Role of chest ultrasonography in assessment of diaphragmatic mobility in chronic obstructive pulmonary disease patients on pulmonary rehabilitation program

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Background Chronic obstructive pulmonary disease (COPD) affects all skeletal muscles including the diaphragm as an extra pulmonary complication. Diaphragmatic mobility improves by pulmonary rehabilitation (PR). Chest ultrasound can be used in assessment of diaphragmatic mobility.

Aim Evaluation of chest ultrasound as a simple, noninvasive tool in assessment of diaphragmatic mobility in COPD patients undergoing PR and its correlation with maximal inspiratory pressure (Pi MAX), 6-min walk test (6MWT) and clinical chronic obstructive pulmonary disease questionnaire (CCQ).

Patients and methods This study was conducted upon 30 COPD male patients aged 54.50±8.81 years old. All patients were recruited in to a PR program including 16 sessions over 8 weeks. The program included upper limb exercise, lower limb exercise and inspiratory muscle training. Baseline spirometry, Pi MAX, modified medical research council (mMRC) dyspnea scale, CCQ, 6MWT and sonographic assessment of diaphragmatic excursion and thickness were done. Follow-up sonographic evaluation of the diaphragm, CCQ and mMRC every 2 weeks were done. Re-evaluation after the program by the same baseline parameters was done.

Results There was statistically significant improvement in diaphragmatic excursion and thickness after PR program as evidenced by chest ultrasound. There was also significant functional improvement evidenced by 6MWT and Pi MAX. Also, there was significant improvement in mMRC and CCQ, but PR did not significantly affect spirometric parameters as forced expiratory volume in first second (FEV1)%, FEV1 value in liter or FEV1/forced vital capacity.

Conclusion Chest ultrasound is a beneficial tool in diaphragmatic assessment in COPD patients undergoing PR.
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Keywords: chest ultrasound, chronic obstructive pulmonary disease, diaphragmatic mobility, pulmonary rehabilitation

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Introduction

Chronic obstructive pulmonary disease (COPD) is a common preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and or alveolar abnormalities usually caused by significant exposure to noxious particles or gases [1].

The diaphragm is a major respiratory muscle contributing 75% of resting lung ventilation with an excursion of 1–2 cm. During forced breathing its excursion reaches 7–11 cm varying with the individual characteristics and methods [2].

All skeletal muscles including the diaphragm can be affected by COPD as an extra pulmonary complication of COPD. Yet, both diaphragmatic mobility and thickness can be increased by pulmonary exercise training [3].

The diagnostic tools traditionally used to study the diaphragmatic dysfunction like fluoroscopy, phrenic nerve conduction study, and transdiaphragmatic pressure measurement present some limitations and disadvantages including: the usage of ionizing radiations, low availability, invasiveness, the need for patient transportation and skilled or specifically trained operators. Recently, ultrasound has been used to evaluate the diaphragmatic function. Advantages of ultrasound include safety, avoidance of radiation hazards, and availability at the bedside [4].

Patients and methods

The present study was conducted upon 30 COPD male patients. The study was performed at Ain Shams University Hospitals Chest Clinic during the period between August 2015 and August 2017. The mean ±SD of age of the patients was 54.50±8.81 years old.

Patients meeting the following criteria were excluded

Conditions that might interfere with pulmonary rehabilitation (PR) process such as advanced arthritis, conditions that might place the patient at

risk during exercise training such as unstable cardiac, hepatic or renal conditions or cases of hematological malignancies, unstable chest condition such as acute exacerbation of COPD, pneumonia, respiratory failure and pneumothorax, patients with pleural effusion and/or ascites that might interfere with diaphragmatic mobility, patients with diaphragmatic paralysis or diaphragmatic hernia, patients with chest deformities which can affect diaphragmatic mobility such as kyphoscoliosis, patients requiring long term O_2 therapy, patients who are living alone and patients encountered in previous PR program during the previous 12 months.

