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The role of diaphragm thickness and mobility in chronic obstructive pulmonary disease classification and exacerbations

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Abstract:

BACKGROUND AND AIM: Chronic obstructive pulmonary disease (COPD) is a systemic condition. Oxidative stress and air trapping may lead to alterations in diaphragm mobility and thickness. Therefore, assessing diaphragm function in these patients is of great importance. The aim of this study is to evaluate diaphragm thickness and mobility using ultrasonography in COPD patients and to determine their relationship with clinical classification and exacerbation frequency.

METHODS: This single-center, prospective study assessed diaphragm excursion, diaphragm thickness, inspiratory and expiratory durations, contraction speed, and thickening fraction using ultrasound. Spirometry and diffusing capacity for carbon monoxide were performed, and lung volumes and capacities were calculated. Patients were followed for three months to record the number and severity of exacerbations and hospitalizations. Diaphragm parameters were compared with clinical and functional tests to examine their association with COPD classification and exacerbations.

RESULTS: A total of 81 patients, 70 of whom were male, were included in the study. Diaphragm excursion during deep inspiration showed a significant negative correlation with FEV₁ classification ($r=-0.38$, $p<0.001$). Significant correlations were also observed between diaphragm excursion during deep inspiration and residual volume (RV) (%; L) ($r=-0.39$, $p<0.001$; $r=-0.37$, $p<0.001$) and the residual volume/total lung capacity ratio (RV/TLC) ($r=-0.52$, $p<0.01$). Diaphragm excursion during deep inspiration significantly decreased with increasing Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage ($p=0.007$). No significant differences were found between diaphragm thickness and either GOLD or FEV₁ classification. During the three-month follow-up, patients with lower diaphragm excursion during deep inspiration experienced significantly more exacerbations ($p=0.012$).

CONCLUSIONS: Our study demonstrated that diaphragmatic excursion during deep inspiration is associated with GOLD classification, FEV₁ severity, and the frequency of acute exacerbations. Our findings suggest that diaphragmatic dysfunction in this context is more closely related to impaired mobility than to reduced muscle thickness. Although diaphragmatic excursion was significantly associated with exacerbation risk in univariate analysis, it did not remain an independent predictor after multivariable adjustment. Further longitudinal studies are warranted to better define the prognostic significance of diaphragmatic excursion in COPD.

Keywords:

Chronic obstructive pulmonary disease, diaphragm, exacerbation, ultrasonography

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Introduction

Chronic obstructive pulmonary disease (COPD) is a heterogeneous lung disease characterized by persistent, progressive airway obstruction accompanied by chronic respiratory symptoms and structural abnormalities in the airways, alveoli, or parenchyma.^[1] In COPD, air trapping occurs as a result of the inability of the airways to remain patent during expiration, and hyperinflation develops as a result of alveolar destruction and parenchymal damage.^[2]

In patients with COPD, systemic changes can occur in addition to pulmonary alterations due to systemic inflammation and oxidative stress. The most common of these systemic changes is skeletal muscle dysfunction.^[3] This dysfunction affects not only the limb muscles but also the diaphragm, which is the most essential muscle for respiration.^[4] Diaphragm dysfunction results from a reduction in both strength and movement of the diaphragm muscle. The loss of strength is associated with decreased myosin filaments and increased apoptosis in muscle cells, caused by muscle remodeling, oxidative stress, and diminished protein synthesis.^[5] The reduction in diaphragm mobility is thought to result from mechanical restrictions due to hyperinflation and air trapping.^[6]

One reliable method for evaluating diaphragm dysfunction is ultrasonography (US), which is highly reproducible, cost-effective, and free of radiation exposure.

The aim of this study is to evaluate diaphragm thickness and diaphragm excursion in patients with COPD using ultrasonography and to compare these parameters with symptom questionnaires, pulmonary function tests, lung volumes, and exercise capacity. Additionally, the study aims to demonstrate the prognostic impact of diaphragm parameters in terms of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) classification, COPD classification according to FEV₁, and exacerbation frequency.

Materials and Methods

This single-center, prospective study was conducted at a hospital. The study protocol was approved by the Lutfi Kirdar City Hospital Clinical Research Ethics Committee (Approval Number: 2022/514/234/9, Date: 28.09.2022), and performed in accordance with the Declaration of Helsinki. Patients who presented to the Chest Diseases Clinic

between July 2022 and March 2023 and met the diagnostic criteria for COPD according to the GOLD 2022 guidelines were included. Written informed consent was obtained from all participants prior to inclusion in the study.

