Clinical Utility of Chest Sonography in COPD Patients with a Focus on Diaphragmatic Measurements

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Keywords: COPD, transthoracic chest ultrasound, diaphragm thickness, diaphragm excursion.

Conflict of interest
The authors have no conflicts of interest with the content of this paper.

Data availability statement
The authors confirm that all data supporting the findings of this study are available within the article, its supplementary material, and upon reasonable request.

Funding statement
No funding to declare.

Ethics approval statement
The Research Ethics Committee of the Faculty of Medicine at our University approved the study design. The IRB registration number: Soh-Med-22-10-0013006. The study was conducted by adhering to the principles of the 1964 Declaration of Helsinki and its 2013 amendment.

Patient consent statement
In accordance with the Declaration of Helsinki, all patients provided their informed consent after proper counselling before participation in the study.

All supporting data are available within the article

Contribution Details:
HME and KAA contribute to the conceiving of the study and its design; HME, KAA and DG contributed to the administrative support, SK collected the clinical data and clinical samples, HME and DG wrote the manuscript, All authors provided clinical input and collected and interpreted the data, read, critically reviewed, and edited the
manuscript and approved of the final version.

Word counts
- for abstract: 245
- for the text: 2856

Total number of tables: 8
Total number of figures: 3
Total number of references: 40
Supplementary file: 1
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Abstract

Background: There are many methods of evaluating diaphragmatic function, such as trans-diaphragmatic pressure measurements, which are considered the key rule of diagnosis, we studied the clinical usefulness of chest ultrasonography in evaluating stable COPD patients and those in exacerbation, we focus on diaphragmatic measurements and their correlation to spirometry and other clinical parameters.

Methods: In a prospective case control study, we enrolled 100 COPD patients divided into 40 stable COPD patients and 60 patients with exacerbation. The analysis included 20 age-matched controls. In addition to the clinical assessment of the study population, radiological evaluation included chest radiographs and chest computed tomography. Transthoracic ultrasonography (TUS) was done for all included subjects.

Results: Multiple A lines (more than 3) were more frequent in COPD exacerbation than in stable patients, the same for B Lines. TUS significantly showed high specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy in detecting pleural effusion, consolidation, pneumothorax, and lung mass. Diaphragmatic measurements were significantly lower among stable COPD subjects than healthy controls. Diaphragmatic thickness and excursion illustrated a significant negative correlation with BMI and dyspnea scale and a positive correlation with spirometry measures. Patients in GOLD group D showed lower diaphragmatic measurements (thickness and excursion).

Conclusion: The TUS of COPD patients both in stable and exacerbated conditions and the assessment of diaphragm excursion and thickness by TUS in COPD patients and their correlations to disease-related factors proved informative and paved the way for the better management of COPD patients.

Keywords: COPD, chest ultrasound, diaphragm thickness, diaphragm excursion
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Introduction

Chronic obstructive pulmonary disease (COPD) represents a common, preventable, and treatable illness with chronic respiratory symptoms and limited airflow because of airway and/or alveolar abnormalities. It often results from being significantly exposed to harmful gases or particles.

COPD is related to high morbidity, mortality, increased economic and social problems throughout the world. Patients with COPD have diaphragmatic dysfunction and weakness due to different causes, including, over-inflation of the lungs, remodeling, oxidative stress, as well as a reduced myosin filament because of the reduction in producing protein and more apoptosis of muscle cells. The literature on the weakness of inspiratory muscles in patients with COPD always address the diaphragm as the main source of tidal volume. The diaphragmatic dysfunction relates to altered pulmonary function parameters, e.g., FEV1. Diaphragmatic weakness is detected by below normal amplitude excursion on deep breathing with or without paradoxical motion on sniffing.

There are many methods of evaluation of the diaphragmatic function, such as trans-diaphragmatic pressure measurements, which are considered the key rule of diagnosis.

In 1975, Haber et al. introduced M- and B-mode ultrasonography (US) for evaluating diaphragm movement. This measurement was considered as quick, simple-accessible, as well as non-ionizing evaluation. Traditional ultrasound with a frequency range of 2-10MHz is being utilized in the evaluation and differentiation of COPD from other mimicking conditions based on observing the diaphragmatic function, air trapping, as well as A lines.

