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Frailty in elderly chronic obstructive pulmonary disease patients: a cross-sectional study

Fragilidad en pacientes adultos mayores con enfermedad pulmonar obstructiva crónica: estudio transversal

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Palabras clave
Enfermedad pulmonar obstructiva crónica, enfermedad crónica, fragilidad, anciano frágil, progresión de la enfermedad, fenómenos fisiológicos, hospitalización, pruebas de función respiratoria, salud pública.

Abstract

Objective

This study aimed to determine frailty prevalence among patients aged ≥65 diagnosed with Chronic Obstructive Pulmonary Disease (COPD) and investigate its relationship with disease severity, hospitalization rates, and acute exacerbation frequency.

Methods

This cross-sectional study evaluated 112 elderly patients with COPD. Patient records, pulmonary function tests, Modified Medical Research Council (mMRC) dyspnea scores, COPD *Assessment Test* (CAT) scores, and the previous year's exacerbations and hospitalizations were analyzed. Frailty was assessed using the FRAIL scale.

Results

Frailty prevalence was 49.1% (55/112). A significant negative correlation was found between FRAIL and FEV1% values (r_s: -0.695, 95% CI: -0.782 to -0.581, p <0.001). Conversely, FRAIL Scores correlated positively with CAT (r_s: 0.840, 95% CI: 0.773 to 0.888, p <0.001) and mMRC values (r_s: 0.733, 95% CI: 0.631 to 0.811, p <0.001). Significant differences in CAT, mMRC, and FEV1% were observed between high and low frailty groups. COPD exacerbations and hospitalizations were significantly higher in patients with higher FRAIL Scores (p <0.001).

Conclusion

The FRAIL scale is strongly associated with higher rates of exacerbations and hospitalizations in elderly COPD patients, reflecting increased disease severity and poorer clinical outcomes.

Conflict of interest

The authors have no conflicts of interest to declare.

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CRediT authorship contribution statement

M.I.B.: Conceptualization, Investigation, Supervision. **F.O.:** Formal analysis, Validation, Writing - review & editing. **M.C.:** Formal analysis, Writing - original draft, Writing - review & editing, Supervision. **G.A.A.:** Investigation, Resources.

Data Availability

The datasets generated and analyzed during the current study are not publicly available due to patient privacy and institutional confidentiality protocols, but are available from the corresponding author on reasonable request.

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Resumen

Objetivo

Determinar la prevalencia de la fragilidad en pacientes de 65 años o más diagnosticados con Enfermedad Pulmonar Obstructiva Crónica (EPOC) e investigar su relación con la gravedad de la enfermedad, las tasas de hospitalización y la frecuencia de exacerbaciones agudas.

Métodos

Este estudio de corte transversal evaluó a 112 pacientes de edad avanzada con EPOC. Se analizaron los registros de los pacientes, las pruebas de función pulmonar, las puntuaciones de disnea del Modified Medical Research Council (mMRC), las puntuaciones del COPD *Assessment Test* (CAT) y las exacerbaciones y hospitalizaciones del año anterior. La fragilidad se evaluó mediante la escala FRAIL.

Resultados

La prevalencia de fragilidad fue del 49.1% (55/112). Se encontró una correlación negativa significativa entre los valores de FRAIL y FEV1% (r_s: -0.695, IC del 95%: -0.782 a -0.581, p <0.001). Por el contrario, las puntuaciones de FRAIL se correlacionaron positivamente con los valores de CAT (r_s: 0.840, IC del 95%: 0.773 a 0.888, p <0.001) y mMRC (r_s: 0.733, IC del 95%: 0.631 a 0.811, p <0.001). Se observaron diferencias significativas en CAT, mMRC y FEV1% entre los grupos de fragilidad alta y baja. Las exacerbaciones por EPOC y las hospitalizaciones fueron significativamente mayores en pacientes con puntuaciones de FRAIL más altas (p <0.001).

Conclusión

La escala FRAIL está fuertemente asociada con tasas más altas de exacerbaciones y hospitalizaciones en pacientes ancianos con EPOC, lo que refleja una mayor gravedad de la enfermedad y peores resultados clínicos.

