

Diaphragmatic Thickness in Chronic Obstructive Pulmonary Disease

Jumana Mahdi Kareem, Noor Kathem Al-Waely¹, Ali F. Al-Hashimi

Departments of Physiology, ¹Surgery, College of Medicine, Al-Nahrain University, Baghdad, Iraq

Abstract

Background: Chronic obstructive pulmonary disease, characterized by chronic airway inflammation and progressive airflow limitation, and is considered as common, preventable and treatable disease. The defining standard values for diaphragm thickness and thickening ratio using B-mode ultrasound may provide a simpler, safer means of evaluating diaphragmatic function in chronic obstructive pulmonary disease patients. **Objective:** to assess the diaphragmatic structure and function using B-mode ultrasonography studying the diaphragm muscle inspiratory and expiratory thickness and thickening fraction in patients with COPD compared to healthy controls, and to study their sensitivity and specificity as well as their correlation with certain pathophysiologic parameters namely (peripheral capillary oxygen saturation, body mass index and C-reactive protein) to establish possible relation with the pathophysiology of the disease. **Materials and Methods:** The present study is a case control study was conducted in Al-Imamein Al-Kadhimein Medical City, Baghdad, Iraq in the period extended from November 2019 to October 2021. Forty patients with the diagnosis of COPD underwent B-mode ultrasound analysis. Three images were captured both at end expiration (Tmin) and at maximal inspiration (Tmax). The thickening fraction was calculated as $(T_{max}-T_{min}/T_{min})$, and each set of values was averaged. Findings were compared with a database of 40 healthy control subjects. **Results:** Diaphragm thickness and thickening fraction were significantly higher in COPD patients compared to control subjects with the mean of the Rt. inspiratory diaphragmatic thickness equals $(3.23 \pm 0.68\text{mm})$ versus $(2.8 \pm 0.55\text{mm})$; respectively, $p=0.006$ compared to control, and (2.44 ± 0.71) versus (1.96 ± 0.6) ; respectively, $p=0.004$ for the mean Rt. diaphragmatic thickening fraction, while the mean of the Lt. inspiratory diaphragmatic thickness was $(3.22 \pm 0.63\text{mm})$ versus $(2.79 \pm 0.51\text{mm})$; respectively, $p=0.003$ compared to control, and (2.45 ± 0.63) versus (1.95 ± 0.54) ; respectively, $p=0.003$ for the mean Lt. diaphragmatic thickening fraction, ROC analysis shows that the right and left diaphragmatic fractions had the highest sensitivity and specificity parameter for COPD. No correlations were found between body mass index, SpO₂ with diaphragmatic parameters. **Conclusion:** the current study found diaphragmatic ultrasonographic characteristics in patients with COPD show significant increase in inspiratory thickness and thickening fraction compared to control group, yet they were of low diagnostic accuracy.

Keywords: Chronic obstructive pulmonary disease, diaphragmatic ultrasonography, maximal inspiration, patients

INTRODUCTION

Diaphragmatic dysfunction is not uncommon in patients with chronic obstructive pulmonary disease (COPD).^[1] The commonest and oldest known cause for diaphragmatic dysfunction in patients with COPD is mechanical disadvantage owing to over inflation of the lungs.^[2] More recently recognized reasons for the diaphragmatic weakness are remodelling,^[3] exposure to oxidative stress,^[4] and a reduction of myosin filaments owing to reduced protein production and increased apoptosis of muscle cells.^[4,5]

Electromyographic evaluation of diaphragmatic neuromuscular disease in patients with COPD is technically difficult and potentially high risk. Ultrasound imaging of the diaphragm has been broadly applied in some chronic respiratory diseases, such as COPD, diaphragmatic paralysis, as well as during weaning from

Address for correspondence: Dr. Jumana Mahdi Kareem,
Department of physiology, College of Medicine,
University of Al-Nahrain, Baghdad, Iraq.
E-mail: jumana86.jm@gmail.com

Submission: 10-May-2022 **Accepted:** 21-May-2022 **Published:** 29-Sep-2022

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Kareem JM, Al-Waely NK, Al-Hashimi AF. Diaphragmatic thickness in chronic obstructive pulmonary disease. Med J Babylon 2022;19:427-33.

