Transthoracic ultrasonographic evaluation of diaphragmatic excursion in patients with chronic obstructive pulmonary disease

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Background Chronic obstructive pulmonary disease (COPD) is a multisystem disorder that mainly besides the lungs also affects the muscle mass. The force generated by the respiratory muscles decreases, resulting in a negative effect on ventilation and exercise capacity. Recent studies have reported that M-mode ultrasonography is reliable and relatively easy to use for assessment of diaphragmatic motion.

Objective To evaluate diaphragmatic excursion by M-mode ultrasonography in patients with COPD and to correlate it with different clinical and ventilatory variables.

Patients and methods A total of 40 patients with COPD who attended Chest Diseases Department Al-Azhar University Hospitals from January 2017 to May 2017 were recruited in this study. Informed consent was obtained. Diagnosis and severity of COPD was made according to the Global Initiative for Chronic Obstructive Lung Disease guidelines. All patients in this study were subjected to full medical history, clinical examination, pulmonary function tests, calculation of BMI, arterial blood gases analysis, 6-min walk test, and ultrasound imaging of the diaphragm.

Results Diaphragmatic excursion during quiet breathing did not differ significantly between the patients and the controls (P=0.085). However, during deep breathing, the degree of diaphragmatic excursion was lower in the patients (P=0.001). Diaphragmatic excursion during deep breathing correlated significantly with disease severity(r=0.86); the percentage of the predicted forced expiratory volume in the first second, forced vital capacity, and forced expiratory volume in the first second/forced vital capacity (r=0.84, 0.72, and 0.80, respectively); and the 6-min walk test (r=0.47).

Conclusion M-mode ultrasonography is an easy, noninvasive and inexpensive method for evaluation of diaphragmatic excursion. Patients with COPD had significantly lower diaphragmatic excursion than normal ones.
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Introduction

Diaphragmatic dysfunction is not uncommon in patients with chronic obstructive pulmonary disease (COPD). The commonest and oldest known cause for diaphragmatic dysfunction in patients with COPD is mechanical disadvantage owing to overinflation of the lungs [1]. More recently recognized reasons for the diaphragmatic weakness are remodeling [2], exposure to oxidative stress [3], and a reduction of myosin filaments owing to reduced protein production and increased apoptosis of muscle cells [4].

The best available method, the gold standard, for the measurement of diaphragmatic dysfunction is the measurement of the transdiaphragmatic pressure after stimulation of the phrenic nerve. However, this test is invasive and time consuming [5].

Ultrasound imaging of the diaphragm has been broadly applied in some chronic respiratory diseases, such as COPD, diaphragmatic paralysis, as well as during weaning from mechanical ventilation [6–8]. In comparison with other imaging methods, this technique has many advantages, such as absence of radiation, portability, repeatability, low price, real-time imaging, and noninvasiveness. In COPD, reduced diaphragmatic mobility, as determined by ultrasound, has proven to be a good predictor of failure to wean off mechanical ventilation [9] and has been shown to correlate significantly with disease severity [10].

Aim

To evaluate diaphragmatic excursion by M-mode ultrasonography in patients with chronic obstructive pulmonary disease and to correlate it with different clinical and ventilatory variables.

Patients and methods

This study included two groups,

> Group 1: Forty clinically stable male patients with COPD with a mean age of 54.8±6.51 years attending the Chest Diseases Department, Al-Azhar University Hospitals between January 2017 and May 2017 were included in this study. Female patients were excluded from the study

because the number of female patients during this period was too small for statistical analysis. COPD was diagnosed according to the criteria of the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [11]. All patients were current or former smokers. The study exclusion criteria were as follows: (a) exacerbations of COPD during the last 6 weeks; (b) blood pH less than 7.35; (c) other known pulmonary diseases besides COPD such as pleural effusion, pneumothorax, and phrenic nerve palsy; (d) known cardiac insufficiency; (e) chest deformity; and (f) obesity (patients with a BMI ≥30).

Group 2: Ten apparently healthy individuals were incorporated as control group. The controls were well matched to the patients for age, sex, and BMI.

