Diaphragm Ultrasound Distinguishes Exacerbation From Stable Status in Chronic Obstructive Pulmonary Disease

Tai Joon An
Catholic University of Korea Yeouido Saint Mary's Hospital
Yeun Jie Yoo
Catholic University of Korea Saint Vincent's Hospital
Jeong Uk Lim
Catholic University of Korea Yeouido Saint Mary's Hospital
Wan Seo
Catholic University of Korea Yeouido Saint Mary's Hospital
Chan Kwon Park
Catholic University of Korea Yeouido Saint Mary's Hospital
Chin Kook Rhee
Catholic University of Korea Seoul St. Mary`s Hospital
Hyoung Kyu Yoon (cmcyhg@gmail.com)
Catholic University of Korea Yeouido Saint Mary's Hospital

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Abstract

Background: The importance of evaluating the diaphragm muscle in chronic obstructive pulmonary disease (COPD) is widely accepted. However, the role of diaphragm ultrasound (DUS) in COPD is not fully understood. We set this study to evaluate the role of DUS for distinguishing the status of COPD.

Methods: COPD patients who underwent DUS were enrolled between March 2020 and November 2020. The diaphragm thickening fraction (TF_{max}) and diaphragm excursion (DE_{max}) during maximal deep breathing were measured. Patients were divided into exacerbation and stable groups. Demographics, lung function, and DUS findings were compared between the two groups. Receiver operating characteristic (ROC) curve and univariate/multivariate logistic regression analyses were performed.

Results: Fifty-five patients were enrolled. The exacerbation group had a lower body mass index (BMI) (20.9 vs. 24.2, $p = 0.003$), lower TF_{max} (94.8 ± 8.2% vs. 158.4 ± 83.5%, $p = 0.010$), and lower DE_{max} (30.8 ± 11.1 mm vs. 40.5 ± 12.5 mm, $p = 0.007$) compared to stable group. The areas under the TF_{max} (0.745) and DE_{max} (0.721) curves indicated fair results for distinguishing exacerbation. The patients were divided into low and high TF_{max} and DE_{max} groups based on calculated cut-off values. Low TF_{max} (odds ratio [OR] 8.40; 95% confidence interval [CI] 1.55–45.56) and low DE_{max} (OR 11.51; 95% CI 1.15–115.56) were associated with exacerbation after adjusting for age, sex, BMI, forced vital capacity and forced expiratory volume in 1 sec.

Conclusion: TF_{max} and DE_{max} distinguished exacerbation from stable status. We describe the DUS cut-off values for determining an exacerbation status in this study.

Background

Chronic obstructive pulmonary disease (COPD) is a common chronic airway disease characterized by chronic airway inflammation with persistent airflow limitation[1,2]. The diaphragm muscle is key in the respiration process, and it is important to understand lung exercise physiology and the mechanics of COPD[3,4]. Previous studies have shown that atrophy or dysfunction of the diaphragm is related to poor COPD outcomes[5].

An evaluation of the diaphragm is necessary for COPD patients but is difficult to achieve. The gold standard for evaluating diaphragm function is measuring trans-diaphragmatic pressure using an electromyogram during phrenic nerve stimulation or via maximal static inspiratory pressure, which is an invasive and time-consuming technique[6]. By contrast, diaphragm ultrasound (DUS) is an emerging alternative technique for evaluating the diaphragm muscle[7-13]. It is a non-invasive, real-time, and intuitively understandable method for evaluating various aspects of the diaphragm[10,11]. The method and effects of DUS in COPD patients have been well described by previous studies[7,8]. However, few studies have compared DUS findings between patients with a stable status and those with acute exacerbation of COPD[9,10]. Also, there are no data about the value of diaphragm markers for distinguishing exacerbation

from a stable status. We designed this study to analyze differences in diaphragm markers according to COPD status and identify potential exacerbation factors.

Methods

Study Subjects

COPD patients were retrospectively recruited between March 2020 and November 2020 at Yeouido St. Mary's Hospital. They were diagnosed with COPD by pulmonologists. The patients were ≥ 40 years of age and satisfied the spirometry definition of persistent airflow limitation, such as a post-bronchodilator forced expiratory volume in 1 sec/forced vital capacity ratio (FEV_1/FVC) < 0.70.

