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Ahmed Ali Abunaglah
Department of Chest Diseases, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt

Houssam Eldin Hassanin Abd Elnaby
Department of Chest Diseases, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt

Ahmed Gamal Yousef
Department of Chest Diseases, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt, ahmedgamal4884@gmail.com

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ORIGINAL ARTICLE

Assessment of Diaphragmatic Mobility by Transthoracic Ultrasound in Patients with Interstitial Lung Diseases

Ahmed A. Abunaglah, Houssam Eldin H. Abd Elnaby, Ahmed G. Yousef*

Department of Chest Diseases, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

Abstract

Background: **Interstitial lung diseases (ILDs) may promote respiratory muscle dysfunction due to increased lung elastic recoil, chronic hypoxemia, systemic inflammation, physical inactivity, malnutrition, and corticosteroid therapy. Therefore, measuring diaphragmatic function is quite helpful when assessing patients with ILDs.**

Aim: **The aim of the study was to compare diaphragmatic mobility which was assessed by ultrasonography between healthy individuals and patients with ILDs.**

Patients and methods: **This is a case−control trial, where 30 patients with clinically stable ILDs and 20 healthy persons served as a control. Age, sex, and BMI matched apparently in the control group. Pulmonary function tests such as the 6-min walk test, ultrasonographic measurement of both diaphragmatic excursion, and thicknesses at residual functional capacity and total lung capacity (TLC), with a calculation of the diaphragmatic thickening fraction were done for all participants.**

Results: **Diaphragmatic kinetics are greatly impaired in ILD patients at TLC, but almost not affected at functional residual capacity. Diaphragmatic excursion and thickness at TLC and the diaphragmatic thickening fraction showed considerable positive correlations with forced vital capacity and 6-min walk distance, whereas they exhibited considerable negative correlations with modified Medical Research Council dyspnea scale.**

Conclusion: **Diaphragmatic kinetics measured at TLC and thickening fraction have good correlations with the degree of dyspnea, forced vital capacity, and exercise tolerance.**

Keywords: Diaphragmatic mobility, Interstitial lung diseases, Ultrasound

1. Introduction

Breathlessness, reductions in lung capacity, gas exchange, and exercise tolerance are all characteristics of interstitial lung diseases (ILDs), which are also associated with a reduced quality of life and a shorter life expectancy.[1]

Although these traits were previously primarily associated with parenchymal involvement, a recent study has shown that individuals with ILDs also exhibit reduced muscle function.[2]

In clinical practice, the use of ultrasonographic methods to measure diaphragmatic excursion and thickness of the diaphragm (TD) at various lung volumes in both healthy and ill persons is well established.[3]

In addition, people with ILDs have been shown to exhibit diaphragmatic weakness and expiratory muscle weariness after intense activity.[4]

The current study aimed to explore any possible correlations of mobility elements in such patients with the degree of dyspnea, forced vital capacity (FVC) percentage, and exercise tolerance.

2. Patients and methods

This study was conducted during the period from September 2021 to June 2022 on 50 patients attending the Bab Al-Sha'reia, Al-Azhar University

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* Corresponing author.
E-mail address: ahmedgamal4884@gmail.com (A.G. Yousef).

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Hospital Outpatient Clinic of the Chest Department during the time of the study.

The selected candidates were established into two collections: the first included 30 patients with clinically stable ILDs (due to various etiologies), identified in accordance with 2002 recommendations from the American Thoracic Society and the European Respiratory Society.[1] The second included 20 seemingly healthy participants who were chosen for the research as a control group because they best matched the sick group in terms of age, sex, and BMI.

Patients included in the study were aged from 28 to 72 years. They were not smokers and had no known medical conditions except the ones who had chest diseases other than ILDs, clinical picture suggesting ILD exacerbation, severe cardiac, hepatic or renal dysfunction, diseases that affect the diaphragmatic motility directly, for example, diaphragmatic hernia, or indirectly pregnancy, abdominal organomegaly or causes of increased intra-abdominal pressure, generalized muscular or neurological disorders, general conditions that may attribute to diaphragmatic weakness, for example, thyroid disorders, radiation therapy and electrolyte disturbances, recent thoracic or abdominal surgery, conditions interfering with good ULTRASOUND window, for example, morbid obesity (BMI >40 kg/m^2), chest wall edema, and subcutaneous emphysema, and finally severe malnutrition or those with BMI less than 18 kg/m^2.

