Diagnostic and clinical values of non-cardiac ultrasound in COPD: a systematic review

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## S2. Table 1. Characteristics of included studies on ultrasound measurement of diaphragmatic features in COPD

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Country/ Type of study</th>
<th>Sample size (male=Female=)</th>
<th>Age mean ±SD or range</th>
<th>Targeted population</th>
<th>GOLD severity</th>
<th>Type of assessment</th>
<th>Outcome measures</th>
<th>Result specifically for ultrasound (with numbers and p values)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yamaguti et al 2008</td>
<td>Brazil/O</td>
<td>M= 58 F= 14</td>
<td>52-70</td>
<td>Stable</td>
<td>Gold 2</td>
<td>Assess intervention effect</td>
<td>To assess diaphragm mobility COPD patients had less diaphragm mobility (36.5 ±10.9 mm) than healthy individuals (46.3 ±9.5 mm) (P = 0.001) and this s mainly due to air trapping and is not influenced by respiratory muscle strength or hyperinflation</td>
<td></td>
</tr>
<tr>
<td>Baria et al 2014</td>
<td>US/O</td>
<td>M=23 F=27 (Control Group M=73 F=77)</td>
<td>69 ±9.9</td>
<td>Stable</td>
<td>Gold 2</td>
<td>Diagnose</td>
<td>To find the standard values for diaphragm thickness and thickening ratio There was no significant difference in diaphragm thickness or thickening ratio between sides within groups (control subjects or patients with COPD) or between groups, with the exception of the subgroup with severe air trapping (residual volume. 200%), in which the only difference was that the thickening ratio was higher on the left (P value, 0.04).</td>
<td></td>
</tr>
<tr>
<td>Nair et al 2019</td>
<td>India/RCT</td>
<td>M = 12 F = 8</td>
<td>66.85 ± 8.37</td>
<td>Stable</td>
<td>Gold 2</td>
<td>Assess intervention effect</td>
<td>To compare the effects of diaphragmatic stretch and manual diaphragm release technique on diaphragmatic excursion in patients with COPD. Despite significant differences before and after applying each method, there was no statistically significant difference in diaphragmatic excursion in the comparison of the post intervention values of both techniques.</td>
<td></td>
</tr>
<tr>
<td>Okura et al 2017</td>
<td>Japan/O</td>
<td>M = 32 F = 8</td>
<td>73 ± 7</td>
<td>Stable</td>
<td>Gold 2 Gold 3</td>
<td>Diagnose</td>
<td>To assess the contractile capacity of the diaphragm and its relationship with nocturnal oxygen saturation. NSpO2 mean was positively correlated with (% change in the thickness of the diaphragm) %ΔTdi (P &lt; 0.001).</td>
<td></td>
</tr>
<tr>
<td>Gorman et al 2005</td>
<td>Australia/O</td>
<td>M= 7 F = 5</td>
<td>63 ± 8</td>
<td>Stable</td>
<td>Gold 4</td>
<td>Diagnose</td>
<td>To estimate the diaphragm length after lung volume reduction surgery Increased diaphragm length resulted in lower motor unit firing rates and reduced breathing effort, and this is likely to contribute to improved quality of life and exercise performance after LVRS.</td>
<td></td>
</tr>
<tr>
<td>Gorman et al al 2002</td>
<td>Australia/O</td>
<td>M = 10 F=0 (Control 10)</td>
<td>68 ± 9</td>
<td>Not stable, (Had recurrent hospital admissions)</td>
<td>Gold 4</td>
<td>Diagnose</td>
<td>To estimate the diaphragm length during tidal breathing in COPD Although the diaphragm length during tidal breathing is shorter at FRC in patients with COPD, its motion and change in length during tidal breathing is like that in control subjects.</td>
<td></td>
</tr>
<tr>
<td>Grosu et al 2017</td>
<td>US/O</td>
<td>COPD=8 M = 33 F=24</td>
<td>65.7 ± 16.7</td>
<td>Not Stable (mechanically ventilated)</td>
<td>No data</td>
<td>Diagnose</td>
<td>To estimate the changes in diaphragm thickness in intubated patients. Subjects without COPD had thinner diaphragm at baseline than those with COPD (0.22 ±0.07 vs 0.26 ±0.06, p value, 0.03). No significant association between the rate of thinning and diagnosis of COPD, (P value 0.36).</td>
<td></td>
</tr>
<tr>
<td>El Aziz, Amal et al</td>
<td>Egypt/O</td>
<td>50 COPD M=30 F=10</td>
<td>54.3 ± 6.49 (40±70 Years)</td>
<td>Stable</td>
<td>All 4 categorie s</td>
<td>Diagnose</td>
<td>To assess the diaphragmatic thickness and excursions in COPD patients. Diaphragmatic thickness at different lung volumes (TDRV, TDFRC and TDTLC), and excursion all are decreased in COPD than control. Highly significant positive correlation was found between diaphragmatic thickness at different lung volumes (TDRV, TDFRC and TDTLC) diaphragmatic thickenings and excursion with the spirometric finding as FEV1, MIP and MEP.</td>
<td></td>
</tr>
</tbody>
</table>
| Study           | Country/Cohort | COPD Group | COPD Groups | Stable | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | 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GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | GOLD | Golden