Access this article online

Quick Response Code:



Website:
www.medjbabylon.org

DOI:
10.4103/MJBL.MJBL_68_22

mechanical ventilation.^[6,7] The B-mode ultrasound may provide a simpler, safer means of evaluating diaphragmatic function in COPD patients. In comparison with other imaging methods, this technique has many advantages, such as absence of radiation, portability, repeatability, low price, real-time imaging, and non-invasiveness.^[8-11]

The aims of the present study is to assess the diaphragmatic structure and function using B-mode ultrasonography to measure the diaphragm muscle inspiratory and expiratory thickness and thickening fraction in patients with COPD compared to healthy controls, and to study their sensitivity and specificity in diagnosing diaphragmatic dysfunction in COPD; as well as their correlation with certain pathophysiologic parameters namely peripheral capillary oxygen saturation (SpO₂), body mass index (BMI) and C-reactive protein to establish possible relation with the pathophysiology of the disease.

MATERIALS AND METHODS

This case control study was conducted in Al-Imamein Al-Kadhimein Medical City, Baghdad, Iraq in the period extended from November 2019 to October 2021. All the selected subjects were enlightened about the examination and informed consent for participation in the study was provided. The study was approved by the Institute Review Board of the College of Medicine, Al-Nahrain University.

Forty patients with clinically documented COPD, being diagnosed and referred by a pulmonologist. History and information are taken from the patients which include the patient's name, age, sex, weight, height, occupation, past medical history, disease duration. Those were compared with 40 age and sex matched healthy controls with no history of any medical disease. All participants would be subjected to O₂ saturation analysis by oxymeter, C-reactive protein analysis and perform pulmonary function test (PFT) before commencement of ultrasonographic analysis.

All subjects underwent B-mode ultrasound examination using a LOGIO P6 PRO –GE ultrasound Korea serial no.137540SU1, with the patient in the supine position, the transducer was placed on the chest wall at approximately the anterior axillary line, just cephalad to the lower costal margin. With the transducer spanning/perpendicular to two ribs, the diaphragm can be visualized as a hypoechoic layer of muscle encased in two hyperechoic layers of connective tissue (the parietal pleura and the peritoneum), deep to the intercostal muscles connecting the two ribs. Diaphragm thickness was measured by placing electronic callipers just inside the hyperechoic connective tissue layers. Measurements were taken on three different images to find the average thickness of the diaphragm at maximal inspiration or total lung capacity as well as at end expiration or functional residual capacity. A thickening fraction was derived by dividing the average thickness of

the diaphragm at maximal inspiration minus thickness of diaphragm at end expiration divided by the average thickness of the diaphragm at end expiration.

Most of data were continuous and expressed as mean $\pm$ standard deviation. Comparison of these data was done by using unpaired Student t-test. Only gender ratio and C-reactive protein was expressed as frequency and percentage, comparison of these data was done using Fisher exact test. P value less than 0.5 was considered as significant.

The sensitivity and specificity of all studied diaphragmatic ultrasonographic parameters were evaluated by using receiver operating characteristics curve (ROC) test. Pearson correlation was studied between abovementioned parameters and certain pathophysiologic parameters namely (SpO₂, BMI and C-reactive protein). The software used were Microsoft excel 2016 and SPSS (statistical package for social sciences) version 23.

Ethical approval

The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki. It was carried out with patients verbal and analytical approval before sample was taken. The study protocol and the subject information and consent form were reviewed and approved by a local ethics committee according to the document number (268) in 15/10/2019.

RESULTS

Eighty subjects were enrolled in this study; 40 patients diagnosed with COPD and 40 apparently healthy volunteers. The mean age of patients was (60.83 $\pm$ 9.34 years) comprising (30) males and (10) females, as compared to (62.9 $\pm$ 5.98 years) of apparently healthy volunteers comprising (30) males and (10) females, too. No significant difference was noticed regarding age, gender, weight, height or BMI between COPD patients and control group [Table 1].