Patients included in the study were subjected to the following: full medical history, including determination of the level of dyspnea according to the modified Medical Research Council (mMRC) dyspnea scale,[5] thorough clinical evaluation, laboratory tests including complete blood count, liver and renal activity tests, random blood sugar, serum electrolytes, thyroid hormones, and arterial blood gases. Plain posteroanterior chest radiograph and lateral views and high-resolution computed tomography on chest were also performed. Pulmonary functions tests, 6-min walk test (6MWT), and U/S assessment of diaphragmatic mobility including measuring diaphragmatic excursion and thickness at functional residual capacity (FRC) and total lung capacity (TLC), with a calculation of the diaphragmatic thickening fraction (DTF) (as a percentage) were ultimately applied for all study population.

Pulmonary function tests (PFTs): PFTs took place in the PFT Unit, using a computerized pulmonary function apparatus (Blue Cherry Version 1.2.2.4; Geratherm Respiratory GmbH, Bad Kissingen, Germany).

After an initial period of tidal volume breathing, a full inspiration to TLC was taken followed by a rapid forceful maximal expiration to residual volume into the spirometer. For each participant, three acceptable efforts were implemented, and the best obtained FVC as a percentage from expected and forced expiratory volume in the first second to FVC ratio (as a percentage) were collected for statistical analysis. A good attempt had a full expiration, a quick start, and no leaks or blockage at the mouthpiece.

6MWT: the 6MWT was conducted in accordance with the American Thoracic Society's recommendations.[6]

2.1. Ultrasonography of the diaphragm

Ultrasound machine (Sono-Scape Medical Manufacturer, Shenzhen, China) was utilized to assess the DTF using the high-frequency linear probe (7–12 MHz), and also the diaphragmatic excursion utilizing the low-frequency curvilinear probe (2–6 MHz).

Patients were examined while they were in the supine position as it is more comfortable for the patient, shows less variability and greater reproducibility during spontaneous respiration, and allows better excursion of the diaphragm.

By placing a linear probe at the anterior axillary line, in the longitudinal plane between the seventh and ninth intercostal spaces, or in 'intercostal view', the TD was evaluated. The diaphragm was seen as a hypoechoic layer of muscle surrounded by two hyperechoic layers of connective tissue in the B-mode (the parietal pleura and the peritoneum). When performing a breath-holding technique at the end of tidal expiration (equivalent to FRC) and maximum inspiration (corresponding to TLC), TD was measured in the zone of opposition immediately inside the hyperechoic connective tissue layers.[7]

The curvilinear probe, which was positioned between the midclavicular and anterior axillary lines, was used to measure the diaphragmatic excursion in the anterior subcostal region (also known as the 'anterior subcostal view'). In the B-mode, the diaphragmatic interface was visualized as a hyperechogenic line encircling the liver. At this point, utilizing the gallbladder as a reference point when present, we angled the probe to get the greatest convexity. Following that, imaging was switched to M-mode with the line of sight set up to acquire the greatest excursion.

As a hyperechogenic line in M-mode, the diaphragmatic interface eventually took on a sinusoidal

shape, with the peak matching the maximal inspiration and the dip corresponding to expiration. The diaphragmatic excursion was measured as it represented the height of the curve.[8]

The following equation was used to compute the DTF:

$$\text{DTF} = \frac{\text{thickness at (TLC)} - \text{thickness at (FRC)}}{\text{thickness at (FRC)}} \times 100$$

