### Original Article Clinical outcome of a novel breathing training maneuver in stable COPD patients

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**Abstract:** Pulmonary rehabilitation (PR) programs have been shown to improve exercise capacity and health-related quality of life. Breathing training is considered an important component of PR for individuals with chronic obstructive pulmonary disease (COPD). The current study designed a breathing training method based on expiratory airflow limitation and impaired inspiratory muscle function in COPD patients with rapid deep inspiration and prolonged expiration. It was hypothesized that this novel breathing training maneuver can provide effective inspiratory muscle training and alleviate dynamic hyperinflation during breathing training, improving dyspnea. To test the hypothesis, patients with stable moderate or severe COPD symptoms were randomized into one of the three groups, including group A with novel breathing training, group B with diaphragmatic breathing training, and group C as control. Exercise tolerance and quality of life were measured at baseline and post-training. The training groups (groups A and B) improved significantly compared to baseline in mMRC scale, 6-MWD, MIP and MEP, SGRQ total score, and BODE index. Significant improvements were present in exercise capacity, health-related quality of life, and dyspnea of groups A and B, compared with those of group C, with no statistical differences shown between groups A and B. Breathing training improves dyspnea, exercise capacity, respiratory muscle function, and quality of life in patients with moderate to severe COPD. Results prove that this novel breathing training is an effective rehabilitation method.

**Keywords:** Chronic obstructive pulmonary disease, pulmonary rehabilitation, breathing training, diaphragmatic breathing, respiratory muscle dysfunction

### Introduction

Chronic obstructive pulmonary disease (COPD) is characterized by incompletely reversible airflow limitation and dyspnea. As the disease progresses, systemic symptoms occur in the majority of patients, including exercise limitation and respiratory and peripheral muscle dysfunction and malnutrition [1-3]. Recent guidelines [4] for management of COPD emphasize the importance of pulmonary rehabilitation (PR) as a part of an integrated multidisciplinary approach. PR programs have shown the ability to improve exercise capacity, health-related quality of life, and dyspnea. Breathing training is considered an important component of PR for individuals with COPD. Several breathing training methods have been reported in the literature, including slow and deep breathing, pursed lips breathing, and diaphragmatic breathing. However, diaphragmatic breathing (DB) may be difficult for patients to employ. It accompanies increased asynchronous and paradoxical breathing movements when this breathing is used during dyspnea. Pursed lips breathing is difficult to learn for many patients. This self-designed novel breathing training is based on expiratory airflow limitation and impaired inspiratory muscle function in COPD patients with rapid deep inspiration and prolonged expiration. It was hypothesized that this novel breathing training method can provide effective inspiratory muscle training, alleviate dynamic hyperinflation during breathing training, and improve dyspnea.

A prospective, randomized, and controlled study was conducted to evaluate clinical effects and potential mechanisms of this novel breathing training method with the following outcome: improvement of dyspnea and exercise tolerance.

Novel breathing training is another frequently used type of respiration that differs from DB. Although use of DB is growing in rehabilitation, there is little scientific research on this new novel breathing training maneuver.

### Material and methods

### Subjects

Patients with stable moderate or severe COPD symptoms were enrolled in Outpatient Clinics of The First Affiliated Hospital of Guangzhou Medical University, from April to December 2013. COPD diagnosis was confirmed with clinical presentation and spirometric testing. Inclusion criteria were as follows: (1) Age  $\geq$  50 years; (2) Post-bronchodilator FEV, < 80% predicted and FEV, /FVC ratio < 70%; (3) Subjects that had neither acute exacerbation nor systemic use of glucocorticosteroids in the past 4 weeks; (4) No history or diagnosis of bronchial asthma; and (5) Ex-smokers. Exclusion criteria included: (1) Subjects that had participated in the PR program before; (2) Complicated with respiratory failure; (3) Disorders involving pleural cavity, thoracic wall, bone and joint, or neurological or muscular system; (4) Subjects with history or previously diagnosed with major disorders including cardiac, hepatic, or renal disorders or tumors; (5) Psychological or cognitional abnormalities; and (6) Incompliance or refusal to sign informed consent. All patients signed informed consent before entering the study. This study was approved by the Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University (Protocol: 2010-36).

### Procedure

Patients were randomly assigned into one of the three groups: group A with novel breathing training, group B with diaphragmatic breathing training, and group C as control. The maneuver of novel breathing training consists of a fastforceful deep inspiration to total lung capacity, holding for a short period with total inspiratory time of 0.8~1.0 seconds, followed by a relaxed expiration for 3~4 seconds. The maneuver of diaphragmatic breathing for group B was as described in the literature. Breathing training was instructed and supervised by researchers in the hospital until the patient could follow the technique. Patients underwent a 15-minute training at home, 3 times a day, with a daily diary record for eight weeks. Group C was managed with stable pharmacological therapy and followed up for eight weeks. Measurements at baseline and post-training were as follows: mMRC scale of dyspnea, 6 minutes walking distance, pulmonary function, respiratory muscle strength (MIP and MEP), quality of life (St George's Respiratory Questionnaire, SGRQ), and BODE index.