Among them, patients who underwent DUS were enrolled. DUS was performed in the stable COPD group when they visited the outpatient clinic for a regular follow-up. DUS was performed within 48 hours of admission in patients with acute exacerbation. Exacerbation was defined by an acute change in respiratory symptoms requiring a medication change, such as a systemic steroid or antibiotics. Patients who required hospitalization had the following indications: 1) acute respiratory failure, 2) cyanosis or edema, 3) very severe symptoms, such as dyspnea at rest or mental change, 3) severe comorbidities, such as cardiovascular disease, and 4) need for refractory to acute management. Patients who did not undergo DUS or underwent DUS after 48 hours of admission were excluded. Patients with confounding factors of diaphragm function, such as hemiplegia, quadriplegia, sequelae from an abdominal or thoracic operation, or diaphragm paralysis due to phrenic nerve palsy, were also excluded. All patients enrolled in this study completed the modified Medical Research Council (mMRC) scale, COPD assessment test (CAT), and history taking for comorbidities.

Comorbidities

Histories of medication and comorbidities were collected during the DUS exam. Electrical medical records were reviewed to confirm the comorbidities of the patients. The modified Charlson Comorbidity Index (mCCI), in which the chronic pulmonary disease categories are removed, was calculated to predict prognosis and mortality based on the ICD-10 diagnosis for the COPD patients[14].

Diaphragm ultrasound protocol

All DUS exams were performed with a single high-resolution ultrasound machine (Affiniti 70, Phillips, Inc., Best, the Netherlands). The exams were conducted by a respiratory physician who specializes in DUS. DUS findings are well established in many studies[7,8,13]. Patients were placed in a supine position, and the tests were performed at the right hemidiaphragm. A linear ultrasound probe (5–12 MHz) was used to measure the thickness of the diaphragm. Diaphragm excursion was measured with a convex ultrasound probe (1–5 MHz). B-mode was used to measure the thickness of the diaphragm (DT), and diaphragm

excursion (DE) was measured in M-mode. These measurements were repeated three times in the same position and the mean value was used as the representative value.

Diaphragm thickness and diaphragm excursion

DT was measured in the zone of opposition in the right hemithorax over the mid-axillary line between the eighth and eleventh intercostal spaces in longitudinal intercostal view. DT was defined by the distance between the diaphragmatic pleura and the peritoneal membrane. First, it was measured at the end of expiration, which is correlated with functional residual capacity. Then, it was measured at the end of the inspiration during both quiet tidal breathing and maximal deep breathing.

DE was measured at the anterior subcostal margin of the right hemidiaphragm. A convex probe was positioned below the costal margin at the mid-clavicular line. The incidence angle of the ultrasound beam was perpendicular to the posterior third of the diaphragm, or the so-called DE line. The DE was the diaphragm inspiratory amplitude during respiration measured at the DE line in M-mode. DE was measured during quiet tidal breathing and maximal deep breathing (DE_{max}) (see Supplemental Figure 1).

Diaphragm thickening fraction

The thickening fraction of the diaphragm (TF) has been evaluated in many studies[7,8,12]. It is related to the generation of diaphragm muscle pressure. The TF was calculated with the DT value. TF was defined as the ratio of DT changes between the end of expiration and the end of inspiration. The TF equation was [(DT at end-inspiration) - (DT at end-expiration)]/(DT at end-expiration) × 100. TF was also calculated during tidal breathing and maximal deep breathing (TF_{max}).

Statistical analyses

We used Student's *t* test and the Mann-Whitney *U* test for analyzing continuous variables according to the normality test results. Pearson's chi-square test or Fisher's exact test were used to compare categorical variables between groups. A receiver operating characteristic (ROC) curve analysis was performed to evaluate the usefulness of the DUS findings for classifying the exacerbation group. The Youden index was used to identify the optimal cut-off value and compare the ROC curves. Binary univariate and multivariate logistic regression analyses were conducted to calculate the odds of being classified in the exacerbation group. A *p*-value < 0.05 was considered to indicate significance. Student's *t* test, the Mann-Whitney *U* test, Pearson's chi-square test, Fisher's exact test, and the logistic regression analyses were performed using IBM SPSS Statistics for Windows, version 26.0 (IBM Corp., Armonk, NY, USA). The ROC curve analyses, the Youden's index, and the comparison of the ROC curves were performed using MedCalc® Statistical Software version 19.5.6 (MedCalc Software Ltd., Ostend, Belgium; https://www.medcalc.org; 2020).

Ethics approval

This study was approved by the Institutional Review Board of The Catholic University of Korea Yeouido St. Mary's Hospital (approval no. SC20RIS0181). The need for informed consent was waived due to the retrospective nature of the study.