Patient characteristics

Age, gender, smoking history, comorbidities, body mass index (BMI), and triceps skinfold thickness (measured using a caliper) were recorded. To assess symptoms and conduct a combined evaluation of COPD, the Modified Medical Research Council Dyspnea Score (mMRC) and the COPD Assessment Test (CAT) were administered. The number of COPD exacerbations and hospitalizations during the past year was documented. Based on these data, patients were classified according to the GOLD 2022 combined assessment strategy.

Pulmonary function tests

Spirometry, single-breath diffusing capacity for carbon monoxide, and lung volumes and capacities (measured via the helium dilution technique) were performed by an experienced respiratory nurse. Additionally, the six-minute walk test (6MWT) was conducted.

Ultrasonographic evaluation of the diaphragm

Ultrasound evaluations were performed using a GE Logic 7 device (Germany) with convex and linear probes by a single experienced physician. During ultrasonography, diaphragm excursion during deep inspiration and tidal breathing, inspiratory and expiratory durations during tidal breathing, contraction speed, end-inspiratory and end-expiratory diaphragm thickness, and diaphragm thickening fraction were measured.

For excursion and contraction speed, a low-frequency convex probe was placed subcostally along the midclavicular or anterior axillary line, perpendicular to the diaphragm, with the patient in a dorsal recumbent position and the head of the bed elevated 30–45 degrees. Diaphragmatic motion was observed in M-mode. The diaphragm, seen as a hyperechoic line adjacent to the liver, was tracked across 5–6 respiratory cycles, and the peak excursion was measured in centimeters (cm). A vertical line was drawn from the peak of diaphragm movement to separate inspiration and expiration. The time from the beginning of inspiration to the peak defined inspiratory duration, and the time from the peak to the end of expiration defined expiratory duration. Diaphragm contraction speed was calculated using the slope method on ultrasound [Fig. 1].

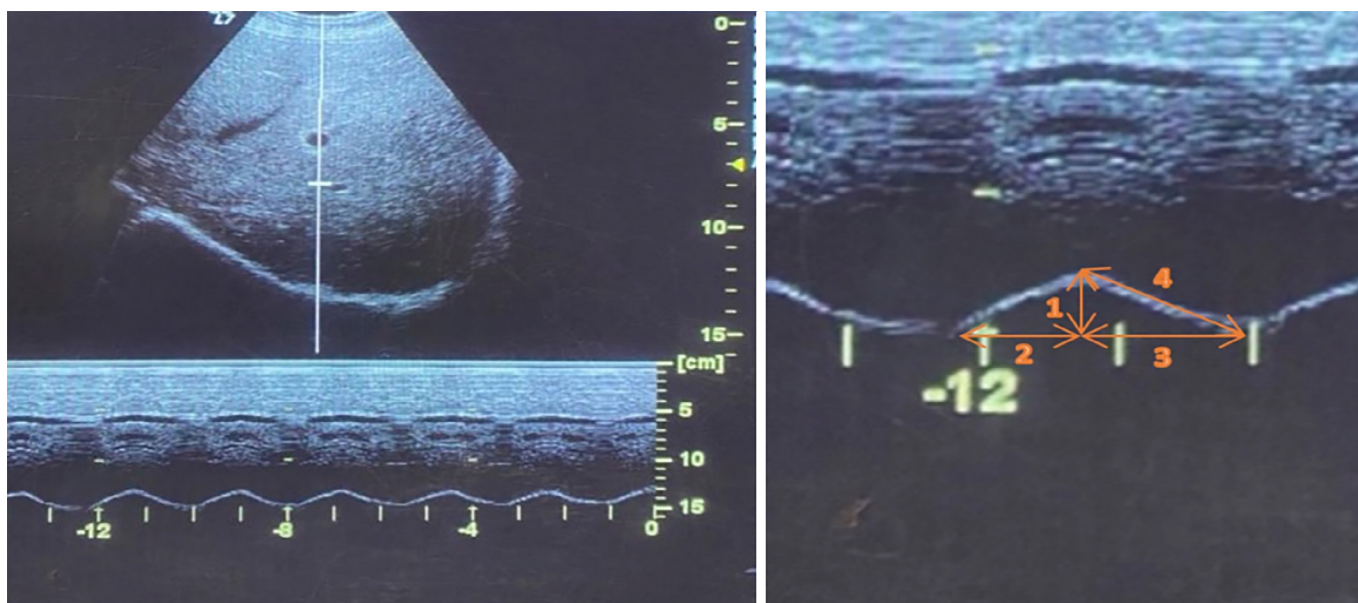


Figure 1: Diaphragm movement with M-mode during tidal volume (1: Diaphragm excursion, 2: Inspiratory time, 3: Expiratory time, 4: Diaphragm contraction speed)