Remark

1) Why was this study conducted?

Human life expectancy is increasing both in our country and worldwide. As a natural consequence of this, the time spent in advanced age increases. Therefore, specific markers and predictors are needed to help older adults better cope with disease and improve their quality of life. Although frailty is a feature of many diseases, it has not been extensively studied in COPD. Research on this topic in our country is also limited, and frailty specifically in patients with COPD has not been previously evaluated. We planned this study for this purpose.

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

In our study, the FRAIL scale was significantly higher in COPD patients aged 65 and over with severe symptoms, low FEV1, high CAT scores, and high mMRC scores. This elevation suggests that the FRAIL Score may serve as a novel prognostic predictor.

3) What do these results contribute?

These findings suggest that using the FRAIL scale may help realign treatment management strategies for these patients. Patients should be evaluated not only in terms of respiratory health but also in terms of whole-body health.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is a significant cause of morbidity and mortality worldwide. In the 2010 Global Burden of Disease Study, COPD ranked third among all deaths [1]. The Global Initiative for Chronic Obstructive Lung Disease (GOLD) defines COPD as a heterogeneous disease characterized by chronic respiratory symptoms (dyspnea, cough, sputum production) and a persistent airflow limitation that is usually progressive and caused by airway and/or alveolar abnormalities [2]. Acute exacerbations of COPD occur with increases in local and systemic inflammation, often in response to infections, air pollution, or other exposures. These exacerbations result in a worsening of the patient's respiratory condition over the previous 14 days, which may be accompanied by tachypnea and/or tachycardia [2]. COPD exacerbations are significant events that increase the risk of hospitalization and mortality in patients [3]. Moreover, these exacerbations account for a large proportion of the healthcare costs attributable to COPD [4].

The increasing life expectancy and aging population are major risk factors contributing to the increased morbidity and mortality of COPD, posing a significant public health problem worldwide [5,6]. Although not a new concept, there is a need to accurately define frailty and its subcomponent, weakness, in the elderly. This is because weakness represents a propensity for disability and should therefore be distinguished from functional impairment [7]. Frailty, on the other hand, is the loss of a person's ability to cope with stress due to a decrease in physiological reserves or dysfunction. Physical frailty is closely associated with an increased risk of disability, falls, hospitalization, and death [8]. Frailty can result from physiological processes, such as aging, as well as from chronic diseases, such as COPD [9,10]. In fact, the prevalence of frailty among COPD patients worldwide is estimated to range from 6% to 82% [11,12].

Frailty is a significant clinical syndrome consistently associated with adverse outcomes in the elderly [13]. A study in Brazil estimated an annual frailty incidence of 6.4% and found that frailty both prolonged hospitalization and reduced quality of life [14]. Frail COPD patients have been found to be more likely to complete rehabilitation programs, and short-term reversibility of frailty has been reported in a significant proportion of these patients [13]. The prevalence of frailty among older adults living in the community ranges from 5% to 58%, and it has been observed that the incidence of frailty varies according to gender, region, country income level, and diagnostic criteria used [15,16]. However, there is limited information available on the prevalence of frailty and predictive factors associated with frailty in individuals with COPD in Turkey.

This study aims to determine the prevalence of frailty among COPD patients admitted to our hospital's pulmonary clinic and to evaluate the relationship between frailty and disease severity, the number of hospitalizations, and the number of emergency department visits due to acute exacerbations of COPD.

Materials and Methods

Study population and design

This cross-sectional study includes the records of 250 COPD patients who were screened and referred to the pulmonary diseases outpatient clinic at Şişli Hamidiye Etfal Training and Research Hospital between April 1st and July 1st, 2024. These records were reviewed; 138 patients were excluded based on the exclusion criteria listed below, and 112 patients were included in the study. All necessary records for these included patients were collected, including the number of hospitalizations in the past year and the number of COPD exacerbations.

