Number of comorbidities	0.222	0.119
BMI kg/m2	-0.088	-0.226
COPD combined assessment	0.135	-0.061
FEV_1 (% predicted)	-0.084	0.065
FVC (% predicted)	-0.002	-0.064
FEV_1/FVC (% predicted)	-0.236*	0.202
SO2%	0.007	-0.160
CAT score	0.015	-0.010
Spirometric grading (FEV1%)	0.109	0.110
BODE index	-0.046	-0.113
mMRC points	-0.005	0.027
Exacerbation history of previous year	0.138	-0.086
6 Minutes Walk Test	0.085	0.215

Spearman Correlation Analysis

FSFI: Female Sexual Function Index, BMI: Body mass index, FEV1%: predicted value of forced expiratory volume in 1st second, FVC%: predicted value of forced vital capacity, SO2%: oxygen saturation%, CAT score: Chronic Obstructive Pulmonary Disease assessment test, mMRC: Modified Medical Research Council scale.

* *p* <0.05

Table 4. Correlation of patient characteristics with FSFI scores according to age groups

	FSFI scores	
Ages between 36-51	**Ages between 36-51(r)**	**Ages between 52-65 (r)**
Age (years)	-0.195	0.144
BMI kg/m2	0.044	-0.397*
Number of comorbidities	-0.005	0.189
FEV1% predicted	0.026	0.067
CAT score	0.073	-0.068
mMRC points	0.005	-0.267
6MWT	0.292	0.173
BODE points	0.013	-0.212
Exacerbation history of the previous year	-0.318	0.040
BECK depression inventory scores	-0.185	0.007

Spearman correlation analysis

BMI: Body mass index, CAT score: Chronic Obstructive Pulmonary Disease assessment test, FEV1%: predicted value of forced expiratory volume in 1st second, SO2%: oxygen saturation, mMRC: Modified Medical Research Council scale, 6MWT: Six- min walk test.

* $p<0.05$

Table 5. Comparison of demographic and clinical data between patients with and without sexual dysfunction

Parameteres	Female Sexual Dysfunction	
	-	+
	Mean ±SD	**Mean ±SD**
Age	51.7±9.7	53.9±6.4
FEV1% predicted	56.3±12.8	57.7±12.1
SO2%	96.3±1.6	96.3±1.1
CAT score	24.6±6.2	23.5±6.4
BODE points	2.17±1.03	2.36±1.15
mMRC points	2.08±1.16	1.83±0.94
BECK depression score	17.7±4.7	20.7±6.0

Mann Whitney U Test

FEV1%: predicted value of forced expiratory volume in 1st second, SO2%: oxygen saturation, CAT score: Chronic Obstructive Pulmonary Disease assessment test, mMRC: Modified Medical Research Council scale. No result was significant.

Table 6. Relationship of COPD 'patients' characteristics with FSFI and BECK Depression Inventory scores

Parameters		BECK Depression Inventory Scores		Female Sexual Function Index (FSFI)	
		Mean ± Standard Deviation	***p***	**Mean ± Standard Deviation**	***p***
Smoking status	Never	19.7±5.5	0.857#	22.6±3.7	0.609
	Current	20.2±6.9		22.6±3.0	
	Ex-smoker	21.1±4.1		22.5±4.2	
Comorbidites	-	15.9±6.9	0.039*	24,9±3,6	0.092
	+	18.4±6.9		23,5±4,2	
COPD combined assessment	GOLD A	3	0.533#	22.5±4.3	0.86
	GOLD B			22.9±4.2	
	GOLD E			22.4±2.3	
Spirometric grading (FEV1% predicted)	Mild	17.5±3.5	0.517*	23.5±2.5	0.273
	Moderate	20.0±5.8		22.2±3.4	
	Severe	20.8±6.2		23.3±3.7	
Inhalation therapy	+	20.4±6.0	0.293*	22.9±3.4	0.370
Long-term Oxygen Treatment	+	21.9±4.4	0.188*	21.4±3.7	0.440
NPPV	+	23.7±6.7	0.031*	22.6±3.3	0.993
β-2 mimetic use before intercourse	+	19.9±5.8	0.365*	22.6±3.6	0.852
Living as a couple	+	19.6±5.6	0.088*	22.6±3.5	0.753
Occupation status	+	20.1±7.1	0.487*	23.1±3.6	0.293
Educational status	Low	19.8±6.0	1.000*	22.4±2.9	0.599
	High	21.0±5.5		23.0±4.5	
Residence area	Suburban	19.3±7.0	0.447*	22.9±4.0	0.960
	Urban	20.6±5.2		22.5±3.2	
Fatigue+ dyspnea during intercourse	+	20.7±7.6	0.875*	21.7±2.9	0.251
Fatigue during intercourse	+	20.9±6.0	0.170*	21.8±3.1	0.027*
Dyspnea during intercourse	+	20.2±6.6	0.721*	22.9±3.5	0.507

