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Frailty phenotype in chronic obstructive pulmonary disease patients: prevalence and relation to disease severity

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Abstract

Frailty is considered a high risk for falls, disability, hospitalization, and mortality in geriatric and certain chronic-disease populations. So, this study was planned to determine the prevalence of frailty phenotype in Chronic obstructive pulmonary disease (COPD) patients. **Methods.** 70 stable COPD patients were included in this study. Age, comorbidities (The FRAIL (***F**atigue, **R**esistance, **A**mbulation, **I**llness, and **L**oss of weight*) scale, BODE index, and *modified Medical Research Council dyspnea score* (mMRC) were recorded. In addition, each patient performed the Six-minute walk test (6-MWT) and underwent a pulmonary function test. **Results.** Frailty was detected in 37.3% of studied patients. However, 43.1% were classified as pre-frail. The presence of frailty was not significantly associated with the age of studied patients ($p = 0.7$). Comorbidities were significantly associated with frailty ($p = 0.009$). Also, the BODE index was significantly higher among patients with frailty ($p < 0.001$). Frailty was significantly associated with forced expiratory volume in 1 second, residual lung volume/Total Lung Capacity, and GOLD (*Global Initiative for Chronic Obstructive Lung Disease*) classification of COPD ($p = 0.001$; $p = 0.003$; $p = 0.003$ respectively). Frailty was significantly associated with 6-MWD and Borg scale difference (Lowest 6-MWD, highest Borg scale difference were detected in frail patients ($p = 0.008$; $p = 0.001$). **Conclusion.** Frailty is frequent among COPD patients. The presence of frailty is related to disease severity and functional impairment. Evaluation of frailty should be considered as a part of COPD assessment in clinical practice.

Key words: frailty, chronic obstructive pulmonary disease (COPD), FRAIL scale, frailty phenotype.

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Ethical expertise: This study was performed within the essential ethics guidelines of the Mansoura institutional research board (code number: R.22.01.1587). Each patient gave written informed consent to participate in the study.

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Фенотип старческой астении у больных хронической обструктивной болезнью легких: распространенность и связь с тяжестью заболевания

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Резюме

В гериатрической популяции пациентов с некоторыми хроническими заболеваниями при старческой астении отмечается высокий риск падений, инвалидизации, госпитализации и смерти. **Целью** исследования явилась оценка распространенности фенотипа старческой астении у пациентов с хронической обструктивной болезнью легких (ХОБЛ). **Методы.** В исследование были включены пациенты ($n = 70$) со стабильной ХОБЛ, у которых регистрировались возраст, информация о сопутствующих заболеваниях, оценка по шкалам FRAIL (***F**atigue, **R**esistance, **A**mbulation, **I**llness, and **L**oss of weight* (усталость, устойчивость, ходьба, болезнь и потеря массы тела)) и mMRC (*The Modified Medical Research Council Dyspnea Scale* – модифицированная шкала одышки Совета медицинских исследований), а также индекс BODE. Кроме того, у каждого пациента проводился 6-минутный шаговый (6-МШТ) и оценивалась функция легких. **Результаты.** У 37,3 % обследованных выявлена старческая астения, состояние еще 43,1 % классифицировано как близкое к старческой астении. Значимой связи старческой астении с возрастом у обследованных пациентов не обнаружено ($p = 0,7$). Связь между старческой астенией и сопутствующими заболеваниями являлась значимой ($p = 0,009$). У пациентов со старческой астенией отмечен достоверно более высокий индекс BODE ($p < 0,001$). Показано также, что старческая астения была значимо связана с показателями объема форсированного выдоха за 1-ю секунду, остаточного объема легких / общей емкости легких и стадией ХОБЛ согласно классификации GOLD (*Global Initiative for Chronic Obstructive Lung Disease* – Глобальная инициатива по диагностике и лечению ХОБЛ) ($p = 0,001$; $p = 0,003$; $p = 0,003$ соответственно). Также выраженность старческой астении была в значимой степени связана с результатом 6-МШТ и разницей по шкале Борга, при этом самый низкий результат 6-МШТ и самая высокая разница по шкале Борга обнаружены у пациентов со старческой астенией ($p = 0,008$; $p = 0,001$ соответственно). **Заключение.** У пациентов с ХОБЛ часто наблюдается ослабленное состояние, что связано со степенью тяжести болезни и функциональными нарушениями. При обследовании пациентов с ХОБЛ в клинической практике необходимо включать оценку степени старческой астении.

Ключевые слова: старческая астения, хроническая обструктивная болезнь легких (ХОБЛ); шкала FRAIL; фенотип старческой астении.