Results

Demographics of study subject

Fifty-five COPD patients were enrolled in the study. Twenty-two were classified as having an acute exacerbation status (AE group) and the remainder had a stable status (stable group). No significant differences in age, sex, mCCI, or COPD medication were observed between the groups. The AE group had a lower BMI than the stable group (20.9 vs. 24.2 kg/m^2, $p = 0.003$). Scores of the symptom and dyspnea scales, such as the CAT (25.4 ± 8.2 vs. 13.7 ± 3.8, $p < 0.001$) and mMRC (3.1 ± 1.0 vs. 1.7 ± 1.2, $p < 0.001$), were significantly higher in the AE group than in the stable group. Smoking status and the baseline Global Initiative for Chronic Obstructive Lung Disease grouping differed between the two groups. Lung function was different between the two groups. Absolute values and predictive percentages of FVC and FEV_1 were significantly lower in the AE group than in the stable group. The air-trapping index (residual volume/total lung capacity) was higher in the AE group than in the stable group (51.7 ± 9.4 vs. 43.7 ± 8.1, $p = 0.019$) (Table 1).

DT at end-expiration and end-inspiration during quiet tidal breathing, and at end-inspiration during maximal deep breathing did not differ between the two groups. TF and DE during quiet tidal breathing did not differ between the AE and stable groups. TF_{max} and DE_{max} were significantly lower in the AE group than in the stable group compared to values during tidal breathing (94.8 ± 8.2% vs. 158.4 ± 83.5%, $p = 0.010$; 30.8 ± 11.1 mm vs. 40.5 ± 12.5 mm, $p = 0.007$, respectively) (Table 1).

Diaphragm ultrasound distinguished acute exacerbation from stable status in COPD patients well

ROC curve analyses of TF_{max} and DE_{max} for distinguishing the AE group were performed. The areas under the curve (AUC) for TF_{max} and DE_{max} were 0.745 and 0.721, respectively (Figure 1 and Table 2). The maximal Youden's index was summarized for the maximum potential effectiveness of variables with optimal cut-off values. The TF_{max} cut-off value was 93.8% (sensitivity 68.4%, specificity 78.8%) and that of DE_{max} was 44.9 mm (sensitivity 95.2%, specificity 44.8%) (Table 2). No significant difference in TF_{max} and DE_{max} ($p = 0.608$) was observed when the ROC curves were compared (Figure 1).

We also conducted ROC curve analyses for the other variables, such as the absolute values of FVC, FEV_1, and BMI, because these variables are well-known exacerbation factors from previous studies. These

variables exhibited clinical significance in the ROC curve analyses (Table 2). Therefore, we conducted multiple comparisons of the ROC curves to compare the performance of the TF_{max} (Figure 2a) and DE_{max} (Figure 2b) models with that of the others. The TF_{max} and DE_{max} models for the AE group were non-inferior to those of FVC, FEV_1, and BMI (Figure 2c).

Differences in demographics according to low or high TF_{max} and low or high DE_{max}

We set new variables according to optimal TF_{max} and DE_{max} cut-off values. The low TF_{max} and high TF_{max} groups were divided by a cut-off value of 93.8%. The low DE_{max} and high DE_{max} groups were divided by a cut-off value of 44.9 mm. No significant differences in age, sex, mCCI, BMI, CAT score, or mMRC score were observed between the two groups. The low TF_{max} and low DE_{max} groups usually had many symptoms and exacerbation histories. Lung function was lower in the low TF_{max} and low DE_{max} groups than in the high TF_{max} and high DE_{max} groups. The percentage of AE patients was significantly higher in the low TF_{max} (63.2%) and low DE_{max} (55.6%) groups than in the high TF_{max} (23.5%) and high DE_{max} (7.1%) groups (Table 3).

The low TF_{max} and low DE_{max} groups were associated with acute COPD exacerbation status

We performed multivariate logistic regression analyses to determine whether a low TF_{max} and low DE_{max} could be used for distinguishing exacerbation status. The variables were entered into two models that included age, male sex, mCCI, and BMI. Model 1 included variables such as age, male sex, mCCI, BMI, and a low TF_{max}, and model 2 included a low DE_{max} as the variable instead of TF_{max}. In model 1 univariate analyses, a high mCCI, low BMI, and low TF_{max} were associated with exacerbation. In the adjusted analyses, a low BMI (odds ratio [OR] 0.70; 95% confidence interval [CI] 0.56–0.88) and low TF_{max} (OR 8.40; 95% CI 1.55–45.56) were associated with exacerbation. Similar results were observed for model 2. A high mCCI (OR 2.68; 95% CI 1.09–6.60), low BMI (OR 0.79; 95% CI 0.64–0.97), and low DE_{max} (OR 11.51; 95% CI 1.15–115.56) were associated with exacerbation after adjustment. Therefore, low TF_{max} and low DE_{max} groups were associated with an exacerbation status (Table 4).