- DBTP in patients with COPD leads to improvements in abdominal motion during NB and in functional capacity. We also showed that patients with a baseline level predominance of costal breathing and worse diaphragmatic mobility experienced a greater improvement in abdominal motion
- The diaphragmatic mobility demonstrated significant differences between the subjects with COPD and the healthy controls. During resting breathing, mobility was statistically and clinically higher, especially at the beginning of the rehabilitation program, without improvements thereafter.
- Diaphragmatic mobility during deep inspiration was lower than in the healthy controls, but improved after rehabilitation, and those improvements were followed by improvements of the inspiratory capacity. Second, diaphragmatic mobility reduction was correlated to loss in lung function.
- COPD patients, especially those with severe COPD, showed significantly lower diaphragmatic motion than IPF patients or healthy controls. Right diaphragmatic motion during deep breathing was negatively correlated with emphysema scores (r=-0.60, p value, 0.001).
- M-mode ultrasonographic evaluation of diaphragmatic motion during deep breathing may be a useful tool in diagnosing CPFE and in discriminating CPFE patients from IPF or COPD patients.
- Diaphragmatic thickness fraction measurements based on ultrasonographic assessment in subjects with COPD seemed to be unable to identify subjects at high risk of symptoms and exacerbations.
- There was no significant difference between the patients and control groups in diaphragmatic thickness.
- Thickness (R) in COPD vs control: 2.74 ± 0.4 vs 2.98 ± 0.8 (p=0.134)
- Thickness (L) in COPD vs control: 2.77 ± 0.4 vs 2.70 ± 0.7, (p=0.647).
- There was also no significant difference between diaphragmatic thickness and COPD severity, respiratory function (P = 0.410), and frequency of exacerbations (P = 0.881) and mMRC (P = 0.667).
<table>
<thead>
<tr>
<th>Study</th>
<th>Country/Clinic</th>
<th>Participants</th>
<th>Age (mean ± SD)</th>
<th>Status</th>
<th>Intervention Effect</th>
<th>Findings</th>
</tr>
</thead>
</table>
| Evrin et al. 2019     | Turkey/O       | M=83 F=18 COPD 61 | 58.72           | Stable | Gold 1 Gold 2 Gold 3 Gold 4 | To determine the use of point-of-care ultrasound in evaluating the disease status and outcomes in COPD patients.  
Five point-of-care US measurements, Lung Sil R, Lung Sil L, Ant B-Mode R, Ant M-Mode R, and Ant M-Mode L, were significantly different among the patient groups (P<0.001 for each).  
FEV₁ positively correlated and annual number of exacerbations were negatively correlated with US findings. |
| Zhang et al. 2019     | China/O        | M= 27 F= 10 | 74.5 ± 7.5      | Stable (On MV, Ready for extubation) | Asses intervention effect | To estimate the diaphragmatic activity and its variation in predicting extubation outcome in mechanically ventilated COPD patients.  
(AUC-ROC) of DE30 and ΔDE30−5 (the variation between 30 and 5 min) were 0.762 and 0.835; a cut-off value of DE30 >1.72 cm and ΔDE30−5> 0.16 cm were associated with a successful extubation with a sensitivity of 76% and 84%, a specificity of 75% and 83.3%, respectively.  
Combination of diaphragmatic excursion (DE30 and ΔDE30−5) estimated by the bedside ultrasound could improve the predictive value and could be used as the predictor of extubation outcome in mechanically ventilated patients with COPD. |
| Sun et al. 2017       | China/O        | M = 13 F = 2 | 78.6 ± 7.01     | Stable (Mechanically ventilated COPD) | Assess intervention effect | Ultrasonic assessment of the diaphragm activities during NAVA and PSV mode during the weaning phase of mechanical ventilation.  
The diaphragm activity in patients with AECOPD decreased when the support level increased for both PSV and NAVA. However, the diaphragm activities were higher during NAVA compared to the same sup-port level during PSV.  
There was a positive correlation between the diaphragm activity and ventilation distribution in the most dependent regions (ROI4, $R^2=0.56$, P< 0.01). |
| Priori et al. 2013    | Italy/O        | 23 COPD 12 Control | 66.4 ± 6.9      | Stable | Gold 3 | Assess intervention effect | To assess the kinematics of the diaphragm by ultrasonography  
In COPD patients, the Diaphragm displacement estimated by ultrasonography was 23.6 ± 9.3 mm while seated and 17.5 ± 5.7 mm supine (P = 0.05). COPD patients showed significantly greater diaphragmatic displacement seated compared with control subjects (P = 0.04), but when supine the degree of displacement was similar in both groups.  
Rib cage paradox was noticed in approximately one-half of the COPD patients while seated but was not related to impaired diaphragm motion. In the supine posture, the rib cage paradox disappeared, suggesting that, in this posture, diaphragm mechanics improves. |
| Rocha et al. 2015     | Italy/RCT      | M=14 F=5 71 years | 63.61 ± 5.6     | Stable | Gold 3 | Assess intervention effect | To evaluate diaphragmatic mobility  
The Manual Diaphragm Release Technique produced statistically significant improvements in diaphragmatic mobility, 6-minute walking distance and inspiratory capacity in people with COPD.  
The improvement in diaphragmatic mobility showed moderate correlation with abdominal volume during inspiratory capacity manoeuvres. |
| Elsawy et al. 2017    | Egypt/O        | COPD M= 100 F= 0 Control 100 | 63.61 ± 5.6     | Stable | Gold 1 Gold 2 Gold 3 Gold 4 | Diagnostic  
To assess the diaphragm thickness and its impact on disease severity in COPD patients.  
The right (25.3 ± 5.1 vs 30.8 ±5.4) and left thickness fraction (31.3 ±7.2 vs 34.1 ±8.5) were significantly lower in COPD group than control group.  
The right and left thickness fraction were significantly decreased through progression of COPD (mild, moderate, severe and very-severe grades) (p = 0.020, 0.002 respectively).  
The right and left thickness fraction were positively correlated with BMI, FEV₁/FVC, FEV₁%, and PaO₂, while it was negatively correlated with PaCO₂, which indicates that diaphragm... |
### Paulin et al. 2007

**Brazil/O**  
M=42  
F=12  
Control=20  

<table>
<thead>
<tr>
<th>COPD= 54</th>
<th>62.15± 8.06</th>
<th>Stable</th>
<th>Gold 3</th>
<th>Diagnostic</th>
</tr>
</thead>
</table>

To evaluate the influence of diaphragmatic mobility on exercise tolerance and dyspnea in patients with COPD.

