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Ultrasonographic evaluation of diaphragmatic thickness and movement for assessment of diaphragmatic dysfunction in COPD patients

Eman Mohamed Dahma^{1*}, Walaa Mowafy El-lawaty², Dalia Ezzat Shaarawy², Mohammed Mahmoud Dawoud³ and Wafaa Saleh El-Shimy²

Abstract

Backgrounds Chronic obstructive pulmonary disease (COPD) is often ascribed to the disparity that exists between ventilatory loading and diaphragmatic function. The principal factor contributing to this imbalance is the mechanical difficulties brought about by pulmonary hyperinflation. This causes the fiber lengths of the respiratory muscles to be suboptimal, thereby decreasing the tension generated. The frailty of the respiratory musculature is further exacerbated by hypercapnia, acidosis, nutritional deficiency, and steroid therapy. As the principal respiratory muscle, the diaphragm is responsible for 75% of quiescent lung ventilation. Ultrasonography has exhibited substantial promise in evaluating the effectiveness of the diaphragm. The goal of the research was to assess the diaphragmatic function in COPD patients using ultrasonographic examination and to study its correlation with pulmonary function tests.

Methods This work was performed on 60 individuals with COPD and 20 healthy volunteers (control group). All the subjects were sequentially examined by chest X-ray and spirometry in one time and then repeated 15–45 min after the first dose of inhalation therapy (salbutamol); then, 6MWT, ABG, and ultrasonography were done for all patients.

Results In COPD patients, diaphragmatic thickness and excursion were substantially reduced in comparison to the control group; these parameters were also significantly correlated with pulmonary function tests.

Conclusions A reduction in diaphragmatic thickness and excursion is observed in patients diagnosed with COPD.

Keywords Chronic obstructive pulmonary disease, Diaphragmatic thickness, Diaphragmatic movement

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Background

Chronic obstructive pulmonary disease (COPD) is a treatable and preventable condition with a high prevalence. Persistent respiratory symptoms and ventilation obstruction resulting from abnormalities in the airway and/or alveoli define this condition [1]. Around 60–80% of the respiratory workload is executed by the diaphragm, the principal muscle responsible for human respiratory movements, during respiration [2]. As a result, the diaphragm's function in COPD has drawn more



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attention and is now thought of as an indicator for disease progression. Diaphragmatic dysfunction is caused by the absence of one of the two main factors that affect muscle action: strength and endurance, leading to a weak contraction. Systemic inflammation, hyperinflation, oxidative stress [3, 4], chronic hypoxia, and malnutrition [5, 6] all are some of the potential causes of diaphragm dysfunction in individuals with COPD. One of the most important aspects of evaluating individuals with COPD is the assessment of the diaphragm. Measuring the transdiaphragmatic pressure following magnetic stimulation of the phrenic nerve is the gold standard for determining diaphragmatic dysfunction, but it requires considerable expertise, invasive, and is not available at the bedside [7]. Chest x-ray, fluoroscopy, and computed tomography are used to assess diaphragmatic function, but they are not sensitive beside the hazards of ionizing radiation [8]. Ultrasonography has emerged as a noninvasive and effort-independent tool to assess diaphragmatic function [9, 10]. Diaphragmatic performance was also used to assess weaning from mechanical ventilation [11] as well as evaluation of acute exacerbation of COPD [12].

Methods

Inclusion criteria

This was an observational prospective, case–control study. It was conducted over the interval between April 2020 and April 2021 after approval of the committee for scientific research ethics at Faculty of Medicine, Tanta University (no. 33703) and consent was obtained in writing form from every participant.

Sixty patients > 40 years with clinically stable COPD were recruited throughout their follow-up in outpatient department of Chest University Hospital. They were classified and diagnosed in accordance with GOLD 2021 criteria [1]. Also, 20 age-matched apparently healthy volunteers were included.

Exclusion criteria

Patients with age less than 40 years, COPD exacerbation within the previous 6 weeks, additional pulmonary conditions including pneumothorax, pleural effusion, lung cancer, phrenic nerve palsy, pneumonia, or musculoskeletal diseases, recognized cardiovascular insufficient supply (Ejection fraction < 50%), upper abdominal surgeries, ascites, and being obese [those who have a body mass index (BMI) that is greater than 30] were excluded.

All participants were subjected to the following: detailed history taking, clinical evaluation, BMI evaluation, radiological examination, arterial blood gases assessment, spirometric assessment according to American Thoracic Society guidelines (2019) [13] using computerized spirometry apparatus "Spirosoft spirometry SP-5000, Fukuda Denshi, Japan," a 6-min walk test in accordance with American Thoracic Society recommendations [14], and ultrasonography of the diaphragm using (ProSound Aloka F37, Hitachi Ltd., Japan) ultrasound machine.