# Pulmonary function test and respiratory muscle function

Pulmonary function was determined by forced spirometry. Bronchodilator tests were performed according to American Thoracic Society guidelines [5] with a PonyFX spirometer (COS-MED, Italy).

Maximal inspiratory pressures (MIP) and maximal expiratory pressures (MEP) were measured to evaluate respiratory muscle strength. MIP was measured with airway occlusion and maximal inspiration for  $\geq$  1.5 seconds (Mueller manoeuver) at FRC position and MEP was measured with maximal expiration (Valsalva manoeuvre) at TLC position.

### Quality of life

Quality of life was assessed by Saint George's Respiratory Questionnaire [6]. It consists of 76 items, divided into three domains. It measures symptoms, activity limitation, and social and emotional impact of disease. Each item is accorded a weight determined by the degree of distress according to each symptom or state described. SGRQ has a 100-point scale in which higher scores indicate poorer quality of life.

### Dyspnea assessment

Dyspnea was measured with the Modified Medical Research Council (mMRC) dyspnea scale [7]. Patients were asked about their perceived breathlessness. They were then classified into the five mMRC dyspnea grades (0 minimal to 4 maximum), according to how they perceived their disability.

an subjects				
	Group A (N=22)	Group B (N=23)	Group C (N=20)	Р
Age, yrs	65.18±6.25 66.52±6.90 67.55±7.50		67.55±7.50	0.538
Gender, M/F	21/1	23/0	19/1	0.489
BMI, kg/m²	20.60±3.99	21.09±3.33	20.22±3.03	0.715
FEV1 (L)	0.96±0.41	0.97±0.29	0.94±0.35	0.953
FEV1%pre	36.31±13.37	31±13.37 37.91±12.84 37.41±12.4		0.914
FEV <sub>1</sub> /FVC (%)	41.88±9.19	40.60±10.48	43.15±10.07	0.704
FVC (L)	2.26±0.57	2.40±0.46	2.22±0.74	0.572
IC (L)	1.68±0.42	1.86±0.37	1.59±0.43	0.112
PIF (L/s)	3.73±1.37	3.86±1.12	3.17±1.35	0.190
PEF (L/s)	3.22±1.52	3.15±1.11	2.62±0.93	0.231
MVV (L/min)	40.05±18.76	39.49±12.73	34.64±14.06	0.466
6-MWD (m)	424±101.77	437.30±69.44	411.70±90.37	0.636
mMRC	2.77±1.06	2.39±0.94	2.60±1.18	0.488
MIP (cmH <sub>2</sub> 0)	74.35±24.81	70.29±18.98	63.39±22.89	0.284
$MEP (cmH_2O)$	106.30±35.64	113.56±31.04	102.74±31.26	0.542
SGRQ				
Total score	47.81±14.09	44.56±12.42	48.35±19.05	0.673
Symptoms	57.81±15.05	58.26±13.79	53.70±21.33	0.631
Activity	66.00±21.98	58.52±16.98	69.20±24.19	0.237
Impact	35.13±13.72	33.17±13.71	35.30±18.85	0.879
BODE index	4.86±2.35	4.21±1.83	5.00±2.38	0.454

 
 Table 1. Demographics and baseline clinical characteristics of all subjects

BMI: body mass index; FEV1: forced expiratory volume in one second; FEV1%pre: forced expiratory volume in 1 s in percentage of predicted; FEV1/FVC: forced expiratory volume in one second to forced vital capacity; FVC: forced vital capacity; IC: inspiratory capacity; PIF: peak inspiratory flow; PEF: peak expiratory flow; MVV: maximal voluntary ventilation; 6-MWD: 6 minute walk distance; mMRC: Modified Medical Research Council Dyspnea Scale; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; SGRQ: St. George's Respiratory Questionnaire.

### Minute walking test

The 6 Minute Walking Test (6-MWT) was conducted following the recommendation of ATS [8] in a 60-m flat-surface corridor.

### BODE index

The BODE index, a multidimensional classification system, was calculated according to Celli et al. It is composed of four dimensions: body mass index (weight in kilograms divided by the square of the height in meters), degree of airflow obstruction (FEV<sub>1</sub> as percentage of prediction), level of functional dyspnea (mMRC), and exercise capacity (the best of two 6-MWT). Overall scores range from 0 to a maximum score of 10, with higher scores indicating greater mortality [9].