Seven out of forty patients had CRP positive results, as compared to none in the control group and the difference

Table 1: Comparison of demographic parameters, SpO₂ between COPD patients and control group

Parameter	Patients N=40 mean $\pm$ SD	Control N=40 mean $\pm$ SD	P value
Age (yr)	60.83 $\pm$ 9.34	62.9 $\pm$ 5.98	0.241*
Weight (kg)	80.3 $\pm$ 17.51	83.58 $\pm$ 12.63	0.340*
Height (cm)	165.83 $\pm$ 9.22	168.43 $\pm$ 10.58	0.245*
BMI (kg/m ²)	29.03 $\pm$ 5.17	29.46 $\pm$ 3.52	0.669*
SpO ₂ (%)	95.0 $\pm$ 5.48	98.68 $\pm$ 0.53	<0.001*

BMI= Body mass index, CRP= C-reactive protein, * p value by unpaired t-test

was significant (p value = 0.012). Finally, results of SpO₂ were significantly lower in COPD patients as compared to control group (p value <0.001) [Tables 1, 2].

Diaphragm thickness and thickness ratio were significantly higher in COPD patients compared to control subjects, with the mean of the Rt. inspiratory diaphragmatic thickness equals $(3.23 \pm 0.68\text{mm})$ versus $2.8 \pm 0.55\text{mm}$; respectively, $p=0.006$ compared to control, and (2.44 ± 0.71) versus 1.96 ± 0.6 ; respectively, $p=0.004$ for the mean Rt. diaphragmatic thickening ratio; while the mean of the Lt. inspiratory diaphragmatic thickness was $(3.22 \pm 0.63\text{mm})$ versus $2.79 \pm 0.51\text{mm}$; respectively, $p=0.003$ compared to control, and (2.45 ± 0.63) versus 1.95 ± 0.54 ; respectively, $p=0.003$ for the mean Lt. diaphragmatic thickening ratio. Although the expiratory diaphragmatic thickness was also higher in these patients, the difference was not significant [Table 3]. ROC analysis was done for diaphragmatic thickness and thickening fraction [Figures 1 and 2]. The Rt. and Lt. diaphragmatic fractions showed the highest sensitivity and specificity parameter for COPD, with both sensitivity and specificity equals (70.0% versus 74.3% at cutoff value 2.31 and 73.3% versus 74.3% at cutoff value 2.20 for the Rt. and Lt. diaphragmatic ratios; respectively). The Lt. diaphragmatic expiratory thickness showed a lesser sensitivity and specificity percentages (70.0% versus 71.4% at cutoff value 3.05mm). However, other studied parameters were of lower sensitivity and specificity percentages [Tables 4]. No correlations were found between body mass index, SpO₂ with diaphragmatic

ultrasound parameters in COPD patients and control groups apart from positive correlation between Rt. and Lt. diaphragmatic expiratory thickness and BMI [Tables 5 and 6]. Finally, patients with positive C-reactive protein level had significantly lower diaphragmatic expiratory thickness compared to those with negative results for both Rt. and Lt. diaphragms [Table 7].

DISCUSSION

In the current study, no significant differences were noticed regarding gender, height or age between the two studied groups, which would exclude any possible source of error which might be anticipated if any significant differences were present and this is important to exclude their effects as co-factors that would compromise study results. In addition, no significant differences were observed regarding weight and hence, BMI results between patients and control group. This can be explained that all of the patient included in the study were not in the advanced severe stages of the disease, and most of them were overweight, thus, malnutrition was not found in all of the studied patients and therefore, no statistical significant differences were found regarding weight and BMI as compared to control subjects. However, the significant decrease in SpO₂ percentages observed in COPD patients as compared to control subjects, can be explained by the effects of hypoxemia which is a major complication of COPD compared to controls. Gas exchange abnormalities in COPD result in hypoxemia and hypercapnia, and have several mechanisms.^[12] Finally, C-reactive protein was positive in seven patients compared to none in the control group, which is statistically significant and might ring a bell about the possible effect of inflammation in the pathophysiology of the disease. A study by Agarwal R and his colleagues revealed the circulating levels of the inflammatory marker hs-CRP are significantly elevated in patients with COPD, supporting the view that COPD is in part an inflammatory disorder.^[13]