- The COPD patients presented less diaphragmatic mobility than the controls (36.27± 10.96 mm vs. 46.33±9.46 mm).
- Diaphragmatic mobility was found to correlate with RV (r= -0.60; p<0.000), IC (r=0.41; p<0.002), the RV/TLC ratio (r= -0.72; p<0.000), and the IC/TLC ratio (r=0.55; p<0.000).
- Diaphragmatic mobility also correlated significantly with performance on the 6MWT (r=0.38; p<0.005) and dyspnea score (r=-0.36; p=0.007).

### Kang et al. 2011

**South Korea/O**  
M=31  
F=6  

<table>
<thead>
<tr>
<th>69.1 ± 9.0</th>
<th>Stable</th>
<th>Gold 2,3,4</th>
<th>Diagnostic</th>
</tr>
</thead>
</table>

The purpose of the study was to investigate the relationship between diaphragm mobility and pulmonary function parameters, as well as that between arterial blood gas values and diaphragm mobility in COPD patients.

- Diaphragm mobility (mm) 19.8 ± 7.5
- Diaphragm mobility correlated with the (FEV$_1$: r = 0.415, P = 0.011) and pulmonary hyperinflation (RV: r = -0.501, P = 0.021; TLC: r = -0.281, P = 0.030; RV/TLC: r = -0.527, P = 0.001).
- It also correlated significantly with (FVC: r = 0.302, P = 0.029; MVV: r = 0.481, P = 0.003).
- Negative correlations between diaphragmatic mobility and PaCO2 (r = 0.373, P = 0.030).

### Souza et al. 2019

**Brazil/O**  
M=13  
F=8  

<table>
<thead>
<tr>
<th>65.80 ± 7.00</th>
<th>Stable</th>
<th>Gold 2,3,4</th>
<th>Diagnostic</th>
</tr>
</thead>
</table>

To evaluate inspiratory muscle strength, diaphragmatic mobility and body composition in COPD subjects and to correlate these variables.

- Subjects with inspiratory muscle weakness had reduced diaphragmatic mobility compared to those without, (76.64 ± 12.87 vs 62.53 ± 7.92; P=0.007).
- Maximal inspiratory pressure exhibited a weak positive relationship to diaphragmatic mobility (r= 0.496, p= 0.022).
- Inspiratory muscle weakness had repercussions on the mobility of the diaphragm muscle.

### Lim et al. 2019

**South Korea/O**  
M=10  
F=0  

<table>
<thead>
<tr>
<th>79.8 ± 8.1</th>
<th>acute exacerbation</th>
<th>Gold 3,4</th>
<th>Diagnostic</th>
</tr>
</thead>
</table>

To investigate the changes in diaphragmatic function during acute exacerbation of COPD by US.

- The significant increase in the diaphragmatic thickness from the initial (at exacerbation) to the follow-up (stable phase) values (80.1 ± 104.9 mm vs. 159.5 ± 224.6 mm, p = 0.011);
- Diaphragmatic excursion did not vary significantly between the initial and follow-up values (22 ± 6 mm vs 23 ±12 mm).
- The change in excursion between the stable and exacerbation periods was positively correlated with time to the next exacerbation (r=0.89; p=0.04) and negatively correlated with the time taken to recover from the exacerbation (r=-0.77; p=0.07).
- Diaphragmatic dysfunction occurs during AECOPD, and patients showing greater improvement of function during recovery will likely have delayed appearance of future exacerbations.

### Abbas et al. 2018

**Egypt/O**  
M = 34  
F =16  

<table>
<thead>
<tr>
<th>61.9±7.47</th>
<th>Stable</th>
<th>Gold 2, 3</th>
<th>Diagnostic</th>
</tr>
</thead>
</table>

Mechanically Ventilated

To validate the D-RSBI as a new predictor of weaning outcome in patients with AECOPD and to compare its accuracy with that of the traditional RSBI.

- D-RSBI (RR/DD) is superior to the traditional RSBI (RR/VT) in predicting weaning outcome in AECOPD patients.
- The areas under the ROC curves for D-RSBI and RSBI were 0.97 (p<0.001) and 0.67 (p<0.001), respectively.
- DD (mm), 16.57±2.4 vs 9.23±2.42, (P= <0.001)
- D-RSBI = Successful weaning, 3.27±0.84 (P= <0.001)

### McKenzie et al. 2000

**Australia/O**  
M = 9  
F =0  

<table>
<thead>
<tr>
<th>65 (10)</th>
<th>Stable</th>
<th>Gold 4</th>
<th>Diagnostic</th>
</tr>
</thead>
</table>

To measure the Diaphragm length (LDi) via measurements of transverse diameter of the rib.