### Statistical analysis

Data were analyzed using the Statistical Package for the Social Sciences (Windows Release 13.0; SPSS; Chicago, IL). Paired t-test or paired rank sum test method was performed to compare pre- and post-study parameters. Quantitative variables are expressed as mean ± SEM. *P* values (two tailed) smaller than 0.05 indicate statistical significance.

### Results

## Baseline demographic and clinical characteristics

Demographic and clinical characteristics of the study groups are shown in Table 1. Figure 1 shows the flowchart of inclusion/exclusion and dropout of patients. Only those subjects that completed the study were included in the following analysis. There were no significant differences in baseline measurements, including average age, BMI, pulmonary function, exercise capacity, dyspnea, respiratory muscle strength, quality of life, and BODE index among the three groups (all P values > 0.05).

### Impact on dyspnea

mMRC scale declined significantly after 8 weeks, compared to baseline values in groups A and B (all P < 0.001). At the end of 8 weeks, no significant change was observed in mMRC scale in group C (P > 0.05).  $\Delta$ mMRC: Significant decrease (P < 0.01) was present in  $\Delta$ mMRC of groups A and B compared with that of group C, with no statistical differences being shown between groups A and B (P > 0.05) (**Tables 2**, **3**).

### Impact on exercise capacity

6-MWD increased significantly after 8 weeks, compared to baseline values in groups A and B (all P < 0.001). At the end of 8 weeks, no significant differences were observed in 6-MWD in

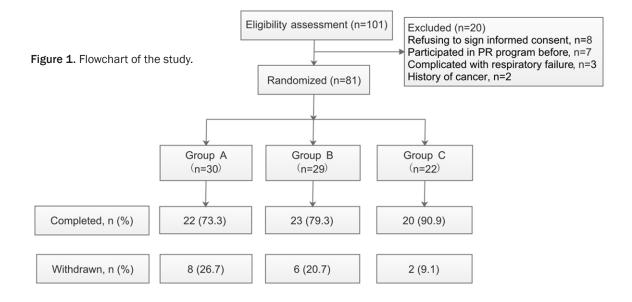


Table 2. Comparison of clinical parameters before and after 8 weeks in 3 study groups

Parameters -	Group A		Group B		Group C				
	Baseline	After 8 weeks	Р	Baseline	After 8 weeks	Р	Baseline	After 8 weeks	Р
BMI (kg/m²)	20.60±3.99	20.86±3.96	0.005	21.09±3.33	21.39±3.29	0.008	20.22±3.03	20.18±3.07	0.555
$\text{FEV}_1\%$ pred	36.31±13.37	37.50±13.31	0.131	37.91±12.84	38.37±14.14	0.662	37.41±12.41	36.96±12.25	0.272
6-MWD (m)	424±101.77	475.77±107.15	< 0.001	437.30±69.44	486.34±57.40	< 0.001	411.70±90.37	410.05±93.58	0.579
mMRC	2.77±1.06	1.90±0.75	< 0.001	2.39±0.94	1.52±0.89	< 0.001	2.60±1.18	2.60±1.27	0.869
MIP (cmH <sub>2</sub> 0)	74.35±24.81	85.20±22.59	< 0.001	70.29±18.98	80.26±19.32	< 0.001	63.39±22.89	63.64±22.70	0.892
MEP (cmH <sub>2</sub> 0)	106.30±35.64	129.60±39.07	< 0.001	113.56±31.04	127.98±32.61	< 0.001	102.74±31.26	102.05±30.66	0.873
SGRQ									
Total score	47.81±14.09	35.40±12.98	< 0.001	44.56±12.42	32.04±14.09	< 0.001	48.35±19.05	47.95±18.68	0.779
Symptoms	57.81±15.05	39.00±12.44	< 0.001	58.26±13.79	44.91±14.72	< 0.001	53.70±21.33	51.20±22.59	0.254
Activity	66.00±21.98	53.59±19.03	< 0.001	58.52±16.98	44.30±19.39	< 0.001	69.20±24.19	66.40±25.69	0.384
Impact	35.13±13.72	25.00±13.88	< 0.001	33.17±13.71	22.04±14.75	< 0.001	35.30±18.85	35.00±18.07	0.876
BODE index	4.86±2.35	3.86±1.78	< 0.001	4.21±1.83	3.21±1.73	< 0.001	5.00±2.38	4.90±2.55	0.428

BMI: body mass index; FEV1: forced expiratory volume in one second; FEV1%pred: forced expiratory volume in 1 s in percentage of predicted; 6-MWD: 6 minute walk distance; mMRC: Modified Medical Research Council Dyspnea Scale; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; SGRQ: St. George's Respiratory Questionnaire.

group C (P > 0.05).  $\Delta$ 6-MWD: a significant increase (P < 0.001) was present in  $\Delta$ 6-MWD of groups A and B compared with group C. No statistical differences were shown between groups A and B (P > 0.05) (**Tables 2, 3**).