In the current study, the COPD patients showed a significant increment in inspiratory diaphragmatic thickness and diaphragmatic ratio in comparison to control people, and although the expiratory diaphragmatic

Table 2: Comparison of gender and C-reactive protein between COPD patients and control group

Parameter		Patients N=40 mean $\pm$ SD	Control N=40 mean $\pm$ SD	P value
		N (%)	N (%)	
Gender	Male	30 (75.0)	30 (75.0)	1.000**
	Female	10 (25.0)	10 (25.0)	
CRP	Negative	33 (82.5)	40 (100)	0.012**
	Positive	7 (17.5)	0 (0.0)	

CRP= C-reactive protein, ** p value by Fisher Exact test

Table 3: Comparison of the Diaphragmatic Ultrasound Parameters between COPD patients and control

Ultrasound Parameter	Patients N=30 mean $\pm$ SD	Control N=35 mean $\pm$ SD	P value
Rt. diaphragmatic inspiratory thickness (mm)	3.23 ± 0.68	2.8 ± 0.55	0.006
Rt. diaphragmatic expiratory thickness (mm)	2.53 ± 0.53	2.32 ± 0.44	0.089
Rt. Diaphragmatic thickening fraction	2.44 ± 0.71	1.96 ± 0.6	0.004
Lt. diaphragmatic inspiratory thickness (mm)	3.22 ± 0.63	2.79 ± 0.51	0.003
Lt. diaphragmatic expiratory thickness (mm)	2.5 ± 0.54	2.3 ± 0.43	0.103
Lt. diaphragmatic thickening fraction	2.45 ± 0.63	1.95 ± 0.54	0.001