Mann Whitney U Test, Kruskal Wallis Test

COPD: Chronic Obstructive Pulmonary Disease, FEV1%: predicted value of forced expiratory volume in 1st second, NPPV: Noninvasive Positive Pressure Ventilation

Table 7. Multivariable analysis of parameters that may predict female sexual dysfunction

Enter method	OR	95% CI	
Age	1.049	0.901	1.221
Presence of comorbidities	0.635	0.093	4.327
Duration of the disease	1.059	0.860	1.303
FEV1% predicted	1.026	0.921	1.144
SO2%	1.018	0.509	2.038
mMRC points	0.675	0.190	2.396
6MWT	0.968	0.928	1.009
BECK depression scores >17	2.291	0.429	12.225
Fatigue during intercourse	10.216*	1.822	57.277
Smoking status			
Current smoker	0.802	0.119	5.395
Ex-smoker	0.444	0.045	4.359

Hosmer and Lemeshow Test Enter Method p= 0.232, OR: Odds Ratio, CI: Confidence Interval
Cox & Snell R Square Enter Method= 0.203.
* *p* <0.05
FEV1%: predicted value of forced expiratory volume in 1st second, SO2%: oxygen saturation, mMRC: Modified Medical Research Council scale, 6MWT: Six-min walk test.

the duration of COPD, FEV_1%, 6MWT, oxygen saturation %, having a comorbidity, BECK depression scores, and being a current or a former smoker were not shown to predict sexual dysfunction in females with COPD (Table 7).

Discussion

This study indicated that female patients with COPD experienced difficulties in their sexual activities compared to similar age individuals who did not have COPD (*p* <0.001). 82.9% of study patients presented sexual dysfunction according to FSFI questionnaire, which was consistent with earlier reports that were concentrating on sexual life of females with COPD [8,9,18]. Since the sexuality of females was a rare topic and erectile dysfunction was a biological deficit and a more noticeable disorder, sexual dysfunction in male COPD patients was much more expressed than 'females' in the published literature. Despite the health-related quality of life is accepted as an important outcome measure in the management of COPD, there is still lack of awareness to the problems of these patients regarding sexuality. FSFI is an easy-to- apply psychometric diagnostic test, that provides a fast screening of female sexual dysfunction in outpatient visits [17]. Since women hesitate to share their complaints, this questionnaire may be useful for physicians to increase their ability to communicate with female patients and to disclose sexual problems in a rapid and efficient way.

Dyspnea is the major symptom of COPD and described as perception of hunger for air, breathlessness, and increased work of breathing [1]. Several studies reported that sensation of dyspnea influenced exercise capacity and daily activities stronger than FEV_1% [19,20]. According to COPD combined assessment, our study group comprised 40% GOLD B and 42% GOLD E patients, who had high symptom burden. In spirometric grading, 65.7% of patients corresponded to moderate severity of disease with 50 ≥ FEV_1% ≥79.

All our patients were in the stable state. No correlation was noted between predicted FEV_1% values, oxygen saturation %, CAT scores, spirometric grading, COPD combined assessment and FSFI scores in Spearman correlation analysis (r= 0.065 *p*= 0.595 r= 0.110 *p*= 0.363 r= -0.061 *p*= 0.613 respectively). Moreover, mMRC points which measured the decrease in daily physical activities, 6MWT which showed exercise capacity were not found to be correlated with sexual functionality in our analysis (r= 0.027 *p*= 0.826 r= 0.215 *p*= 0.073 respectively). Our results did not comply with the study comprising female COPD patients in terms of the association between FEV_1% values and sexual dysfunction [18]. In addition, another recent report pointing the relation of increased mMRC scores which directly evaluated dyspnea sensation in daily life activities, and decreased quality of sexual life did not match with our findings [9]. Hypoxemia is the main cause of dyspnea and reduced exercise capacity in COPD [1]. In Schönhofer et al., among the patients who had chronic respiratory failure, the

ones who were sexually active had higher partial pressure of oxygen and better FVC than the patients who were not [21]. Interestingly, 12.6% of these patients reported an improvement in their sexual activities after initiating ventilatory support at home, which suggested that not only the severity of the disease might contribute to the decrease in the sexual relationship [21]. Furthermore, unlike former studies, smoking status, and having LTOT or NPPV at home did not seem to affect the sexual relations of females in our research [21].