- Diaphragm dimensions in patients with severe COPD can be predicted from measurements of LZapp and Drc.
- The findings validate the use of non-invasive.
<table>
<thead>
<tr>
<th>Study</th>
<th>Country/Gender</th>
<th>COPD Status</th>
<th>Study Group</th>
<th>Diaphragm Measurement and Analysis</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Jain et al. 2019</td>
<td>India/O</td>
<td>COPD</td>
<td>Not reported</td>
<td>Stable Gold 1,2,3,4 Diagnostic</td>
<td>Mean diaphragmatic thickness during inspiration and expiration and zone of apposition were significant decreased in patients with small airways, mild to moderate obstruction and increased in cases with severe airway obstruction as compared to controls. Mean diaphragmatic thickness during inspiration and expiration in COPD patients in Indian population with the help of ultrasound guided examination.</td>
</tr>
<tr>
<td>Smargiassi et al. 2014</td>
<td>Italy/O</td>
<td>M=23, F=9</td>
<td>Stable</td>
<td>Gold 1,2,3 Diagnostic</td>
<td>TD at different lung volumes was closely related to IC, vital capacity (VC) and TLC, showing TDTLC to have the closest relationships with IC and VC (r=0.42 and p = 0.0001 in both cases). TDTLC was related to all indices of air trapping: directly to IC/TLC (p = 0.01), inversely to FRC/TLC and to RV/TLC (p = 0.01 and p = 0.02, respectively). FFM showed significant direct correlations with all TD measurements (i.e. TDFRC, TDTLC and TDRV), with closer relationships with TDFRC and TDTLC (r=0.39 and p = 0.0002 and r= 0.32 and p = 0.0008, respectively). Echographic measurements of TDTLC and thickening at TLC might be a useful tool to estimate lung hyperinflation, especially when adjusted for FFM.</td>
</tr>
<tr>
<td>Cişmî et al. 2016</td>
<td>Turkey/O</td>
<td>M=47, F=6</td>
<td>Stable</td>
<td>Gold 2,3,4 Diagnostic Ultrasound evaluation of the diaphragm thickness to determine the relationship between pulmonary function tests, and symptom scores</td>
<td>Mean thickness value was 2.3 mm in females and 2.06 mm in males. There was a moderate correlation between diaphragmatic muscle thickness and %FEV1 in mild COPD patients (r=0.62, p=0.017&lt;0.05). No significant difference in diaphragmatic thicknesses of GOLD subgroups was found. There were no correlations between diaphragmatic muscle thickness, symptom scores, BMI, age, and gender.</td>
</tr>
<tr>
<td>Marchioni et al. 2018</td>
<td>Italy/O</td>
<td>M=38, F=37</td>
<td>Exacerbation</td>
<td>Gold 1,2,3,4 (Categorized based on the previous history) Diagnostic</td>
<td>Early and noninvasive US assessment of DD during severe AECOPD is reliable and accurate in identifying patients at major risk for NIV failure and worse prognosis. Diaphragmatic thickness ΔTD&lt; 20% showed better accuracy in predicting NIV failure than baseline pH value and early change in both arterial blood pH and partial pressure of carbon dioxide following NIV start (AUCs 0.84 to DTdi &lt; 20%, 0.51 to pH value at baseline, 0.56 to early change in arterial blood pH following NIV start, and 0.54 to early change in partial pressure of carbon dioxide following NIV start, respectively; p = 0.0001).</td>
</tr>
<tr>
<td>Crimi et al. 2018</td>
<td>Italy/O</td>
<td>M=23, F=2</td>
<td>Stable</td>
<td>Gold 1,2,3,4 Assess intervention effect To estimate the role of US assessment of diaphragm function and change of rectus femoris area in COPD patients undergoing a PR program and in the detection of post rehabilitation outcomes.</td>
<td>A correlation was found between the intradividual percentage of change in the diaphragmatic length of zone of apposition at functional residual capacity (ΔLzapp%) and the change in 6-minute walking distance (6MWD) after PR (r=0.49, P=0.02). ΔLzapp% was significantly higher in patients with improved 6MWD and COPD Assessment Test (CAT) score (mean rank=12.03±2.57 vs 6.88±4.37; P=0.02).</td>
</tr>
</tbody>
</table>
Diaphragm US assessment represents a useful prognostic marker of PR outcomes in COPD patients.

### Diaphragm Excursion (mm)

<table>
<thead>
<tr>
<th>Study</th>
<th>Country/RCT</th>
<th>Gender</th>
<th>Age</th>
<th>GOLD</th>
<th>Diastolic Function</th>
<th>IVW</th>
<th>6MWT Improvement</th>
<th>US Measurement</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bhatt et al. 2013</td>
<td>USA/RCT</td>
<td>M=10 F=4</td>
<td>53.1 ± 7.4</td>
<td>Stable</td>
<td>Gold</td>
<td>2,3,4</td>
<td>To measure the diaphragmatic movement during tidal and FVC Maneuver to estimate the changes in exercise capacity</td>
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</tr>
<tr>
<td>Andrews et al. 2017</td>
<td>Canada/RCT</td>
<td>M=67 F= 33</td>
<td>76.3 ± 11.9</td>
<td>Stable</td>
<td>GOLD 1, 2, 3</td>
<td>Assess intervention</td>
<td>To assess the effect of EMT on lung function and outcomes in patients that completed PR.</td>
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</tr>
<tr>
<td>Scheibe et al. 2015</td>
<td>Germany/O</td>
<td>COPD 60 Control 20</td>
<td>Stable</td>
<td>Gold</td>
<td>2,3,4</td>
<td>Diagnostic</td>
<td>To compare sonoanographic measurement of the lung silhouette movement and investigate the correlation between both measures and lung function parameters in COPD patients</td>
<td></td>
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</tr>
<tr>
<td>Maynard-Paquette et al. 2020</td>
<td>Canada/O</td>
<td>M=20 F= 0</td>
<td>66±6</td>
<td>Stable</td>
<td>Gold</td>
<td>1,2,3,4</td>
<td>Diagnostic</td>
<td>To evaluate the relationship between quadriceps size, and symptoms, lung function and diaphragm contractility in COPD patients using ultrasound.</td>
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</tr>
</tbody>
</table>