Discussion

We designed this study to analyze the association between DUS findings and COPD exacerbation status. Many significant differences in DUS findings, such as the DT fraction during maximal deep breathing (TF_{max}) and DE during maximal deep breathing (DE_{max}) were observed between patients with a stable or acute COPD exacerbation status. However, no significant difference in DT was observed at end-expiration

or end-inspiration. In this study, differences in breathing effort produced different results. The maximal effort measurements were significantly associated in the AE group, whereas those of quiet tidal breathing were not. Respiratory muscle reserve or contractile strength was related to the change of diaphragm thickness (TF) or change of length (DE), not by muscle mass itself (DT) in previous studies. These findings support the results of those articles[8,9,12,13].

The results of the ROC curve analyses suggest the usefulness of TF_{max} and DE_{max} in classifying the exacerbation and stable conditions. TF_{max} and DE_{max} were not inferior markers to each other and they have complementary roles. TF_{max} was highly specific (78.8%) and DE_{max} was highly sensitive (95.2%). Both were non-inferior to other classical factors of exacerbation, such as age, sex, FVC, FEV_1, and BMI. After dividing the patients into those with low or high TF_{max} and those with low or high DE_{max}, the low TF_{max} and low DE_{max} groups exhibited poorer lung function and a higher proportion of exacerbation. After adjusting for age, sex, mCCI, and BMI, low TF_{max} patients were classified into the AE group 8.40-times higher than high TF_{max} patients, and low DE_{max} patients were classified into the AE group 11.51-times higher than high DE_{max} patients. These findings suggest that DUS findings can be used as distinguishing markers for COPD exacerbation.

These are valuable results regarding the use of DUS in patients with COPD. This study compared TF_{max} and DE_{max}. We firstly showed that they were non-inferior to each other and were complementary markers for detecting an acute exacerbation status, as far as we know. No previous study has examined differences in DUS findings between quiet breathing and maximal breathing both in stable and exacerbation status. Only the maximal deep breathing findings were different between the groups and those were associated with an exacerbation status. TF and DE should be checked together during maximal breathing effort when DUS is performed on a patient with COPD.

Another interesting finding is the usefulness of the DUS findings. The results were associated with exacerbation status after adjustment, and the markers were not inferior to FVC, FEV_1, and BMI for classifying exacerbation. DUS is a real-time test that can be performed immediately when exacerbation is suspected. With these results, we have identified novel markers for distinguishing patients with severe exacerbation who need hospitalization.

Several limitations of this study should be discussed. First, the cut-off value of the DUS findings reflected maximal potential efficiency only. More studies on proper cut-off values are needed. However, the cut-off values in this study were not inferior to those of conventional markers for classifying COPD status. More studies should specifically evaluate proper cut-off values. Second, we retrospectively included patients in this study. However, we compared the diaphragm marker itself without another intervention in this setting. Prospective research is required for further analyses.

Conclusions

This study describes the utility of DUS in COPD patients. This is the first study to report the role of DUS for distinguishing exacerbation from a stable status. We also showed the value of DUS findings with the consideration of other contributing factors, such as sex, age, and BMI. Based on the results, we suggest using DUS findings as indicators of exacerbation status in COPD patients.

List Of Abbreviations

COPD, chronic obstructive pulmonary disease; DUS, diaphragm ultrasound; $FEV_{1,}$ forced expiratory volume in 1 sec; FVC, forced vital capacity ratio; mMRC, modified Medical Research Council scale; CAT, COPD assessment test; mCCI, modified Charlson Comorbidity Index; DT, thickness of the diaphragm; DE, diaphragm excursion; DE_{max}, diaphragm excursion during maximal deep breathing; TF, diaphragm thickening fraction; TF_{max}, diaphragm thickening fraction during maximal deep breathing; ROC, receiver operating characteristic; AE, acute exacerbation; AUC, area under the curve; OR, odds ratio; CI, confidence interval; BMI, body mass index; SD, standard deviation; GOLD, Global Initiative for Chronic Obstructive Lung Disease; LABA, long-acting β agonist; LAMA, long-acting muscarinic antagonist; ICS, inhaled corticosteroid; RV, residual volume; TLC, total lung capacity

Declarations

Ethics approval and consent to participate: This study was approved by the Institutional Review Board of The Catholic University of Korea Yeouido St. Mary's Hospital (approval no. SC20RIS0181). Informed consent was waived due to the retrospective nature of the study.

Consent for publication: all authors agreed with the publication of this study.

Availability of data and materials: Researchers may request datasets which were used in this study to the corresponding author with reasonable request.