Inclusion criteria and exclusion criteria

Inclusion criteria. A total of 112 patients were included in the study. Eligible participants were aged 65 years or older, had attended the Pulmonary Diseases Outpatient Clinic during the specified study period, had a confirmed diagnosis of COPD according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria, and were under follow-up by a pulmonologist. Patients were also required to have no known chronic lung disease other than COPD, a recorded Fatigue, Resistance, Ambulation, Illnesses, and Loss of Weight (FRAIL) scale score in their medical records, and stable chronic conditions affecting other organ systems.

Exclusion criteria. Patients under the age of 65, with missing FRAIL scale and laboratory information, and with previously known chronic lung disease other than COPD were excluded from this study.

Additionally, patients with neurological diseases such as advanced dementia, Alzheimer's, cerebrovascular disease, and patients with a history of major orthopedic or other surgical operations, or those for whom a pulmonary function test (PFT) could not be performed, and sufficient information was not obtained for identification criteria, were not included in the study.

Data collection

The medical records of all patients aged 65 years or older with COPD who attended the outpatient clinic during the study period were reviewed. Anamnestic data, physical examination findings, laboratory test results, PFT parameters, and radiological imaging results were recorded in the study file. Smoking habits, systemic and pulmonary comorbidities, Modified Medical Research Council (mMRC) dyspnea scale score, COPD *Assessment Test* (CAT) score, the number of moderate (conditions requiring systemic corticosteroids and/or antibiotics) and severe (conditions requiring an emergency department visit and/or hospitalization) COPD exacerbations (in accordance with the GOLD criteria) in the previous year, and the number of hospitalizations due to COPD in the previous year were also recorded in our files.

Collection of data using the FRAIL Scale. Due to its rapid screening capability and ease of use in clinical practice, the FRAIL scale, which assesses patients for fatigue, resistance, ambulation, illnesses, and weight loss, was preferred in this study over other patient frailty assessment tools, such as the Fried Criteria and the Edmonton Frailty Scale.

This scale is a five-item self-report questionnaire with possible responses of "yes" or "no," and each item is scored 1 or 0. Individuals were classified as non-frail (0 points), pre-frail (1 or 2 points), or frail (3 or more points) [17].

Ethical considerations and peer review

The study was conducted in strict accordance with the principles of the Declaration of Helsinki. Ethics committee approval was officially obtained from the University of Health Sciences, Şişli Hamidiye Etfal Training and Research Hospital Clinical Research Ethics Committee (Decision No. 2694). Due to the study's cross-sectional design, the ethics committee formally waived the requirement for written informed consent. To ensure data quality and confidentiality, all patient data were collected anonymously and processed using coded records. The manuscript underwent external peer review.

Statistical method

The IBM SPSS 22.0 package program was used in the statistical analysis of the study. Descriptive statistics of demographic data, clinical values, and laboratory results of the study participants were calculated. Accordingly, Pearson Correlation Analysis was used for normally distributed parameters, and Spearman Correlation Analysis for non-normally distributed parameters in the relationship analysis. To compare the FRAIL Low/High groups on the relevant parameters, an independent samples *t*-test was used for normally distributed parameters, and a Mann-Whitney U test was used for non-normally distributed parameters. Chi-square test was used to compare categorical data. Statistical significance was evaluated at $p < 0.05$.

As no studies similar to the present cross-sectional study were identified in the literature regarding the selection of groups and independent variables, a power analysis was conducted using G*Power software (*t*-test for the difference between the means of two independent groups). The analysis, based on the assumption of a one-tailed test, 80% power, a significance level of α= 0.05, and an effect size of d= 0.5, determined that a minimum of 51 subjects were required for each comparison group. The planned total sample size for the study was set at N= 112 for the two main groups (Group 1 - FRAIL ≤ 2: n= 57, Group 2 - FRAIL > 2: n= 55).

