Marmara Medical Journal 2016; 29: 8-13
DOI: 10.5472/MMJoa.2901.02

ORIGINAL ARTICLE / ÖZGÜN ARAŞTIRMA

Ultrasound assessment of diaphragm thickness in COPD

KOAH'ta diyafragm kalınlığının ultrasonografi ile değerlendirilmesi

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ABSTRACT

Objective: Thickness of the diaphragm was evaluated by B-mode ultrasonography (US) in chronic obstructive pulmonary disease (COPD) to determine the relationship between diaphragm thickness measurement, pulmonary function tests, and symptom scores.

Patients and Methods: Fifty-three clinically stable patients with COPD were enrolled in this study for diaphragmatic thickness evaluation with B- mode US. The severity of COPD was determined by spirometric measurements in terms of %FEV1. Patients were also analyzed according to GOLD criteria. Correlation between diaphragm thickness and symptom scores like Medical Research Council (mMRC), COPD Assessment Test (CAT), composite scores and body mass index (BMI) were sought.

Results: There was a moderate correlation between diaphragmatic muscle thickness and %FEV1 in mild COPD patients ($r=0.62$, $p=0.017<0.05$). 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.

Conclusion: No correlation was found between diaphragmatic thickness in COPD patients and pulmonary function tests except for %FEV1 in mild COPD patients. There were no correlations between diaphragmatic muscle thickness and symptom scores. Further US studies should take place for functional evaluation of the diaphragm in COPD subgroups.

Keywords: Diaphragm, Ultrasonography, Chronic obstructive pulmonary disease, Thickness.

ÖZ

Amaç: Kronik obstruktive akciğer hastalığı (KOAH) olan hastaların, diyafram kalınlıklarını ultrasonografi ile ölçerek solunum fonksiyon testleri ve semptom skorları ile ilişkisinin araştırılmasıdır.

Gereç ve Yöntem: KOAH nedeniyle takip edilmekte olan, son iki aydır klinik olarak stabil seyirli 53 hasta çalışmamıza dahil edildi. Bronkodilatör sonrası FEV1 değerlerinde %12 artış, çalışmada uygulanan testlerden herhangi birine uyumsuzluk, oksijen bağımlılığı, abdominal ya da torasik cerrahi geçirme hikayeleri çalışmadan dışlanma kriterleri olarak belirlendi. KOAH düzeyi spirometri ölçümlerine ve GOLD kriterlerine göre sınıflandırıldı.

Hayat kalitesi değerlendirmesi için mMRC ve CAT semptom skorları testleri ile kompozit KOAH skor ölçümü hesaplanması için alevlenme sayıları sorularak kaydedildi.

Bulgular: KOAH düzeyi hafif olan hastalarda FEV1 % ile diyafram kalınlığı arasında anlamlı ilişki bulundu ($r=0.62$, $p=0,017<0,05$). Diyafram kalınlığı ile GOLD alt grupları, semptom skorları, BMI , yaş ve cinsiyet gibi parametreler arasında anlamlı ilişki bulunamadı.

Sonuç: KOAH hastalarında ultrasonografi ile ölçülen diyafram kalınlığı ile solunum fonksiyon testleri arasında hafif KOAH'lı hasta grubu haricinde anlamlı ilişki gösterilememiştir. Diyafram kalınlığı ile semptom skorları arasında anlamlı ilişki bulunamadı. Ultrasonografi ile planlanacak yeni çalışmalarda, KOAH alt gruplarında diyafram fonksiyonunu yansıtacak diyafram kalınlık oranları irdelenmelidir.

Anahtar kelimeler: Diyafram, Ultrasonografi, Kronik obstrüktif akciğer hastalığı, Kalınlık.

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Submitted/Gönderilme: 12.11.2015 **Accepted/Kabul:** 29.12.2015

Introduction

Sonographic evaluation of diaphragm has gained wide acceptance to assess the presence of postoperative diaphragm dysfunction, identify ventilator induced injuries, and evaluate diaphragmatic motion in intensive care units. There are ongoing studies about diaphragmatic thickness evaluation in search for the correct timing for discontinuation of mechanical ventilation and adjustment of ventilator settings [1, 2].

COPD is mainly defined as a disease characterized by airway obstruction and air trapping that is not fully reversible. Studies dealing with inspiratory muscle weakness in COPD patients focus mostly on diaphragm since it is the principal generator of tidal volume [3]. US findings of diaphragm muscle in COPD patients is not concluded yet because of the varying results [3-7].These studies address the structure and the motion of the diaphragm [4]. The impairment of diaphragm is suggested to be an important factor which is associated with alterations in the principal pulmonary function parameters such as FEV1 [8]. In our study, diaphragmatic muscle thickness is measured in COPD patients with B-Mode US to determine the relationship between thickness and clinical and functional parameters. Our aim is to determine if US assessment of the diaphragm muscle thickness could be a useful tool for evaluating diaphragmatic function and disease progression in COPD subgroups.