This work aims to explore the clinical usefulness of chest ultrasound in the evaluation of stable COPD patients and those in exacerbation, with a focus on diaphragmatic measurements and correlation to spirometry parameters and other clinical parameters was intended.

Patients and Methods

Study Design and Setting:

The present prospective, case-control study recruited 100 cases diagnosed with COPD and admitted in ward and/or attending our outpatient clinic in tertiary care hospital in the period from June 2021 to February 2022.
Sample size:

The study populations were classified into the following groups: Group (1): patients with stable COPD numbered (40), Group (2): patients with COPD exacerbation numbered (60), and 20 aged matched healthy controls.

COPD patients were classified based on the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2020 classification into four groups: GOLD A, GOLD B, GOLD C, and GOLD D. While Groups A and B included low-risk cases, Groups C and D included high-risk ones.

an exacerbation of chronic obstructive pulmonary disease (COPD) was defined as "an acute event characterized by a worsening of the patient's respiratory symptoms that is beyond normal day-to-day variations and leads to a change in medication".

An exacerbation of chronic obstructive pulmonary disease (ECOPD) is characterized by increased dyspnea, increased sputum purulence and volume together with increased cough and wheezes and is often associated with increased local and systemic inflammation caused by infection, pollution, or other insult to the airways.

Data collection method:

The study included all patients with confirmed COPD diagnosis by clinical evaluation together with post bronchodilator spirometry, FEV1/FVC < 70% and presented to our department throughout the period of the study. It excluded patients with clinical and/or radiographic evidence of other chest diseases apart from COPD. Patients with cardiogenic pulmonary edema were also excluded. All studied population (cases and controls) were subjected to: taking history, including respiratory symptoms, such as cough, exertional dyspnea, as well as chest pain) and clinical examination and radiological evaluation, including (chest radiograph, high resolution computed tomography scanning of the chest, as well as echocardiography if needed).

Ultrasonography was done for all patients. The machine used in the study was Medison SonoAceR3 ultrasound system with 2-8 MHz curvilinear and 5-12 MHz linear probes. Same operator performed the chest US to all the study population. Cases were examined by oblique and longitudinal scans both on the posterior and anterior chest in the seated and supine position by high and low frequency probes, application of ultrasound gel on the selected probe, it was positioned on the chest wall perpendicular to the skin with the probe marker pointing to patient's head, the image marker on the screen correspond to the probe marker and was positioned to the right of the screen.

To analyze data, each hemithorax was divided into six regions delineated by the anterior and posterior axillary lines, three in upper fields (anterior, posterior, and lateral), and the other three in the lower fields (anterior, posterior, and lateral).

The Sonographic finding includes B-lines, Pneumothorax, Lung consolidation was indicated by (Air bronchogram, Fluid bronchogram, Shred sign), Lung abscess, pleural Effusion, pulmonary infarction, and lung mass.
**Diaphragmatic assessment:** The diaphragm is identified by TUS as a three-layer structure consisting of one hypoechoic inner muscle layer surrounded by two hyperechoic outer membranes (the peritoneum and pleura) \(^{11,12}\). TUS was used for the assessment of diaphragmatic excursion and thickness.

**Diaphragm thickness:** The thickness of the diaphragm muscle at deep inspiration was evaluated by B-Mode US. (Figure 1S A)

**Technique of examination:** All participants underwent B-mode US examinations in supine position. Probe was placed between the anterior and the mid axillary lines in the 9\(^{th}\) intercostal space perpendicular to two ribs (9\(^{th}\)-10\(^{th}\)). Diaphragm muscle appears as hypoechoic lines between two parallel echoic lines, i.e., the peritoneal membrane and diaphragmatic pleura. The patient was advised to take spontaneous breathing and deep inspiration. Thickness was evaluated by putting the calipers inside the hyperechoic lines, three diaphragmatic thickness measurement of the right diaphragm were taken for each patient, and the best value was registered \(^{13}\). (Figure 1S A)

**Diaphragm excursion:** is the movement of the diaphragm during breathing. Normal diaphragmatic excursion should be 3–5 cm.