Results

Demographic characteristics and laboratory findings

The study was conducted with 112 COPD patients, regardless of gender. Table 1 shows that 112 patients were included in the study, with a mean age of 72.31 ± 7.27 years (range: 65-96). The majority of the patients were male (n= 86, 76.8%), while 26 (23.2%) were female. The mean body mass index was 26.24 kg/m^2 (range: 15.57-44.44). The mean smoking pack-year history was 39.53 ± 6.1 (range: 25-56). Laboratory parameters were as follows: glucose 102.4 ± 19.7 mg/dL (67-197), urea 42.63 ± 19.5 mg/dL (17-153), creatinine 1.01 ± 0.4 mg/dL (0.32-3.82), alanine aminotransferase 18.69 ± 10.7 U/L (7-71), aspartate aminotransferase 22.68 ± 9.4 U/L (6-62), C-reactive protein 12.93 ± 24.33 mg/L (0.5-199.81), hemoglobin 13.26 ± 1.7 g/dL (8.6-17.5), hematocrit 40.35 ± 4.9% (26.7-52.6), and platelet count 250,070 ± 85,400 platelets/µL (range: 108,000–713,000 platelets/µL).

Pulmonary function test, CAT, mMRC, and FRAIL scale data of all patients

Pulmonary function test, CAT, mMRC, and FRAIL scale data of all patients are presented in Table 2. The FRAIL Score was calculated for all patients and was 2.12 ± 1.4 (range: 0-5). According to the FRAIL scale, 19 patients (17%) were classified as normal, 38 (34%) as pre-frail, and 55 (49%) as frail.

Comparison of data

A comparison was made between the FRAIL scales and FEV1%, CAT, and mMRC. There was a statistically significant, moderate negative correlation between participants' FRAIL Scores and FEV1 (%) values (Spearman Correlation r(r_s)= -0.695; 95% CI: -0.782 to -0.581, p <0.001).

Table 1. Baseline demographic and laboratory findings of the study population.

Characteristics	Patients (N= 112) Mean ± SD (min - max)
Gender, n (%)	
Male	86 (76.8%)
Age in years	72.31 ± 7.27 (65 - 96)
BMI, kg/m^2	26.24 ± 5.1 (15.57 - 44.44)
Smoking habit	
Pack-years	39.53 ± 6.1 (25 - 56)
Laboratory parameters	
White blood cell count (cells/µL)	8,330 ± 2,100
Hemoglobin (g/dL)	13.26 ± 1.7 (8.6-17.5)
Hematocrit (%)	40.35 ± 4.9 (26.7-52.6)
Platelet count (platelets/µL)	250,070 ± 85,400 (108,000-713,000)
C-reactive protein (mg/L)	12.93 ± 24.33 (0.5-199.81)
Glucose (mg/dL)	102.4 ± 19.7 (67-197)
Urea (mg/dL)	42.63 ± 19.5 (17-153)
Creatinine (mg/dL)	1.01 ± 0.4 (0.32-3.82)
Alanine aminotransferase (U/L)	18.69 ± 10.7 (7-71)
Aspartate aminotransferase (U/L)	22.68 ± 9.4 (6-62)
Albumin (g/dL)	3.81 ± 0.47
Total cholesterol (mg/dL)	173.53 ± 36.3

SD: Standard deviation, min-max: minimum-maximum, BMI: Body mass index.

Table 2. Pulmonary function test, CAT, mMRC, FRAIL Score data of all patients.

Characteristics	Patients (N= 112) Mean ± SD (min - max)
Pulmonary function test	
FVC (L)	1.53 ± 0.6 (0.42 - 3.07)
FVC (%)	46.5 ± 14.6 (15 - 80)
FEV1 (L)	1.08 ± 0.4 (0.29 - 2.14)
FEV1 (%)	42.31 ± 13.1 (13 - 75)
FEV1/FVC	71.6 ± 13.2 (38 - 100)
FRAIL	2.12 ± 1.4 (0 - 5)
Number of exacerbations	2.3 ± 2.1 (0 - 9)
Hospitalization n (%)	35 (31.25)
CAT	17.83 ± 6.8 (7 - 34)
mMRC	2.19 ± 1.1 (0 - 4)

SD: Standard deviation, min-max: minimum-maximum, FEV1: forced expiratory volume in 1 second, FVC: forced vital capacity, CAT: COPD *Assessment Test*, mMRC: Modified *Medical Research* Council, FRAIL: Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight.