**Comments:**
- There was a significant correlation between improvement in 6MWT distance and increase in diaphragmatic excursion during forced breathing when measured by US ($r=0.59$, $p<0.03$).
- Tidal excursion (cm), Pre-PLB 2.01±0.7 vs Post 2.23±0.5
- PLB increases functional exercise tolerance. This effect could be mediated by a reduction in RR and increased diaphragmatic movement.
- Ultrasound assessment revealed no difference in the RFcsa or diaphragm thickness between the EMT and control group
- US diaphragm in EMT and control (cm ± SD 0.3 ± 0.) respectively.
- US rectus femoris in EMT and control (cm ± SD 2.8 ± 0.5 vs 2.9 ±0.7) respectively.
- There was a significant correlation between improvement in 6MWT distance and increase in diaphragmatic excursion during forced breathing when measured by US ($r=0.59$, $p<0.03$).
- Tidal excursion (cm), Pre-PLB 2.01±0.7 vs Post 2.23±0.5
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- There was a significant correlation between improvement in 6MWT distance and increase in diaphragmatic excursion during forced breathing when measured by US ($r=0.59$, $p<0.03$).
- Tidal excursion (cm), Pre-PLB 2.01±0.7 vs Post 2.23±0.5
- PLB increases functional exercise tolerance. This effect could be mediated by a reduction in RR and increased diaphragmatic movement.
- Ultrasound assessment revealed no difference in the RFcsa or diaphragm thickness between the EMT and control group
- US diaphragm in EMT and control (cm ± SD 0.3 ± 0.) respectively.
- US rectus femoris in EMT and control (cm ± SD 2.8 ± 0.5 vs 2.9 ±0.7) respectively.

**References:**
- Bhatt et al. 2013
- Andrews et al. 2017
- Scheibe et al. 2015
- Maynard-Paquette et al. 2020
**Abbreviations:**  
- %ΔTdi: percentage changes in diaphragm thickness;  
- 6MWD: six minute walk distance;  
- AECOPD: acute exacerbation of chronic obstructive pulmonary disease;  
- AUC-ROC: Area under the curve, receiver-operating characteristic;  
- BMI: body mass index;  
- CAT: COPD Assessment Test;  
- COPD: chronic obstructive pulmonary disease;  
- CPFE: Combined pulmonary fibrosis and emphysema;  
- DBTP: diaphragmatic breathing training program;  
- DD: diaphragmatic dysfunction;  
- DE: diaphragmatic excursion;  
- DRC: diameter of the rib cage;  
- D-RSBI: diaphragmatic rapid shallow breathing index;  
- EMT: exercise maintenance therapy;  
- F: female;  
- FEV₁: Forced expiratory volume in one second;  
- FFM: fat-free mass;  
- FRC: functional residual capacity;  
- FVC: forced vital capacity;  
- GOLD: global initiative for chronic obstructive lung disease;  
- IC: inspiratory capacity;  
- IPF: interstitial pulmonary fibrosis;  
- LDi: diaphragm length;  
- LVRS: lung volume reduction surgery;  
- LZapp: length of the zone of apposition;  
- M: male;  
- MEP: maximum expiratory pressure;  
- MIP: maximum inspiratory pressure;  
- mm: Millimetre;  
- mMRC: modified medical research council;  
- NAVA: neurally adjusted ventilatory Assist;  
- NB: normal breathing;  
- NIV: noninvasive ventilation;  
- NSpO₂: nocturnal oxygen saturation;  
- O: observational;  
- PaCO₂: carbon dioxide pressure in arterial blood;  
- PaO₂: oxygen pressure in arterial blood;  
- PR: pulmonary rehabilitation;  
- PSV: pressure support ventilation;  
- Qc: quadriceps contractile index;  
- QcSA: quadriceps cross-sectional area;  
- Qthick: quadriceps thickness;  
- RCT: randomised control trial;  
- RFCSA: rectus femoris cross-sectional area;  
- RR/DD: respiratory rate/diaphragmatic displacement;  
- TD: diaphragm thickness;  
- TDFRC: diaphragm thinness at functional residual capacity;  
- TDRV: diaphragm thinness at residual volume;  
- TDTLC: diaphragm thinness at total lung capacity;  
- TFf: thickening fraction;  
- US: ultrasound;  
- VC: vital capacity.
S2. Table 2 – Characteristics of included studies on ultrasound measurement of muscles features and bone mineral density in COPD