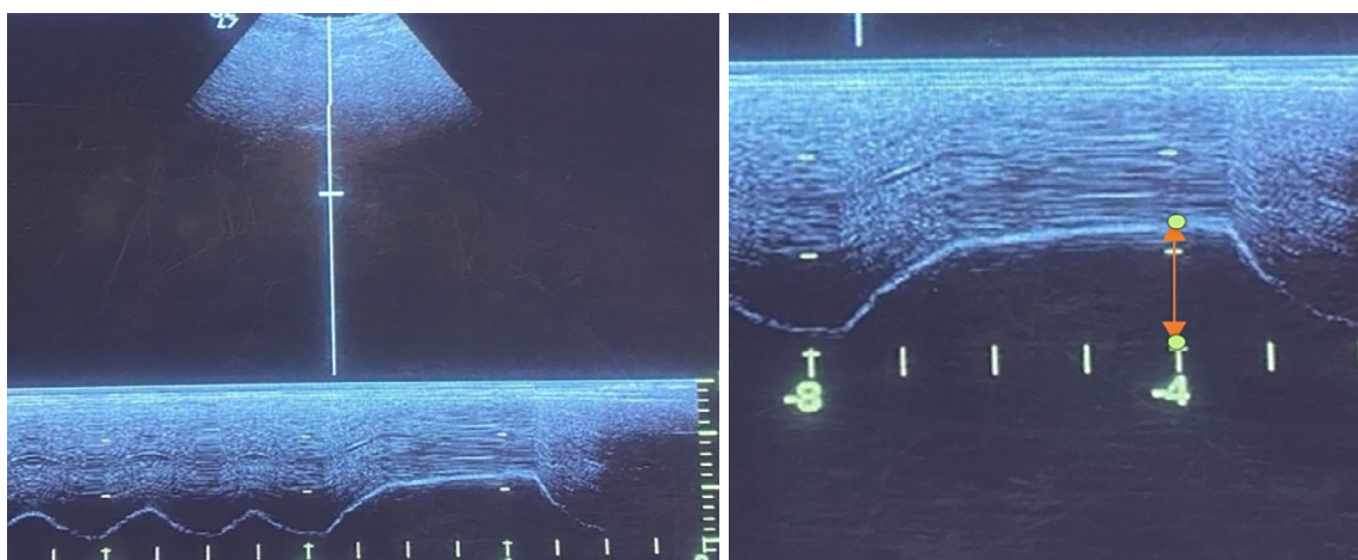


Figure 2: Evaluation of diaphragm movement with M-mode during deep inspiration (the area indicated by the arrow represents deep inspiratory excursion)

For deep inspiratory excursion, after observing 3–4 tidal excursions, patients were instructed to take a deep breath. Measurements were taken from the peak of the fixed image, and the vertical distance from the start of inspiration to the peak excursion was recorded as the deep inspiratory excursion [Fig. 2].

Diaphragm thickness was measured using a linear probe in the same patient position. The diaphragm was visualized in B-mode as a hypoechoic area between two parallel hyperechoic lines, with a central hyperechoic line, at the midaxillary or anterior axillary line between the

9th and 10th ribs. End-inspiratory and end-expiratory thicknesses were measured three times, and the averages were recorded in centimeters [Fig. 3]. The diaphragm thickening fraction was calculated by subtracting the end-expiratory thickness from the end-inspiratory thickness, dividing this value by the end-expiratory thickness, and expressing the result as a percentage.