2.2. Statistical analysis

Statistical analyses were carried out utilizing the program R version 4.1.1 with packages (The R Foundation for Statistical Computing, Auckland, New Zealand). Mean ± SD was used to describe continuous normally distributed numerical (quantitative) data, while the median (minimum–maximum) was used to describe abnormally distributed numerical data. The categorical data were expressed as frequency and percentages. Bivariate analyses were carried out using the following tests according to normality and type of data; independent sample *t*-test was used for comparing normally distributed numerical data between two groups. Between two groups of people, skewed numerical data can be compared utilizing the Mann–Whitney test, categorical data can be compared utilizing the χ^2-test, and the strength and direction (positive or negative) of a relationship between two variables can be summarized utilizing Spearman's correlation coefficient. *P* value at the level of significance was less than 0.05.

3. Results

The median age of patients was 57.13 ± 10.2 years, while the median age of controls was 55.8 ± 6.14 years. The median BMI of the patient group was 29.84 ± 3.89 kg/m^2, while that of the control group was 28.84 ± 3.27 kg/m^2. Females represented 70% of the total number of each of the studied groups, whereas males accounted for the remaining 30% in each of them. There were no statistically substantial variations in age, BMI, and sex between patients and control groups ($P > 0.05$) (Table 1).

As illustrated in Table 2, a highly statistically substantial variation was detected between the mean diaphragmatic excursion at TLC in the patient group (4.29 ± 1.28 cm) and its match in the control group (5.94 ± 0.64 cm) ($P < 0.001$). Another high statistically substantial variation was detected between the median diaphragmatic thickness at TLC in the patient's group (2.05 ± 0.51 mm) and its match in the control group (2.87 ± 0.61 mm) ($P < 0.001$). The median of calculated DTF in the patient group (40.69%) was greatly lower than the median DTF in the control group (114.31%) ($P < 0.001$).

Strong highly significant ($P < 0.001$) positive correlations of diaphragmatic excursion at TLC, diaphragmatic thickness at TLC, and DTF in ILD patients with FVC (% of predicted) and 6MWD were noticed. However, strong highly significant negative correlations of the same ultrasonographic findings with the mMRC dyspnea scale were detected. Weak nonsignificant ($P > 0.05$) positive correlations of diaphragmatic excursion at FRC, diaphragmatic

Table 1. Demographic characteristics in patients and control groups.

Demographic variables	Patients group ($N = 30$) (mean ± SD)	Control group ($N = 20$) (mean ± SD)	Statistical test	*P*
Age	57.13 ± 10.2	55.8 ± 6.14	$t = 0.57$	0.567
BMI	29.84 ± 3.89	28.84 ± 3.27	$t = 0.98$	0.33
Sex [*N* (%)]				
Females	21 (70)	14 (70)	$\chi^2 = 0$	1
Males	9 (30)	6 (30)		

t, independent sample *t*-test.

Table 2. Diaphragmatic excursion, thickness, and thickening fraction in patients and control groups.

Variable	Patients group ($N = 30$)	Control group ($N = 20$)	Statistical test	*P*
Diaphragmatic excursion (cm)				
FRC	1.6 (1.13–2.3)	1.65 (1.26–2.31)	$W = 241.5$	0.251
TLC	4.29 ± 1.28	5.94 ± 0.64	$t = 6.01$	<0.001[a]
Diaphragmatic thickness (mm)				
FRC	1.34 ± 0.37	1.38 ± 0.17	$t = 0.55$	0.58
TLC	2.05 ± 0.51	2.87 ± 0.61	$t = 4.5$	<0.001[a]
Thickening fraction (%)	40.69 (0.001–238.57)	114.31 (15.72–200.81)	$W = 129$	<0.001[a]

FRC, functional residual capacity; *t*, independent sample *t*-test; TLC, total lung capacity; *W*, Mann–Whitney test.
[a] Statistically highly significant.

thickness at FRC in ILDs patients with FVC (% of predicted), and 6MWD were revealed whereas weak nonsignificant negative correlations of the same ultrasonographic findings with the mMRC dyspnea scale were explored (Table 3).