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Authors` contributions:

Conceptualization: TJ An, YJ Y

Data curation: TJ An, YJ Y, W Seo

Formal analysis: TJ An

Investigation: W Seo, CK Park, HK Yoon

Methodology: JU Lim, CK Rhee, HK Yoon

Project administration: TJ An, YJ Y

Resources: TJ An, YJ Y

Software: TJ An

Supervision: CK Rhee, CK Park, HK Yoon

Validation: JU Lim, CK Rhee, CK Park, HK Yoon

Visualization: TJ An

Writing – original draft: TJ An

Writing – review & editing: TJ An

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Tables

Table 1. Patient demographics

	Stable (n=33)	AE (n=22)	*p*-value
Age (years), mean ± SD	73.5 ± 8.3	72.6 ± 11.6	0.897*
Male sex, n (%)	23 (69.7)	18 (81.8)	0.361
mCCI (points), mean ± SD	0.7 ± 0.9	1.4 ± 1.6	0.078*
BMI (kg/m^2), mean ± SD	24.2 ± 3.8	20.9 ± 4.0	0.003
CAT (points), mean ± SD	13.7 ± 6.9	25.4 ± 8.2	< 0.001
mMRC (points), mean ± SD	1.7 ± 1.2	3.1 ± 1.0	< 0.001
Smoking, n (%)			
Never	11 (33.3)	11 (50.0)	0.040
Ex-smoker	14 (42.4)	11 (50.0)	
Current smoker	8 (24.2)	0 (0.0)	
Pack-years, mean ± SD	28.3 ± 24.5	22.3 ± 25.5	0.387
Duration of COPD (years), mean ± SD	5.1 ± 4.4	5.4 ± 6.1	0.839
GOLD group, n (%)			
A	14 (42.4)	0 (0.0)	< 0.001
B	10 (30.3)	7 (31.8)	
C	5 (15.2)	0 (0.0)	
D	4 (12.1)	15 (68.2)	
Baseline COPD medication, n (%)			
None	2 (6.1)	2 (9.1)	0.255
LABA or LAMA	1 (3.0)	0 (0.0)	
ICS/LABA	5 (15.1)	0 (0.0)	
LABA/LAMA	12 (36.4)	7 (31.8)	
ICS/LABA/LAMA	13 (39.4)	13 (59.1)	
DT (mm), mean ± SD			
at end-expiration	17.0 ± 6.0	18.9 ± 7.4	0.542*
at tidal inspiration	24.5 ± 7.9	24.9 ± 11.3	0.862*
at maximal deep inspiration	41.8 ± 14.9	35.7 ± 14.1	0.151

TF of diaphragm (%), mean ± SD			
at tidal inspiration	51.3 ± 51.0	42.3 ± 45.3	0.523
at maximal deep inspiration	158.4 ± 83.5	94.8 ± 81.4	0.010
DE (mm), mean ± SD			
at tidal inspiration	19.6 ± 5.4	20.9 ± 8.7	1.000*
at maximal deep inspiration	40.5 ± 12.5	30.8 ± 11.1	0.007
Lung function test, mean ± SD			
FEV_1/FVC (%)	52.5 ± 14.9	52.0 ± 17.4	0.922*
FVC (L)	2.82 ± 0.93	2.11 ± 0.81	0.006
FVC (%)	73.2 ± 16.1	55.0 ± 18.6	< 0.001
FEV_1 (L)	1.42 ± 0.52	1.00 ± 0.38	0.002
FEV_1 (%)	54.6 ± 19.4	40.5 ± 18.1	0.010
RV/TLC (%)	43.7 ± 8.1	51.7 ± 9.4	0.019

SD, standard deviation; mCCI, modified Charlson Comorbidity Index; BMI, body mass index; CAT, COPD assessment test; mMRC, modified Medical Research Council; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; LABA, long-acting β agonist; LAMA, long-acting muscarinic antagonist; ICS, inhaled corticosteroid; DT, diaphragm thickness; TF, Thickening fraction; DE, diaphragm excursion; FEV_1, forced expiratory volume in 1 sec; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity

*Mann-Whitney *U* test

Table 2. Results of the receiver operating characteristic curve analysis for COPD exacerbation

	AUC	95% CI	Cut-off values	*p*-value	Sensitivity	Specificity
TF_{max}	0.745	0.605–0.856	≤ 93.8%	0.001	68.4%	78.8%
DE_{max}	0.721	0.576–0.838	≤44.9 mm	0.003	95.2%	44.8%
FEV_1/FVC	0.508	0.368–0.647	≤64%	0.927	57.1%	21.2%
FVC	0.709	0.570–0.825	≤1.78 L	0.003	47.6%	87.9%
FEV_1	0.747	0.610–0.855	≤1.21 L	< 0.001	85.7%	57.6%
BMI	0.729	0.592–0.840	≤22.5 kg/m^2	0.002	77.3%	66.7%

COPD, chronic obstructive pulmonary disease; AUC, area under curve; CI, confidence interval; TF_{max}, thickening fraction at maximal inspiration; DE_{max}, diaphragm excursion at maximal inspiration; FEV_1, forced expiratory volume in 1 sec; FVC, forced vital capacity; BMI, body mass index

