Correlation Between Ultrasonographic Evaluation of Diaphragm Excursion, Thickness and Spirometry in COPD patients: A Case-Control Study

Anjaly K Chandrakumar, Jacob Baby, Elizabeth Sunila Chakkalakkal Xavier, Praveen Valsalan, Rohith Puthanveettil

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Abstract
Background: Weakness of the diaphragm is associated with dyspnea, exercise intolerance and affects survival in chronic obstructive pulmonary disease (COPD) patients. The present study aimed to evaluate diaphragm excursion, and thickness using ultrasonography (USG) and spirometry values in patients with COPD, correlate these values and compare them with healthy controls.
Methodology: This case-control study was conducted in a tertiary care center in South India for 1 year. A total of 70 patients with COPD and 70 healthy controls were recruited. Data were collected and statistically analyzed.
Results: The absolute value of forced expiratory volume in 1 (FEV1) and the percentage of predicted FEV1, forced vital capacity (FVC), and FEV1/FVC was significantly lower in COPD patients (p < 0.0001). Diaphragm excursion at normal inspiration, deep inspiration, and while sniffing was significantly lower in COPD patients (p < 0.01). Diaphragm thickness at end-inspiration, end-expiration, and diaphragm thickness fraction (DTF) was significantly lower in COPD patients compared to normal healthy subjects (p < 0.01).
Conclusion: A mild positive correlation was found between diaphragm excursion at normal inspiration and FEV1. There was a strong correlation between FEV1 and diaphragm excursion during deep inspiration and sniffing. A linear equation was developed to calculate FEV1. FEV1 = 2.99 – (0.042 × age) + (0.224 × deep inspiration) + (0.015 × sniffing). This could predict risks for any major surgeries, decide on treatment options for COPD patients, and can be used for prognosis and follow-up while the patient is on inhaler therapy.
Keywords: Chronic obstructive pulmonary disease, Diaphragmatic paralysis, Forced expiratory volume 1, Forced vital capacity, Spirometry, Ultrasonography

Introduction
Chronic obstructive pulmonary disease (COPD) has become the second most common cause of mortality in India. Different studies have shown a variable spectrum of COPD prevalence in different states in India. Prevalence ranged between 2 and 22% in males and between 1.2 and 19% in females in various population-based studies in India. A negative effect on ventilation and exercise capacity is observed in patients with COPD when the force generated by the respiratory muscles diminishes. M-mode USG is a reliable and relatively easy tool for assessing diaphragm function. Patients with COPD suffer diaphragm dysfunction, which may be due to overinflation of the lungs, remodeling, oxidative stress, a reduction in myosin filaments due to reduced protein production, and increased apoptosis of muscle cells. Hence it is necessary to assess diaphragm function in inpatients and outpatients diagnosed with COPD during emergencies. Transdiaphragm pressure measurement after phrenic nerve stimulation is the gold standard for diagnosis of diaphragm dysfunction. However, the test is invasive and time-consuming. The traditionally invasive techniques were used to diagnose diaphragm weakness or paralysis, and the techniques like electromyography and fluoroscopy expose patients to radiation. These traditional techniques consume time and are indirect, uncomfortable, complex, and expensive.

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Lung hyperinflation among COPD patients may be determined by measuring the DTF. Point-of-care USG to examine the diaphragm helps to assess the disease status and outcomes in COPD patients. The present study aims to investigate the relationship between diaphragm excursion, thickness during respiratory maneuvers, and spirometry values in COPD patients using diaphragm movements and evaluate the use of USG as a diagnostic tool to assess diaphragm thickness and excursion and find the correlation with spirometry values.
USG Evaluation of Diaphragm Alternative to Assess Lung Function

**Methodology**

This is a prospective, observational, case-control study conducted on 70 COPD patients aged ≥ 45 years who came to the Department of Pulmonology and 70 healthy volunteers of the same age group who attended the Wellness clinic at a tertiary care center in Cochin, South India. The study was conducted from 1st January 2019 to 31st December 2019.

### Inclusion criteria
- Age ≥ 45 years
- Healthy volunteers who were non-smokers
- Patients diagnosed with COPD
- Those who gave informed consent for the study and agreed to diaphragm USG in addition to standard spirometry.