All patients received medical treatment for COPD according to guidelines applied by GOLD 2015 [5] all through the program. All the patients were submitted to thorough history and clinical general and local chest examination, some routine laboratory investigations such as: complete blood count and hepato – renal profile, ECG, chest radiography posteroanterior view, initial spirometry to all the patients, initial symptoms evaluation of patients by clinical chronic obstructive pulmonary disease questionnaire (CCQ) with validated translation translated in to Arabic [6], modified medical research council (mMRC) dyspnea scale after explanation of the scale to the patients in Arabic, baseline maximal inspiratory pressure test (Pi MAX) and maximal expiratory pressure test (Pe MAX) according to ATS/ERS statement on respiratory muscle testing 2002 [7]. Baseline 6-min walk test (6MWT) according to ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories [8], baseline ultrasound evaluation of diaphragmatic mobility (excursion) both at rest and with forced respiration, in addition to assessment of diaphragmatic thickness using Mindray M7 (Guangzhou Medsinglong Medical Equipment Co., Ltd Guangdong, China) Ultrasound device with the following steps while the patients at supine position:

For diaphragmatic excursion

Examination was done using a 3.5C (bandwidth 2–5 MHz) convex phased array probe (low frequency probe with greater depth and allowing to assess excursion), with B mode set as the default mode on the device screen.

Probe of ultrasound was put at anterior axillary line, right subcostal after application of ultrasound gel and is directed medially, cephalic and dorsally using the liver as acoustic window for better illustration of diaphragm.

Then switch to M mode observing diaphragmatic movement during inspiration and expiration during quiet breathing, then press freeze button on ultrasound device, then measurement the difference between the diaphragmatic position during inspiration and expiration was done and recorded as diaphragmatic excursion during quiet breathing which corresponds to diaphragmatic excursion during rest.

The same steps were followed but with asking the patient to take a deep inspiration followed by a deep expiration to measure diaphragmatic excursion during forced respiration which corresponds to diaphragmatic excursion during patients exercise.

For diaphragmatic thickness

An M12L linear array probe (bandwidth 5–13 MHz) was put at right anterior axillary line at seventh or eighth intercostal space, obtaining an image showing liver and lung and a zone of apposition between them using B mode. Both pleural lining and peritoneal lining appeared clearly as two approximately parallel echogenic lines. The space between them resembling diaphragmatic thickness was measured during inspiration. Diaphragmatic thickness corresponds with muscle endurance.

Then the patients were encountered in a PR program (mainly exercise training program), according American Thoracic Society/European Thoracic Society statement for PR (2013) [9] including: two sessions weekly for 8 weeks (total 16 sessions) as follows: at the first session and the sessions at each visit were performed at pulmonary function unit of Ain Shams University Hospital, while the rest of sessions were performed at home with regular follow-up by phone at each predetermined date for training sessions to ensure performing exercise, and detecting any obstacles or complaints from the patients. Regular 2 weeks interval visits were done till the end of the program, at each visit re-check on the program goals and steps was done.

The exercise training program was explained for each patient with written exercise details at the beginning of the study to be followed at home.

(1) Warm up for 15 min.
    (a) Upper limb exercise for 15–20 min.
(2) Aerobic regimen: arm cycling.
(3) Resistance training: free weights (dumb bells) or bottle of water lifting.
    (a) Lower limb exercise: Endurance training including walking sessions were conducted during first 2 weeks lasting 15–20 min on

the patient's own pace, then exercise sessions were increased by 5 min every 2 weeks until 35–40 min per session during the final week.
(b) Respiratory muscle exercise for 15 min.

(4) Breath holding technique, by taking deep inspiration lasting 3 s then holding breath for another 3 s followed by slow expiration through pursed lip lasting for about 4 s.
(5) Training by incentive spirometer device by holding the device opening between lips then taking deep inspiration trying to elevate the three balls in the device, or blowing a balloon taking in consideration to be less compliant, with fair elastic resistance. Once the balloon became more compliant and easily inflatable, patients were advised to discard it to be replaced by a new one.

Follow-up visits was done at 2 weeks interval during which two sessions were to be completed. During the visit, diaphragmatic ultrasound was done in addition to symptoms evaluation by CCQ and mMRC. After completion of 16 sessions along 8 weeks, the following was done: follow-up spirometry, Pi MAX, Pe MAX, follow-up 6MWT, follow-up diaphragmatic evaluation by ultrasound regarding excursion and thickness and follow-up symptoms evaluation by CCQ and mMRC.