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Этическая экспертиза. Исследование проводилось в соответствии с основными этическими принципами институционального исследовательского совета Mansoura (кодовый номер: R.22.01.1587). От каждого пациента получено письменное информированное согласие на участие в исследовании.
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Chronic obstructive pulmonary disease (COPD) is the third major cause of death, with significant clinical and economic consequences [1]. COPD is a heterogeneous illness; some COPD patients have characteristics that many do not (e. g., frequent exacerbations), which impact prognosis [2].

Frailty is a vulnerability syndrome caused by physiologic malfunction and deterioration. It is typically defined as a greater susceptibility to adverse effects. In elderly and some chronic-disease patients, frailty is linked with high morbidity and death [3]. Frailty is frequently measured using the Fried frailty phenotype 3. Individuals with respiratory insufficiency are more prone to frailty [4]. Frailty is a potential risk for non-completion of pulmonary rehabilitation in COPD patients [5].

So, this study was planned to determine the prevalence of frailty phenotype in COPD patients. Also, to verify whether the frailty phenotype is linked with the severity and functional assessment of COPD.

Methods

Stable COPD patients (n = 70) were included in this cross-sectional study. COPD patients who attend the outpatient clinic of the chest medicine department Mansoura University was enrolled. The diagnosis and classifications of COPD were built on *Global Initiative for Chronic Obstructive Lung Disease* (GOLD) guidelines (2021) [6]. This study was performed within the essential ethics guidelines of Mansoura institutional research board (code number: R.22.01.1587).

Age, comorbidities (The FRAIL (***F**atigue, **R**esistance, **A**mbulation, **I**llness, and **L**oss of weight*)) scale, BODE index, and *modified Medical Research Council dyspnea score* (mMRC) were recorded. In addition, each patient performed the Six-minute walk test (6-MWT) and underwent a pulmonary function test.

Six-minute walk test. The Six-minute walk test (6-MWT) was conducted according to the *American Thoracic Society* (ATS) guidelines [7]. Each patient was asked to walk as far as possible in six minutes, during which peripheral oxygen saturation (SpO_2) was recorded. Changes in SpO_2 (ΔSpO_2) throughout the 6-MWT were analyzed by subtracting the measurements at baseline from those instantly after walking 6 minutes [8]. Borg scale was also detected at baseline and after 6 minutes.

Pulmonary function test. The lung function test was completed corresponding to the ATS guidelines [9] and measured forced vital capacity (FVC), forced expiratory volume in one second (FEV_1), the diffusion capacity of the lung for carbon monoxide (DL_{CO}) and RV/TLC. Each one was stated as percentages of the predicted values (FVC, FEV_1, DL_{CO}, RV, RV/TLC, respectively).

FRAIL scale [10]. The **F**atigue, **R**esistance, **A**mbulation, **I**llnesses, and **L**oss of weight (FRAIL) scale was used to assess frailty. It is a questionnaire with five self-report questions with potential replies of "yes" or "no", with a point value of 1 or 0 assigned to each. Persons were classed as non-frail (0 points), pre-frail (1 or 2 points), or frail (1 or 2 points) (3 or more points).

BODE index [11]. An index determines the 4-year survival of COPD patients depending on BMI, FEV_1, level of dyspnea (based on the Medical Research Council dyspnea score), and exercise ability (6-minute walk distance). As the score increases, the 4-year survival rate declines.

Statistical analysis. The acquired data was compiled, tabulated, and statistically analyzed using SPSS version 16. Categorical data was displayed as a number (percent), whereas continuous data was provided as a mean (SD) or median (interquartile range) based on the findings of the Shapiro – Wilk test, which was used to evaluate the assumption of normal data distribution. The analysis of variance (ANOVA) (normal distribution data) and Kruskal – Wallis test (non-normal distribution data) were used to compare three groups of frailty. Significant testing was done by using the Chi-Square test or Fisher's exact test for ordinal data.

Results

This study included 70 COPD patients (the mean age was 58 years old). Most of them were males (91.4%). GOLD 3 of airflow limitation and COPD group D were reported in 54.3% and 35.3% respectively. In addition, 32.9% had grade 3 of mMRC. 49% of studied patients had hypertension and about 16% had diabetes Miletus (table 1).