Patients and Methods

Patients

This prospective study was approved by the Ethics Committee of our institution. Informed written consent was obtained from all individual participants included in the study. Patients were referred from the Pulmonary Diseases and Critical Care Department between February 2013 and February 2014. Fifty-three patients with COPD (47 male and 6 females with a mean age 62.57 ± 10. 1) were enrolled in this study for diaphragmatic thickness evaluation with US. Clinical history, physical examination, and pulmonary function tests (post bronchodilator FEV1/FVC < 0.7) were used for COPD diagnosis. Patients under medical treatment for COPD and who are clinically stable for at least two months period were included in the study. None of the subjects were hospitalized because of exacerbations nor did they have history of steroid or theophylline treatment. A positive response to bronchodilators (an increase in FEV1 from baseline that is more than 200ml and more than 15 per cent of the prebronchodilator value), oxygen dependency, discordance between test results, history of major thoracic or abdominal surgery were the exclusion criteria. The severity of COPD was determined by spirometric measurements as mild (FEV1 >%80), moderate (%80<FEV1 >%50) or severe (%50<FEV1 >%30). Patients were also analyzed according to GOLD criteria (A, B, C, and D). All patients completed questionnaire assessing globally the impact of COPD on health status and symptom levels were assessed by using the modified Medical Research Council (mMRC) dyspnea scale and the COPD Assessment Test (CAT). The number of exacerbations was questioned for evaluation of composite scores. Body mass index (BMI) and smoking status were also recorded. The patient characteristics of the study population are shown in Table I.

Table I. Descriptive Statistics

	Minimum	Maximum	Mean	Std. Deviation
Diaphragm thickness (mm.)	0.6	2.8	2.05	0.45
Age	41	78	62.57	9.8
BMI (kg/m^2)	18	45	27.70	52.9
Smoking (pack/year)	10	120	47.05	25.41
CAT	0	29	12.09	8.58
mMRC	0	4	2	1.12
FEV1 (litre)	0.6	2.8	1.81	0.45

BMI: Body mass index; CAT: COPD Assessment Test;
mMRC: modified Medical Research Council dyspnea scale

Pulmonary function test

The pulmonary function tests were performed in the pulmonary function laboratory of our institution with a whole-body plethysmograph (Collins GS II, Collins, Braintree, MA, USA). Spirometric parameters, static lung volumes, airway resistance and COPD were quantified in accordance with the technique recommended by the American Thoracic Society and the European Respiratory Society, based on criteria of reproducibility and acceptability (variation of < 5%) [9].

US Technique

Thickness of the diaphragm muscle at end-expiration was measured using B-Mode US. All subjects underwent B-mode US examinations in supine position. US was performed using a Logiq E9 (GE Healthcare, Milwaukee, USA) ultrasound system equipped with a 9-15 MHz linear transducer.

The diaphragm was visualized by placing the transducer in the ninth intercostal space perpendicular to two ribs (9^{th}-10^{th}), between the anterior and the midaxillary lines where the zone of apposition can be observed optimally 0.5 to 2 cm below the costophrenic sinus (Figure 1). The hypoechoic diaphragm muscle lays between two parallel echoic lines namely the diaphragmatic pleura and the peritoneal membrane. Thickness was measured by placing the calipers inside the hyperechoic lines (Figure 2). The patient was instructed to perform spontaneous breathing. Three diaphragm thickness measurement of the right diaphragm were recorded at end-expiration and averaged. Radiologists performing B-Mode US was blind to the patient groups.

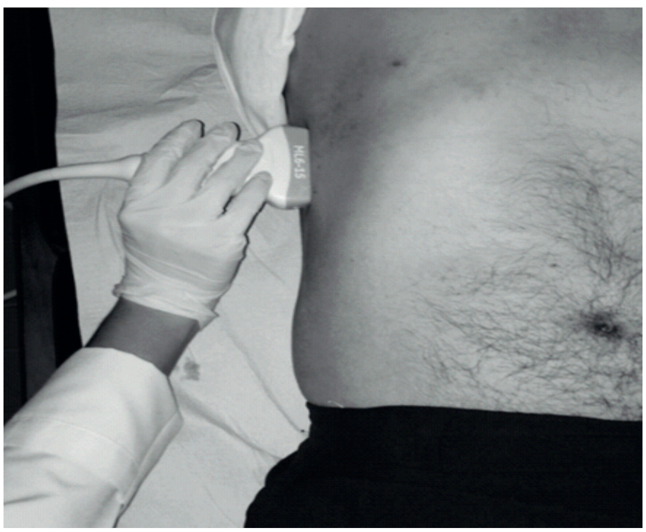

Figure 1. Transducer placement for intercostal view.