Prospective follow-up of patients

Patients were followed for three months after the measurements to monitor the number and severity of exacerbations, as well as any hospital or intensive care unit

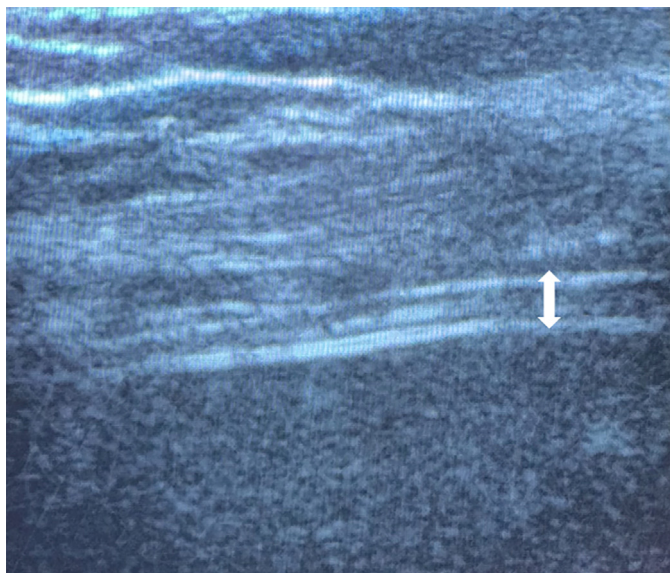


Figure 3: Measurement of diaphragm thickness by ultrasonography (US), showing the hypoechoic area between two hyperechoic lines with a central hyperechoic line

(ICU) admissions due to COPD. The severity of exacerbations was categorized as mild, moderate, or severe according to the GOLD 2022 guidelines.

Statistical analysis

Statistical analyses were performed using IBM SPSS version 23.0 (IBM Corporation, Armonk, NY, USA). The normality of continuous variables was assessed using the one-sample Kolmogorov-Smirnov test. Chi-square tests were used for categorical comparisons, and t-tests or analysis of variance (ANOVA) were applied to normally distributed continuous variables. For non-normally distributed variables, the Mann-Whitney U test was used. Correlation analyses were performed using Pearson or Spearman tests based on data distribution. Logistic regression analysis was applied to identify predictors of COPD exacerbations, and odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. A p-value <0.05 was considered statistically significant.

Results

Eighty-one patients (70 males) were included in the study. The mean age of the patients was 62.4 ± 18.1 years. Based on the GOLD 2022 classification, 31 patients were categorized as Group A, 26 as Group B, 5 as Group C, and 19 as Group D. According to the forced expiratory volume in one second (FEV_1) classification, 18 patients had mild, 44 had moderate, 13 had severe, and 6 had very severe COPD.

A significant negative correlation was found between deep inspiratory excursion and the COPD Assessment Test (CAT) score ($r = -0.39$, $p < 0.001$), as well as a positive correlation with the 6MWT-minute walk test ($r = 0.48$, $p < 0.001$). Deep inspiratory excursions also showed a negative correlation with the number of exacerbations ($r = -0.34$, $p = 0.001$) and hospitalizations ($r = -0.23$, $p = 0.018$) in the past year. Additionally, there was a significant negative correlation with both GOLD classification ($r = -0.373$, $p < 0.001$) and FEV_1 classification ($r = -0.515$, $p < 0.001$).

Deep inspiratory excursion was positively correlated with forced vital capacity (FVC) ($r = 0.52$, $p < 0.001$), FEV_1 ($r = 0.51$, $p < 0.001$), and FEV_1 /FVC ratio ($r = 0.25$, $p = 0.01$). However, there was no significant correlation between deep inspiratory excursion and the diffusing capacity of the lungs for carbon monoxide (DLCO) or diffusing capacity of the lungs for carbon monoxide corrected for alveolar volume (DLCO/VA). Among lung volumes, residual volume (RV) (%) ($r = -0.39$, $p < 0.001$; $r = -0.37$, $p < 0.001$) and residual volume to total lung capacity ratio (RV/TLC ratio) ($r = -0.52$, $p < 0.01$) were negatively correlated with deep inspiratory excursion, while no significant relationship was found with total lung capacity.

During the three-month follow-up, patients with lower deep inspiratory excursion had significantly higher numbers of exacerbations ($r = -0.31$, $p = 0.002$), greater exacerbation severity ($r = -0.34$, $p = 0.001$), increased likelihood of hospital admission ($r = -0.29$, $p = 0.004$), and a higher number of hospitalizations ($r = -0.23$, $p = 0.019$). All statistically significant results are presented in Table 1.

A weak but significant correlation was found between end-inspiratory diaphragm thickness and FVC ($r = 0.22$, $p = 0.021$), and between end-expiratory diaphragm thickness and both FVC ($r = -0.22$, $p = 0.023$) and DLCO/VA ($r = 0.23$, $p = 0.01$). No significant correlations were observed between diaphragm thickening fraction and any clinical or functional parameters.