<table>
<thead>
<tr>
<th>Study Name</th>
<th>Country</th>
<th>Sample size (male/female)</th>
<th>Age mean ±SD or range</th>
<th>Targeted population</th>
<th>COPD GOLD</th>
<th>Location of use</th>
<th>Type of assessment</th>
<th>Outcome measures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maddocks et al. 2014</td>
<td>UK/O</td>
<td>M=10 F=7 Healthy M= 16 F = 22</td>
<td>68 (10)</td>
<td>Stable</td>
<td>GOLD 3</td>
<td>Tibialis anterior cross-sectional area</td>
<td>Diagnose</td>
<td>To assess change in strength, loss and change in the composition of skeletal muscles in patients with COPD.</td>
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<td>➢ Reduction in ankle dorsiflexor muscle strength (ADMVC, 100 HzAD) in COPD patients compared to age-matched and younger healthy subjects when normalized to TA&lt;sub&gt;CSA&lt;/sub&gt; (P&lt;0.01). TA&lt;sub&gt;AE&lt;/sub&gt; increased in COPD patients compared healthy young (P=0.0008) and elderly (P=0.025) subjects.</td>
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<td></td>
<td>➢ There were no significant differences in TACSA between healthy young, healthy elderly and COPD patient groups</td>
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<td>➢ In all participants ADMVC and 100 HzAD positively correlated with TA&lt;sub&gt;CSA&lt;/sub&gt; (r=0.78, P&lt;0.0001) and negatively correlated with TA&lt;sub&gt;AE&lt;/sub&gt; (r=−0.46, P&lt;0.0005).</td>
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<td>➢ Muscle Infiltration of non-contractile tissue is related to loss in muscle strength observed in COPD patients.</td>
</tr>
<tr>
<td>Greening et al. 2015</td>
<td>UK/O</td>
<td>M=78 F=113</td>
<td>71.6 (9.1)</td>
<td>Exacerbate</td>
<td>Gold 1,2,3,4</td>
<td>Quadriceps RFcsa</td>
<td>Diagnose</td>
<td>To determine whether muscle (quadriceps) function as assessed by ultrasound can predict hospital readmission at 1 year or death in COPD patients</td>
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<td>➢ Quadriceps RFcsa was associated with readmission or death (OR=0.34, 95% CI= 0.17–0.65, P= 0.001), and hospitalization in the previous year (OR, 4.82; 95% CI, 2.42–9.58; P=0.001).</td>
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<td>➢ Subjects in the smallest muscle group were more likely to be readmitted or die (as expected) but also had more days in hospital over the subsequent 12 months.</td>
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<td>➢ Q&lt;sub&gt;c&lt;/sub&gt;sa, cm&lt;sup&gt;2&lt;/sup&gt;:4.76 (1.41)</td>
</tr>
<tr>
<td>Ye X et al. 2017</td>
<td>China/O</td>
<td>M=27 F=23 Control 21</td>
<td>65.76±8.07</td>
<td>Stable</td>
<td>Gold 1,2,3,4</td>
<td>Rectus femoris</td>
<td>Diagnose</td>
<td>To investigate the relationship between rectus femoris echo intensity and COPD (HRQoL) using ultrasound.</td>
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<td>➢ EI was significantly higher in GOLD I/II/III COPD than in non-COPD subjects (P=0.019) P&lt;0.005/ P&lt;0.0001.</td>
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<td>➢ QMT (mm) was lower in GOLD III-IV COPD compared to non-COPD and GOLD I COPD subjects (P=0.000 and P=0.001).</td>
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<td></td>
<td>➢ RF&lt;sub&gt;CSA&lt;/sub&gt; (cm&lt;sup&gt;2&lt;/sup&gt;) was lower in GOLD III-IV COPD compared to non-COPD (7.07±1.78) and GOLD I COPD (6.84±2.67) (P=0.006 and P=0.01).</td>
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<td>➢ In stable COPD patients QMT, RFcsa, FACITF and 6MWD showed positive correlation with lung function, while EI showed significant negative correlation with lung function (r=−0.413, P&lt;0.01).</td>
</tr>
<tr>
<td>Alcazar et al. 2019</td>
<td>Spain/R</td>
<td>M=24 F=5</td>
<td>77.7 ± 7.9</td>
<td>Stable</td>
<td>Gold 1,2,3,4</td>
<td>Vastus lateralis (VL) muscle</td>
<td>Assess intervention effect</td>
<td>To assess the effects of ET on systemic oxidative stress and limb muscle dysfunction in older people with COPD via measurement of plasma protein carbonylation and muscle ultrasonography respectively.</td>
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<td>➢ In ET subjects there was a significant change in mid-thigh muscle CSA (+4%), VL muscle thickness (+1%) and pennation angle (+19%).</td>
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<td>➢ Also, protein carbonylation decreased in the ET group compared to the control group (-27%, P&lt;0.05) and correlated with changes in Muscle size and pennation angle (r = −0.44 to −0.57), exercise capacity (r = −0.46). muscle strength (r = −0.45) and sit-to-stand performance (r = 0.60).</td>
</tr>
<tr>
<td>Vrieze et al. 2007</td>
<td>Netherla nds/O</td>
<td>M=62 F=53</td>
<td>60.0±10.8</td>
<td>Stable</td>
<td>Gold 2,3,4</td>
<td>Bone mineral density</td>
<td>Diagnostic</td>
<td>To investigate the prevalence and predictors of abnormal</td>
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<td></td>
<td>➢ The prevalence of abnormal BMD in COPD rises from 27% in GOLD II to 75% in GOLD IV COPD.</td>
</tr>
<tr>
<td>Reference</td>
<td>Country/Region</td>
<td>N</td>
<td>Gender</td>
<td>Airflow Limitation</td>
<td>Site of Interest</td>
<td>Methodology</td>
<td></td>
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<tr>
<td>Wallbridge et al, 2018</td>
<td>Australia/O</td>
<td>M=16 F=4</td>
<td>Stable</td>
<td>Gold 2,3,4</td>
<td>Parasternal intercostal muscle</td>
<td>To investigate the validity of parasternal intercostal muscle ultrasound as an alternative to computed tomography-based measurement and correlation of the ultrasound measurements with COPD severity.</td>
<td></td>
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</tr>
<tr>
<td>Seymour et al, 2012</td>
<td>UK/RCT</td>
<td>M=12 F=8 Control 18</td>
<td>Stable</td>
<td>Gold 3,4</td>
<td>RF&lt;sub&gt;CSA&lt;/sub&gt; and (TA&lt;sub&gt;CSA&lt;/sub&gt;)</td>
<td>To assess difference in strength and size of skeletal muscles in COPD and elderly group.</td>
<td></td>
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<tr>
<td>Coratella et al, 2018</td>
<td>Italy/O</td>
<td>M=35 F=0</td>
<td>Stable</td>
<td>Gold 3,4</td>
<td>Vastus lateralis (VL) muscle</td>
<td>To compare muscle strength and architecture in COPD versus healthy subjects using ultrasound.</td>
<td></td>
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</tr>
<tr>
<td>Kaneko et al, 2008</td>
<td>Japan/O</td>
<td>M=15 Control 15</td>
<td>Stable</td>
<td>Gold 3,4</td>
<td>Abdominal Muscles</td>
<td>To assess the relationship between resting expiratory activity of the lateral abdominal muscle and exercise tolerance in COPD patients compared to healthy control.</td>
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<tr>
<td>Gorka et al, 2016</td>
<td>Poland/O</td>
<td>M=24 F=9</td>
<td>Stable</td>
<td>Gold 2,3,4</td>
<td>Bronchial wall layer thickness</td>
<td>To assess the relationship between emphysema severity, bronchial wall thickness using EBUS, and markers of remodelling (MMP-9) in BALF in COPD patients.</td>
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</tbody>
</table>