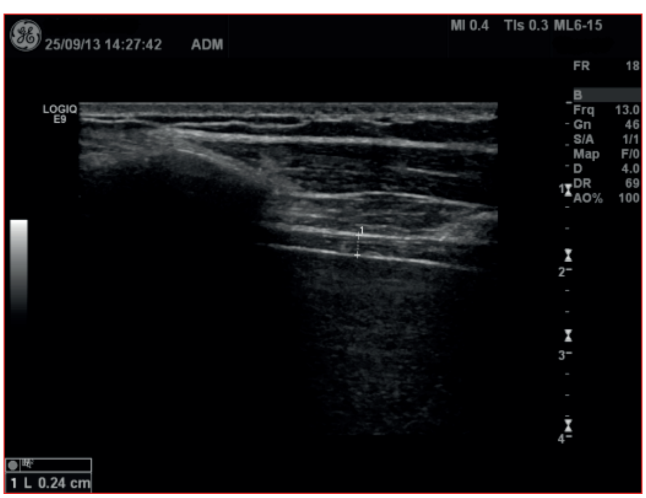

Figure 2. Ultrasound image of diaphragm thickness at end-expiration (2.4mm). The hypoechoic diaphragm muscle lies between two hyperechoic lines namely the diaphragmatic pleura and the peritoneal membrane.

Statistical analysis

Statistical analysis was performed with SPSS software version 21.0 (SPSS Inc., Chicago, IL). Kolmogorov - Smirnov test was used to examine the normal distribution of descriptive statistics (frequency, percentile, mean, standard deviation). Mann Whitney U test was used to compare the quantitative data parameters between groups. Pearson chi-square test and Fisher's exact test were used to compare the qualitative data parameters. The Spearman coefficient was used to evaluate correlations.

Results

Fifty-three COPD patients (47 male and 6females) with a mean age 62.57 ± 10.1 were enrolled in this study. Average BMI was 27.7 ± 5.1 with a minimum value of 18 and maximum value of 45. The distribution of COPD patients determined by spirometric measurements is as follows: mild (n=14), moderate (n=28), severe (n=11). Descriptive characteristics are summarized in Table I.

The diaphragmatic thickness was 2, 03± 0.39mm in females and 2, 06±0,55mm in males. There was no significant correlation between diaphragmatic muscle thickness regarding gender, age, and BMI (p>0.05). There was a moderate correlation between diaphragmatic muscle thickness and patients with mild COPD (r=0.62, p=0,017<0, 05). As %FEV1 decreased, the thickness decreased. There was no significant correlation between thickness and moderate and severe COPD (Tables II, III).

Table II. Severity of COPD and diaphragm thickness

	Mild (n=14)		Moderate (n=28)		Severe (n=11)		KW	p
	Mean	**Std**	**Mean**	**Std**	**Mean**	**Std**		
Thickness	2.207	0.369	1.975	0.624	2.073	0.476	4.658	0.097

Diaphragm thickness was 2,367mm in GOLD A; 1,8mm in GOLD B; 2,014mm in GOLD C; and 2,065mm in GOLD D. There was no significant difference in diaphragmatic thickness of GOLD A, B, C; D groups (Table IV).

Average mMRC score was 2±1; CAT grade was 12±8. There were no correlations between diaphragmatic muscle thickness and symptom scores (mMRC, and CAT).

Table III. Functional and anthopometric characteristics of classification of COPD according to the severity of obstruction

			Mild (n=14)			Moderate (n=28)			Severe (n=11)	
n		r	p	n	r	p	n	r	p	
Thickness (mm)	smoking	11	-0.533	0.091	24	0.066	0.760	11	-0.012	0.973
	BMI	14	0.151	0.606	28	0.083	0.681	11	0.220	0.515
	Attack (n)	9	-0.094	0.810	20	0.165	0.486	9	-0.026	0.948
	FEV/FVC	14	-0.256	0.378	28	0.035	0.858	11	0.067	0.846
	FEV1 %	14	-0.623	**0.017**	28	-0.209	0.285	11	-0.108	0.752
	mMRC	14	-0.431	0.124	28	0.256	0.189	11	0.036	0.917
	CAT	14	-0.162	0.580	28	0.006	0.974	11	0.009	0.978

BMI: Body mass index; CAT: COPD Assessment Test; **mMRC:** modified Medical Research Council dyspnea scale