Statistical analysis

The collected data was revised, coded, tabulated and introduced to a PC using statistical package for the social sciences (SPSS 17). Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

(1) Description of quantitative variables as mean, SD and range.
(2) Description of qualitative variables as number and percentage.
(3) Paired *t*-test was used to test the difference in two means.
(4) The comparison between more than two independent groups regarding quantitative data with parametric distribution was done by using one-way analysis of variance.
(5) Spearman's correlation coefficients were used to assess the correlation between two quantitative parameters in the same group.
(6) Pearson's correlation was used to measure of the strength of a linear association between two variables.

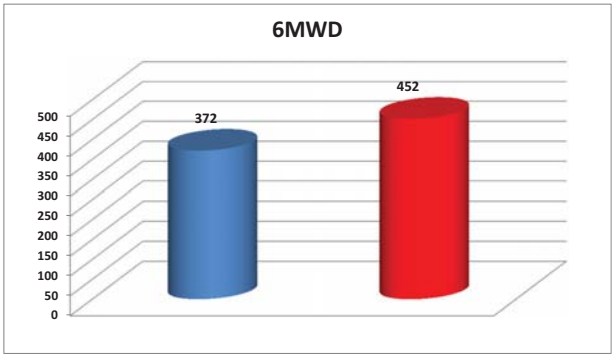
The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the *P*-value was considered significant as the following:

$P>0.05$, nonsignificant.
$P<0.05$, significant.
$P<0.01$, highly significant.

Results

The present study was conducted upon 30 COPD male patients. The mean±SD of age of the patients was 54.50±8.81 years old. The following results were obtained from the study; there was statistically significant improvement in diaphragmatic excursion both during quiet breathing and forced respiration (Fig. 1), in addition to diaphragmatic thickness after PR program evidenced by M-mode ultrasound (Table 1). There was also significant functional improvement evidenced by 6-min walking distance (6MWD) (Fig. 2) and Pi MAX (Fig. 3) following PR program. In addition to this, there was significant improvement in health related quality of life evidenced by improvement in mMRC dyspnea scale (Table 2) and CCQ (Table 3). On the other hand, PR did not significantly affect spirometric parameters [forced

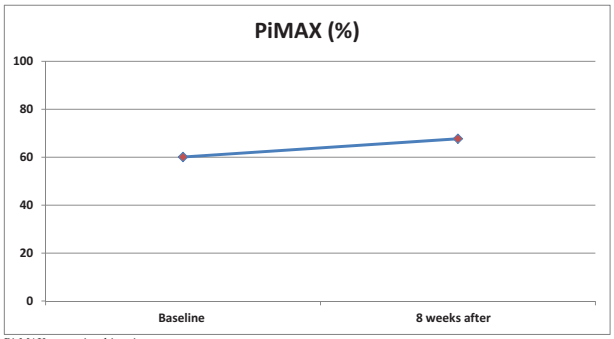
Figure 1



6MWD = 6 minute walking distance in meters

Comparison between baseline data and different follow-up periods regarding DE (forced respiration). DE, diaphragmatic excursion.

Figure 2



Pi MAX = maximal inspiratory pressure

Comparison between 6MWD before and after pulmonary rehabilitation program. 6MWD, 6-min walking distance (m).

Table 1 Comparison between baseline data and different follow-up periods regarding ultrasound findings

	Diaphragmatic excursion (quiet breathing) (mean±SD) (cm)	Diaphragmatic excursion (forced respiration) (mean±SD) (cm)	Diaphragmatic thickness (mean±SD) (cm)
Baseline (before pulmonary rehabilitation)	2.0±0.38	4.0±0.71	0.22±0.10
2 weeks	3.08±0.67	4.8±1.42	0.27±0.10
4 weeks	2.8±0.65	5.03±1.23	0.26±0.11
6 weeks	3.26±0.70	6.13±1.59	0.38±0.12
8 weeks (at the end of pulmonary rehabilitation)	3.69±1.03	6.40±1.76	0.33±0.08
P-value	0.0001*	0.0001*	0.0001*

*Statistically significant difference.

Table 2 Comparison between modified medical research council before and after pulmonary rehabilitation program

Modified medical research council	Before pulmonary rehabilitation [*n* (%)]	8 weeks later (end of pulmonary rehabilitation) [*n* (%)]	*P*-value
Class 1	0 (0)	15 (50)	0.0001*
Class 2	9 (30)	15 (50)	0.001*
Class 3	21 (70)	0 (0)	0.0001*

*Statistically significant difference.