**Technique of examination:** The participants were scanned based on a low anterior subcostal approach and/or a coronal intercostal approach. The 2D mode was utilized to define the best approach and choose the exploration line. The M-mode line of sight was angled to get the highest diaphragmatic excursion. M-mode was used to measure diaphragmatic excursion during deep inspiration at the right hemidiaphragm. The liver was employed as a window. The distance between echogenic lines was evaluated on frozen images from the M-mode. Calipers were centered on the echogenic lines. For each patient, three measurements were carried out, recording the best value. All diaphragmatic excursion measurements were given in centimeters \(^{14}\). (Figure 1S B,C)

**Statistical analysis:**

The authors carried out statistical analysis using SPSS for window (v. 21, IBM Corp., Armonk, NY, USA). Median, standard deviation, mean, and interquartile range (IQR) represented the quantitative data. Moreover, the Shapiro-Wilk test was used to test data for normality. The student t-test to compared the means of two groups, but ANOVA was used for more than two groups. When the data were not normally distributed, the Mann-Whitney test was used to make a comparison between the means of two groups, and the Kruskal Wallis Test was employed for the comparison of the means of different groups. Qualitative data were shown in the form of number and percentage. Comparison of data was carried out using either the Chi-square test or the fisher exact test. McNemar test was used to compare the results of the different methods used for diagnosis of lung pathology. Pearson's correlation coefficient was adopted to evaluate the association between diaphragmatic measurements and quantitative data, and spearman's correlation coefficient test was used to evaluate the association between diaphragmatic measurements and qualitative data. By utilizing the receiver operating characteristic curve analysis, we could get the accuracy, specificity, and sensitivity of chest ultrasound. Graphs were created using Excel or SPSS. P value was significant if it was below 0.05.
Results:

This paper studied sixty (60) cases with COPD exacerbation, forty (40) with stable COPD, and twenty (20) healthy controls of the same age group. The mean age of the study population was 61.55±6.92. No statistically significant differences were found in the two groups in gender and age (P=0.342, P=0.220, respectively). Significantly higher percentage of exacerbated group were current smoker than stable COPD (P <0.0001). There was a highly significant relationship between COPD exacerbation and moderate to severe grades of smoking index (P <0.0001) (table 1).

Patient characteristics as regard gasometric parameters, pulmonary function and echocardiographic finding are presented in supplementary data Table S1 and Table S2. Ultrasound evaluation revealed that multiple A lines (more than 3) were more frequently found in COPD exacerbation than in stable patients, the same for B Lines. The difference showed statistical significance. (P value=0.008 and <0.0001, respectively) (table 2). Other Sonographic findings in both groups are shown in (Table 3).

The diagnostic validity of chest ultrasound in comparison with CT as the gold standard was assessed. TUS significantly showed high specificity, negative predictive value (NPV), positive predictive value (PPV), and accuracy in detecting pleural effusion, consolidation, pneumothorax, as well as lung mass. Sensitivity values were lower. In detection of emphysematous bullae, the sensitivity was very low (18.18%) (Table 4).

Diaphragmatic measurements showed that the mean value of the diaphragmatic thickness and the diaphragmatic excursion decreased significantly in stable COPD patients compared to healthy controls. The difference between stable and exacerbated COPD was statistically insignificant (fig. 1, 2).

In terms of Correlation between diaphragmatic measurements (thickness and excursion), and COPD patient's Characteristics, diaphragmatic thickness showed a statistically significant negative correlation with BMI and dyspnea grades (r = -0.300, -0.274, P=0.014, P=0.00016, respectively), and diaphragmatic excursion illustrated a statistically significant negative correlation with the frequency of exacerbation, BMI, and dyspnea grades (P=0.003, P<0.001, P=0.012, respectively). No statistically significant correlation of diaphragmatic measurements (thickness and excursion) was reported with age (table 5).

Concerning the correlation between diaphragmatic measurements (thickness and excursion), and spirometric results of COPD patients, Pearson Correlations analysis showed that diaphragmatic thickness and excursion had a significant positive correlation with spirometric measures, including FEV1 and FVC. (Table 6 & fig. 2S and Fig 3S).

The assessment of diaphragmatic thickness in different GOLD groups revealed that the mean value of diaphragmatic thickness was higher in low-risk groups (A, B) than high risk groups (C, D) of COPD patients, although the difference was not statistically significant (P=0.09) (table 7).