- **BMD in COPD by ultrasound densitometer.**
- **Risk factors of low BMD abnormal (T-score < -1.0) are FFM, BMI and FEV\(_1\).**
- **GOLD IV COPD patients have 7.6 times greater risk of abnormal BMD than GOLD II patients (95% CI 2.4 – 24.3, P<0.05).**
- **Advanced COPD, low BMI and low FFM are risk factors for the presence of low BMD.**
- **In stable COPD, ultrasound measurements of parasternal intercostal muscle thickness and density (quality) is a reliable technique for clinical use.**
- **In general, ultrasound-measured intercostal thickness correlated with FEV\(_1\) (r=0.33), quadriceps thickness (r=0.32).**
- **Ultrasound-measured mean echogenicity (indicating poorer muscle quality) showed a moderate negative correlation with FEV1% predicted.**
- **Reduced quadriceps size and strength in COPD patients (mean MVC difference: -10.9 kg 95% CI= -17.1kg to -4.8kg, P=0.01 and mean RF<sub>CSA</sub> difference: -119 mm\(^2\), 95% CI= -180 mm\(^2\) to -58 mm\(^2\), P<0.01).**
- **No significant difference in FFM index, TA<sub>CSA</sub> or ankle dorsiflexor strength recorded.**
- **The eccentric peak-torque of COPD and control group at low (2.57 ± 0.55 and 2.80 ± 0.60 N m kg\(^{-1}\), p=0.128 respectively) and high (2.44 ± 0.51 and 2.58 ± 0.46 N m kg\(^{-1}\), p=0.259 respectively) angular velocity was similar.**
- **Greater vastus lateralis pennation angle and muscle thickness were found in CON vs COPD, although no difference was observed in fascicle length.**
- **FEV\(_1\) and FEV\(_1\)/FVC correlated negatively (r=-0.465 and r=-0.414 respectively) and moderately (p<0.05) with eccentric-to-concentric peak-torque ratio and peak-torque respectively.**
- **Overall, Tdiff of the lateral abdominal muscle was higher (20.7±5.2% vs 18.4±3.5% P<0.05).**
- **Significant negative correlation was observed between Tdiff and distance walk (r=−0.58, p<0.05).**
- **No significant correlation between Tdiff and FEV\(_1\), in both the COPD and control groups.**
- **Expiratory muscle activity during breathing is more linked with exercise intolerance than airflow limitation.**
- **Matrix metalloproteinase 9 (MMP-9) significantly higher in severe COPD and negatively correlated with FEV\(_1\).**
- **Thickness of mucosa/submucosa and smooth muscle positively correlated with BALF TGF-β (r=0.366, P=0.046 and r=0.425, P=0.02), while the mucosa/submucosa thickness negatively correlated with neutrophil elastase (r=−0.508, P=0.004). No correlation between the BALF markers and emphysema score.**
<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Gender</th>
<th>N</th>
<th>Add. Info</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Diagnostic Goals</th>
<th>Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cruz-Montecinos et al. 2016</td>
<td>Spain/O</td>
<td>M = 11</td>
<td>70 ± 7</td>
<td>Stable</td>
<td>Gold 3,4</td>
<td>Rectus femoris, Vastus intermedius and anterior compartment of the right thigh</td>
<td>To assess the relationships between 6MWT and MVCQ and quadriceps thickness and echo intensity in COPD patients</td>
<td>Positive correlation between MVCQ and thickness of rectus femoris and vastus intermedius (r=0.427; P=0.003; r=0.469; P=0.018, respectively). Negative correlation between MVCQ and echo intensity of rectus femoris and vastus intermedius (r=-0.500; P=0.012; r=-0.482; P=0.016). 6MWT and MVCQ not correlated (r=0.319; P=0.085). Accordingly, 70% of variance in 6MWT result is explained by vastus intermedius thickness and echo intensity and the echo intensity of rectus femoris. In COPD, exercise capacity and quadriceps force are linked to quantity and quality of quadriceps muscle.</td>
</tr>
<tr>
<td>Nijholt et al. 2019</td>
<td>Netherland/O</td>
<td>M = 19</td>
<td>59.8 ± 8.6</td>
<td>Stable</td>
<td>Gold 4</td>
<td>Rectus femoris size</td>
<td>To correlate ultrasound measured rectus femoris size with fat-free mass and muscle function in patients with COPD</td>
<td>RFCSA and thickness positively correlated with FFMI (r = 0.57, P&lt;0.001; r = 0.53, P=0.003, respectively) and HGS (CSA r = 0.58, p &lt; 0.001, thickness r = 0.48, p = 0.009). No significant correlations between RF-thickness, CSA, and leg muscle power (r=0.33, p&lt;0.091; r=0.35, p=0.073, respectively). Furthermore, no correlation between RF size and maximal exercise capacity was observed (thickness r = 0.21, p=0.297, CSA r=0.22, p = 0.274).</td>
</tr>
<tr>
<td>Navarro-Cruz et al. 2019</td>
<td>Spain/O</td>
<td>COPD M= 26</td>
<td>79 ± 7</td>
<td>Stable</td>
<td>Gold 3,4</td>
<td>Vastus lateralis muscle</td>
<td>Assess intervention effect</td>
<td>Lower physical function and concentric maximal muscle power were lower in COPD patients compared to non-COPD subjects (P&lt;0.05). SSC-induced potentiation at 50-100% and 80-100% of V0 negatively correlated with physical function (r=0.40 to -0.50) and VL thickness and pennation angle (r=0.43–0.52) (all P&lt;0.05). SSC-induced potentiation is higher in adults with COPD than in non-COPD adults and is associated with lower physical function, VL thickness and pennation angle values. SSC-induced potentiation is a possible interventional candidate in older adults with decreased concentric muscle actions.</td>