When diaphragm parameters measured via thoracic ultrasound were compared across GOLD classes, deep inspiratory excursion showed a statistically significant difference between groups ($p = 0.007$). These comparisons are detailed in Table 2.

Patients were followed prospectively for three months to assess the number and severity of exacerbations, hospi-

Table 1: Correlation analysis of deep inspiratory excursion movement and other variables from M-mode diaphragm ultrasonography measurements

Main variable	Other variables	Correlation coefficient	p
Deep inspiratory excursion movement	GOLD classification	-0.37**	<0.001
	According to the FEV ₁ classification	-0.38**	<0.001
	CAT score	-0.39**	<0.001
	Six minute walk test	0.48**	<0.001
	The number of exacerbations in the last year	-0.30**	0.003
	The number of hospitalizations in the last year	-0.23*	0.018
	FVC (L)	0.52**	<0.001
	FVC (%)	0.43**	0.009
	FEV ₁ (L)	0.51**	<0.001
	FEV (%)	0.44**	<0.001
	FEV ₁ /FVC	0.25**	0.010
	RV (L)	-0.37**	<0.001
	RV (%)	-0.39**	<0.001
	RV/TLC	-0.52**	<0.001
	In the three-month follow-up of patients with the number of exacerbations	-0.31**	0.002
	In the three-month follow-up of patients with the severity of exacerbations	-0.34**	0.001
	In the three-month follow-up of patients with the presence of hospital admissions	-0.29**	0.004
	In the three-month follow-up of patients with the number of hospital admissions	-0.23*	0.019

Values are Pearson correlation coefficients (r). *: Weak correlation, **: Moderate correlation. GOLD: Global Initiative for Chronic Obstructive Lung Disease, CAT: COPD Assessment Test, FVC: Forced vital capacity, RV: Residual volume, TLC: Total lung capacity

Table 2: Comparison of diaphragm parameters according to GOLD classification

Variables	GOLD A (n=31)	GOLD B (n=26)	GOLD C (n=5)	GOLD D (n=19)	p
Excursion movement in tidal volume	2.11±0.74	2.06±0.75	1.98±0.51	1.93±0.53	0.852
Excursion movement in deep inspiration	6.1±1.1	5.53±1.1	5.42±1.42	4.95±1	0.007
Inspiratory time	1.18±0.34	1.15±0.35	1.12±0.13	1.05±0.25	0.602
Expiratory time	1.39±0.4	1.41±0.41	1.72±0.24	1.75±0.41	0.408
Contraction speeds	1.58±0.53	1.68±0.51	1.48±0.32	1.63±0.49	0.823
Diaphragm thickness in deep inspiration	0.57±0.15	0.58±0.2	0.58±0.25	0.53±0.12	0.788
Diaphragm thickness in deep expiration	0.428±0.13	0.440±0.17	0.446±0.17	0.404±0.10	0.853
Diaphragm thickness fraction	36.2±16.7	34.4±13.9	33.4±9.1	32.05±14.4	0.809

GOLD: Global Initiative for Chronic Obstructive Lung Disease

talizations, and ICU admissions. Exacerbations occurred in 28 patients. In the group with exacerbations, deep inspiratory excursion was significantly lower ($p=0.012$), whereas other diaphragm parameters did not differ significantly between those with and without exacerbations. These results are presented in Table 3.

Logistic regression analysis was conducted to identify variables that might predict exacerbations. Variables found significant in prior analyses, as well as clinically relevant parameters, were included in the model. Both GOLD classification ($p=0.016$, 598 (3.2–110100)) and COPD severity based on FEV₁ ($p=0.028$, 1635 (2.2–1208976)) were significant predictors of exacerbation risk. These results are presented in Table 4. Although di-

aphragmatic excursion showed a significant association with exacerbation frequency in univariate analysis, it did not remain an independent predictor in the multivariate logistic regression model.