P value by unpaired t-test

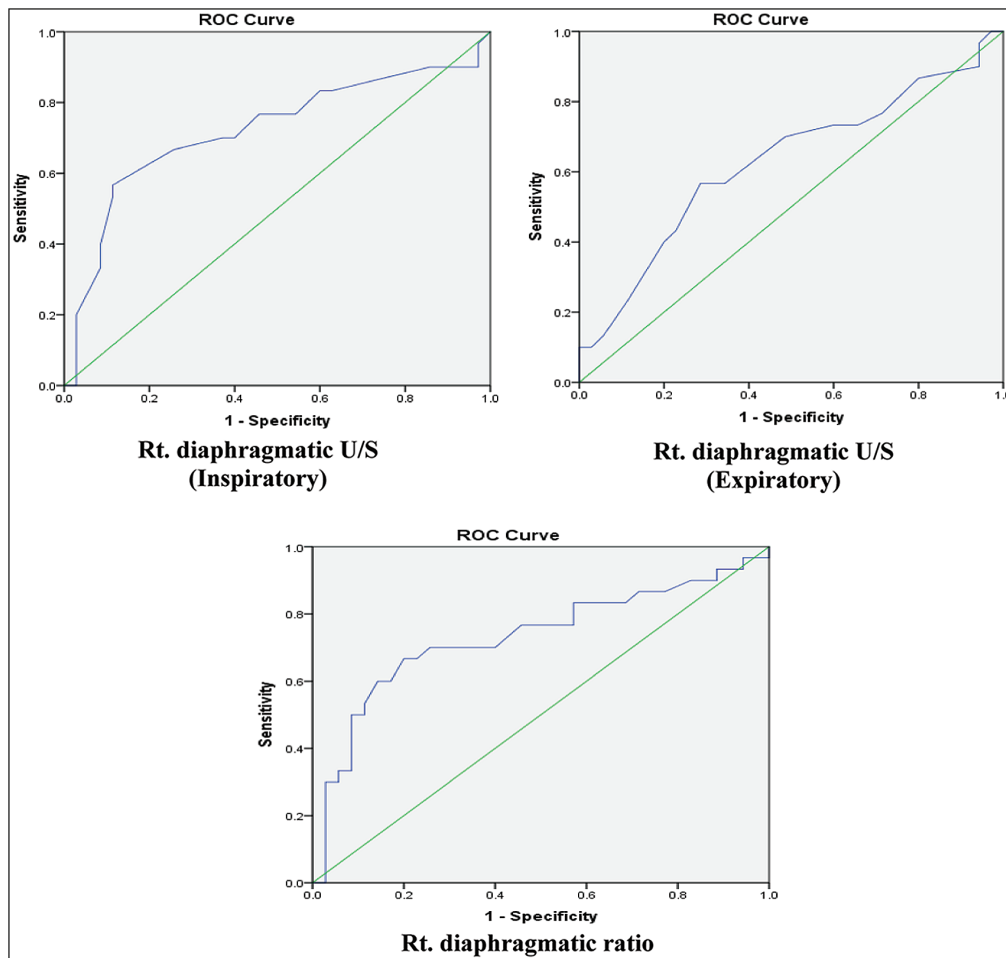


Figure 1: ROC Curve of Rt. Diaphragmatic Ultrasound Parameters in Patients with COPD

thickness was also higher in these patients, the difference was not significant. These findings are in harmony with the results of several studies^[7,14] Jane and his associates have found that in severe COPD, an increase in movement, diaphragm thickness, zone of apposition were observed, perhaps due to increased transpulmonary pressure variations and adaptive diaphragmatic changes like collagen accumulation.^[15] The progressive limitation of the airflow in COPD patients causes a pathological adaptation of the diaphragm, the dome of the diaphragm is lowered, in inspiratory position. The muscle thickness is increased, especially with decreased mechanical excursion, probably due to fibers' shortening. A decrease of anaerobic type fibers (type II) and an increase in aerobic fibers (type I) are observed; this process progressively increases with the pathology worsening. The increase in the oxidative process, however, does not correspond to an improvement of the diaphragmatic function. The rate of detectable myosin decreases, resulting in altered sarcomeric organization and further decreasing of the contractile strength.^[16]

Contrary to these results, Eryüksel and his colleagues reported a normal diaphragm structure, diaphragm

function, and respiratory drive in patients with COPD, explaining their results that in patients with COPD, the diaphragm is overburdened against an increased mechanical load because of airway obstruction. It has been suggested that the resulting mechanical load may lead to a chronic endurance training-type effect on the diaphragmatic muscle.^[17]

Therefore, it is possible that pathological adaptation of the diaphragm during inspiration, and the transformation of muscle fiber type into the aerobic high endurance fatigue resistant type I fiber with decreased fiber length and increased thickness are of the possible explanation for increased inspiratory thickness and thickening ratio; not to mention the accumulation of non-contractile proteins like collagen and the altered sarcomeric organization.

Receiver Operating Characteristic (ROC) analysis of different ultra-sonographic parameters in COPD, were of low sensitivity and specificity, with the highest sensitivity and specificity were in the thickening fraction (70.0% versus 74.3% at cutoff value 2.31 and 73.3% versus 74.3% at cutoff value 2.20 for the Rt. and Lt. diaphragmatic ratios; respectively)). These findings point to the lower