Table 3 Comparison between clinical chronic obstructive pulmonary disease questionnaire before and after pulmonary rehabilitation program

	Before pulmonary rehabilitation	8 weeks later (end of pulmonary rehabilitation)	Paired *t*-test	*P*-value
Clinical chronic obstructive pulmonary disease questionnaire (mean±SD)	26.8±8.03	10±4.54	16.929	0.000*

*Statistically significant difference.

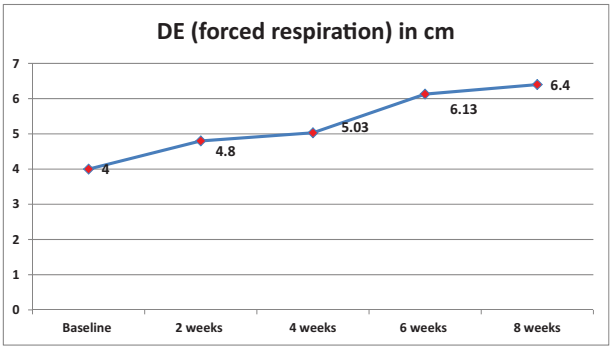
Table 4 Comparison between pulmonary function tests before pulmonary rehabilitation program and after 8 weeks (at the end of pulmonary rehabilitation program)

	Before pulmonary rehabilitation	8 weeks later (at the end of the program)	Paired *t*-test	*P*-value	Significance
FEV1/FVC% (mean±SD)	53.3±8.8	53.3±8.4	–0.010	0.992	NS
FEV1% (mean±SD)	47.9±21.7	48.7±23.1	–0.912	0.369	NS
FEV1 (l) (mean±SD)	1.46±0.7	1.50±0.73	–1.072	0.293	NS
Pi MAX% (mean±SD)	60.1±25.3	67.7±22.7	–3.306	0.001	HS
Pe MAX% (mean±SD)	72.4±22.9	77.1±20.9	–1.350	0.188	NS

FEV1, forced expiratory volume in first second; FVC, forced vital capacity; HS, highly statistically significant; Pe MAX, maximal expiratory pressure; Pi MAX, maximal inspiratory pressure.

expiratory volume in first second (FEV1)% of predicted, absolute FEV1 value in liter or FEV1/forced vital capacity (FVC)] (Table 4). There was statistically significant correlation between FEV1 and diaphragmatic excursion (both at quiet breathing and at forced respiration) at the end of PR program, while there was no statistically significant correlation between FEV1 and diaphragmatic thickness (Table 5). There was statistically significant correlation between diaphragmatic excursion during forced respiration and 6MWD, while there was no statistically significant correlation between diaphragmatic excursion (forced respiration) and Pi MAX, CCQ, mMRC at the end of PR program (after 8 weeks) (Table 6).

Figure 3



DE = diaphragmatic excursion, cm = centimeter.

Comparison between baseline Pi MAX and after 8 weeks (at the end of pulmonary rehabilitation program). Pi MAX, maximal inspiratory pressure.

Table 5 Correlation between forced expiratory volume in first second at 8 weeks (end of pulmonary rehabilitation program) and diaphragmatic assessment data

	FEV1		
	r	*P*-value	Significance
DE by US (quiet breathing) (cm)	0.559	0.001	S
DE by US (forced respiration) (cm)	0.647	0.000	S
Diaphragmatic thickness (cm)	0.320	0.085	NS

DE, diaphragmatic excursion; FEV1, forced expiratory volume in first second; *r*, correlation; S, statistically significant difference; US, ultrasound.

Table 6 Correlation between diaphragmatic excursion (forced respiration) at the end of pulmonary rehabilitation program (after 8 weeks) and other data

	DE (forced respiration)		Significance
	r	*P*-value	
Pi MAX	0.258	0.169[a]	NS
CCQ	−0.208	0.269[a]	NS
mMRC	−0.244	0.194[b]	NS
6MWD	0.375	0.041[a]	S

CCQ, clinical chronic obstructive pulmonary disease questionnaire; DE, diaphragmatic excursion; mMRC, modified medical research council; 6MWD, 6-min walking distance; Pi MAX, maximal inspiratory pressure; *r*, correlation; S, statistically significant difference. [a]Pearson's correlation. [b]Spearman's correlation.