Discussion

In our study, deep inspiratory excursion was found to vary significantly across classifications based on the GOLD guidelines. Additionally, a significant negative correlation was observed between deep inspiratory excursion and COPD classification based on FEV₁. Similarly, Topçuoğlu et al.^[7] categorized COPD patients as having mild, moderate, or severe disease and found statistically significant differences in diaphragm excursion

Table 3: Comparison of diaphragm parameters of patients according to the presence or absence of exacerbation

Variables	Exacerbation present (n=28)	Exacerbation absent (n=53)	p
Age	63.11±8.5	62.04±7.99	0.578
Smoking history (pack-years)	55.96±29.55	38.68±21.6	0.004*
mMRC	2.32±1.4	1.2±1.08	<0.001*
CAT	16.9±7	9.08±7.05	<0.001*
FVC (L)	2.8±0.7	3.4±0.9	0.003*
FVC (%)	80.6±16.9	100.4±22.1	<0.001*
FEV ₁ (L)	1.46±0.6	2.06±0.6	<0.001*
FEV ₁ (%)	51.2±18.2	74.7±20.1	<0.001*
FEV ₁ /FVC (%)	48.2±12.7	57.6±8.5	<0.001*
DLCO (mL/dk/mm-Hg)	75.5±26.1	85.4±21.4	0.07*
DLCO/VA	89.8±25.7	94.8±23.6	0.377
TLC (L)	8.4±1.9	7.05±1.68	0.009*
TLC (%)	130.29±27.01	115.4±24.8	0.015*
RV (L)	4.7±1.6	3.5±1.4	<0.001*
RV (%)	202.6±62.9	149.8±61.4	<0.001*
RV/TLC	57.2±9.4	48.5±10.7	0.001*
6 MWT (m)	398±125.2	496.3±93.2	<0.001*
Excursion movement in tidal volume	2.01±0.48	2.06±0.7	0.75
Excursion movement in deep inspiration	5.16±1.07	5.84±1.1	0.012*
Inspiratory time	1.1±0.3	1.1±0.3	0.520
Expiratory time	1.4±0.3	1.4±0.4	0.432
Contraction speeds	1.6±0.5	1.6±0.4	0.921
Diaphragm thickness in deep inspiration	0.56±0.14	0.57±0.18	0.883
Diaphragm thickness in deep expiration	0.42±0.10	0.43±0.15	0.823
Diaphragm thickness fraction	34.3±14.2	34.6±15	0.944

Mean±Standard deviation, *: p<0.05 value was accepted as significant. CAT: COPD Assessment Test, FVC: Forced vital capacity, DLCO: Diffusing capacity of the lungs for carbon monoxide, DLCO/VA: Diffusing capacity of the lungs for carbon monoxide corrected for alveolar volume, TLC: Total lung capacity, RV/TLC: Residual volume/total lung capacity ratio

Table 4: Results of Binary Logistic Regression Analysis for determining the risk of COPD exacerbation

Variables	Relative risk (95% CI)	p
GOLD group D	598 (3.2–110100)	0.016*
Having an exacerbation in the past year	0.13 (0–1.1)	0.059
Very severe COPD based on FEV ₁	1635 (2.2–1208976)	0.028*
mMRC	1.2 (0.4–3.3)	0.666
CAT	1.08 (0.8–1.3)	0.446
Smoking history (pack-years)	1.05 (0.9–1.1)	0.059
FEV ₁ (L)	14.2 (0.3–525)	0.150
Age	0.9 (0.8–1.1)	0.662
6 MWT (m)	0.9 (0.9–1.01)	0.555
Excursion movement in deep inspiration	1.06 (0.2–4.05)	0.922

Model Fit Statistics: -2 log likelihood: 47.5, Cox & Snell R²: 0.504, Nagelkerke R²: 0.696, *: p<0.05 considered statistically significant. RR: Estimated odds ratio, CI: Confidence Interval

among the groups. Yalçın et al.^[8] also reported a strong negative correlation between GOLD classification and deep inspiratory excursion.

No significant difference or correlation was found between diaphragm thickness and either GOLD classification or FEV₁-based classification. This finding is consistent with studies in the literature that compared

end-inspiratory and end-expiratory diaphragm thickness across GOLD classes and found no statistically significant differences.^[9,10] In the study by Cimşit et al.,^[10] patients were additionally grouped by FEV₁ severity, and again, no significant relationship with diaphragm thickness was noted. In contrast to our findings, Elsayy et al.^[11] reported a negative correlation between diaphragm thickness and COPD severity based on FEV₁.

This discrepancy may be due to their study including only male patients to eliminate gender-related variability and having an equal distribution of patients across COPD severity categories.