Table IV. Diaphragm thickness according to GOLD subgroups

	A (n=19)		B (n=19)		C (n=8)		D (n=7)		KW	p
	Mean	Std	Mean	Std	Mean	Std	Mean	Std		
Thickness	2.367	0.803	1.800	0.372	2.014	0.308	2.065	0.430	6.492	0.090

Discussion

Despite widespread use of ultrasound for diaphragm assessment, there is a lack of reference value for diaphragm parameters in patients with COPD. B-mode US can be used to assess the thickness of the diaphragm over a wide range of lung volumes from residual volume to total lung capacity in the zone of apposition (ZOA), with high reproducibility [1, 7, 10]. Data from a necropsy study indicate that measurement of diaphragm thickness with ultrasonography at the ZOA is as accurate as measurements performed in vitro with a ruler [11]. In our study, diaphragm thickness was measured at the ZOA. Measuring diaphragm thickness at end-expiration was easy for participants to perform, which is important when considering clinical applications in patients with limited alertness and cooperation. Diaphragm thickness measurements in COPD patients varied in different studies. Boon et al. measured diaphragmatic thickness in normal subjects in the ZOA and reported the mean value as 3.3mm. Diaphragm pathology was suggested for sonographically measured thickness less than 1.5mm [12]. McCool et al. proposed cutoff value to define diaphragm atrophy to be less than 2mm at end-expiration [13]. In our study, the mean thickness value was 2.3 mm in females and 2.06 mm in males indicating that diaphragm thickness of the patients enrolled were influenced by COPD.

There are only a few studies in literature about sonographic diaphragm evaluation involving COPD patients [3, 4, 7]. Some studies defined the relationship between diaphragm mobility in COPD patients where the craniocaudal displacement of the portal vein was calculated as an indirect measurement of the diaphragm mobility in B-mode and M- mode US [3, 5, 6]. Baria et al. had a similar study to ours with B-mode US where diaphragmatic thickness and thickening ratio were measured in COPD patients with coexisting neuromuscular respiratory weakness. No significant difference was found between COPD patients and healthy groups in terms of diaphragm thickness with the exception of a subgroup with severe air trapping so Baria et al. concluded that normal values could be applied to COPD patients as reference values [4].

Sonographic assessment of the diaphragm thickness was recently evaluated for disease progression in COPD patients in terms of lung volumes. Smargiassi et al. demonstrated that the alterations in thickness were related to the volumetric changes [7]. They showed that indices of lung hyperinflation like VC, FVC, FEV1 were related to the diaphragmatic thickening by taking measurements at various lung volumes. In our study, we found correlation between diaphragmatic muscle thickness and %FEV1 values in mild COPD patients. The diaphragm thickness decreased as the lung volume decreased. However we could not get significant results in moderate and severe COPD patients. Since the measurements were made only at the end-expiratory phase, we could suggest that the results reflect the structural status rather than functional features of the diaphragm. The low number of patients enrolled in the study might be another factor affecting the relationship between COPD severity and US measurements.

Diaphragm thickening fraction (TF) has been newly proposed to be more sensitive than measurement of thickness since the increase in diaphragmatic thickness during inspiration is used as an indirect measurement of muscle fiber contraction which is analogous to ejection fraction of the heart [14]. TF was calculated as (thickness at end inspiration-thickness at end expiration)/ (thickness at end expiration) [15]. The assessment of TF by US performed as effective as the other weaning indexes in intensive care units [1, 2, 15].

COPD affects the lungs, but it also produces significant systemic consequences like nutritional abnormality, and weight loss [16]. In our study BMI decreased with advancing disease stage as expected. However no correlation was found between BMI and diaphragm thickness. Muscle wasting is called a significant determinant of mortality in severe COPD patients. Recent studies suggest that loss of fat free mass (FFM) is more accurate than BMI for predicting severity of the disease [7].

The small number of patients enrolled is one of the limitations of the study. Having no comparison with any other methods that might be considered to be a gold standard for assessing diaphragm function is another limitation of our study. Trans-diaphragmatic pressure measurement using esophageal or gastric transducers is considered to be the gold standard for evaluation of diaphragmatic function [15]. Electromyography is also an invasive and uncomfortable method and fluoroscopy expose the patients to radiation. Ultrasound has been shown to be similar in accuracy to most other imaging modalities for diaphragm assessment and measurements correlated well with lung volumes and inspiratory pressure values [17, 18].

Conclusions

No correlation was found between diaphragmatic thickness in COPD patients and pulmonary function tests except for %FEV1 in mild COPD patients. There were no correlations between diaphragmatic muscle thickness and symptom scores. Further US studies assessing thickness fraction should take place for functional evaluation of the diaphragm in COPD subgroups to determine disease progression.

Conflict of interest: Authors declared no conflicts of interest.

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