The high-frequency (5-13 MHz) linear probe was used for observing hemidiaphragms in order to determine the diaphragmatic thickness. While the individual was in a semi-sitting position, the probe was positioned above the area of apposition perpendicular to the ninth intercostal space between the midaxillary and anterior axillary lines. Using B-mode, the diaphragm was identified as a threelayer structure, comprising two hyper-echoic outer layers (the peritoneum and pleura) surrounding a hypo-echoic inner muscle layer. As demonstrated in Fig. 1, the thickness of each hemidiaphragm was determined by directly measuring the distance between the center of the pleural membrane and the center of the peritoneal membrane on the frozen B-mode images. The measurements were collected at the ending of maximal inspiration and maximal expiration, specifically at the point of total lung capacity (Tmax) and residual volume (Tmin), respectively. Average measurements from at least three separate breathing cycles were taken. By dividing the average diaphragmatic thickness during maximal inspiration (Tmax) by the average diaphragmatic thickness during maximal expiration (Tmin), the TH ratio was calculated.

Diaphragmatic excursion (DE) shown in Fig. 2 was assessed by visualizing the right hemidiaphragm via the low-frequency (2–6 MHz) convex probe through the hepatic window. In a semi-recumbent posture, the anterior subcostal region between the anterior axillary line and midclavicular line was scanned by B-mode. The right hemidiaphragm, which separates the air-inflated lung and liver parenchyma, appears as a thick hyperechoic line. By positioning calipers at the base and summit of the diaphragmatic slope throughout deep breathing, the diaphragmatic excursion's amplitude was determined in M-mode. Because of technical issues with the left diaphragmatic excursion caused by the spleen's limited acoustic window and the interposed stomach gas, only the right diaphragmatic excursion was measured.

Statistical analysis

The statistical analysis was conducted using SPSS (SPSS Inc., Chicago, USA, Version 25.0). In order to compare categorical qualitative parameters expressed as frequency and percentage, the chi-square test was applied. To compare continuous quantitative parameters, the ANOVA test was utilized; the parameters were presented as mean \pm SD. In order to ascertain the correlation between the measured ultrasonographic parameters and the clinical characteristics of the patients, Spearman's correlation



Fig. 1 Diaphragmatic thickness



Fig. 2 Diaphragmatic excursion

analysis was conducted. The receiver operating characteristics curve (ROC) test was employed to evaluate the sensitivity and specificity of all components comprising diaphragmatic ultrasonography.

Results

Of 123 COPD patients were evaluated for eligibility criteria of the study, we selected 20 patients in each COPD GOLD 2, 3, and 4 groups, and 63 patients were excluded as 51 patients with exacerbations over the past 3 months, 7 patients with umbilical hernia, 3 patients with right minimal pleural effusion detected by ultrasound, 1 patient with upper abdominal surgery, and 1 patient with moderate ascites.

Basic demographic and clinical data of all individuals are displayed in Table 1. There were highly significant variations among groups regarding age, smoking prevalence, pH, Pao₂, Paco₂, and 6MWT.

Regarding diaphragmatic thickness, the mean values of Rt Tmax, Lt Tmax, Rt Tmin, and Lt Tmin were noticeably reduced in COPD groups when contrasted to control group (Table 2).

Significantly higher mean values of Tmax and Tmin were observed in COPD grade 2 compared to grades 3 and 4, and in grade 3 compared to grade 4, although