Although our results demonstrated a trend toward increased diaphragm thickness in GOLD A, B, and C groups followed by a decrease in GOLD D, these observations did not reach statistical significance. We believe this may reflect initial diaphragm hypertrophy in early disease due to increased respiratory load, followed by atrophy in later stages due to tissue destruction and oxidative stress.^[2]

Both our study and the existing literature suggest that diaphragm mobility, rather than thickness, is more critical in COPD classification. Deep inspiratory excursion may serve as a valuable functional parameter for classifying COPD. In contrast, diaphragm thickness provides structural rather than functional information and appears less relevant to disease classification.

When considering exacerbation outcomes, patients with lower deep inspiratory excursion had more frequent exacerbations and hospitalizations in the preceding year. Similarly, during prospective follow-up, reduced excursion was associated with more frequent and severe exacerbations and higher hospitalization rates. Other diaphragm parameters did not show a meaningful correlation with exacerbations, either retrospectively or prospectively.

In further analysis, patients were divided into two groups based on whether they experienced exacerbations during follow-up. Only deep inspiratory excursions differed significantly between the groups. In the study by Ogan et al.,^[9] no relationship was found between diaphragm thickness and the number of exacerbations. Additionally, when patients were divided into those with fewer than two or more than two exacerbations, diaphragm thickness did not differ significantly. There are limited studies in the literature examining diaphragm mobility and COPD exacerbations. Yalçın et al.^[8] found that decreased diaphragm mobility was associated with a shorter time to the next exacerbation, but they did not assess exacerbation severity or frequency. These findings suggest that deep inspiratory excursion may be a useful parameter in evaluating prognosis and exacerbation risk in patients whose clinical course cannot be

adequately predicted by current tools. Conversely, diaphragm thickness appears to have limited predictive value for exacerbations. However, due to the scarcity of studies on this topic, future research with larger cohorts and longer follow-up periods is warranted.

In our study, deep inspiratory excursion was positively correlated with FVC (L and %), FEV₁ (L and %), and FEV₁/FVC ratio. However, no correlation was found with DLCO or DLCO/VA. In contrast, Scheibe et al.^[12] reported a strong correlation between diaphragm mobility and diffusion capacity. This discrepancy may be due to methodological differences; Scheibe et al.^[12] used the lung silhouette method with patients in a seated position, which may have enhanced the correlation with lung function parameters.

Regarding diaphragm thickness and pulmonary function, we found no correlation between thickness and FEV₁ (L or %), or the FEV₁/FVC ratio. This is consistent with the findings of Schulz et al.,^[13] who studied 140 COPD patients and observed no significant relationship between diaphragm thickness and FEV₁, although they did find a correlation between FEV₁ and diaphragm excursion. These results reinforce the idea that diaphragm mobility plays a more central role than thickness in COPD pathophysiology.

The diaphragm thickening fraction, considered an indirect marker of muscle fiber contractility, has recently been proposed as a more sensitive parameter than thickness alone.^[14] Contrary to expectations, no significant association was found between diaphragm thickening fraction and GOLD classification or exacerbation outcomes in our study. In the study by Elsayy et al.,^[11] although diaphragm thickness did not differ between COPD and control groups, the thickening fraction was significantly reduced in COPD patients. Baria et al.^[15] also reported no significant changes in thickness or thickening fraction in COPD patients, suggesting that diaphragm dysfunction is likely due to mechanical limitation caused by hyperinflation rather than intrinsic changes in muscle contractility. In contrast, Schulz et al.^[13] found a significant correlation between thickening fraction and FEV₁. It is worth noting that the method of calculating thickening fraction differed between studies, which may explain the variation in findings. Our results suggest that further research is needed to clarify the clinical value of diaphragm thickening fraction in COPD.

We observed a negative correlation between deep inspiratory excursion and RV (% and L), as well as RV/TLC ratio, but no significant association with TLC. Similarly, no relationship was observed between diaphragm thickness and lung volumes. Paulin *et al.*^[16] reported that patients with lower diaphragm mobility had significantly higher RV, but not TLC, aligning with our findings. Yamaguti *et al.*^[17] found strong correlations between diaphragm motion and RV and RV/TLC, but only a weak correlation with TLC. In COPD, parenchymal destruction and airway narrowing result in air trapping, increased RV and TLC, and dynamic hyperinflation. This flattens the diaphragm and reduces its mobility. Our findings support the hypothesis that impaired diaphragmatic mobility is more closely associated with air trapping than with pulmonary hyperinflation. The lack of correlation with TLC in our study may be due to differing body positions during testing—semi-recumbent during ultrasonography and seated during lung volume measurements.