Discussion

COPD is a common preventable and treatable disease affecting the lung with some extra pulmonary manifestations [1]. All skeletal muscles including the diaphragm can be affected by COPD [3]. PR plays a vital role in improvement of diaphragmatic functions [3]. Chest ultrasound provides a simple, safe and available tool in assessment of diaphragmatic excursion and thickness [4].

The aim of this study was to evaluate chest ultrasound as a simple, noninvasive test in assessment of diaphragmatic mobility in COPD patients undergoing PR program and its correlation with Pi MAX, 6MWT and CCQ.

At this study, there is highly statistically significant improvement in diaphragmatic excursion, both at quiet breathing from 2.0±0.38 to 3.69±1.03 cm (P=0.0001) and forced breathing from 4.0±0.71 to 6.40±1.76 cm (P=0.0001) after PR program. This matches with Corbellini *et al.* [10] who compared diaphragmatic mobility before and after PR using M-mode ultrasonography. In his study, 30 patients completed the PR program for 31±8 days, diaphragmatic mobility during deep respiration increased from 4.58±1.83 to 5.45±1.56 cm (P<0.01), but as regard diaphragmatic mobility during quiet breathing; it was not significantly changed (ranged from 2.25±0.83 to 2.53±0.82 cm).

Also, these results agree with Chun *et al.* [11] who analyzed diaphragmatic mobility in COPD patients before and after PR through home-based training. Chun *et al.* [11] used fluoroscopy as an imaging tool in assessment of diaphragmatic mobility. In his study, 37 COPD patients were enrolled in a PR program for 3 months. Diaphragmatic mobility significantly improved after PR (P=0.001).

This work showed that there was statistically positive correlation between FEV1 and diaphragmatic mobility both at quiet breathing (P=0.001) and forced respiration (P<0.001). This coincides with Corbellini *et al.* [10] study in which diaphragmatic mobility both at rest and deep inspiration correlated significantly with FEV1% (P<0.001). These results also corresponds with Akturk *et al.* [12] who studied the role of M mode ultrasound in 76 COPD patients and its correlation with pulmonary function tests. There was a significant correlation between FEV1 and diaphragmatic motion.

It has been found that there was statistically significant improvement in 6MWD from 372±80.4 to 452±8.7 m (P<0.001). This is in agreement with El-Khateeb *et al.* [13] study, in which 4 COPD patients were included in a PR program for 6–8 weeks, there was a statistically significant improvement in 6MWD with an increase of 78 m. This also was in concordance with Dourado *et al.* [14] who compared different pulmonary exercise programs upon 35 COPD patients, 11 of which were applied on combined strength training with low intensity general training, the 6MWD improved by 48±50 m (P<0.05). Also, these results match with Chaicharn *et al.* [15] who assessed the efficacy of simple PR program upon 30 COPD patients along 1 year; 6MWD improved significantly at 2 month interval from 307.9±87.4 to 371.2±80.4 m (P<0.001). Also, this coincides with Nicole *et al.* [16] who studied the efficacy of at home tele-rehabilitation on 23 COPD patients on average 65.2 years old (SD=7.1), and found that 6MWD significantly improved after 8 weeks of PR program (15 sessions at home) with P value of less than 0.05. Also, Ghanem *et al.* [17] whose study was carried out on 39 COPD patients (25 patients underwent PR for 2 months, 14 COPD patients as control who did not undergo PR) found that there was statistically significant improvement in 6MWD in group 1 in comparison with the control group with P value of less than 0.05.

It has been found that there was no statistically significant difference between FEV1/FVC% and FEV1% before and after PR. This was in concordance with Chun *et al.* [11] whose study included thirty seven COPD patients recruited in a PR program. They found that there was no significant differences in FVC% (P=0.137), FEV1% (P=0.297), or forced expiratory flow at 25–75% (P=0.921) in the subjects after the 3 months of PR, compared with pre-rehabilitation.