All patients and healthy individuals after providing written informed consent were subjected to the following:

(1) Full history taking and clinical examination.
(2) Pulmonary function tests: the forced vital capacity (FVC) and the forced expiratory volume in the first second (FEV1) were measured, and the ratio of FEV1 to FVC was calculated. All included patients had an FEV1/FVC of less than 70%. According to the GOLD guidelines, patients with an FEV1 more than or equal to 80% predicted were classified as GOLD I (mild), patients with an FEV1 between 50 and 80% predicted were classified as GOLD II (moderate), patients with an FEV1 between 30 and 50% were classified as GOLD III (severe), and finally, patients with an FEV1 less than 30% were classified as GOLD IV (very severe) [12].
(3) Height and weight were measured, and BMI was calculated. Obese patients (BMI ≥30 kg/m^2) were excluded from the study.
(4) Arterial blood gases analysis.
(5) Six-min walk test (6MWT): this was conducted in a 30-m long, flat corridor. Standardized instructions and encouragement were given, according to ATS guidelines [13].
(6) Ultrasound imaging of the diaphragm: In all patients and controls, we performed ultrasound imaging of the diaphragm. During the procedure,

patients were in a semirecumbent position. For the evaluation of diaphragmatic mobility, a 2–5 MHz convex transducer was placed over the anterior subcostal region between the midclavicular and anterior axillary lines. The transducer was angled medially and anteriorly so that the ultrasound beam would reach the posterior third of the right hemidiaphragm. The greatest craniocaudal excursion occurs in this region of the diaphragm [14]. The ultrasound was used in B-mode to visualize the diaphragm. The right hemi-diaphragm appeared as a thick, curved line with hyperechogenicity. In this position, imaging was then changed to M-mode to measure the amplitude of the craniocaudal diaphragmatic excursion during quiet breathing and deep breathing [15,16]. Three consecutive respiratory cycles were recorded for each type of breathing, and maximal values were selected. We also assessed the mobility of the diaphragm during a sniff test to exclude the presence of paradoxical movement.

Statistical analysis
Data analysis was performed using statistical package for the social sciences, version 20.0 (SPSS; SPSS Inc., Chicago, Illinois, USA). P less than or equal to 0.05 was considered statistically significant. Parametric data were expressed as mean±SD and were compared using the paired or independent Student's t-test. Pearson's correlation coefficient (r) was used to calculate correlations between various variables.

Results
This study included two groups:

Group 1: Forty clinically stable male patients with COPD with a mean age of (54.8±6.51) attending Chest Diseases Department, Al-Azhar University Hospitals between January 2017 to May 2017.

Group 2: Ten apparently healthy individuals as control group.

All the patients with COPD and control individuals were males. No statistically significant difference was detected between the two groups regarding age (P=0.085) and BMI (P=0.487), with a statistically significant difference regarding smoking index (P=0.001) (Table 1).

Table 1 Demographic data of the patients with chronic obstructive pulmonary disease and controls

	Group 1 (N=40) (mean±SD)	Group 2 (N=10) (mean±SD)	t	P
Age	54.8±6.51	52.6±5.65	1.77	0.085
Smoking index	300.00±23.08	100.00±9.89	6.16	0.001
BMI	26.74±1.53	28.36±2.37	0.72	0.487

Regarding FEV1 (%predicted), FVC (%predicted), and FEV1/FVC (%), there was a statistically significant difference between patients with COPD and normal individuals (P=0.001, 0.040, and 0.001, respectively).

Moreover, there was a statistically significant difference between patients with COPD and normal individuals regarding PaO_2, $PaCO_2$, SO_2, and 6MWT (P=0.001, 0.002, 0.046, and 0.001, respectively) with no statistically significant difference regarding pH (P=0.065) (Table 2).

According to severity, patients with COPD were categorized as moderate COPD cases (n=20), severe COPD cases, (n=13), and very severe COPD cases (n=13). No mild cases were included (Table 3).

On assessment of diaphragmatic motion by M-mode ultrasonography, diaphragmatic excursion during quiet breathing did not differ significantly between the patients and the controls (P=0.085). However, there was a statistically significant difference in diaphragmatic excursion during deep breathing (P=0.001) (Table 4).

Assessment of diaphragmatic motion during quiet breathing in different GOLD stages revealed that there was no statistically significant difference in diaphragmatic excursion among patients of different GOLD stages (P=0.099). During deep breathing, diaphragmatic excursion values among patients of GOLD stages II, III, and IV were 4.52±1.64, 3.73±1.12, and 3.22±1.08 cm, respectively, with statistically significant difference (P=0.002) (Table 5).

This study demonstrated that there was a statistically significant negative correlation between GOLD staging of patients with COPD and diaphragmatic excursion (P=0.001). There was a statistically significant positive correlation between spirometric variables (FEV1% predicted, FVC% predicted, and FEV1/FVC) and diaphragmatic excursion (P=0.001, 0.002, and 0.012, respectively). Regarding arterial blood gases variables (PaO_2, $PaCO_2$, SO_2%, and pH), there was a statistically insignificant positive correlation between PaO_2, SO_2%, and pH on one side and diaphragmatic excursion on the other side (P=0.163, 0.142, and 0.202, respectively). However, there was a statistically significant negative correlation between $PaCO_2$ and diaphragmatic excursion (P=0.022). There was a statistically significant positive correlation between 6MWT and diaphragmatic excursion (P=0.020) (Table 6).

