Editorial

Diaphragmatic dysfunction in chronic obstructive pulmonary disease

Chronic obstructive pulmonary disease (COPD) is truly a multisystem disease. However, primarily, the respiratory system has to bear the onslaught of ongoing pathophysiological insult. Diaphragm is a major respiratory muscle, and therefore, alterations in its structure and function in stable COPD as well as during exacerbations could have significant adverse clinical consequences. Moreover, it would be interesting to explore whether, for these alterations, corrective measures could be applied effectively as a part of the comprehensive pulmonary rehabilitation program. Therefore, research based on diaphragmatic dysfunction in COPD is important, and this field definitely needs to be explored further. This issue *Lung India* includes an article based on the measurement of diaphragmatic dysfunction in patients with COPD by ultrasonography.[1]

DIAPHRAGM IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Diaphragm is a dome- or umbrella-shaped anatomical partition between thorax and abdomen, which is highly active throughout the life span of an individual. Grossly, it consists of central tendon and a peripheral sheet of muscle fibers that take origin from the circumference of the thoracic outlet. It has costal, lumbar, and sternal portions corresponding to its insertion on ribs, vertebral bodies, and xiphoid process, respectively. Each hemidiaphragmatic muscle is innervated by the ipsilateral phrenic and the vagus nerve.

During inspiration, muscle fibers of the diaphragm are activated and it shortens in its axial diameter. Due to this contraction, the dome, which primarily consists of the central tendon, descends. This downward displacement produces both an expansion of the pleural cavity leading to a caudal shift of the abdominal viscera and an outward motion of the ventral wall of the abdomen.

In this regard, diaphragm and rib interactions during the process of respiration are equally important as there are differential effects of diaphragmatic contractions on the upper and lower rib cages.[2] Different models have been proposed for understanding physiological mechanism of this activity. In a model by Troyer and Wilson, although the upper rib cage and lower rib cage pistons are connected by a spring representing the coupling between the two pistons, the rib cage inspiratory muscles act only on the upper rib cage piston whereas the diaphragm acts only on the lower rib cage piston.[2] Optoelectronic plethysmography technique might provide a useful method for quantifying the forces exerted by the diaphragm on the rib cage in humans, and it is important to remember that posture might have a significant effect on these parameters.[3]

Significant diaphragmatic muscle dysfunction exits in different disease-related and physiological conditions, including COPD, and in age-related sarcopenia. Critical illness, cancer cachexia, and diseases related to hypoxic stress are other conditions that can potentially alter diaphragmatic functions.[4]

It has been theorized that acute pulmonary inflammation leads to diaphragmatic fiber atrophy. Although the exact pathophysiological mechanism of diaphragmatic muscle dysfunction in COPD is not clear, there is participation of proteolysis and nuclear factor B (NF-B) signaling in inflammation occurring in the diaphragm muscle. Acute respiratory distress syndrome (ARDS) and sepsis are also accompanied by local and systemic inflammation and diaphragmatic dysfunction similar to COPD and its exacerbations.[5]

As per Levine *et al.*, the following micro-alterations are proposed to occur in the diaphragm in COPD:[6]

1. Deletion of sarcomeres from the costal diaphragm.
2. Increased proportion of slow-twitch fibers and decreased proportion of fast-twitch fibers making the diaphragm resistant to fatigue.
3. Increased capacity for oxidative metabolism due to peroxisome proliferator-activated receptor-γ coactivator-1α-induced switch to oxidative fiber types.
4. Fast-to-slow isoform shift in sarcoplasmic reticulum Ca–ATPase decreasing ATP utilization by diaphragm.
5. Oxidative stress leading to the degradation of myofibrils, and
6. Myofiber atrophy due to the activation of signaling myostatin and NF-κB pathways.

ASSESSMENT OF DIAPHRAGMATIC FUNCTIONS IN CHRONIC OBSTRUCTIVE PULMONARY DISEASE

The diaphragm may be assessed by various techniques which have their own advantages and disadvantages. Interestingly, human touch can distinguish minor variation measurable in microns, and therefore, mobility and function of diaphragm can also be assessed effectively with manual palpation technique.[7] Looking at the simplicity

of the procedure, this modality may be effectively incorporated into pulmonary rehabilitation for COPD patients.

Various other modalities, including chest radiographs, computed tomographic (CT) scan or magnetic resonance imaging, nerve stimulation, and electromyography (EMG), are used for diaphragmatic assessment. It is important to note that four-dimensional CT provides exceptional *z*-axis coverage and time-resolved volumetric datasets of the whole chest. Fluorodeoxyglucose (FDG)-positron emission tomography has also been used to assess diaphragmatic dysfunction. In a study using this modality, increased 18F-FDG uptake in the diaphragm, the intercostal muscle, and the scalene muscle was found to correlate with the severity of COPD.[8]

Ultrasonography and fluoroscopy are used for real-time assessment of the diaphragm. M-mode or B-mode ultrasound (US) has significant advantages over other techniques as it is an easily available, relatively inexpensive, and safer method for diaphragmatic assessment. In addition, it can be used to enhance the safety and accuracy of needle EMG of the diaphragm.[9]