In the multivariable analysis performed to predict sexual dysfunction, not the clinical variables, but only fatigue during intercourse was found as the significant predictive variable (p=0,08). In line with our results, in an important systematic review of sexual health, it was noted that breathing difficulties and fatigue were the most common causes of sexual impairment in the qualitative studies [22]. There had been discrepancies in the previous reports investigating the impact of comorbidities on sexual dysfunction [8,23]. Despite the fact that 58.6% of our patients had comorbidities, no association was demonstrated between sexual dysfunction and these co-existing diseases in our research, which all were controlled by medication.

Similar to the results of Abd-Elsalam et al, 60% of our patients reported fatigue during intercourse, 55.7% reported dyspnea, 17% reported both fatigue and dyspnea, and 60% required β-2 mimetic before intercourse [18]. Sexuality is a broad term referring to a combination of psychological and physical acts and, intercourse is only one part of it. But, easy fatigability seemed to reduce the patient's willingness to engage in sexual relations [18,22].

Fatigue and shortness of breath decreased sexual appetite and desire in Zysman et al. COPD cohort [10]. Therefore, not the symptom itself but the distressing experience of fatigue and shortness of breath during intercourse might impact COPD 'females' sexual health. As defined in Kinsman et al.'s study, dyspnea and fatigue frequently concurred in COPD and inevitably contributed to the disease process and progression [24]. Contrary to previously mentioned reports age, duration of the disease, and partner status were not found as the determinants of limitations in sexual relations in our study [9,10,18]. In the age group between 52-65, we noted an inverse correlation between BMI and sexual function which supported the abovementioned studies [10].

In several studies, low education level and unemployment were assumed to have a negative effect on sexual life, but we observed no relation between qualification or employment and sexual functionality in our study [25]. Hence, sexual dysfunction in COPD was more than breathing difficulties that spoiled sexual activities according to our findings. The underlying mechanisms of the pathophysiology of sexual dysfunction in COPD remain unclear.

COPD patients are at higher risk for having depressive symptoms and depression is a cause or a consequence of impaired sexual life [26]. We documented higher scores of BECK depression inventory in our COPD patients when compared to the control group, which may indicate the increased prevalence of possible depression or depressive symptoms in this population ($p < 0.001$). This corroborated earlier findings describing depression, which was not correlated with $FEV_1\%$ values and showed varying prevalence according to the stages of COPD [26,27]. BECK depression scores were not a significant variable in predicting sexual dysfunction in this current study ($p= 0.465$). Since we were unable to demonstrate a causal link between sexual dysfunction and depression, which was not parallel with the previous studies, depression might be considered a distinct entity in this present research [8,9].

Depressive symptoms cause a decrease in functional capability. The multi-center study examining depression in COPD revealed that in younger age subjects (age <60) and particularly in females, depressive symptoms were more prevalent; moreover; fatigue and dyspnea were found significantly worse in the subjects with depression [28]. It is a fact that COPD is a highly symptomatic disease, and its fundamental elements include not only shortness of breath and fatigue but anxiety and depression also [28]. A psychiatrist's counseling is required when specific symptoms were discovered in outpatient visits.

Until recent years, the concept of grading COPD was defined by lung function indices like the FEV_1% value. However as we are still learning about the heterogeneous and complex course of the disease, the definitions broadened to symptom burden, exacerbation history, and comorbidities [1]. Several studies revealed that subjective fatigue in COPD patients is significantly related to functional restrictions and level of disability and had negative consequences on 'patients' daily lives [29,30]. In a population-based study investigating low physical activity in COPD subjects, fatigue was an important factor associated with decreased exercise capacity [31]. Some others demonstrated fatigue associated with the depressive mood in COPD concerning dyspnea and exertion [32]. However, this key symptom goes unnoticed and is understudied in COPD.

Although we avoided including patients who received systemic steroids four weeks prior to the survey, it should be kept in mind that glucocorticoids which were used in the treatment of COPD, might lead to hormonal imbalance and contribute to sexual dysfunction in these patients [33].

Our study had some limitations; since participation in the study was optional and the study was conducted in a single center, one should be cautious when generalizing the results. The assessments were gone through questionnaires, and medical information about the sexual life of the patients before the diagnosis of COPD was not available. Research primarily focusing on women's sexual health in COPD is scarce, and most of the report's healthcare providers have stated that sexual dysfunction has been more likely to be discussed with men than women [34]. This current study emphasizes the broad range of sexual dysfunction that female patients with COPD face and the need for clinicians to be proactive in screening extrapulmonary symptoms like fatigue, depression, and impairment in sexual relations.