Table 3. Clinical characteristics of COPD patients according to diaphragm ultrasound findings

	TF_{max}			DE_{max}		
	Low (n=19)	High (n=34)	*p*-value	Low (n=36)	High (n=14)	*p*-value
Age (years), mean ± SD	71.3 ± 12.9	74.2 ± 7.7	0.315	72.9 ± 10.0	73.9 ± 9.4	0.755
Male sex, n (%)	15 (78.9)	24 (70.6)	0.746	25 (69.4)	12 (85.7)	0.303
mCCI (points), mean ± SD	1.1 ± 1.5	0.8 ± 1.0	0.411	0.9 ± 1.1	0.5 ± 0.9	0.389
BMI (kg/m^2), mean ± SD	22.4 ± 4.9	22.9 ± 3.8	0.689	22.1 ± 4.4	24.3 ± 3.4	0.237
CAT (points), mean ± SD	20.5 ± 7.1	16.2 ± 9.7	0.167	19.2 ± 9.6	13.9 ± 8.2	0.089
mMRC (points), mean ± SD	2.7 ± 1.2	2.0 ± 1.3	0.061	2.5 ± 1.2	1.7 ± 1.4	0.055
Smoking, n (%)						
Never	9 (47.4)	13 (38.2)	0.325	18 (50.0)	2 (14.3)	0.052
Ex-smoker	9 (47.4)	14 (41.2)		14 (38.9)	8 (57.1)	
Current smoker	1 (5.3)	7 (20.6)		4 (11.1)	4 (28.6)	
Pack-years, mean ± SD	23.2 ± 27.5	25.7 ± 23.2	0.727	23.9 ± 27.5	32.3 ± 17.4	0.209
Duration of COPD (years), mean ± SD	6.7 ± 5.9	4.7 ± 4.5	0.190	5.4 ± 5.3	5.1 ± 5.3	0.838
GOLD group, n (%)						
A	1 (5.3)	13 (38.2)	0.044	6 (16.7)	7 (50.0)	0.009
B	6 (31.6)	10 (29.4)		11 (30.6)	3 (21.4)	
C	2 (10.5)	3 (8.8)		2 (5.6)	3 (21.4)	
D	10 (52.6)	8 (23.5)		17 (47.2)	1 (7.1)	
Baseline COPD medication, n (%)						
None	0 (0.0)	3 (8.8)	0.111	3 (8.3)	0 (0.0)	0.005
LABA or LAMA	1 (5.3)	0 (0.0)		0 (0.0)	1 (7.1)	
ICS/LABA	0 (0.0)	5 (14.7)		0 (0.0)	4 (28.6)	
LABA/LAMA	6 (31.6)	12 (35.3)		14 (38.9)	4 (28.6)	
ICS/LABA/LAMA	12 (63.2)	14 (41.2)		19 (52.8)	5 (35.7)	
Lung function test, mean ± SD						

FEV_1/FVC (%)	53.9 ± 15.4	51.3 ± 16.4	0.569	51.0 ± 16.4	53.6 ± 15.9	0.619
FVC (L)	2.20 ± 0.92	2.72 ± 0.94	0.060	2.20 ± 0.83	3.08 ± 0.83	0.002
FVC (%)	55.8 ± 17.7	71.6 ± 18.4	0.004	59.7 ± 18.9	77.3 ± 14.7	0.003
FEV_1 (L)	1.13 ± 0.50	1.31 ± 0.51	0.232	1.026 ± 0.32	1.60 ± 0.59	< 0.001
FEV_1 (%)	44.6 ± 21.2	51.4 ± 19.7	0.254	41.9 ± 15.7	60.9 ±23.2	0.002
RV/TLC (%)	51.9 ± 10.8	44.8 ± 7.0	0.044	50.4 ± 8.1	41.5 ± 7.7	0.014
Exacerbation status, n (%)	12 (63.2)	8 (23.5)	0.007	20 (55.6)	1 (7.1)	0.003