Age Mean±SD 54.8 ± 6.4 56.2 ± 5.9 62.2 ± 6.9 64.6 ± 5.8 $F=10.5$ Gender Male $12 (60\%)$ $14 (70\%)$ $15 (75\%)$ $16 (80\%)$ $\chi^2 = 2.1$ Female $8 (40\%)$ $6 (30\%)$ $5 (25\%)$ $4 (20\%)$ $\chi^2 = 84.9$ Smoking Current $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $0 (0\%)$ $\chi^2 = 84.9$ Smoking Current $0 (0\%)$ $1 (5\%)$ $1 (5\%)$ $1 (5\%)$ $\chi^2 = 84.9$ BMI Nonsmoker $20 (100\%)$ $1 (5\%)$ $0 (0\%)$ $0 (0\%)$ $\chi^2 = 84.9$ BMI Mean±SD 25.5 ± 2.5 26.6 ± 2.6 24.7 ± 3.1 1.8 PH Mean±SD 7.4 ± 0.01 7.4 ± 0.04 7.39 ± 0.03 7.36 ± 0.01 8.5	 -6.9 64.6±5.8 5%) 16 (80%) %) 4 (20%) 	F = 10.5	0.214	* 0000					
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PO2 Mean±SD 85.7±4.2 67.6±6.8 62±7.3 48.1±9.7 90.4	7.3 48.1±9.7	90.4	0.001*	0.001*	0.001*	0.031*	0.001*	0.001*	< 0.05
pCO2 Mean±SD 39.5±3.5 43.1±4.7 50.2±9 59.2±7.4 34.9	-9 59.2±7.4	34.9	0.013*	0.001*	0.001*	0.001*	0.001*	0.001*	< 0.05
6MWT (m) Mean±SD 545±79.7 388.5±63.5 283±63.7 150±40 138.4	·63.7 150±40	138.4	0.001*	0.001*	0.001*	0.001*	0.001*	0.001*	< 0.05
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 Table 2
 Statistical comparison of ultrasonographic parameters among different groups

		Controls	Grade 2	Grade 3	Grade 4	F-test	P1	P2	P3	P-total
Rt Tmax (mm)	$Mean \pm SD$	4.4±1.2	4.1±0.7	3±0.8	2.5±0.8	18.1	0.00*	0.00*	< 0.05*	0.006*
Rt Tmin (mm)	$Mean \pm SD$	3.1 ± 1.4	2.8 ± 0.9	2±0.9	1.7 ± 0.7	8.8	0.001*	0.00*	< 0.05*	0.03*
Rt TH ratio	$Mean \pm SD$	1.4 ± 0.5	1.5 ± 0.4	1.5 ± 0.3	1.4±0.1	0.4	0.8	0.3	0.7	0.2
Lt Tmax (mm)	$Mean \pm SD$	4.1 ± 1.05	4.1 ± 0.7	2.9±0.7	2.4±0.7	21	0.00*	0.00*	< 0.05*	0.003*
Lt Tmin (mm)	$Mean \pm SD$	2.8 ± 1.1	2.8±0.7	1.9±0.7	1.7±0.6	9.5	0.00*	0.00*	< 0.05*	0.02*
Lt TH ratio	$Mean \pm SD$	1.5 ± 0.38	1.5 ± 0.3	1.5 ± 0.2	1.4 ± 0.1	0.5	0.7	0.4	0.6	0.2
Excursion (mm)	$Mean\pmSD$	41.8±13.4	29.4 ± 8.1	25.4 ± 6.9	17.7±4.1	25.9	0.001*	0.001*	< 0.05*	0.001*

Data are presented as mean \pm SD (standard deviation), *P** significant *P*-value \leq 0.05, *P*1 between grades 2 and 3,

P2 between grades 2 and 4, P3 between grades 3 and 4, Rt Tmax thickness of right hemidiaphragm total lung capacity, Rt Tmin thickness of right hemidiaphragm at residual volume, Rt TH ratio thickness ratio resulting from the equation of Rt Tmax/Rt Tmin, Lt Tmax thickness of left hemidiaphragm at total lung capacity, Lt Tmin thickness of left hemidiaphragm at residual volume, Lt TH ratio thickness ratio resulting from the equation of Rt Tmax/Rt Tmin, Lt Tmax thickness of left hemidiaphragm at total lung capacity, Lt Tmin thickness of left hemidiaphragm at residual volume, Lt TH ratio thickness ratio resulting from the equation of Lt Tmax/Lt Tmin, excursion diaphragm movement between total lung capacity and residual volume

there were nonsignificant differences between patients and controls regarding Rt TH ratio and Lt TH ratio. In contrast to the control group, DE levels were significantly lower in the COPD group. The mean values of diaphragmatic excursion were significantly higher in grade 2 than grades 3 and 4 and were higher in grade 3 than grade 4.

Receiver operating characteristic (ROC) analysis was done for diaphragmatic thickness and excursion (Table 3, Fig. 3). The diaphragmatic excursion showed the highest sensitivity and specificity parameters for COPD with both sensitivity and specificity equal (88% versus 70%) respectively at cutoff value 3.4 cm. Tmax and Tmin showed a lesser sensitivity and specificity percentages (81% versus 60% at cutoff value 4 mm and 77% versus 55% at cutoff value 2.6 mm) for Tmax and Tmin sensitivity and specificity respectively.