Similarily, El-Khateeb *et al.* [13] found that there was no statistically significant improvement in FEV1, but on the contrary, FEV1/FVC showed statistically significant difference (P=0.033). These results also match with Ghanem *et al.* [17] who compared the results of 25 COPD patients before and after PR program as regard FEV1 (l), FEV1% and FVC; they found that these spirometric parameters did not statistically improve following the program (P=0.79). Moreover, the results were in concordance with Yoshimi *et al.* [18] study; in which 31 COPD patients with mean±SD of age 68±7 who attended rehabilitation sessions at Juntendo University Hospital from 1999 to 2006. They found that although there was statistically significant improvement in 6MWD and Saint George's Respiratory Questionnaire (SGRQ) dyspnea scale, neither FEV1% predicted nor FEV1/FVC was affected to a significant extent.

Regarding Pi MAX and Pe MAX; this study shows that there was statistically significant improvement in Pi MAX after PR program in comparison with pre-rehabilitation (P=0.001). This was in agreement with Elmorsi and AbdAllah [19] whose study included 60 COPD patients divided into three groups (group A received combined inspiratory muscle training with general exercise training, group B received general exercise alone, group C did not receive any training). The PR program was for 8 weeks. They found that there was highly statistically significant improvement in Pi MAX in group A more than group B with P=0.000. This also matches with Sykes and Hang [20] who found that Pi MAX improved significantly with inspiratory muscle training in addition to general training, while O'Donnel *et al.* [21] found that Pi MAX improved with general exercise without performing inspiratory muscle training. Even though, Pe MAX improved following the PR program, it was not statistically significant (0.188). This coincides with Larson *et al.* [22], in contrast to Elmorsi and AbdAllah [19] who found that there was statistically significant improvement in Pe MAX (P=0.000).

Regarding symptoms evaluation before and after PR, this work shows statistically significant improvement in patient's symptoms by CCQ with P=0.000. This matches with Dourado *et al.* [14] who assessed patients symptoms by SGRQ before and after different pulmonary exercise programs, patients symptoms statistically improved following the programs (P<0.05). This also agrees with Chaicharn *et al.* [15] who assessed symptoms of 30 COPD by SGRQ before and after PR with statistically significant improvement after 2 months (P=0.001). Similarily, Ghanem *et al.* [17] who enrolled 25 COPD patients in a PR and 14 COPD control patients over 2 months using chronic respiratory questionnaire for symptoms evaluation, there was statistically significant improvement in chronic respiratory questionnaire score in patients who underwent PR before and after the program (P=0.05) and in comparison with control group with P value of less than 0.01. This also corresponds with Elmorsi and AbdAllah [19] who used SGRQ for symptoms evaluation in COPD patients on PR program versus control group along 2 months. There was highly statistically significant improvement (P=0.000) in patients on PR in comparison with the control group.

This study shows that there was statistically significant improvement among study group regarding mMRC dyspnea score (P<0.001) after PR program. This matches with El-Khateeb *et al.* [13] study, in which there was improvement in mMRC score (P=0.02) among 45 COPD patients undergoing PR. This also agrees with Chaicharn *et al.* [15] on 30 patients after 2 months of PR with P value of less than 0.01. Elmorsi and AbdAllah [19] also found that there was highly statistically significant improvement in mMRC dyspnea scale among COPD patients on PR (P=0.000) versus control group (P=0.317).

This study aimed at not only diaphragmatic assessment before and after the PR program, but also all through the program at equal intervals. This was done to detect whether improvement in diaphragmatic excursion or thickness would be at a specific time (forming peak improvement) then would take a plateau attitude at the rest of PR program or not. It has been found that the improvement took a gradual course all through the program to some extent. As regard diaphragmatic thickness, the overall evaluation revealed that there was improvement in diaphragmatic thickness after PR in comparison with pre-rehabilitation assessment; which is the main target of this work. Although there was decrease in diaphragmatic excursion by ultrasound in the last 2 weeks, it can be explained ultrasound assessment of

diaphragmatic thickness carries some variability during interpretation, yet, it was a fraction of mm and did not affect the overall results statistically.It is important to notice that there were some limitations facing this work such as compliance of patients regarding adherence to the program involving regular 2-week interval visits. This affected the overall number of patients recruited in this study as many patients were excluded due to nonadherence to the program. But this has been overcome by regular follow-up by phone, motivation and tailoring exercise training to be suitable for each patient.

Conclusion

From this study, it can be concluded that chest ultrasound is a beneficial tool in diaphragmatic assessment in COPD patients undergoing PR; which plays a fundamental role as a nonpharmacological treatment of COPD patients. It improves health related quality of life in addition to exercise tolerance.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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