Frailty was detected in 37.3% of studied patients. However, 43.1% were classified as pre-frail. The remaining

Table 1
Characteristics and functional assessment of studied patients (n = 70)
Таблица 1
Характеристика пациентов и результаты оценки функционального состояния (n = 70)

Age, years (n = 51) (mean ±SD)	58.7 ± 8.7
Sex, n (%):	
• males	64 (91.4)
• females	6 (8.6)
Comorbidity* (n = 51), n (%):	
• diabetes miletus	8 (15.7)
• hypertension	25 (49)
• ischemic heart disease	4 (7.8)

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FEV_1 (mean ± SD), %	46.4 ± 16.2
FVC (mean ± SD), %	65.5 ± 17.9
DL_{CO} (mean ± SD), %	70.4 ± 20.6
RV/TLC, median (min/max)	134.5 (39 – 273)
mMRC, *n* (%):	
• 0	5 (7.1)
• 1	18 (25.7)
• 2	20 (28.6)
• 3	23 (32.9)
• 4	4 (5.7)
GOLD, *n* (%):	
• 1	3 (4.3)
• 2	22 (31.4)
• 3	38 (54.3)
• 4	7 (10)
Frailty (*n* = 61), *n* (%):	
• non	12 (19,6%)
• prefrail	26 (43,1%)
• frail	23 (37,3%)

Note: FEV_1 – Forced Expiratory Volume in 1 sec; FVC – Forced Vital Capacity; DL_{CO} – Diffusing capacity of the Lungs for carbon monoxide; RV – Residual lung Volume; TLC – Total Lung Capacity; mMRC – modified Medical Research Council dyspnea score; GOLD – Global Initiative for Chronic Obstructive Lung Disease; *, Not mutually exclusive.

Примечание: * – не взаимоисключающие.

19.6% did not have a frailty table 1. The presence of frailty was not significantly associated with the age of studied patients ($p = 0.7$). Comorbidities were significantly associated with frailty (comorbidities were noticed in 73.9% of patients had frailty and in 25% of patients without frailty; $p = 0.009$). Also, the BODE index was significantly higher among patients with frailty ($p < 0.001$), table 2. Most of the frail patients had group D COPD. However, most of the non-frail patients had group A with borderline statistical significance ($p = 0.04$), table 2.

As regards the association between frailty and pulmonary function results of studied patients, frailty was significantly associated with FEV_1, RV/TLC, and GOLD classification of COPD ($p = 0.001$, 0.003, and 0.003 respectively). Moreover, a non-significant association was detected with DL_{CO} ($p = 0.2$), table 3.

Frailty was significantly associated with 6-MWD and Borg scale difference (Lowest 6-MWD, highest Borg scale difference were detected in frail patients ($p = 0.008$, and 0.001). Although no statistically significant association was detected with ΔSpO_2 ($p = 0.08$), the highest ΔSpO_2 was detected in frail patients.

Discussion

Considerable heterogeneity of clinical presentation and disease progression occurs within COPD. Although FEV_1 insufficiently explains this heterogeneity, an obvious substitute has not appeared [2].

Frailty is considered a high risk for falls, debility, hospitalization, and death. Frailty has been thought identical to comorbidity, and other physical attributes, but it is known that it might have a biological origin and be a definite clinical syndrome [3]. As a result of the contribution of frailty with important health consequences in patients' chronic diseases, frailty could be an essential predictor in patients with COPD [12].

Frailty was detected in 37.3% of patients in this study. *C.C.Kennedy et al.* 12 found the prevalence of frailty in COPD to be 6%. 25.6% of elderly COPD patients in *M.Maddocks et al.* [5] were frail. However, *L.Lahousse et al.* [13], studied the association between COPD and frailty in the elderly and found that the frailty prevalence was signifi-

Table 2
Association between frailty and characteristics of studied patients; n (%)
Таблица 2
Связь между ослабленностью и другими характеристиками пациентов; n (%)

	Nonfrail	Prefrail	Frail	Significance	
				p	X^2
Age (mean ± SD)	61.5 ± 10	60.2 ± 8	59 ± 7	0.7*	
Comorbidity:					
• yes	3 (25)	14 (53.8)	17 (73.9)	0.009**	9.3
• no	9 (75)	12 (46.2)	6 (26.1)		
mMRC:					
• 0 – 1	10 (83.3)	23 (88.4)	11 (47.8)	0.001**	14.3
• 2 – 4	2 (16.7)	3 (11.6)	12 (52.2)		
COPD group:					
• A – B	10 (83.3)	13 (50)	10 (43.4)	0.04**	6.4
• C – D	2 (16.7)	13 (50)	13 (56.6)		
BODE index	1 (0 – 6)	3 (0 – 7)	6 (1 – 9)	< 0.001***	

Note: mMRC – modified Medical Research Council dyspnea score; COPD – Chronic Obstructive Pulmonary Disease; *, ANOVA test; **, χ^2 test; ***, Kruskal – Wallis test.

Примечание: * – критерий дисперсионного анализа ANOVA; ** – критерий χ^2; *** – тест Крускала–Уоллиса.