### Exclusion criteria
- Age < 45 years
- Those with underlying musculoskeletal/neurological disorders
- Any other known pulmonary disease besides COPD
- Morbidity with body mass index > 30 kg/m²
- Recent thoracic/abdominal surgeries
- Subcutaneous emphysema/chest wall edema

The study was approved by the Institutional Ethics Committee (Ref No: AM/EC/59-2018, dated 03/09/2018), and all participants provided their informed consent. The diagnosis and severity of COPD were determined in accordance with the guidelines of the Global Initiative for Chronic Obstructive Lung Disease (GOLD).10

Detailed medical history and clinical examination were conducted for all subjects. Reversibility, pulmonary function test, was completed for each patient and healthy volunteer by standard spirometry (Smart Pulmonary Function Test (PFT) body, Medical Equipment, Germany, Europe) following American Thoracic Society (ATS)/European Respiratory Society (ERS) guidelines for spirometry.11

| GOLD 1: Mild FEV1 ≥ 80% predicted |
| GOLD 2: Moderate 50% ≤ FEV1 < 80% predicted |
| GOLD 3: Severe 30% ≤ FEV1 < 50% predicted |
| GOLD 4: Very severe FEV1 < 30% predicted |

Patients included in the study were diagnosed with COPD based on their history, clinical examination, and spirometry values (FEV1/FVC ratio of < 0.7, with no postbronchodilator reversibility). Most of the COPD patients had chest X-ray findings of hyperinflated lung fields. Classification of airflow limitation severity (based on postbronchodilator FEV1) in COPD patients was done, and they were assigned grades 1–4 as per GOLD guidelines.12

Symptoms were assessed using a modified British Medical Research Council (mMRC) Questionnaire and COPD Assessment Test (CAT).13 A combined COPD assessment was based on their history of exacerbations (moderate or severe), mMRC grade, and CAT score. Patients were categorized as A, B, C, and D.12

Ultrasoundographic (USG) imaging of the diaphragm was performed with a GE Logiq-e portable USG imaging system (GE co, New York, United States of America) using a curvilinear transducer to assess diaphragm excursion in M mode during quiet breathing, deep inspiration, and while performing sniff test and with a linear transducer to assess diaphragm thickness in B mode at the end of inspiration and end of expiration. Healthy volunteers who attended the Wellness clinic and belonged to the same age group as COPD patients and those who signed the informed consent were evaluated through the same procedures.

The patient was evaluated supine because it provides less overall variability, side-to-side variation, increased reproducibility, and greater excursion. Supine position increases any paradoxical movement and limits compensatory active expiration through the anterior abdominal wall masking the paralysis.14

The right diaphragm was observed through the liver window. In contrast, the left diaphragm is generally harder to view due to the smaller acoustic window created by the spleen and can be minimized by a more coronal plane parallel to the ribs.14

The thickness of the diaphragm at the anterior axillary line, between the seventh and ninth intercostal space, was measured using a high-frequency linear (12 MHz) probe. The zone of apposition, inferior to the costophrenic angle, where the diaphragm touches the inner aspect of the chest wall, was measured. We measured the thickness by visualizing the pleural and peritoneal membranes with an angle of incidence of the USG beam close to 90 degrees, and 0.2 cm is the cut-off below which diaphragm atrophy was defined.15

We used the formula (thickness at end-inspiration – thickness at end-expiration)/thickness at end-expiration × 100) to calculate the DTF. A DTF value below 20% is consistent with paralysis.14 We measured the diaphragm excursion with a lower frequency curvilinear probe (4 MHz probe) in the anterior subcostal view. The transducer was placed between the mid-clavicular and anterior axillary lines, directed medially, cranially, and dorsally to visualize the posterior third of the right diaphragm, approximately 5 cm lateral to the inferior vena cava foramen.15 Measurement for normal breathing and sniffing was made in the M-mode, from the point of the maximal excursion to the baseline. We measured from the maximal to the lowest point of excursion while subjects performed deep breathing.15

### Statistical Analysis

Data were recorded in Microsoft Excel 2019 and exported into IBM Statistical Package for Social Sciences Statistics for Windows, Version 20.0. Categorical variables were expressed as frequency and percentages. Normally distributed data were expressed as mean and standard deviation and compared using the student t-test. Non-normally distributed data were expressed as the median and interquartile range (IQR) (Q1, Q3) and compared using the Mann–Whitney U test. Spearman rank correlation was used for the estimation of the correlation between variables. A p-value of <0.05 was considered statistically significant.

### Results

A total of 140 samples were included in this study, of which 70 were COPD patients; 10 patients were in the intensive care unit with COPD exacerbation and had oxygen support, and 70 were controls. Age ranges from 45 to 84 years, and the median age of the COPD patients was significantly higher than healthy controls [median, IQR; 70.0 (66.0, 74.2) vs 54.0 (50.0, 60.25.0); p < 0.0001]. The gender distribution of the study population showed that the patient group had 65 males and five females; in the control group, there were 51 males and 19 females.