Discussion

On assessment of diaphragmatic motion by M-mode ultrasonography, the excursion at the right hemi-diaphragm using the liver as an ultrasound window was only measured as the left hemidiaphragm has a smaller ultrasonographic window owing to the spleen and also is frequently masked by the descending lung on full inspiration. During quiet breathing, diaphragmatic excursion was 2.23±0.50 cm in group 1 and 2.28± 0.59 cm in group 2, with no significantly significant difference (P=0.085). However, during deep breathing, diaphragmatic excursion was 3.83±1.13 cm in group 1 and 6.32±0.88 cm in group 2, with a statistically significant difference (P=0.001). None of the patients exhibited paradoxical movement of the diaphragm during sniffing.

These findings are in agreement with Dos Santos Yamaguti et al. [10] who in their study on 54 patients with COPD using B-mode ultrasonography

Table 2 Mean and SD of the studied variables in patients with chronic obstructive pulmonary disease and controls

Variables	Group 1 (N=40) (mean±SD)	Group 2 (N=10) (mean±SD)	t	P
FEV1 (% predicted)	59.55±6.11	90.26±4.81	6.37	0.001
FVC (% predicted)	84.13±4.84	91.88±5.21	2.86	0.040
FEV1/FVC	59.30±6.09	86.91±4.94	4.72	0.001
PaO_2	77.58±6.57	88.38±8.21	5.07	0.001
$PaCO_2$	44.58±3.15	36.62±3.69	4.25	0.002
SO_2%	91.08±2.90	96.33±2.85	2.66	0.046
pH	7.36±0.00	7.38±0.02	1.88	0.065
6-min walking test	328.50±41.60	482.00±68.30	5.66	0.001

FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; $PaCO_2$, partial arterial carbon dioxide tension; PaO_2, partial arterial oxygen tension; pH, hydrogen ion concentration; SO_2, oxygen saturation.

Table 3 Staging of patients with chronic obstructive pulmonary disease according to severity

Stage	n (%)
GOLD stage I	0 (0)
GOLD stage II	20 (50)
GOLD stage III	13 (32.5)
GOLD stage IV	7 (17.5)
Total	40 (100)

GOLD, Global Initiative for Chronic Obstructive Lung Disease.

Table 4 Diaphragmatic excursion in patients with chronic obstructive pulmonary disease and controls

Diaphragmatic excursion	Group 1 (N=40) (mean±SD)	Group 2 (N=10) (mean±SD)	t	P
Quiet breathing	2.23±0.50	2.28±0.59	1.77	0.085
Deep breathing	3.83±1.13	6.32±0.88	4.72	0.001

Table 5 Diaphragmatic excursion in patients with chronic obstructive pulmonary disease of different Global Initiative for Chronic Obstructive Lung Disease stages

Diaphragmatic excursion	Total patients (N=40) (mean±SD)	Gold stage II (N=20) (mean±SD)	Gold stage III (N=13) (mean±SD)	Gold stage IV (N=7) (mean±SD)	ANOVA	
					F	P value
Quiet breathing	2.23±0.50	2.32±0.58	2.26±0.56	2.16±0.50	1.34	0.099
Deep breathing	3.83±1.13	4.52±1.64	3.73±1.12	3.22±1.08	3.12	0.002

ANOVA, analysis of variance; GOLD, Global Initiative for Chronic Obstructive Lung Disease.

Table 6 Correlation between diaphragmatic excursion and the studied variables in patients with chronic obstructive pulmonary disease

Relation	Correlation coefficient (r)	P value
Diaphragmatic excursion and staging	−0.86	0.001
Diaphragmatic excursion and FEV1% predicted	0.84	0.001
FVC% predicted	0.72	0.002
FEV1/FVC%	0.80	0.012
Diaphragmatic excursion and PaO$_2$	0.14	0.163
PaCO$_2$	−0.45	0.022
SO$_2$	0.18	0.142
pH	0.11	0.202
Diaphragmatic excursion and 6-min walking test	0.47	0.020

FEV1, forced expiratory volume in the first second; FVC, forced vital capacity; PaCO$_2$, partial arterial carbon dioxide tension; PaO$_2$, partial arterial oxygen tension; pH, hydrogen ion concentration; SO$_2$, oxygen saturation.

assessed the diaphragmatic motion indirectly through measurement of the craniocaudal displacement of the left branch of the portal vein. They reported that patients with COPD had less diaphragmatic mobility than healthy controls (P=0.001).