Comparison of diaphragmatic excursion among different GOLD groups showed no statistically significant differences in diaphragmatic excursion were reported among the different GOLD groups. Diaphragmatic excursion decreased toward group D (fig. 4).
Ultrasonographic findings in different GOLD groups showed that there was a significant difference between GOLD groups in some sonographic finding. Multiple A and B lines were significantly more in GOLD group D (P= 0.01, 0.001 respectively). Also, pleural effusion was detected significantly more in patients with high symptom severity and high risk (GOLD D) than other groups of patients (P=0.001). The analysis of pleural effusion was found to be related to right ventricular failure. No statistically significant differences of the other ultrasonography finding were reported among patients in different GOLD groups (table 8).

Discussion

COPD represents the fourth primary reason for mortality worldwide, denoting a major public health issue. COPD exacerbation causes changes in airway caliber and hyperinflation in the parenchyma. Scholars have introduced ultrasonography to provide tools of simple, accessible, quick, as well as and non-ionizing evaluation of several physiological variables, such as diaphragm function and integrity. This work aimed to evaluate the clinical utility of chest ultrasonography in stable and exacerbated COPD patients with the attention to diaphragm thickness and excursion. Here, we had a mean age of the study population at 61.55±6.92. COPD exacerbation was highly related to smoking state and smoking index. Those findings matched the results of Dong et al. that both old age and high smoking index are risks for COPD exacerbation, which can be attributed to lung dysfunction with age.

On ultrasound examinations of the lung, the detection of prominent A-lines at the lateral and anterior surfaces of the lung is indicative to exacerbation.

In our study, multiple A lines were significantly more frequent in the exacerbation group. This finding matched with the findings of Youssuf et al. who showed that prominent A lines were detected in (60% ) of the total COPD patients. This result was attributed to more prominent hyperinflation, which explained this finding during exacerbation.

B-lines become evident when the lung parenchymal air content is partially reduced and/or the interstitial space is volumetrically increased, as is the case of the interstitial lung disease.

In the current study, we reported that 24 cases (24%) showed one or two B-lines, and 8 cases (8%) showed more than 3 B-lines. At the same context, we also reported
statistically significant differences between the stable COPD group and the exacerbation group.

In agreement with this finding, the study of Sriram et al. 23 observed, on performing lung ultrasound, B-lines in cases with COPD exacerbations. Acute respiratory distress, interstitial lung disease, or subclinical heart failure were the proposed aetiologies 24.

In our study, the diagnostic validity of chest ultrasound compared to CT as the key standard in detecting pleural effusion and consolidation showed an accuracy of 94% and 91%, respectively with (P<0.0001 for both). Those findings matched with the results of Elnaem et al. 25. They diagnosed pleural effusion and consolidation by TUS with an accuracy of 97.8 and 96.7%, respectively.

Transthoracic ultrasound is an outstanding diagnostic tool of community acquired pneumonia, as a common cause of consolidation, with excellent sensitivity and specificity. It is available and simple with no ionizing radiation 26. According to Agamy et al. 27, this tool has much better sensitivity, specificity, and accuracy than chest X-ray in the diagnosis of most chest pathology, such as pleural effusion, pneumothorax, consolidation, and interstitial lung syndrome.

We conducted a diagnosis of 4 cases with pneumothorax by CT chest as the best standard. Ultrasound detected pneumothorax in 3 cases with a perfect agreement with final diagnosis with 75% sensitivity, 100% specificity, as well as a diagnostic accuracy of 99%.

In accordance with our results, Lichtenstein et al., 28 found that ultrasound demonstrated a sensitivity of 79% and a specificity of 100% in diagnosing pneumothorax.

Here, we compared the mean value of diaphragmatic thickness and excursion between healthy controls and stable COPD group and observed a highly significant correlation between the presence of COPD and the reduction in diaphragmatic thickness and excursion. Following our results, multiple studies showed similar findings. For instance, Essawy et al. 29 and Paulin et al. 30 showed a statistically significant difference between the control group and the group with COPD as regard diaphragmatic thickness, diaphragmatic thickness fraction, and excursion.

Furthermore, Gerscovich et al. 31 illustrated the accuracy of ultrasound in evaluating the diaphragm motion because this method did not have any technical failures and
proved easy to utilize. It should be the best technique for examining the diaphragm motion.

The reduction of diaphragm thickness and excursion in COPD could be explained by the restriction of peripheral airflow that increasingly traps gas in the expiration, which causes hyperinflation. This static hyperinflation declines the inspiratory capacity, which causes higher dyspnea and limited exercise capacity. Also, it results in deteriorating the diaphragm’s contractile property.