For assessing the severity of airway obstruction in COPD patients, 47.1% were in GOLD grade 2, followed by 45.7% in GOLD grade 3, 4.3% in GOLD grade 1, and only 2.9% of patients were...
in GOLD grade 4. Also, 42.9% of patients were in COPD stage B, followed by 41.4% of patients in COPD stage D. Only 15.7% were in COPD stage C (Fig. 1).

Spirometry values were lower in the COPD group compared to the control group, which was found to be significant ($p < 0.0001$). Diaphragm excursion during normal inspiration, deep inspiration, and sniffing was significantly lower in COPD patients compared to healthy controls ($p < 0.01$). Diaphragm thickness during end-inspiration, end-expiration, and DTF was significantly lower in COPD patients in comparison to controls ($p < 0.01$) (Table 1).

Correlation between FEV1 with diaphragm excursion showed that diaphragm excursion during normal inspiration had a weak positive correlation with FEV1 ($r = 0.222$). However, excursion of the diaphragm during deep inspiration and sniffing had a good positive correlation ($r = 0.700$ and 0.610, respectively) with FEV1. Age showed a good negative correlation with FEV1, and all the observed relations were statistically significant ($p < 0.001$) (Table 2).

**Discussion**

The present study aimed to evaluate diaphragm thickness, excursion, and spirometry values in patients with COPD and compare them with healthy controls. In our study, the median value of predicted FEV1 was 51.5% in COPD patients, indicating that most of the COPD patients had moderate airflow limitations and belonged to the GOLD grade 2. They had significantly lower ($p < 0.0001$) FEV1 (0.56 L) and FVC (1.2 L) in comparison to healthy controls (2.21 and 2.58 L, respectively).

In obstructive disease, FEV1/FVC ratio is less than 70%; and in our study median percentage of FEV1/FVC in COPD patients was 55%. Our findings concord with Topalovic et al., who reported similar observations in COPD patients. They compared lung function patterns in healthy subjects and COPD patients and showed that out of 222 COPD patients, 197 had an obstructive pattern.

On assessing the diaphragm excursion by USG, we observed that diaphragm excursion at deep inspiration (3.49 ± 0.8 cm) and while sniffing (1.42 ± 0.56 cm) was significantly lower among COPD patients compared to the healthy controls ($p < 0.001$). Amin and Zedan reported that the diaphragm excursion during quiet breathing was 2.23 ± 0.50 cm in COPD patients and 2.28 ± 0.59 cm in healthy controls, with no statistically significant difference ($p = 0.085$). The conclusions of our study agreed with Dos Santos Yamaquiti et al. They used B-mode USG and reported that the diaphragm excursion during tidal breathing was 2.21 ± 0.56 cm in the control group and 1.65 ± 0.66 cm in patients with COPD. Diaphragm dysfunction is common among patients with COPD. Numerous reasons could explain this; pulmonary hyperinflation and malnutrition are the most common causes of muscular weakness. Lung hyperinflation causes the diaphragm to move caudally, causing a mechanical disadvantage.

We also observed that diaphragm thickness measurements based on USG assessment were significantly reduced ($p < 0.0001$) in patients with COPD at end inspiration (0.34 cm) in comparison to healthy controls (0.45 cm). Similarly, the DTF was significantly reduced ($p < 0.0001$) in COPD patients (36.25%) in comparison to controls. However, there are only a few studies measuring diaphragm function due to the lack of standardization of measurement methods. The complex function of the diaphragm muscle and

**Table 1:** Comparison of spirometry values, diaphragm excursion, and thickness between COPD patients and controls

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Healthy controls</th>
<th>COPD patients</th>
<th>$p$-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spirometry values [median (IQR)]</td>
<td>FEV1</td>
<td>2.20 (1.68, 2.5)</td>
<td>0.56 (0.46, 0.86)</td>
</tr>
<tr>
<td></td>
<td>% of predicted FEV1</td>
<td>85.0 (76.0, 90.0)</td>
<td>51.5 (40.0, 65.25)</td>
</tr>
<tr>
<td></td>
<td>FVC</td>
<td>2.50 (1.94, 2.81)</td>
<td>1.2 (0.87, 1.5)</td>
</tr>
<tr>
<td></td>
<td>FEV1/FVC</td>
<td>88.0 (84.0, 90.0)</td>
<td>55.0 (47.0, 62.5)</td>
</tr>
<tr>
<td>Diaphragm excursion (mean ± SD)</td>
<td>Normal inspiration</td>
<td>2.46 ± 0.46</td>
<td>2.18 ± 0.6</td>
</tr>
<tr>
<td></td>
<td>Deep inspiration</td>
<td>5.76 ± 1.02</td>
<td>3.49 ± 0.8</td>
</tr>
<tr>
<td></td>
<td>Sniffing</td>
<td>2.41 ± 0.44</td>
<td>1.4 ± 0.56</td>
</tr>
<tr>
<td>Diaphragm thickness [median (IQR)]</td>
<td>End inspiration</td>
<td>0.45 (0.41, 0.50)</td>
<td>0.34 (0.25, 0.44)</td>
</tr>
<tr>
<td></td>
<td>End expiration</td>
<td>0.28 (0.23, 0.32)</td>
<td>0.23 (0.18, 0.31)</td>
</tr>
<tr>
<td></td>
<td>DTF</td>
<td>68.0 (46.9, 93.0)</td>
<td>36.25 (27.63, 54.23)</td>
</tr>
</tbody>
</table>