Moreover, the findings of this study are in agreement with Paulin et al. [17] who found that patients with COPD had lower diaphragmatic mobility compared with controls.

Moreover, Aka Aktürk et al. [18] studied 76 patients with COPD and 30 controls to assess the diaphragmatic motion using M-mode ultrasonography. They found that diaphragmatic excursion during tidal breathing was 2.21±0.56 cm in the control group and 1.65±0.66 cm in patients with COPD. During deep breathing, the mean diaphragmatic excursion was 6.23±0.74 cm in the control group and 4.64±1.34 cm in patients with COPD, which was statistically significant (P<0.001).

Boussuges et al. [15] studied 210 healthy adults (150 men, 60 women) using M-mode ultrasonography to display the movement of the diaphragm. They reported that the mean diaphragmatic excursion was 3.7 cm for women and 4.7 cm for men during deep breathing. It was noticed that diaphragmatic excursions of controls in our study (6.32±0.88) were higher than those recorded

by Boussuges et al. [15] (4.7 cm); this may be explained by differences in posture during the ultrasonographic study. Participants in the study conducted by Boussuges et al. [15] were in standing position, whereas subjects in this study were in the semirecumbent position. Diaphragmatic motion is greater in the supine position than in the erect or sitting position [19].

Diaphragmatic dysfunction is a frequent finding in patients with COPD. There are many reasons that could explain this; lung hyperinflation and malnutrition are the most common causes resulting in muscle weakness. Lung hyperinflation shifts the diaphragm caudally, imposing a mechanical disadvantage upon it [20]. More recently recognized reasons for the diaphragmatic weakness are remodeling [2], exposure to oxidative stress [3], and a reduction of myosin filaments owing to reduced protein production and increased apoptosis of muscle cells [4].

According to severity, patients with COPD in this study were categorized as moderate COPD cases (n=20), severe COPD cases, (n=13), and very severe COPD cases (n=13). No mild cases were included.

This study reported that diaphragmatic excursion among patients of GOLD stages II, III, and IV were 4.52±1.64, 3.73±1.12, and 3.22±1.08 cm, respectively, with a statistically significant difference

among patients of different GOLD stages (P=0.002). Moreover, there was a statistically significant negative correlation (r=−0.86) between GOLD staging of patients with COPD and diaphragmatic excursion (P=0.001).

These results agree with that reported by Dos Santos Yamaguti et al. [10] who found that diaphragmatic mobility using B-mode ultrasound in patients with COPD with mild obstruction was 44.2± 12.3 mm and in patients with COPD with moderate and severe obstruction were 34.7±8.0 and 30.7± 7.5 mm, respectively, with a statistically significant difference (P<0.001). They concluded that diaphragmatic mobility correlated moderately with airway obstruction (r=0.55, P<0.001).

In the present study, there was a significant positive correlation between diaphragmatic excursion during deep breathing and spirometric volumes (FEV1% predicted: r=0.84, P=0.001; FVC% predicted: r= 0.72, P=0.002; and FEV1/FVC%: r=0.80, P=0.001).

These results agree with that reported by Dos Santos Yamaguti et al. [10], Kang et al. [21], and Scheibe et al. [22].

The presence of significant correlation between diaphragmatic excursion and spirometric volumes during deep breathing may be attributed to the characteristics of the FVC and FEV1 maneuvers [23].

In the present study, there was a nonsignificant positive correlation between diaphragmatic excursions and PaO_2, SO_2%, and pH. However, there was a statistically significant negative correlation between $PaCO_2$ and diaphragmatic excursion.

These results agree with that reported by Kang et al. [21] who reported nonsignificant correlation between PaO_2 and diaphragmatic mobility (r=0.028, P=0.873), and Scheibe et al. [22] who reported nonsignificant correlation between oxygen saturation and diaphragmatic mobility (r=0.13, P=0.185).

There was a statistically significant positive correlation between 6MWT and diaphragmatic excursion (P=0.020). This agrees with Scheibe et al. [22] who reported moderate correlation (r=0.67) between diaphragmatic mobility and distance walked in the 6MWT.

In patients with COPD with diaphragmatic dysfunction, the force generated by the respiratory muscles decreases resulting in a negative effect on ventilation and exercise capacity. The negative effect of decreased diaphragmatic mobility on exercise capacity could explain the positive correlation between 6MWT and diaphragmatic excursion [17].

Conclusion

M-mode ultrasonography is an easy, noninvasive, and inexpensive method in evaluation of diaphragmatic excursion. Patients with COPD had significantly lower diaphragmatic excursion than normal ones.

Conflicts of interest
There are no conflicts of interest.

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