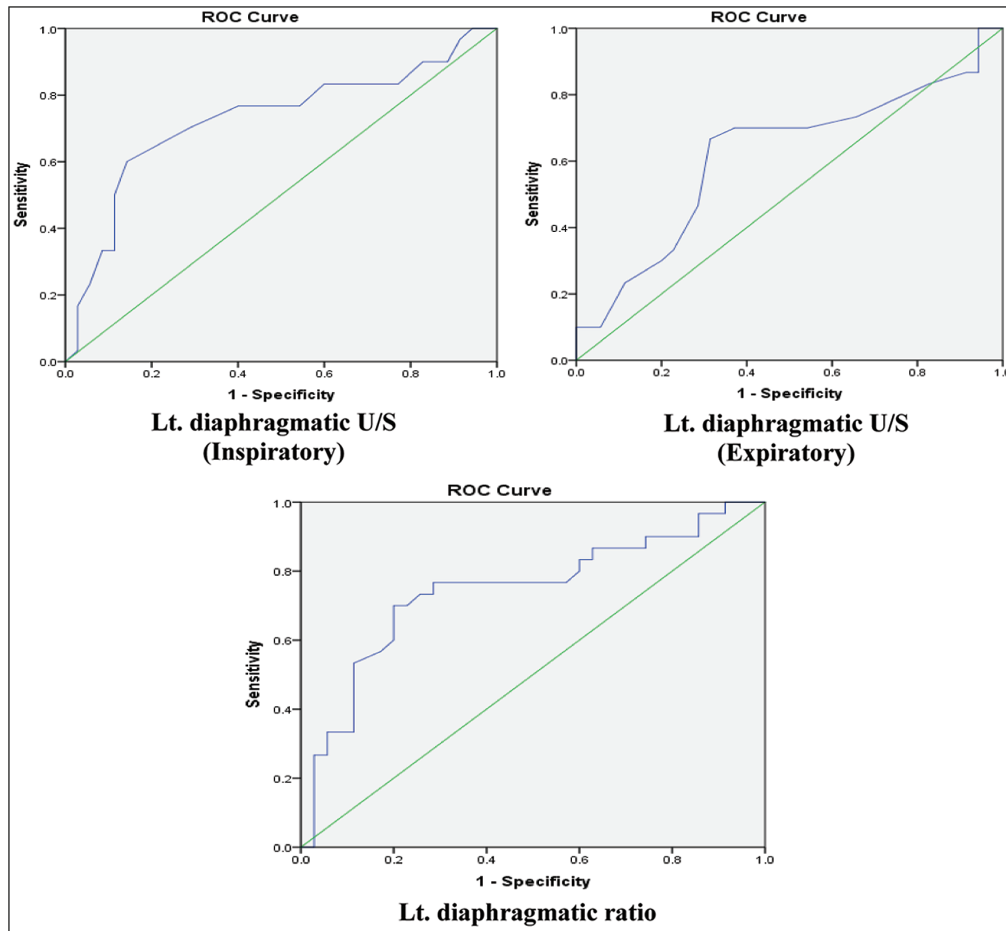


Figure 2: ROC Curve of Lt. Diaphragmatic Ultrasound Parameters in Patients with COPD

Table 4: Area under Curve, Sensitivity, Specificity and Cutoff Value of the Rt. Diaphragmatic Ultrasound Parameters in COPD Patients

Parameter	Area under curve	Sensitivity	Specificity	Cutoff value
Rt. diaphragmatic inspiratory thickness	0.721	66.7%	74.3%	3.15
Rt. diaphragmatic expiratory thickness	0.627	56.7%	65.7%	2.45
Rt. diaphragmatic thickening fraction	0.731	70.0%	74.3%	2.31

Table 5: Correlation of body mass index with ultrasound parameters in patients and control groups

Parameter	BMI (kg/m ₂)		
		Patients	Control
Rt. diaphragmatic inspiratory thickness (mm)	R	0.232	-0.210
	P	0.217	0.227
Rt. diaphragmatic expiratory thickness (mm)	R	0.383	-0.152
	P	0.037	0.383
Rt. Diaphragmatic thickening fraction	R	0.195	-0.199
	P	0.301	0.252
Lt. diaphragmatic inspiratory thickness (mm)	R	0.249	-0.218
	P	0.184	0.208
Lt. diaphragmatic expiratory thickness (mm)	R	0.383	-0.153
	P	0.037	0.381
Lt. diaphragmatic thickening fraction	R	0.213	-0.208
	P	0.258	0.231

Table 6: Correlation of SPO₂% with ultrasound parameters in patients and control groups

Parameter	SPO ₂ %		
		Patients	Control
Rt. diaphragmatic inspiratory thickness (mm)	R	-0.152	0.025
	P	0.421	0.885
Rt. diaphragmatic expiratory thickness (mm)	R	-0.007	-0.125
	P	0.971	0.476
Rt. Diaphragmatic thickening fraction	R	-0.183	0.050
	P	0.334	0.777
Lt. diaphragmatic inspiratory thickness (mm)	R	-0.163	0.005
	P	0.388	0.979
Lt. diaphragmatic expiratory thickness (mm)	R	-0.067	-0.161
	P	0.724	0.355
Lt. diaphragmatic thickening fraction	R	-0.184	0.040
	P	0.331	0.817