The present study showed that diaphragmatic measurements (thickness and excursion) had a significant negative correlation with BMI, mMRC dyspnea scale. Also, we found a significant negative relationship between the frequency of COPD exacerbation and diaphragmatic excursion. Targeting prevention of exacerbation is a fundamental goal in COPD management.

In this regard, several previous studies reported that the patients who had lower diaphragmatic mobility had more dyspneic and shorter 6-min walk distances. Smargiassi et al. reported a direct significant correlation between diaphragmatic excursion and BMI only.

Unlike our results, Ogan et al. and Yalcin et al. reported the lack of correlations between diaphragmatic thickness and frequency of exacerbations, BMI, and symptom score based on mMRC.

The present work found that diaphragmatic thickness and excursion had a significant positive correlation with spirometry measures, including FEV1 and FVC. These results correlated with those of Lim et al. who reported a significant correlation between diaphragmatic thickness and FEV1%, but no correlation between diaphragm excursion and FEV1%. Similarly, the study of Yalcin et al. and the study of Shiraishi et al. reported that diaphragmatic excursion significantly lower in COPD patients with low FEV1 values.

In the current study, based on the classification of our patients according to GOLD ABCD categorization tool, we found that the mean value of diaphragmatic thickness and excursion were significantly declined with risk progression from group A subgroup up to subgroup D.

This result matched with the study of Essawy et al. who assessed the diaphragmatic function in each COPD subgroup, diaphragmatic thickness. Diaphragmatic thickness fraction among COPD subgroups A, B, C, and D showed significant reduction of each parameter toward the groups with more frequent exacerbation. The recently issued
GOLD report replaced groups C and D with one E (Exacerbated) group. This reflects the prognostic effect of exacerbation in COPD patients.

The present paper is an addition to the literature about the clinical significance of transthoracic sonographic evaluation of COPD patients both in stable and exacerbated conditions. The assessment of diaphragmatic excursions and thickness by TUS in patients with COPD and their correlations with disease-related factors proved informative and paved the way for better management of COPD patients.

We recommended in the future research to include the follow up of COPD patients after implementing rehabilitation and other therapeutic option using TUS.

**Conclusion**

Because the diaphragm is a powerful inspiratory muscle, its impaired functioning greatly influences deteriorating the respiratory functioning in patients with COPD. TUS measurements of diaphragm excursion and thickness in COPD patients in consortium with detection of other findings during transthoracic ultrasonography evaluation may have a pivotal role in managing COPD patients.

**Ethical Consideration**

The Research Ethics Committee of the Faculty of Medicine at our University approved the study design. The IRB registration number: Soh-Med-22-10-0013006. The study was conducted by adhering to the principles of the 1964 Declaration of Helsinki and its 2013 amendment.

**Availability of data and materials**

The datasets utilized or analyzed in this study can be obtained from the corresponding author on reasonable requests.

**Funding**

The researchers declare that they have not received any funding for publishing the manuscript.

**Declaration of Competing Interests**

The researchers declare no conflict of interests.

Figure legands
Figure (1): Comparison of diaphragmatic thickness between healthy controls and stable COPD (A), as well as between stable COPD and COPD exacerbation group (B).
Figure (2): Comparison of diaphragmatic excursion between healthy controls and stable COPD (A), as well as between stable COPD and COPD exacerbation group (B).
Figure (3): Comparison of diaphragmatic excursion among different GOLD groups.
References:


Table (1): Demographic data of both COPD groups and control.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Total cases N=100</th>
<th>Controls N=20</th>
<th>Stable COPD cases</th>
<th>Exacerbation N=60</th>
<th>P1 value</th>
<th>P2 value</th>
<th>P3 value</th>
<th>P value</th>
</tr>
</thead>
</table>