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Table 3
Association between frailty and pulmonary function of studied patients
Таблица 3
Связь между ослабленностью и функцией легких пациентов

	Non frail	Prefrail	Frail	Significance	
				p	X^2
FEV_1 (mean ± SD), %	64.2 ± 14.6[a, b]	49.3 ± 17.7[a, c]	39.7 ± 14,0[b, c]	0.001*	
DL_{CO} (mean ± SD), %	78.1 ± 18.0	67.3 ± 19.0	65.2 ± 23.0	0.2*	
GOLD, *n* (%):					
• 1 – 2	9 (75)	13 (50)	5 (21.7)	0.003**	11.7
• 3 – 4	3 (25)	13 (50)	18 (78.3)		
RV/TLC, median (min/max)	122.5 (111 – 142)	128 (39 – 204)	152 (41 – 221)	0.003***	
6-MWD, median (min/max), m	480 (150 – 540)	390 (115 – 720)	210 (105 – 600)	0.008***	
ΔSpO_2 median (min/max), %	0 (0 – 3)	0.5 (0 – 18)	2 (0 – 12)	0.08***	
Borg scale difference	2 (0.5 – 8)	3 (2 – 9)	7 (1 – 9)	0.001***	

Note: FEV_1 – Forced Expiratory Volume in 1 sec; DL_{CO} – Diffusing capacity of the Lungs for carbon monoxide; GOLD – Global Initiative for Chronic Obstructive Lung Disease; RV – Residual lung Volume; TLC – Total Lung Capacity; 6-MWT – Six-Minute Walk Test; SpO_2 – peripheral oxygen saturation; *, ANOVA test, Similar superscripted letters indicate *p* value by Post hoc Bonferroni test ([a], $p = 0.05$; [b], $p = 0.001$; [c], $p = 0.1$; [d], $p = 0.9$); **, χ^2 test; ***, Kruskal – Wallis test.

Примечание: * – критерий дисперсионного анализа (буквы в верхнем индексе обозначают значение *p* по апостериорному критерию Бонферрони ([a] – $p = 0,05$; [b] – $p = 0,001$; [c] – $p = 0,1$; [d] – $p = 0,9$); ** – критерий χ^2; ***, – тест Крускала–Уоллиса.

cantly higher in participants with COPD (10.2%) compared with participants without COPD (3.4%). The prevalence of frailty was 57.8% in *S.K.Park et al.* [14]. The differences between research in frailty prevalence may be caused by the different frailty measurements used and different sample sizes.

In this study, frailty was significantly associated with FEV_1, RV/TLC, and GOLD classification of COPD. Most of the frail patients had group D COPD *L.Lahousse et al.* [13] also detect a higher prevalence of frailty in severe airflow limitation, dyspnea, and frequent exacerbations. Prevalence of frailty increased with age, GOLD stage, MRC score, and age-adjusted comorbidity burden in *M.Maddocks et al.* [5].

C.A.Vaz Fragoso et al. [4] concluded that frailty and respiratory impairment are sharply associated with one another and significantly increase the risk of death when both are present. This strong association could be contributed to frailty and respiratory impairment shares risk factors (tobacco use and aging) and mechanisms (inflammatory cytokines and endocrine dysfunction) [15, 16].

Furthermore, the presence of frailty was not significantly associated with the age of studied patients in this study. *N.Mittal et al.* [17] studied the prevalence of frailty in patients with chronic lung diseases and found that patients in the frail group did not vary from other patients (prefrail and healthy) as regard comorbid conditions, age, and gender. Frail patients in *N.Mittal et al.* [16] had higher self-reported hospitalizations and falls, increased mortality, and lower gait speeds. Similarly, frailty was significantly associated with 6-MWD, Borg scale difference from 6-MWT, Comorbidities, and BODE index in this study.

In *S.K.Park et al.* [14], COPD patients who had self-stated shortness of breath and comorbid diabetes were more probable to be frail than those who did not.

Several of the changes that occur in the lungs as we age, such as decreased lung function, increased gas trapping, loss of lung elastic rebound, and expansion of the distal air gaps, are also evident in COPD. COPD is two to three times more common in adults over the age of 60 than in younger age groups. COPD has long been thought to be a form of accelerated lung aging. Many aging-related processes are found in the lungs of COPD patients [18]. Despite this fact, the presence of frailty was not significantly associated with the age of studied patients in this study.

This study has limitations. Such as a small sample size and we used only one frailty assessment tool. Functional evaluation was only measured at our study's baseline. Further research on larger numbers of studied patients with a follow-up of functional parameters and mortality is recommended.

Conclusion

Frailty is frequent among COPD patients. The presence of frailty is related to disease severity and functional impairment.

Evaluation of frailty should be considered as a part of COPD assessment in clinical practice.

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All authors have made a significant contribution to the search, analysis, and preparation of the article, read and approved the final version before publication, and accepted responsibility for the integrity of all parts of the article.

Участие авторов

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