4. Discussion

Transthoracic ultrasound approach shows several benefits over other imaging modalities, including the lack of radiation, portability, real-time imaging, and noninvasive nature. U/S is a simple tool for determining diaphragmatic excursion and thickness. Patients with ILDs have had their measures' repeatability and the connections between diaphragmatic kinetics and respiratory function metrics examined.[9]

The insignificant differences between the studied groups as regards age, sex, and BMI supported the reliability of the results of the current study, because the variability of these factors may affect diaphragmatic strength and function.

Sharma and Goodwin[10] reported an age-related decline in diaphragmatic strength in older individuals, which can precipitate diaphragmatic fatigue during increased ventilatory load on the respiratory system.

A study included 164 healthy participants which documented that females had a statistically significant decreased diaphragmatic motion than male participants, and that the median diaphragmatic motion was significantly less in underweight individuals when compared with patients with normal or increased body weight.[11]

Seok et al.[12] concluded that sex and BMI had a substantial impact on diaphragmatic thickness, but they had little impact on the thickening fraction, during investigating 80 healthy volunteers using the ultrasound technique.

In this study, diaphragmatic excursion (expressed in centimeters) measured at FRC showed a nonsignificant variability between the two study groups ($P = 0.251$). On the opposite side, the mean diaphragmatic excursion measured at TLC was substantially greater in the control group compared with the patient group ($P < 0.001$).

These results come in agreement with those obtained by an Italian study, which aided the concept that diaphragmatic weakness in patients with fibrotic lung disease is manifested by a decreased excursion on deep breathing compared with healthy volunteers ($P < 0.001$). In the same study, no significant difference between the mean diaphragmatic excursion in patients and controls at spontaneous breathing was recorded ($P = 0.503$).[13]

Alongside, our observations are extremely close to those obtained by a study that included 40 ILD patients and 16 healthy volunteers performed by Santana and colleagues. In a previous work, the mean diaphragmatic excursion did not greatly differ during quiet breathing in controls versus ILD patients ($P = 0.91$). However, the mean diaphragmatic excursion was substantially reduced in the patients during deep breathing compared with the controls ($P < 0.01$).[14] Our feedbacks also coincide with those of another study that reported similar findings.[15]

The results we get sail in the exact stream with those of a Brazilian study, in which the motion of the right diaphragm during deep breathing (TLC) was found to be reduced in ILD patients when compared with healthy volunteers ($P < 0.001$).[16]

On the contrary, our findings are not parallel to those of He and colleagues. A mixed group of patients with pulmonary fibrosis and emphysema, patients with idiopathic pulmonary fibrosis, and healthy controls were examined for diaphragm movement during quiet breathing and deep breathing. In that research, it was shown that individuals with idiopathic pulmonary fibrosis did not substantially differ from healthy controls in terms of their diaphragmatic excursions during silent breathing and deep breathing.[17]

In the current study, we found a statistically substantial variation between the median thickness of the diaphragm at TLC (TDTLC) of ILDs patients and

Table 3. Correlation of diaphragmatic excursion, thickness, and thickening fraction in ILD patients with FVC (% of predicted), 6MWD, and mMRC dyspnea scale.

Variables	Diaphragmatic excursion				Diaphragmatic thickness					
	FRC		TLC		FRC		TLC		DFT	
	r	*P*	*r*	*P*	*r*	*P*	*r*	*P*	*r*	*P*
FVC%	0.13	0.36	0.71	<0.001[a]	0.09	0.52	0.66	<0.001[a]	0.53	<0.001[a]
6MWD	0.24	0.08	0.79	<0.001[a]	0.17	0.22	0.74	<0.001[a]	0.55	<0.001[a]
mMRC dyspnea scale	−0.24	0.09	−0.75	<0.001[a]	−0.12	0.42	−0.70	<0.001[a]	−0.58	<0.001[a]

6MWD, 6-min walk distance; DTF, diaphragmatic thickening fraction; FVC, forced vital capacity; mMRC, modified Medical Research Council; *r*, Spearman's correlation coefficient; TLC, total lung capacity.