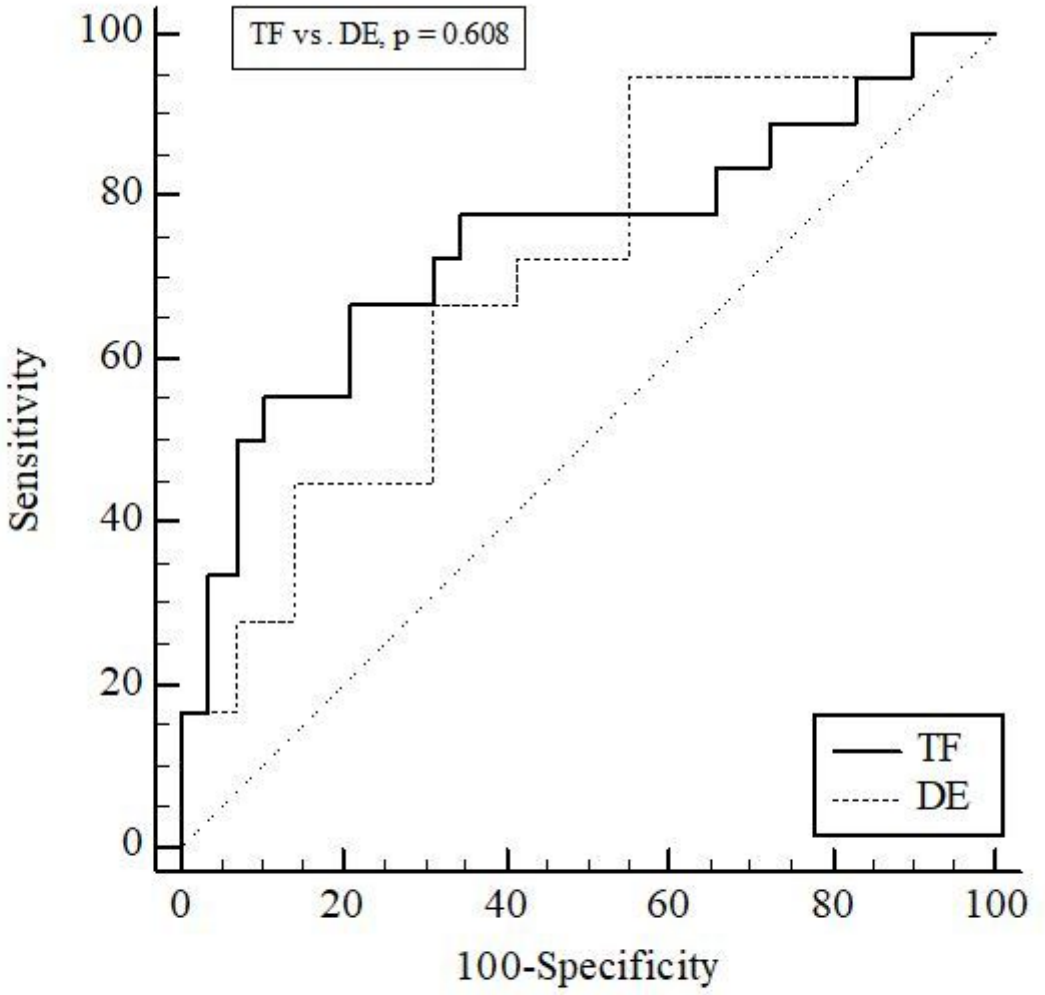
COPD, chronic obstructive pulmonary disease; AUC, area under curve; CI, confidence interval; TF_{max}, thickening fraction at maximal inspiration; DE_{max}, diaphragm excursion at maximal inspiration; mCCI, modified Charlson Comorbidity Index; BMI, body mass index; CAT, COPD assessment test; mMRC, modified Medical Research Council; COPD, chronic obstructive pulmonary disease; GOLD, Global Initiative for Chronic Obstructive Lung Disease; LABA, long-acting β agonist; LAMA, long-acting muscarinic antagonist; ICS, inhaled corticosteroid; FEV_1, forced expiratory volume in 1 sec; FVC, forced vital capacity; RV, residual volume; TLC, total lung capacity

Table 4. Logistic regression analysis for estimating exacerbation of chronic obstructive pulmonary diseases

Model 1	Univariate		Multivariate	
	p-value	OR (95% CI)	*p*-value	OR (95% CI)
Age	0.722	0.99 (0.94–1.05)	0.682	0.98 (0.91–1.06)
Male sex	0.317	1.96 (0.53–7.28)	0.544	1.74 (0.29–10.34)
mCCI	0.049	1.62 (1.00–2.62)	0.157	1.73 (0.81–3.70)
BMI	0.007	0.80 (0.68–0.94)	0.002	0.70 (0.56–0.88)
Low TF_{max}	0.006	5.57 (1.64–18.94)	0.014	8.40 (1.55–45.56)
Model 2	**Univariate**		**Multivariate**	
Age	0.722	0.99 (0.94–1.05)	0.233	0.95 (0.88–1.03)
Male sex	0.317	1.957 (0.53–7.28)	0.393	2.16 (0.37–12.67)
mCCI	0.049	1.62 (1.00–2.62)	0.032	2.68 (1.09–6.60)
BMI	0.007	0.80 (0.68–0.94)	0.022	0.79 (0.64–0.97)
Low DE_{max}	0.011	16.25 (1.92–137.78)	0.038	11.51 (1.15–115.56)

mCCI, modified Charlson Comorbidity Index; BMI, body mass index; TF_{max}, diaphragm thickening fraction during maximal deep breathing; DE_{max}, diaphragm excursion during maximal deep breathing