Table 7: Comparison of ultrasound parameters in patients group according to positivity of C-reactive protein

Parameter	Negative N=24 mean±SD	Positive N=6 mean±SD	P value
Right diaphragmatic U/S (Inspiratory)	3.34±0.67	2.78±0.6	0.073
Right diaphragmatic U/S (Expiratory)	2.63±0.5	2.1±0.41	0.024
Right diaphragmatic Ratio	2.55±0.69	2.01±0.69	0.098
Left diaphragmatic U/S (Inspiratory)	3.32±0.61	2.85±0.58	0.103
Left diaphragmatic U/S (Expiratory)	2.63±0.51	2.02±0.33	0.011
Left diaphragmatic Ratio	2.53±0.61	2.13±0.64	0.174

diagnostic ability of the diaphragmatic ultrasonographic thickness characteristics in COPD, probably because these changes were minor changes or similar changes can occur in several respiratory diseases. These results are in agreement with several study groups.^[17-19]

Essawy and his co-worker found the cut-off point to differentiate between COPD group and control group as regard to thickness fraction was 0.927cm with sensitivity 75% and specificity 80%, they concluded that measuring diaphragmatic thickness fraction is more accurate than measuring diaphragmatic thickness alone for evaluation of diaphragm in COPD patients.^[18] While, Eryüksel and his group reported that diaphragmatic thickness ratio represents a more sensitive measurement than diaphragmatic thickness measurements. An analogy between cardiac ejection and increased diaphragmatic thickness during inspiration as an indirect measure of muscle fiber contractions has been proposed. Similar to the cardiac ejection fraction, this reflects the diaphragmatic functions and magnitude of effort.^[17]

Findings of the present study showed no correlations between body mass index, SpO₂ with diaphragmatic parameters in COPD patients and control groups apart from positive correlation between Rt. and Lt. diaphragmatic expiratory thickness and BMI. However, no significant changes were observed in the current study in the expiratory diaphragmatic thickness between patients and control groups, and the fact that all of the patients included in this study were not in the advanced severe stages of the disease, and most of them were overweight, thus, not malnourished and therefore, these factors could affect the findings of positive correlations between BMI and the expiratory diaphragmatic thickness.

Finally, patients in the current study with positive C-reactive protein level had significantly lower diaphragmatic expiratory thickness compared to those with negative results for both Rt. and Lt. diaphragms. The presence of negative relations between diaphragmatic expiratory thickness and the inflammatory marker C-reactive protein level might elucidate a point that the structural changes in the diaphragm found in the

current study and the significant increased thickness in COPD patients affect mainly inspiratory diaphragmatic thickness, more than the expiratory thickness, which is measured at the functional residual capacity representing the dual effect of the active expiratory reserve volume and the passive residual volume. It is worth mentioning that Jane and his associates have found that the diaphragm thickness, movement, and zone of apposition were significantly reduced, and not increased, in mild to moderate COPD due to overall reduced muscle mass in COPD because of systemic inflammation, but in severe COPD, an increase in movement, diaphragm thickness, zone of apposition were observed.^[15] All patients included in the study were not in the advanced severe stages of the disease, which might give another explanation for the presence of negative relations between diaphragmatic expiratory thickness and the inflammatory marker C-reactive protein level.

CONCLUSION

Diaphragmatic ultrasonographic characteristics in patients with COPD show significantly increase in inspiratory thickness and thickening ratio compared to control; yet of low diagnostic accuracy. There was no correlations between body mass index, SpO₂ with diaphragmatic parameters in COPD patients and control groups.

Financial support and sponsorship

Nil.

Conflict of interest

There are no conflicts of interest.

REFERENCES

- Sharma BB, Singh V. Diaphragmatic dysfunction in chronic obstructive pulmonary disease. *Lung India* 2019;36:285-7.
- Similowski T, Yan S, Gauthier AP, Macklem PT, Bellemare F. Contractile properties of the human diaphragm during chronic hyperinflation. *N Engl J Med* 1991;325:917-23.
- Levine S, Nguyen T, Kaiser LR, Rubinstein NA, Maislin G, Gregory C, *et al.* Human diaphragm remodeling associated with chronic obstructive pulmonary disease: Clinical implications. *Am J Respir Crit Care Med* 2003;168:706-13.