</tr>
<tr>
<td>Shinkoshina et al. 2012</td>
<td>UK/O</td>
<td>COPD M=88</td>
<td>67 ± 9</td>
<td>Stable</td>
<td>Gold 1, 2, 3, 4</td>
<td>Rectus femoris</td>
<td>Assess intervention effect</td>
<td>RFCSA was reduced in COPD GOLD I-IV patients compared with healthy subjects (P&lt;0.001). Physical activity was also reduced in GOLD I-IV COPD patients compared with healthy adults (P&lt;0.05). While in COPD GOLD I RFCSA was linked with physical activity, only lung spirometry was the only predictor of physical activity in COPD GOLD II-IV. Quadriceps muscle loss is present in mild to advanced COPD and independently predicts physical activity in COPD GOLD I. USRFCSA has potential as a physiological biomarker in COPD, and the identification of these patients may guide early lifestyle and therapeutic interventions.</td>
</tr>
<tr>
<td>Menon et al. 2012</td>
<td>UK/O</td>
<td>COPD M=27</td>
<td>68.2 ± 8.2</td>
<td>Stable</td>
<td>Gold 1, 2, 3, 4</td>
<td>Lower limb muscle mass</td>
<td>Ultrasound assessment for Quantifying the improvements in lower limb or quadriceps muscle mass following resistance training in COPD patients.</td>
<td>Resistance training resulted in significant increase in thigh lean mass, RFCSA and quadriceps muscle thickness in both COPD (+5.7%, +21.8%, +12.1% respectively) and non-COPD (+5.4%, +19.5%, +10.9% respectively) subjects. Effect size for RFCSA (COPD=0.77; Healthy=0.83) and quadriceps muscle thickness (COPD=0.36; Healthy=0.7) changes were greater than</td>
</tr>
<tr>
<td>Firstname Surname et al. Year</td>
<td>Country</td>
<td>COPD</td>
<td>Control</td>
<td>F</td>
<td>M</td>
<td>Rectus femoris muscle</td>
<td>Diagnostic</td>
<td>Description</td>
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<tr>
<td>Ramirez-Fuentes et al. 2019</td>
<td>Spain</td>
<td>COPD M=18 F=0 Control 17</td>
<td>67.5 (SD 9.0)</td>
<td>Stable</td>
<td>Gold 3, 4</td>
<td>To determine the relationship of the size of the rectus femoris muscle, assessed by ultrasoundography, with parameters of muscle strength and body composition used in diagnosis of sarcopenia in COPD patients undergoing rehabilitation.</td>
<td>Reduced RFcsa in COPD patients (4.3±1.03 cm²) compared with healthy subjects (5.6±1.25 cm²).</td>
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<tr>
<td>Maynard-Paquette et al. 2020</td>
<td>Canada</td>
<td>COPD M=20 F=0 Control 26</td>
<td>66±6</td>
<td>Stable</td>
<td>Gold 1,2,3,4</td>
<td>To evaluate the relationship between quadriceps size, and symptoms, lung function and diaphragm contractility in COPD patients using ultrasound.</td>
<td>Mean Qcsa, Qthick and Qci were 336±145 mm², 1.55±0.53 cm and 64±16%, respectively, and mean TFdi was 91±16%. Qci was significantly correlated with FFM (r=0.41, p=0.008), FEV1 (r=0.43, p=0.001) but not with age (r=0.18, p=0.28).</td>
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<tr>
<td>J M Seymour et al. 2009</td>
<td>UK</td>
<td>COPD M=16 F=14 Control 26</td>
<td>68 (9)</td>
<td>Stable</td>
<td>Gold 1,2,3,4</td>
<td>To measure the quadriceps cross sectional area in COPD patients using ultrasound method and to relate the measurement to fat-free mass and muscle strength.</td>
<td>Reduced RFcsa, also correlated with quadriceps strength (r=0.49, P=0.036) and FFM (r=0.58, P=0.011).</td>
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<tr>
<td>Lee KM et al. 2019</td>
<td>Korea</td>
<td>COPD M=126 F=3 Control M=139 F=125</td>
<td>71 (65–76)</td>
<td>Stable</td>
<td>Gold 1,2</td>
<td>To diagnose peripheral lung lesions</td>
<td>The overall diagnostic yield of EBUS in patients with no or mild emphysema was significantly higher than in those with moderate or severe pulmonary emphysema (78% vs. 61%, P=0.007).</td>
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<tr>
<td>Georgiou et al. 2016</td>
<td>Australia</td>
<td>COPD M=92 F=7</td>
<td>70.1±9.5</td>
<td>Stable</td>
<td>Gold 1-4</td>
<td>To diagnose peripheral lung lesions</td>
<td>EBUS is a safe and effective procedure for the investigation of peripheral solitary pulmonary nodule in advanced COPD.</td>
<td></td>
</tr>
</tbody>
</table>

expiratory volume in one second; FFM: fat-free mass; FFMI: fat free mass index; FVC: forced vital capacity; GOLD: global initiative for chronic obstructive lung disease; HRQoL: health-related quality of life; MMP-9: matrix metallopeptidase 9; MVCQ: maximum voluntary contraction for quadriceps; OR: odd ratio; Qci: quadriceps contractile index; Qcsa: quadriceps cross-sectional area; Qthick: quadriceps thickness; RCT: randomise control trial; SSC: stretch-shortening cycle; TACSA: Tibialis anterior cross-sectional area; TAcsa: Tibialis anterior cross-sectional area; TFdi: Diaphragm thickening fraction; TGF-β: Transforming growth factor beta; VL: Vastus lateralis
References:

19. Rocha T, Souza H, Brandao DC, et al. The manual diaphragm release technique improves diaphragmatic mobility, inspiratory capacity and exercise capacity in people with chronic