17
<table>
<thead>
<tr>
<th>Variables</th>
<th>Total cases N= 100</th>
<th>Controls N=20</th>
<th>Stable COPD cases N=40</th>
<th>Exacerbation N=60</th>
<th>P1</th>
<th>P2</th>
<th>P3</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Line</td>
<td>Less than 3 lines</td>
<td>23(23%)</td>
<td>17(85%)</td>
<td>12 (30%)</td>
<td>11(18.3%)</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>More than 3 lines</td>
<td>77(77%)</td>
<td>3(15%)</td>
<td>28 (70%)</td>
<td>49 (81.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>B Line</td>
<td>No</td>
<td>68(68%)</td>
<td>10(50%)</td>
<td>35(87.5%)</td>
<td>33 (55%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Less than 3 lines</td>
<td>24(24%)</td>
<td>10(50%)</td>
<td>1 (2.5%)</td>
<td>23 (38.3%)</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>More than 3 lines</td>
<td>8(8%)</td>
<td>0(0%)</td>
<td>4 (10%)</td>
<td>4 (6.7%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

P1: Controls versus Stable COPD, P2: Controls versus Exacerbation, P3: Stable versus Exacerbation. P value: For comparison between the three groups.

Table (2): Comparison of ultrasound evaluation of A lines and B lines between the studied groups.

<table>
<thead>
<tr>
<th>Ultrasonographic finding*</th>
<th>Total N=100</th>
<th>Stable COPD N=40</th>
<th>Exacerbation N=60</th>
<th>( \chi^2 )</th>
<th>P value</th>
</tr>
</thead>
</table>

P1: Controls versus Stable COPD, P2: Controls versus Exacerbation, P3: Stable versus Exacerbation. P value: For comparison between the three groups.

Table (3): Comparison between the two COPD groups according to chest ultrasonographic finding.
**Table (4):** The diagnostic validity of chest ultrasound compared to CT as gold standard

<table>
<thead>
<tr>
<th>Variables</th>
<th>AUC (CI: 95%)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>PPV</th>
<th>NPV</th>
<th>Accuracy</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effusion</strong></td>
<td>US 0.92 (0.84-0.99)</td>
<td>88%</td>
<td>96%</td>
<td>88%</td>
<td>96%</td>
<td>94%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Consolidation</strong></td>
<td>US 0.87 (0.74-0.99)</td>
<td>81.25%</td>
<td>98.8%</td>
<td>92.3%</td>
<td>96.5%</td>
<td>96%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td><strong>Pneumothorax</strong></td>
<td>US 0.88 (0.61-1)</td>
<td>75%</td>
<td>100%</td>
<td>100%</td>
<td>98.9%</td>
<td>99%</td>
<td>0.011</td>
</tr>
<tr>
<td><strong>Lung mass</strong></td>
<td>US 0.82 (0.59-1)</td>
<td>83.33%</td>
<td>98.93%</td>
<td>100%</td>
<td>96.87%</td>
<td>96%</td>
<td>0.006</td>
</tr>
<tr>
<td><strong>Emphysematous bullae</strong></td>
<td>US 0.59 (0.39-0.79)</td>
<td>18.18%</td>
<td>100%</td>
<td>100%</td>
<td>90.81%</td>
<td>91%</td>
<td>0.327</td>
</tr>
</tbody>
</table>

AUC: Area under curve  
CI: Confidence interval  
PPV: Positive predictive value  
NPV: Negative predictive value  
CXR: Chest X-ray  
US: Ultrasound

**Table (5):** Correlation between diaphragmatic measurements (thickness and excursion) and patient's factors

<table>
<thead>
<tr>
<th>Variables</th>
<th>Diaphragmatic thickness</th>
<th>Diaphragmatic excursion</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td>R 0.040 0.694</td>
<td>P value 0.014 -0.704</td>
</tr>
<tr>
<td><strong>BMI</strong></td>
<td>-0.300</td>
<td>0.014</td>
</tr>
<tr>
<td><strong>Frequency of exacerbation</strong></td>
<td>-0.118</td>
<td>0.251</td>
</tr>
<tr>
<td><strong>Dyspnea on mMRC scale</strong></td>
<td>-0.274</td>
<td>0.006</td>
</tr>
</tbody>
</table>

**Table (6):** Correlation between diaphragmatic measurements (thickness and excursion), and spirometric results

- The same patient may have more than one ultrasonographic finding.
Table (7): Comparison of diaphragmatic thickness and excursion among different GOLD groups