Furthermore, statistically significant high and moderate positive correlations were found between the participants' FRAIL Scores and CAT and mMRC scores, respectively (r_s = 0.840; 95% CI: 0.773 to 0.888, p <0.001, and r_s = 0.733; 95% CI: 0.631 to 0.811, p <0.001, respectively) (Table 3).

Patients were divided into two groups based on their FRAIL scales: low (score ≤ 2) and high (score > 2). The low FRAIL group included 57 patients (50.9%), whereas the remaining 55 patients (49.1%) were in the high FRAIL group. Groups were compared on CAT, mMRC, and FEV1% scores. Statistically significant differences were observed between the high and low FRAIL groups in CAT, mMRC, and FEV1% scores (Figure 1).

A statistically significant difference in the number of COPD exacerbations was found between the high and low FRAIL groups (Mann-Whitney U test; U= 204.5, Z= -8.088, p= 0.0001). The median number of COPD exacerbations was 1 (range: 0-5) in the low FRAIL group and 3 (range: 1-9) in the high FRAIL group. The number of COPD exacerbations was significantly higher in the high FRAIL group compared to the low FRAIL group.

Additionally, a statistically significant difference in the number of hospitalizations was found between the high and low FRAIL groups (Chi-square test; χ^2= 47.222, p= 0.0001). The hospitalization rate was significantly higher in the high FRAIL group than in the low FRAIL group (Table 4).

Table 3. Correlation of FRAIL with FEV1%, CAT, and mMRC.

Variables	Statistical Markers	FRAIL	FEV1%	CAT	mMRC
FRAIL	*r*	1.000	-0.695*	0.840*	0.733*
	p		0.0001	0.0001	0.0001
	N	112	112	112	112
FEV1%	*r*		1.000	-0.732**	-0.774*
	p			0.0001	0.0001
	N		112	112	112
CAT	*r*			1.000	0.723*
	p				0.0001
	N			112	112
mMRC	*r*				1.000
	p				
	N				112

r: Correlation coefficient; *p: p*-value.
*: Spearman correlation coefficient, **: Pearson correlation coefficient.
FEV1: Forced expiratory volume in 1 second, CAT: COPD Assessment Test, mMRC: Modified Medical Research Council, FRAIL: Fatigue, Resistance, Ambulation, Illness, and Loss of weight.