Conclusion

According to this study, a substantial proportion of female patients with COPD have declared that they experience sexual problems. The sensation of easy fatigability during sexual activities appeared to be prominent in the sexual impairment of these patients regardless of the severity of the disease or exercise capacity. Physicians should be aware that, even if women are diagnosed with COPD in their mid-forties, they are still sexually active. As growing evidence points out, management of COPD not only consists of medications and prevention of exacerbations; supporting patients in coping with the disease in their daily life would be a more helpful and personalized approach to improving health-related quality of life.

References

1. GOLD Assembly. Global Strategy for the Diagnosis, Management, and Prevention of COPD; 2023. https://goldcopd.org/2023-gold-report-2/

2. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PloS Med. 2006; 3(11): e442. Doi: 10.1371/journal.pmed.0030442

3. Halpin DMG, Celli BR, Criner GJ, Frith P, López VMV, Salvi S, et al. It is time for the world to take COPD seriously: a statement from the GOLD board of directors. Eur respir J. 2019; 54(1): 1900914. Doi: 10.1183/13993003.00914-2019

4. Han MK, Agusti A, Celli BR, Criner GJ, Halpin DMG, Roche N, et al. From GOLD 0 to Pre-COPD. Am J Respir Critical Care Med. 2021; 203(4): 414-23. Doi: 10.1164/rccm.202008-3328PP

5. Celli B, Fabbri L, Criner G, Martinez FJ, Mannino D, Vogelmeier C, et al. Definition and Nomenclature of COPD: Time for its Revision.Am J Respir Crit Care Med. 2022; 206(11):1317-1325. Doi: 10.1164/rccm.202204-0671PP

6. World Health Organization. Definiton of sexual health. https://www.who.int/health-topics/sexual-health#tab=tab_2

7. Levack WMM, Poot B, Weatherall M, Travers J,Cochrane Airways Group. Interventions for sexual dysfunction in people with chronic obstructive pulmonary disease (COPD). Cochrane Database of Systematic Reviews. 2015; 2015(9): CD011442. Doi: 10.1002/14651858.CD011442.pub2

8. Macêdo TE, da Silva G, Morano MT, Alcântara HM, Delgado PE. Sexuality and Associated Factors in Chronic Obstructive Pulmonary Disease (COPD) Patients Attending a Referral Hospital in Northeastern Brazil. J Sex Marital Therapy. 2021; 47:3: 253-261, Doi: 10.1080/0092623X.2020.1869124

9. Kaplan SE, Dai NA, Gümüssoy S. Relationship between the symptoms of COPD and the quality of sexual life. Sex Disab. 2022; 40(3): 555-565. Doi: 10.1007/s11195-022-09744-0

10. Zysman M, Rubenstein J, Le Guillou F, Colson RHM, Pochulu C, Grassion L, et al. "COPD burden on sexual wellbeing." Respir Res. 2020; 21(1): 311. doi: 10.1186/s12931-020-01572-0.

11. Kaptein AA, van Klink RCJ, de Kok F, Scharloo M, Snoei L, Broadbent E, Bel EHD, et al. Sexuality in patients with asthma and COPD. Respiratory Med. 2008: 102(2): 198-204. Doi: 10.1016/j.rmed.2007.09.012

12. Graham BL, Steenbruggen I, Miller MR, Barjaktarevic IZ, Cooper BG, Hall GL, et al. Standardization of spirometry 2019 update. An official American thoracic society and European respiratory society technical statement. Am J Respir Crit Care Med. 2019; 200(8): e70-e88. doi: 10.1164/rccm.201908-1590ST.

13. Yorgancioglu A, Polatli M, Aydemir O. Reliability and validity of Turkish version of COPD assessment test. Tuberk Toraks. 2012; 60(4): 314-320. Doi: 10.5578/tt.4321

14. ATS Committee on Proficiency Standards for Clinical Function Laboratories. American Thoracic Society Statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002; 166: 111-117. Doi: 10.1164/ajrccm.166.1.at1102

15. Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, et al. The body mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med 2004; 350: 1005-1012 Doi: 10.1056/NEJMoa021322

16. Jackson-Koku G. Beck depression inventory. Occupat Med. 2016; 66(2): 174-175. Doi: 10.1093/occmed/kqv087

17. Rosen C, Brown JH, Leiblum S, Meston C, Shabsigh R, Ferguson D, et al. The Female Sexual Function Index (FSFI): a multidimensional self-report instrument for the assessment of female sexual function. J Sex Marital Ther. 2011; 26(2): 191-208. Doi: 10.1080/009262300278597