As regarding correlations, there was nonsignificant correlation between age, sex, BMI, pO_2 , pCO_2 , diaphragmatic thickness and excursion. A positive correlation that was statistically significant was identified between diaphragmatic thickness and excursion as well as 6MWT. A statistically significant positive correlation (FEV1% predicted) was identified between spirometric data and diaphragmatic thickness and excursion (Table 4).

Discussion

COPD is a treatable and preventable condition with a high prevalence. Majority of the respiratory workload is executed by the diaphragm. As a result, the diaphragm's function in COPD has drawn more attention. Ultrasonography has emerged as a noninvasive and effortindependent tool to assess diaphragmatic function. We used ultrasonography to assess diaphragmatic thickness and excursion and compared it to pulmonary function results.

In the present study, as compared to the control group, Tmax and Tmin were significantly lower in the COPD group.

Our findings were corroborated by Smargiassi A. et al. [15] who assessed diaphragmatic thickness in 23 participants and documented a precipitous decrease in diaphragmatic thickness among COPD patients compared to the control group.

However, in contrast, Baria M. R. et al. [8] discovered that there were no substantial variations observed in the thickness of the diaphragm or the TH ratio between sides when comparing groups (control participants or COPD individuals) or between groups (50 COPD patients and 150 healthy control individuals). The exclusion of the subgroup exhibiting extensive air entrapment (residual volume surpassing 200%) could have contributed to this outcome.

 Table 3
 ROC analysis of diaphragmatic parameters

	Cutoff	AUC	Sensitivity	Specificity	PPV	NPV	Accuracy
Tmax (mm)	4	0.752	81	60	86	51	76
Tmin (mm)	2.6	0.702	77	55	84	44	71
Excursion (mm)	34	0.860	88	70	90	67	84

PPV positive predictive value, NPV negative protective value, AUC area under the curve



Diagonal segments are produced by ties.

Fig. 3 ROC analysis of diaphragmatic thickness and excursion

Table 4 Correlation between the diaphragmatic thickness and movement using ultrasonography to different demographic and clinical data

Parameters	Age	Age			PO2		pCO ₂		6MWT (m)		FEV1% predicted	
	r	р	r	p	r	p	r	р	r	p	r	p
Grade 2												
Thickness	0.16	0.4	0.13	0.6	0.11	0.9	0.17	0.45	0.7	0.02*	0.49	0.01*
Movement	0.3	0.15	0.12	0.6	0.08	0.7	0.13	0.5	0.8	0.002*	0.7	0.02*
Grade 3												
Thickness	0.14	0.5	0.2	0.3	0.02	0.9	0.09	0.7	0.6	0.03*	0.22	0.02*
Movement	0.04	0.9	0.21	0.3	0.001	0.9	0.06	0.8	0.6	0.004*	0.5	0.03*
Grade 4												
Thickness	0.3	0.1	0.02	0.9	0.1	0.6	0.01	0.9	0.5	0.05*	0.15	0.04*
Movement	0.02	0.9	0.2	0.3	0.01	0.9	0.1	0.6	0.5	0.02*	0.3	0.04*

 P^* significant P-value ≤ 0.05 , BMI body mass index, Po2 partial pressure of oxygen, Pco2 partial pressure of carbon dioxide, 6MWT 6-min walk test, FEV1% forced expiratory volume during the first second (post bronchodilator results)

The current study found that the COPD group exhibited a significantly shorter diaphragmatic excursion than the control group. healthy persons and 60 COPD patients and stated that COPD patients had less diaphragm mobility than did healthy individuals.

This was in agreement with Scheibe N. et al. [16] who studied diaphragmatic thickness and mobility in 20 In the current study, the mean values of diaphragmatic excursion were significantly higher in group 2 than groups 3 and 4 and were higher in group 3 than group 4 with a statistically high significant difference among the three groups.

Scheibe N. et al. [16] also reported decreasing diaphragmatic mobility with enhanced COPD severity.

As determined by the receiver operating characteristics (ROC) analysis, a number of the ultrasonographic parameters utilized in the diagnosis of COPD exhibited inadequate sensitivity and specificity. At a cutoff value of 3.4 cm, the diaphragmatic excursion exhibited the highest sensitivity and specificity (88% versus 70%). These findings increase the diagnostic efficacy of diaphragmatic ultrasonographic excursion measurement in COPD. These results are in agreement with several study groups including Kareem J. et al. [17] and Essawy T. et al. [18].

In the current study, there was a moderate positive association among Tmax and Tmin of both hemidiaphragms and BMI.