[a] Statistically highly significant.

the mean TDTLC of controls ($P < 0.001$). Another statistically substantial variation was observed between the median DTF of the patient's group and the median DTF of the control group ($P < 0.001$). However, no statistically substantial variability was detected between the mean thickness of the diaphragm at FRC (TDFRC) of ILD patients and the measured same parameter in the controls ($P = 0.58$).

The results of a new investigation corroborate these conclusions, which performed diaphragmatic ultrasonography for 30 fibrotic ILD patients and 30 healthy individuals, and measure diaphragmatic excursion and thickness during both quiet (FRC) and deep (TLC) breathing states by calculating the thickening fraction. In the former study, significant differences were found when comparing the median TDTLC and the median thickening fraction between the diseased and control groups ($P < 0.01$), with the higher values met on the healthy side. However, they found an additional significantly higher median TDFRC among the diseases group ($P = 0.01$).[15]

Furthermore, Santana and coworkers observed a greater mean TDFRC in the ILDs group compared with the control group ($P = 0.05$). In spite of that, the mean TDTLC in the same study was substantially greater in the control individuals versus the ILD patients ($P < 0.01$). The patients also showed a significantly lower DTF when compared with the controls ($P < 0.01$). Those findings are merging with ours more than they oppose.[14]

In our study, we disclosed highly significant strong positive correlations of diaphragmatic excursion at TLC with both FVC (% of predicted) and 6MWD ($r = 0.71$ and 0.79, respectively; $P < 0.001$). At the same lung capacity, a strong negative correlation was detected between diaphragmatic excursion and mMRC dyspnea scale ($r = -0.75$, $P < 0.001$). Similar outcomes were obtained when testing the correlation of diaphragmatic thickness at TLC with the same variables ($r = 0.66$, 0.74, and -0.7 for FVC%, 6MWD and mMRC dyspnea scale, respectively; $P < 0.001$). Good correlations were found between DTF and the same variables as well ($r = 0.53$, 0.55, and -0.58 for FVC%, 6MWD, and mMRC dyspnea scale, respectively, $P < 0.001$).

Our results mostly concur with Santana and colleagues, who reported high positive correlations of FVC (% from predicted) with a diaphragmatic excursion at TLC, TDTLC, and DTF ($r = 0.76$, 0.7, and 0.68, respectively; $P < 0.01$). However, they found variable degrees of negative correlations of mMRC dyspnea scale with diaphragmatic excursion at TLC ($r = -0.57$, $P < 0.01$), TDTLC ($r = -0.36$, $P = 0.05$), and DTF ($r = -0.54$, $P < 0.01$).[15]

Matching with our findings, a South American study concluded that FVC (% of predicted) exhibited a good connection with diaphragmatic mobility at TLC ($r = 0.73$, $P < 0.01$). They determined that an FVC% cutoff value of less than 60% presented high sensitivity (92%) and good specificity (81%) for identifying reduced diaphragmatic mobility.[14] Similarly, a strong positive connection between FVC (% of predicted) and diaphragmatic excursion at deep breathing ($r = 0.86$, $P < 0.01$) was observed by another study.[16]

Finally, our outcomes go through with Boccatonda and colleague, as they detected a positive connection between FVC (% of predicted) and diaphragmatic motility at deep breathing in fibrotic patients ($r = 0.56$, $P = 0.05$). However, they recorded a considerable positive connection between FVC (% of predicted) and diaphragmatic excursion at quiet breathing ($r = 0.53$, $P = 0.05$), which comes in disagreement with our results.[13]

4.1. Conclusion

Diaphragmatic kinetics measured at TLC and DTF have good correlations with the degree of dyspnea, PFTs, and exercise tolerance. Further investigation with larger numbers of patients is needed for more reliable and accurate results.

Contribution

All authors have a substantial contribution to the article.

Ethical approval

The study was approved by the Research Ethical Committee of Al-Azhar University and the patients were given all the information they need about the trial. Informed written consent was obtained from each participant in the study.

Consent statement

This work has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans.

Conflict of interest

There are no conflicts of interest.

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