18. Abd-Elsalam F, Mahgoub N. Chronic obstructive pulmonary disease and sexual functioning among women in egypt egyptian. J Chest Dis Tuberculosis 2015; 64: 551-6. Doi: 10.1016/j.ejcdt.2015.02.006ª

19. Crisafulli E, Clini EM. Measures of dyspnea in pulmonary rehabilitation. Multidiscip Respir Med. 2010; 5(3): 1-9. Doi: 10.1186/2049-6958-5-3-202

20. Denis E, Milne KM, James MD, de Torres JP, Neder JA. Dyspnea in COPD: new mechanistic insights and management implications. Adv Ther. 2020; 37(1): 41-60. Doi: 10.1007/s12325-019-01128-9

21. Schonhofer B, von Sydow K, Bucher T, Nietsch M, Suchi S, Köhler D, et al. Sexuality in patients with noninvasive mechanical ventilation due to chronic respiratory failure. Am J Respirat Crit Care Med. 2001; 164(9): 1612-1617. Doi: 10.1164/ajrccm.164.9.2103020

22. Farver-Vestergaard I, Frederiksen Y, Zachariae R, Rubio-Rask S, Løkke A. Sexual health in COPD: a systematic review and meta-analysis. Int J Chron Obstruct Pulmon Dis. 2022; 17: 297-315. Doi: 10.2147/COPD.S347578

23. Polland A, Davis M, Zeymo Z, Venkatesan K. Comparison of correlated comorbidities in male and female sexual dysfunction: findings from the third national survey of sexual attitudes and lifestyles (Natsal-3). J Sex Med. 2018; 15(5): 678-686. doi: 10.1016/j.jsxm.2018.02.023.

24. Kinsman RA, Yaroush RA, Fernandez E, Dirks JF, Schocket M, Fukuhara J. Symptoms and experiences in chronic bronchitis and emphysema. Chest. 1983; 83(5): 755-761. Doi: 10.1378/chest.83.5.755

25. Reda M, Ruby D. Female Sexual Dysfunction Among a Sample of Egyptian Patients with Asthma. Open Respir Med J. 2020; 14: 38-44. doi: 10.2174/1874306402014010038

26. Schütt CB, Grønbaek M, Osler M, Vestergaard PB, Graugaard C, Frisch M. Associations between physical and mental health problems and sexual dysfunctions in sexually active Danes. J Sex Med. 2011; 8(7): 1890-902. doi: 10.1111/j.1743-6109.2010.02145.x

27. Di Marco F, Verga M, Reggente M, Casanova FM, Santus P, Blasi F, et al. Anxiety and depression in COPD patients: the roles of gender and disease severity. Respiratory Med. 2006; 100(10): 1767-1774. Doi: 10.1016/j.rmed.2006.01.026

28. Mengistu YA, Mülerová H, Lavoie K, Vestbo J, Rennard SI, Wouters E, et al. The association of depressive symptoms with rates of acute exacerbations in patients with COPD: results from a 3-year longitudinal follow-up of the ECLIPSE cohort. J Am Med Dir Assoc. 2017; 18(11): 955-959.e6. doi: 10.1016/j.jamda.2017.05.024.

29. Theander K, Unosson M. Fatigue in patients with chronic obstructive pulmonary disease. J Adv Nurs. 2004; 45(2): 172-7. doi: 10.1046/j.1365-2648.2003.02878.x.

30. Kapella MC, Larson JL, Patel MK, Covey MK, Berry JK. Subjective fatigue, influencing variables, and consequences in chronic obstructive pulmonary disease. Nurs Res. 2006; 55(1): 10-7. doi: 10.1097/00006199-200601000-00002

31. Mikael A, Stridsman C, Rönmark E, Lindberg A, Emtner M. Physical activity and fatigue in chronic obstructive pulmonary disease-a population-based study. Respir Med. 2015;109(8): 1048-57. doi: 10.1016/j.rmed.2015.05.007.

32. Panagioti M, Scott C, Blakemore A, Coventry PA. Overview of the prevalence, impact, and management of depression and anxiety in chronic obstructive pulmonary disease. Int J Chron Obstruct Pulmon Dis. 2014; 9: 1289-306. doi: 10.2147/COPD.S72073

33. Geraghty AC, Kaufer D. Glucocorticoid regulation of reproduction. In: Wang J-G, Harris C. Glucocorticoid Signaling: From Molecules to Mice to Man. Advances in Experimental Medicine and Biology. Springer; 2015. 253-278. Doi: 10.1007/978-1-4939-2895-8_11

34. Levack W. Sexual wellbeing for people with chronic obstructive pulmonary disease: relevance and roles for physiotherapy. New Zeal J Physiother. 2014; 42(3):154-161.