Comparable findings were observed in this investigation and the one documented by Smargiassi A. et al. [15] and Boon A. J. et al. [20], who established a correlation between diaphragmatic thicknesses and physical attributes including body mass index (BMI) and height.

But Cimsit C. et al. [19] found out that BMI dropped as the illness stage advanced. The correlation between BMI and diaphragm thickness, however, was not found.

In the current research, there was also a highly substantial positive correlation between diaphragmatic thicknesses and the spirometric data (FEV1% predicted) with a nonsignificant correlation between ratios of diaphragmatic thickness and FEV1% predicted.

According to Smargiassi A. et al. [15] who assessed diaphragmatic thickness in 23 participants, Tmax was most strongly correlated with fat-free mass (FFM), BMI, and lung hyperinflation.

Yalçin B. et al. [21], who assessed diaphragmatic thickness and mobility in 67 COPD patients and 53 healthy volunteers, discovered a significant correlation between pulmonary function tests and diaphragmatic thickness in patients with COPD.

On the contrary, Cimsit C. et al. [19] assert that there is no correlation between diaphragmatic thickness and pulmonary function tests in patients with chronic obstructive pulmonary disease (COPD), with the exception of those with mild COPD. This lack of correlation is likely attributable to the fact that the measurements were exclusively performed during the end-expiratory phase. In addition, the limited sample size of the study group might have an impact on the correlation between ultrasound measurements and the severity of COPD.

In the present study, the diaphragmatic excursion was found to be positively correlated with BMI.

Smargiassi A. et al. [15] who enrolled 23 clinically stable COPD patients found that diaphragmatic excursion was closely related to BMI.

There was a statistically high significant positive correlation between diaphragmatic excursion and 6-min walk test (6MWT).

Scheibe N. et al. [16] who studied diaphragmatic thickness and mobility in 20 healthy persons and 60 COPD patients stated that there is a moderate correlation between diaphragmatic excursion and 6MWT.

A significant correlation among diaphragmatic excursion and the spirometric data (predicted FEV1%) was found in the current study. It has been demonstrated that ultrasonographic measurements of the diaphragmatic excursion in patients with COPD are negatively correlated with the progression of COPD, with grade IV COPD patients exhibiting the lowest ultrasonographic measurements.

In agreement with our results, Scheibe N. et al. [16] who studied diaphragmatic thickness and mobility in 20 healthy persons and 60 COPD patients found out that diaphragmatic movement was related to lung function parameters,

while Smargiassi A. et al. [15] who studied diaphragmatic thickness and mobility in 23 COPD patients found no relation between diaphragmatic excursion and the spirometric data (FEV1) and stated that it is only related to BMI.

Limitations

A limitation of this research is the relatively small sample size of enrolled patients. Lack of comparative analysis with gold standard techniques used to evaluate diaphragm function constitutes an additional limitation of our research.

Conclusion

Diaphragmatic thickness and excursion significantly positively correlated to the spirometric data (FEV1% predicted). Diaphragmatic assessment could be a prognostic factor for COPD severity and could guide the treatment plan.

Future directions

Assessment of diaphragmatic performance could be a worthy substitute for spirometry in the future. Diaphragmatic performance could also be used to assess weaning from mechanical ventilation and estimation of acute exacerbation of COPD.

Abbreviations

6MWT	Six-minute walk test
BMI	Body mass index
COPD	Chronic obstructive pulmonary disease

Diaphragmatic excursion
Fat-free mass
Receiver operating characteristic
Standard deviation
Thickening ratio
Forced expiratory volume during the first second
Thickness of right hemidiaphragm total lung capacity
Thickness of right hemidiaphragm at residual volume
Thickness ratio resulting from the equation of Rt Tmax/Rt Tmin
Thickness of left hemidiaphragm at total lung capacity
Thickness of left hemidiaphragm at residual volume
Thickness ratio resulting from the equation of Lt Tmax/Lt Tmin
Diaphragm movement between total lung capacity and residual
volume

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Nil.

Authors' contributions

MMD and EMD were tasked with data acquisition, while WME and DEE conceived and oversaw the research. The data were analyzed and interpreted by WSE. The manuscript was subject to feedback from all authors at different phases of its development. The final manuscript was reviewed and endorsed by all authors.

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Availability of data and materials

Materials and data are accessible upon the author's reasonable request.

Declarations

Ethics approval and consent to participate

It was approved by the Tanta University Faculty of Medicine's ethics committee and commenced in April 2020 and concluded in April 2021. Written informed assent was acquired from each participant.

Consent for publication

Permission to publish in the journal is obtained from all authors.

Competing interests

The authors declare that they have no competing interests.

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