4. Barreiro E, de la Puente B, Minguella J, Corominas JM, Serrano S, Hussain SN, *et al.* Oxidative stress and respiratory muscle dysfunction in severe chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005;171:1116-24.
5. Gea J, Pascual S, Casadevall C, Orozco-Levi M, Barreiro E. Muscle dysfunction in chronic obstructive pulmonary disease: Update on causes and biological findings. *J Thorac Dis* 2015;7:E418-38.
6. Ottenheijm CA, Heunks LM, Sieck GC, Zhan WZ, Jansen SM, Degens H, *et al.* Diaphragm dysfunction in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2005;172:200-5.
7. Baria MR, Shahgholi L, Sorenson EJ, Harper CJ, Lim KG, Strommen JA, *et al.* B-mode ultrasound assessment of diaphragm structure and function in patients with Copd. *Chest* 2014;146:680-5.
8. Boccatonda A, Decorato V, Cocco G, Marinari S, Schiavone C. Ultrasound evaluation of diaphragmatic mobility in patients with idiopathic lung fibrosis: A pilot study. *Multidiscip Respir Med* 2019;14:1.
9. Matamis D, Soilemezi E, Tsagourias M, Akoumianaki E, Dimassi S, Boroli F, *et al.* Sonographic evaluation of the diaphragm in critically ill patients. Technique and clinical applications. *Intensive Care Med* 2013;39:801-10.
10. Caleffi-Pereira M, Pletsch-Assunção R, Cardenas LZ, Santana PV, Ferreira JG, Iamonti VC, *et al.* Unilateral diaphragm paralysis: A dysfunction restricted not just to one hemidiaphragm. *Bmc Pulm Med* 2018;18:126.
11. Gottesman E, McCool FD. Ultrasound evaluation of the paralyzed diaphragm. *Am J Respir Crit Care Med* 1997;155:1570-4.
12. Wells JM, Estepar RS, McDonald MN, Bhatt SP, Diaz AA, Bailey WC, *et al.*; COPDGene Investigators. Clinical, physiologic, and radiographic factors contributing to development of hypoxemia in moderate to severe Copd: A cohort study. *Bmc Pulm Med* 2016;16:169.
13. Agarwal R, Zaheer MS, Ahmad Z, Akhtar J. The relationship between C-reactive protein and prognostic factors in chronic obstructive pulmonary disease. *Multidiscip Respir Med* 2013;8:63.
14. Epelman M, Navarro OM, Daneman A, Miller SF. M-mode sonography of diaphragmatic motion: Description of technique and experience in 278 pediatric patients. *Pediatr Radiol* 2005;35:661-7.
15. Jain S, Nair G, Nuchin A, Uppe A. Study of the diaphragm in chronic obstructive pulmonary disease using ultrasonography. *Lung India* 2019;36:299-303.
16. Bordoni B, Marelli F, Morabito B, Sacconi B. Manual evaluation of the diaphragm muscle. *Int J Chron Obstruct Pulmon Dis* 2016;11:1949-56.
17. Eryüksel E, Cimşit C, Bekir M, Cimsit Ç, Karakurt S. Diaphragmatic thickness fraction in subjects at high-risk for Copd exacerbations. *Respir Care* 2017;62:1565-70.
18. Essawy TS, Al-Arag AH, Mousa H, Abdelsattar ME, Elsayy R. Ultrasound assessment of diaphragmatic thickness in chronic obstructive pulmonary disease patients as a predictor for disease severity. *Benha Medical Journal* 2021;38:353-67.
19. An TJ, Yoo YJ, Lim JU, Seo W, Park CK, Rhee CK, *et al.* Diaphragm ultrasound is an imaging biomarker that distinguishes exacerbation status from stable chronic obstructive pulmonary disease. *Int J Chron Obstruct Pulmon Dis* 2022;17:3-12.