Diaphragmatic thickness and movements can be assessed effectively by the chest US as shown in Figure 1. B-mode US markers used for diaphragmatic pathology in other conditions (mean diaphragm thickness in the zone of apposition, 0.33 cm, lower limit of normal (LLN) 0.15 cm or thickening ratio, LLN 1.2) may also be applied in the population of patients with COPD.[10] In addition, US measurement of diaphragm thickness at the zone of apposition at the end of a maximal inspiration might be a useful tool to estimate lung hyperinflation in COPD.[11] This parameter has been found to correlate well with improved 6-min walk distance after pulmonary rehabilitation[12] and nocturnal percutaneous arterial oxygen saturation in COPD.[13]

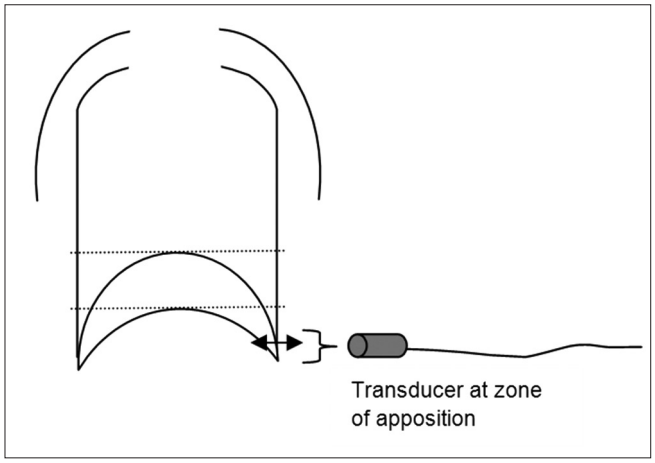

Figure 1: Assessment of diaphragmatic thickness and movements by the ultrasound. Zone of apposition is the place where the diaphragm is in close contact with ribs and is easily accessible by ultrasound. Dotted lines represent diaphragmatic position in expiration and inspiration

US measurements have been found useful in assessing the role of diaphragmatic breathing and pursed lip breathing in pulmonary rehabilitation programs.[14,15] These findings also have important therapeutic implications as it has been seen that in hospitalized patients with acute exacerbation of COPD subjected to noninvasive ventilation (NIV), severe diaphragmatic dysfunction as measured by diaphragmatic US was seen in almost one-quarter of patients. Diaphragmatic dysfunction was also associated with NIV failure and short-term mortality in these patients.[16]

Ultrasonography can be effectively used in the assessment of diaphragm in critically ill COPD patients. Sonographic parameters can provide valuable information in the assessment and follow-up of patients with diaphragmatic dysfunction in the form of weakness or paralysis. It may also prove to be a valuable assessment tool in terms of patient–ventilator interactions during controlled or assisted modalities of mechanical ventilation in the intensive care unit. It can also potentially help in understanding of weaning failure from mechanical ventilation.[17]

The main disadvantage of using US is that it needs the patient's cooperation, and it is not clear which method of the sonographic assessment might be best for a particular group of patients. A simple sonographic measurement of the upward and downward movement of the lung silhouette in the scapular line, similar to the age-old method of tidal percussion, can be a reliable tool to measure diaphragmatic dysfunction in COPD patients. This method might prove very useful for assessment of diaphragm in patients who are more difficult to mobilize, like very obese patients and those undergoing weaning from the ventilator.[18]

In the article being published in this issue of *Lung India* mentioned above, diaphragmatic functions were measured in stable COPD patients by B-mode US.[1] The main objective of the study was to determine the diaphragm muscle thickness, diaphragmatic movement, and zone of apposition in patients with COPD as compared to normal controls. They found that the diaphragm thickness, movement, and zone of apposition were significantly reduced in mild-to-moderate COPD but increased in severe COPD. The paradoxical finding which is difficult to explain in this study is that in patients with severe COPD, diaphragmatic mobility and thickness were increased. On the other hand, in a study by Corbellini *et al.* done in severe-to-very severe COPD patients, the diaphragmatic mobility was significantly lower in severe COPD patients which improved after pulmonary rehabilitation.[19] Although the patients with severe COPD in the study by Jain *et al.*[1] were undergoing pulmonary rehabilitation, there is no clarity regarding other patient characteristics that have led to this conflicting observation. In addition, position of the patient, tissue fluid as in congestive heart failure, anthropometric characteristics, and demographic factors may also influence ultrasonographic measurements.

Finally, we conclude by saying that ultrasonography can be effectively used in the assessment of diaphragmatic structure and functions in COPD. Chest physicians should utilize this technology more frequently for their patients in wards and intensive care units. There is a huge scope of research in this aspect of management of COPD. Clearly, there is a need for standardization of this procedure in different subset of patients with COPD.

Bharat Bhushan Sharma[1], Virendra Singh[2]

[1]Department of Medicine, Division of Allergy and Pulmonary Medicine, SMS Medical College Hospital, Jaipur, Rajasthan, India, [2]Director, Asthma Bhawan, Jaipur, Rajasthan, India
E-mail: drbbshar08@yahoo.co.in

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