A positive correlation was also observed between deep inspiratory excursion and the 6MWT-minute walk test. Shiraishi *et al.*^[18] similarly showed that diaphragm dysfunction is associated with reduced physical activity and increased dyspnea during exertion. Other studies suggest that structural and functional changes in skeletal muscles in COPD contribute to reduced exercise tolerance and increased mortality.^[3] Systemic inflammation, oxidative stress, malnutrition, and apoptosis are believed to impair not only peripheral muscles but also the diaphragm. Additionally, prolonged expiration during exercise may cause dynamic hyperinflation, limiting diaphragm mobility and reducing exercise capacity.

In logistic regression analysis, GOLD group D and very severe COPD based on FEV₁ were identified as significant predictors of exacerbation. However, deep inspiratory excursion did not emerge as an independent prognostic factor. While several models exist to predict exacerbation risk in COPD, studies incorporating diaphragm movement or thickness remain limited. The lack of predictive significance in our model may be attributable to the relatively small sample size, limited follow-up duration, and potential collinearity among clinically related predictors. Additionally, the logistic regression analysis produced very large odds ratios with wide confidence intervals, indicating some instability in the estimates. Consequently, these findings should be interpreted with caution and considered hypothesis-generating, underscoring the need for validation in larger, prospective cohorts.

Limitations

This study has several limitations. First, all ultrasonographic assessments were performed by a single experienced physician. While this ensures methodological consistency, it may introduce observer bias and limit the generalizability of the findings due to the absence of inter-observer variability analysis. Second, the study was conducted over a three-month summer period; seasonal variations such as temperature, allergen exposure, and humidity, which may influence COPD exacerbation frequency, were not specifically analyzed. Third, although the primary focus was on diaphragm dysfunction related to air trapping, patients were not classified into emphysema-predominant or chronic bronchitis-predominant phenotypes. Such classification could provide additional insights into mechanisms underlying diaphragmatic impairment.

In addition, the relatively small sample size and the low number of events per variable in the logistic regression model may have contributed to unstable estimates and inflated odds ratios with excessively wide confidence intervals. Furthermore, several predictors included in the analysis—such as GOLD classification, FEV₁ severity classification, mMRC, and CAT score—are clinically related measures of disease severity and symptom burden, which are likely to be highly correlated. This potential collinearity may have distorted the regression coefficients and reduced the reliability of the effect estimates. Therefore, the logistic regression results should be interpreted with caution and considered exploratory or hypothesis-generating rather than definitive evidence. Validation in larger, independent cohorts is warranted.

Conclusion

This study demonstrates that diaphragm dysfunction in COPD is mainly associated with reduced mobility rather than thickness. Deep inspiratory excursion, measured via ultrasonography, was significantly related to GOLD group D and very severe COPD based on FEV₁, as well as exacerbation frequency and severity in univariate analyses. However, it was not an independent prognostic factor in multivariate analysis, likely due to the relatively small sample size, potential collinearity among predictors, and limited follow-up. These findings should therefore be interpreted with caution and considered exploratory. Further large-scale, long-term studies are needed to clarify the predictive value of diaphragm parameters.

Ethics Committee Approval

The study was approved by the Lutfi Kirdar City Hospital Clinical Research Ethics Committee (No: 2022/514/234/9, Date: 28/09/2022).

Informed Consent

This study was conducted with the informed consent of the patients, ensuring that they were fully aware of the nature of the research, potential risks, and benefits involved. Patient anonymity and confidentiality were maintained throughout the study.

Conflicts of Interest

The authors have no conflicts of interest to declare.

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No artificial intelligence (AI)-assisted technologies, including large language models (LLMs), chatbots, or image creators, were utilized in the production of this submitted work.

Author Contributions

Concept – S.F.E.A., S.Ş.C.; Design – S.F.E.A., S.Ş.C.; Supervision – S.Ş.C., N.K.; Resource – S.F.E.A., E.E.G., E.K.; Materials – S.F.E.A., E.E.G.; Data Collection and/or Processing – S.F.E.A., E.E.G., E.K.; Analysis and/or Interpretation – S.F.E.A., H.Ç.E., A.F.; Literature Review – S.F.E.A., H.Ç.E., N.K.; Writing – S.F.E.A., S.Ş.C.; Critical Review – S.Ş.C., A.F., N.K.

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