A, Mann–Whitney U Test; b, independent t-test; $p < 0.01$ shows the significance
non-standardized measurement methods may be the reasons for contradictory results. Baria et al. used USG to measure the diaphragm thickness in COPD patients and found that the mean right hemidiaphragm thickness was 0.28 cm, and the left hemidiaphragm thickness was 0.32 cm. The healthy controls in their study had a mean right hemidiaphragm thickness of 0.32 cm and a left hemidiaphragm thickness of 0.34 cm, but the difference was not statistically significant. They did not consider the relationship between diaphragm thickness and clinical characteristics. Another study by Cimsit et al. could not determine any correlation between clinical parameters and diaphragm thickness.22

A moderately strong correlation between diaphragm movements during deep inspiration \( (r = 0.700) \) and sniffing \( (r = 0.610) \) was found in this study. Scheibe et al. reported that the measurement of lung silhouette movement using USG measurement was useful and reliable in demonstrating diaphragm dysfunction in COPD patients. A strong correlation between diaphragm movement and FEV1 was reported in their study. Ünal et al. used magnetic resonance fluoroscopy and reported the difference of excursion between the deepest and highest point of the diaphragm as 26 mm for patients with COPD and 69 mm for healthy subjects. They also reported a correlation between diaphragm excursion and FEV1. A positive correlation between diaphragm mobility with FEV1 and FVC and a negative correlation with residual volume, total lung capacity, and partial pressure of carbon dioxide was reported by Kang et al.24

We also evaluated the correlation between the absolute value of FEV1 with diaphragm excursion and age. Age showed a strong negative correlation between FEV1 and diaphragm excursion. Goleczewski et al. derived a mathematical equation of dependence of age with FEV1 and found a negative correlation for healthy males (FEV1 = 0.77 \times FVC + 0.32 – 0.0069 \times age) and females (FEV1 = 0.77 \times FVC + 0.28 – 0.0052 \times age). To the best of our knowledge, our study is the first of its own to derive the equation for predicting FEV1 based on age and diaphragm excursion, FEV1 = 2.99 – (0.042 \times age) + (0.224 \times deep inspiration) + (0.015 \times sniffing).

**Limitations**

The effect of abdominal muscles in the supine position was one of the limitations. In this study, some inpatients were in the intensive care unit and could be examined in a supine position alone. This could influence the USG measurements of diaphragm excursion, thickness, and lung volumes, due to a change in total inspired volume as a result of increased diaphragm excursion and a change in end-expiratory lung volume. However, this technique was chosen to detect the relationship between measurements taken under varying circumstances, even in patients who could not tolerate orthostatic posture. The patients in intensive care units who were included in the study were follow-up patients who were previously diagnosed with COPD using spirometric values, and their latest spirometer values before hospitalization, when they were in a stable state, were taken for the study. The study findings could not be generalized as it was a single-center study, and the sample size was small. Inpatients included in this study were not followed up, so any further changes in their FEV1 to assess disease progression and changes in diaphragm excursion and thickness were not evaluated. As our study was conducted for 1 year, we could not repeat spirometry for the same patient more than once, and as it was not in our objectives to do follow-up spirometry and USG evaluation of the diaphragm, it was not done, and this was another limitation of the study.

**Conclusion**

The absolute value of FEV1 and the percentage of predicted FEV1, FVC, and FEV1/FVC were significantly lower in patients with COPD. Diaphragm excursion at normal inspiration, deep inspiration, and sniffing was significantly lower in these patients compared to healthy controls. The diaphragm thickness at end expiration, end inspiration, and DTF was also significantly lower \( (p < 0.01) \). DTF showed a sensitivity of 74.3% and a specificity of 65.7% at a cut-off value of 54.07. By using the equation FEV1 = 2.99 – (0.042 \times age) + (0.224 \times deep inspiration) + (0.015 \times sniffing), we can predict a person’s FEV1 value by just measuring his diaphragm movements using bedside USG. Thus any risks for major surgeries can be predicted, and treatment options can be made. The FEV1 value could also predict the prognosis and follow-up while on inhaler therapy.

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**References**

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