<table>
<thead>
<tr>
<th>Patient GOLD group</th>
<th>Diaphragmatic thickness (mm)</th>
<th>R</th>
<th>P value</th>
<th>R</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOLD A</td>
<td>5.27±1.39</td>
<td>0.310</td>
<td>0.034</td>
<td>0.572</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>GOLD B</td>
<td>4.09±1.41</td>
<td>0.294</td>
<td>0.043</td>
<td>0.457</td>
<td>0.001</td>
</tr>
<tr>
<td>GOLD C</td>
<td>4.15±1.92</td>
<td>0.035</td>
<td>0.838</td>
<td>0.227</td>
<td>0.122</td>
</tr>
<tr>
<td>GOLD D</td>
<td>3.88±0.88</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>P value</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>0.09</td>
</tr>
</tbody>
</table>

FEV1: Forced expiratory volume in one second  
FVC: Forced volume capacity

Table (8): Comparison of ultrasonographic findings in different GOLD groups

<table>
<thead>
<tr>
<th>Ultrasonographic finding</th>
<th>GOLDA N= 8</th>
<th>GOLD B N= 16</th>
<th>GOLD C N= 13</th>
<th>GOLD D N= 63</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Line</td>
<td>Less than 3 lines</td>
<td>2 (25%)</td>
<td>6 (37.5%)</td>
<td>5 (38.5%)</td>
<td>10 (15.9%)</td>
</tr>
<tr>
<td></td>
<td>More than 3 lines</td>
<td>6 (75%)</td>
<td>10 (62.5%)</td>
<td>8 (61.5%)</td>
<td>53 (84.1%)</td>
</tr>
<tr>
<td>B Line</td>
<td>No</td>
<td>8 (100%)</td>
<td>14 (87.5%)</td>
<td>11 (84.6%)</td>
<td>35 (55.6%)</td>
</tr>
<tr>
<td></td>
<td>Less than 3 lines</td>
<td>0 (0%)</td>
<td>1 (6.3%)</td>
<td>0 (0%)</td>
<td>23 (36.5%)</td>
</tr>
<tr>
<td></td>
<td>More than 3 lines</td>
<td>0 (0%)</td>
<td>1 (6.3%)</td>
<td>2 (15.4%)</td>
<td>5 (7.9%)</td>
</tr>
<tr>
<td>Lung sliding</td>
<td>Present</td>
<td>8 (100%)</td>
<td>15 (93.7%)</td>
<td>13 (100%)</td>
<td>58 (92.1%)</td>
</tr>
<tr>
<td></td>
<td>Abolished</td>
<td>0 (0%)</td>
<td>1 (6.3%)</td>
<td>0 (0%)</td>
<td>5 (7.9%)</td>
</tr>
<tr>
<td>Pleural effusion</td>
<td></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>4 (30.8%)</td>
<td>21 (33.3%)</td>
</tr>
<tr>
<td>Consolidation</td>
<td></td>
<td>0 (0%)</td>
<td>1 (6.4%)</td>
<td>1 (7.7%)</td>
<td>11 (17.7%)</td>
</tr>
<tr>
<td>Lung mass</td>
<td></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>5 (7.9%)</td>
</tr>
<tr>
<td>Pneumothorax</td>
<td></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>3 (4.8)</td>
</tr>
<tr>
<td></td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>2 (3.2%)</td>
<td>0.599</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>--------</td>
<td>--------</td>
<td>--------</td>
<td>----------</td>
<td>-------</td>
</tr>
<tr>
<td>Emphysematous bullae</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Subpleural hypoechoic lesion</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
<td>1 (1.6%)</td>
<td>0.898</td>
</tr>
<tr>
<td>Suggestive of pulmonary Embolism</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>
Supplemental data
Figure S1. Ultrasonography of the diaphragm. (A) Measurement of diaphragm thickness in B-mode (right) and M-mode (left) during tidal breathing. I and E arrows indicate inspiration and expiration. (B) Measurement of diaphragm excursion in B mode. (C) Measurement of diaphragm excursion in M mode; Arrows indicate the start and the end of the diaphragmatic contraction. The distance in between the arrows indicates the diaphragm excursion.
Figure S2. Correlation between diaphragmatic measurements excursion and spirometric results.

Abbreviations: FEV1; Forced expiratory volume in first second. FVC; Forced vital capacity.
**Figure S3.** Correlation between diaphragmatic measurements thickness and spirometric results.