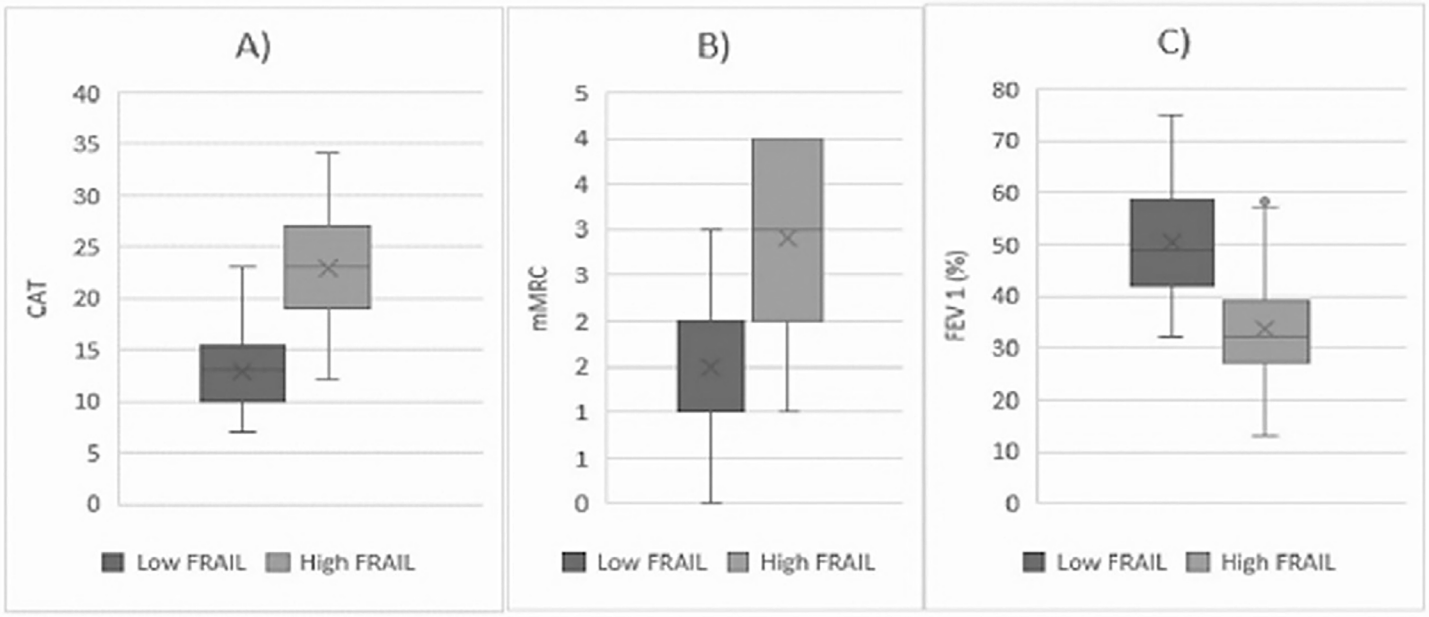

Figure 1. Comparisons between the high and low FRAIL (Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight) groups for clinical scores and lung function parameters. Box plots represent the distribution across FRAIL Score categories for A) CAT (COPD *Assessment Test*), B) mMRC (*Modified Medical Research Council*) dyspnea scale, and C) FEV1% (Forced expiratory volume in 1 second percentage).

Table 4. Comparison of the number of hospitalizations and the number of exacerbations according to FRAIL high and low.

FRAIL	Low FRAIL (≤ 2) (n= 57)	High FRAIL (> 2) (n= 55)	*p*
Median number of exacerbations (Min-Max)	**1 (0-5)**	**3 (1-9)**	**0.0001*[1]**
Number of hospitalizations n (%)			
0	56 (98.2)	21 (38.2)	
1	0 (0)	20 (36.4)	
2	1 (1.8)	11 (20)	0.0001*[2]
3	0 (0)	2 (3.6)	
4	0 (0)	1 (1.8)	

Min-max: minimum-maximum, FRAIL: Fatigue, Resistance, Ambulation, Illnesses, and Loss of weight; [1]: Mann-Whitney U test; [2]: Chi-Square test; *: p <0.01.

Discussion

Frailty, while associated with physiological aging processes, can also be linked to chronic diseases such as COPD [9,10]. Although frailty is considered a geriatric syndrome, its prevalence and mortality risk have not been fully determined in the elderly population with COPD [12,18]. The prevalence of frailty among COPD patients has been reported to vary between 6% and 82% in the literature [11,19]. Our study compared the FRAIL Score with COPD parameters in elderly patients with COPD. Approximately 83% of our patients had FRAIL Scores above the normal range. Pre-frailty was detected in 1/3 of patients, and frailty in 1/2. There was a correlation between the FRAIL Score and FEV1%, CAT, and mMRC values. As our patients' FEV1% decreased, the FRAIL Score increased. Additionally, as CAT and mMRC values increased, the FRAIL Score did so as well. The second aim of our study was to evaluate the correlation between the FRAIL Score and the number of COPD exacerbations and hospitalizations; we also found a correlation between these variables.