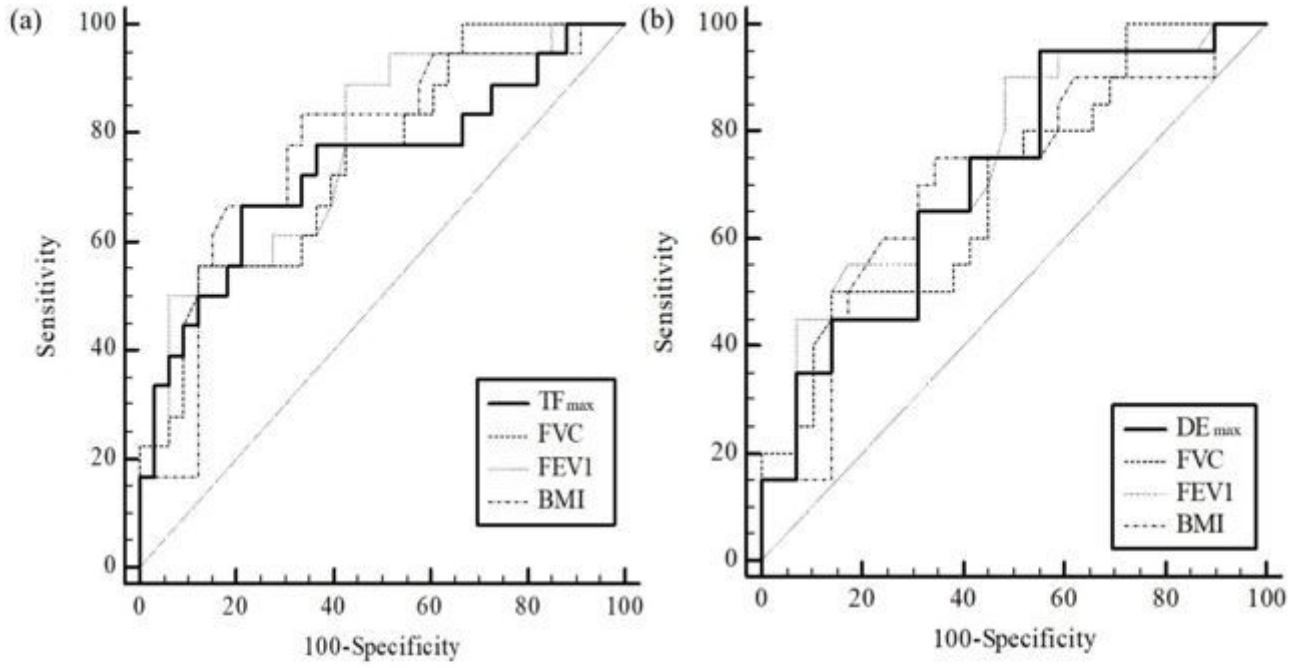
Figures



TF, thickening fraction at maximal inspiration; DE, diaphragm excursion at maximal inspiration

Figure 1

Receiver operating characteristic (ROC) curve analysis for determining chronic obstructive pulmonary disease exacerbation status using diaphragm ultrasound findings The ROC curve for distinguishing exacerbation from a stable status indicated that the outcomes were fair. The area under the curve (AUC) of the thickening fraction during maximal deep breathing (TFmax) was 0.745. The AUC of diaphragm excursion during maximal deep breathing (DEmax) was 0.721. No significant difference was observed between TFmax and DEmax for distinguishing exacerbation status (p = 0.608).



(c)

	TF_{max}			DE_{max}		
	vs. FVC	vs. FEV_1	vs. BMI	vs. FVC	vs. FEV_1	vs. BMI
p-value	0.943	0.631	0.887	0.536	0.303	0.569

BMI, body mass index; TF_{max}, thickening fraction at maximal inspiration; DE_{max}, diaphragm excursion at maximal inspiration; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 sec

Figure 2

Multiple comparative analysis of the receiver operating characteristic (ROC) curve between diaphragm thickening, diaphragm excursion, lung function, and body mass index (BMI). The ROC curve of thickening fraction of diaphragm during maximal breathing (TFmax) (a) and diaphragm excursion during maximal breathing (DEmax) (b) showed in figure 2. (c) There was no significant difference for distinguishing exacerbation both in TFmax and DEmax compared to those of forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and BMI in multiple comparative analysis of the ROC curve analysis.

Supplementary Files

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- Supplementarymaterials.docx