**Abbreviations:** FEV1; Forced expiratory volume in first second. FVC; Forced vital capacity.
Table (S1): ABG and pulmonary function test results of the studied groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Controls N=20</th>
<th>Stable COPD cases N=40</th>
<th>Exacerbation N=60</th>
<th>P1 value</th>
<th>P2 value</th>
<th>P3 value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PH</td>
<td>7.40±0.03</td>
<td>7.43±0.12</td>
<td>7.34±0.07</td>
<td>0.335</td>
<td>&lt;0.000</td>
<td>0.003</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>Pao2</td>
<td>76.7±5.95</td>
<td>67.42±9.56</td>
<td>46.53±15.76</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>PaCO2</td>
<td>41.15±4.4</td>
<td>44.34±5.44</td>
<td>57.14±14.44</td>
<td>0.024</td>
<td>0.861</td>
<td>0.325</td>
<td>0.342</td>
</tr>
<tr>
<td>Hco3</td>
<td>30.3±3.4</td>
<td>30.47±3.68</td>
<td>31.52±3.01</td>
<td></td>
<td></td>
<td></td>
<td>0.490</td>
</tr>
<tr>
<td>FEV1</td>
<td>3.75±0.38</td>
<td>1.28±0.4</td>
<td>0.89±0.36</td>
<td>&lt;0.000</td>
<td>1</td>
<td>&lt;0.000</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>FVC</td>
<td>4.6±0.4</td>
<td>2.14±0.6</td>
<td>1.63±0.61</td>
<td>1</td>
<td>&lt;0.000</td>
<td>1</td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>FEV1/FVC</td>
<td>81.2±7.8</td>
<td>58.97±7.6</td>
<td>55.62±9.15</td>
<td></td>
<td></td>
<td></td>
<td>&lt;0.000</td>
</tr>
<tr>
<td>PASP</td>
<td>17(85%)</td>
<td>14(66.7%)</td>
<td>0(0%)</td>
<td>0.167</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Ejection fraction %</td>
<td>67.35±5.67</td>
<td>60.86±7.78</td>
<td>58.57±7.61</td>
<td>0.004</td>
<td>&lt;0.0001</td>
<td>0.271</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

P1: Controls versus Stable COPD, P2: Controls versus Exacerbation, P3: Stable versus Exacerbation. P value: For comparison between the three groups.

Table S 2: Comparison of Echocardiography results between the studied groups

<table>
<thead>
<tr>
<th>Variables</th>
<th>Controls N=20</th>
<th>Stable COPD N=21</th>
<th>Exacerbation N=44</th>
<th>P1 value</th>
<th>P2 value</th>
<th>P3 value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypokinesia:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>6(30%)</td>
<td>6 (28.6%)</td>
<td>16(35.6%)</td>
<td>0.981</td>
<td>0.662</td>
<td>0.575</td>
<td>0.802</td>
</tr>
<tr>
<td>No</td>
<td>14(70%)</td>
<td>15(71.4%)</td>
<td>29(64.4%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilated left ventricle:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>7(35%)</td>
<td>4(19%)</td>
<td>11(25%)</td>
<td>0.249</td>
<td>0.410</td>
<td>0.594</td>
<td>0.498</td>
</tr>
<tr>
<td>No</td>
<td>13(65%)</td>
<td>17(81%)</td>
<td>33(75%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dilated right ventricle:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>5(25%)</td>
<td>13(61.9%)</td>
<td>41(93.2%)</td>
<td>0.017</td>
<td>&lt;0.0001</td>
<td>0.002</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>No</td>
<td>15(75%)</td>
<td>8(38.1%)</td>
<td>3(6.8%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PASP:</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>17(85%)</td>
<td>14(66.7%)</td>
<td>0(0%)</td>
<td>0.167</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mildly increased</td>
<td>3 (15%)</td>
<td>7(33.3%)</td>
<td>21(47.7%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate increase</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>17(38.6%)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Severe increase</td>
<td>0(0%)</td>
<td>0(0%)</td>
<td>6(13.6%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ejection fraction %</td>
<td>67.35±5.67</td>
<td>60.86±7.78</td>
<td>58.57±7.61</td>
<td>0.004</td>
<td>&lt;0.0001</td>
<td>0.271</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
P1: Controls versus Stable COPD, P2: Controls versus Exacerbation, P3: Stable versus Exacerbation. P value: For comparison between the three groups.

PASP: Pulmonary artery systolic pressure