Our findings were similar to those of Park *et al.* [20], who reported a frailty prevalence of 57.8% and found a direct correlation between dyspnea and frailty [20]. In another study, 257 COPD patients with a mean age of 65 were evaluated, and a frailty prevalence of 82% was found [19]. In a recent

study of 127 patients, three-quarters were found to be frail or pre-frail. Patients with frailty in that study showed lower hemoglobin, hematocrit, and 25-hydroxycholecalciferol levels [21]. Yee *et al.*[22] found in long-term cohort studies that 62% of the study population was pre-frail and 23% was frail [22]. Limpawattana *et al.* [23], found a lower prevalence of frailty compared to other studies. They showed that frailty was 6.6% and pre-frailty was 41.3% in COPD patients. In that study, frailty was associated with cancer, two or more non-elective hospitalizations in the past 12 months, high chest circumference, and sarcopenia [23]. In our study, we included elderly patients with COPD, and half of them exhibited frailty. This result is similar to the few studies on frailty. While the FRAIL scale was used to define frailty in our study, other studies used different scales such as the Frail Non-Disabled (FIND) questionnaire, the Kihon Checklist, and the Modified Frailty Index. This may explain the variation in frailty measurement prevalence.

In our study, we found a significant association between frailty and FEV1, mMRC, and CAT scores. Kusunose *et al.*[24], in a study of patients with mild to severe airflow limitation, found that frail patients had lower FEV1. However, they did not find a difference in FEV1/FVC or Total Lung Capacity (TLC) between the groups [24]. Park *et al.* [20], reported that dyspnea was the strongest predictor of weakness in COPD patients. Additionally, FEV1 was shown to be 1.91 ± 0.53 L in healthy participants and 1.40 ± 0.49 L in frail participants [20]. Lahousse *et al.* [12], found a higher prevalence of frailty in COPD patients with GOLD severity scores B and D. This increased risk of frailty in groups B and D was likely related to mMRC and CAT scores, with patients in group D being 8 times more likely to be frail than those in group B [12]. Similar results were reported by Maddocks and Ierodiakonou[13,19]. In our study, FEV1 was lower in frail patients. A positive correlation was observed between CAT, mMRC, and frailty. This supports our notion that there is a direct relationship between dyspnea and frailty.

Scarlata *et al.* [25], reported that the FRAIL score was higher in patients with frequent COPD exacerbations and dyspnea (mMRC ≥ 2) and was correlated with lung volumes, expiratory flows, and arterial oxygen pressure. The FRAIL Score was positively correlated with the number of comorbidities, depressive symptoms, cognitive decline, and the BODE index [25]. Yee *et al.* [22], found the frail phenotype to be associated with an increased risk of non-COPD hospitalizations but not with COPD exacerbations. Among individual frail components, low grip strength was associated with an increased risk of COPD exacerbations over a 2-year period [22]. In our study, we also found a significant association between frailty and emergency department visits and hospitalizations due to COPD exacerbations. The relationship between frailty and hospitalizations is uncertain, and our study contributes to this area.

Limitations of the study

The sample size may have limited the study's statistical power. Therefore, our findings should be confirmed in larger, multicenter, prospective studies. Another limitation concerns the assessment of muscle strength: because of the retrospective nature of the study, we used the FRAIL scale, which is easy to administer in outpatient settings, rather than more advanced muscle strength tests. Future prospective studies should incorporate more objective and comprehensive assessments of muscle strength.

The retrospective nature of the study and the possibility of missing data on important confounding factors (e.g., objective assessment of nutritional status, detailed information on medication adherence, physical activity levels, and cognitive status) prevented us from performing a multivariable regression analysis adjusted for all relevant confounding factors. This represents a significant limitation. Furthermore, the lack of subgroup and sensitivity analyses limited our ability to assess the consistency and robustness of the findings.

Conclusion

While frailty has significant clinical implications, its assessment is not routinely performed in patients with COPD. In our study, the FRAIL Score was significantly higher among COPD patients aged 65 and over with severe symptoms, low FEV1, high CAT scores, and high mMRC

scores. This elevation suggests that the FRAIL Score may serve as a novel prognostic predictor. Furthermore, we found a strong association between the FRAIL Score and higher rates of exacerbations and hospitalizations in elderly COPD patients. These findings suggest that the use of the FRAIL Score may help tailor management strategies for these patients. Studies with larger sample sizes should further support the validity of the FRAIL Score in COPD patients.

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