### Impact on pulmonary function

(1) group A: IC and PIF increased significantly after 8 weeks, compared to baseline values (1.91 $\pm$ 0.56 L vs 1.68 $\pm$ 0.42 L; 4.45 $\pm$ 1.27 L/s vs 3.73 $\pm$ 1.37 L/s, respectively) (all *P* < 0.01). No significant changes (all *P* > 0.05) were found in other pulmonary function parameters, including FEV<sub>4</sub>, FEV<sub>4</sub>%pre, FEV<sub>4</sub>/FVC, FVC, PEF, and

MVV. (2) group B: IC was the only parameter with a significant increase after 8 weeks, compared to baseline values (2.10±0.34 L vs 2.10±0.34 L) (P < 0.01). No significant changes (all P > 0.05) were found in other pulmonary function parameters, including FEV<sub>1</sub>, FEV<sub>1</sub>%pre, FEV<sub>1</sub>/FVC, FVC, IF, PEF, and MVV. (3) group C: At the end of 8 weeks, no significant changes were observed in all pulmonary function parameters (all P > 0.05). (4) Comparison of changes in pulmonary function among the three groups: there were no significant differences in  $\Delta$ FEV<sub>1</sub>,  $\Delta$ FEV<sub>1</sub>%pre,  $\Delta$ FEV<sub>1</sub>/FVC,  $\Delta$ FVC,  $\Delta$ PEF, and  $\Delta$ MVV among the three groups (all P > 0.05).  $\Delta$ IC: Significant increase (P < 0.01) was present in

	Group A	Group B	Group C	Р
Δ6-MWD (m)	51.77±52.77*	49.04±63.11*	1.65±17.47	< 0.001
ΔmMRC	0.86±0.71*	0.86±0.69*	0.00±0.32	< 0.001
$\Delta MIP (cmH_2O)$	10.85±9.44*	9.96±9.59*	0.24±4.85	< 0.001
$\Delta MEP (cmH_2O)$	23.30±12.83*	14.41±21.28*	0.69±10.13	< 0.001
SGRQ				
ΔTotal score	12.40±6.52*	12.52±9.89*	0.40±6.28	< 0.001
ΔSymptom	18.81±18.61*	13.34±15.97*	2.50±9.50	0.004
ΔActivity	12.40±12.50*	14.21±15.20*	2.80±14.04	0.023
∆Impact	10.13±7.61*	11.13±10.83*	0.30±8.47	< 0.01

**Table 3.** Changes in exercise capacity, dyspnea, respiratory

 muscle function, and quality of life from baseline to week 8

\**P* < 0.001, compared with group C. 6-MWD: 6 minute walk distance; mMRC: Modified Medical Research Council Dyspnea Scale; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; SGRQ: St. George's Respiratory Questionnaire.

 $\Delta$ IC of groups A and B compared with that of group C, with no statistical differences shown between groups A and B (*P* > 0.05).  $\Delta$ PIF: Significant increase (*P* < 0.01) was present in  $\Delta$ PIF of group A compared with that of groups B and C (**Tables 2, 3**).

### Impact on respiratory muscle function

MIP and MEP increased significantly after 8 weeks, compared to baseline values in groups A and B (all P < 0.001). At the end of 8 weeks, no significant changes were observed in all variables of respiratory muscle function in group C (all P > 0.05).  $\Delta$ MIP: Significant increase (P < 0.001) was present in  $\Delta$ MIP of groups A and B compared with that of group C, with no statistical differences shown between group A and group B (P > 0.05).  $\Delta$ MEP had a similar outcome with  $\Delta$ MIP (**Tables 2, 3**).

### Impact on quality of life

SGRQ total scores decreased significantly after 8 weeks, compared to baseline values in groups A and B (all P < 0.001). At the end of 8 weeks, no significant changes were observed in all variables of quality of life in group C (P >0.05).  $\Delta$ SGRQ total score: Significant increase (P < 0.001) was present in  $\Delta$ SGRQ total score of groups A and B compared with that of group C, with no statistical differences shown between groups A and B (P > 0.05). SGRQ symptoms, activity, and impact scores had similar outcomes with SGRQ total score (**Tables 2**, **3**).

### Impact on BODE index

BODE index declined significantly after 8 weeks, compared to baseline values in groups A and B (all P < 0.001). At the end of 8 weeks, no significant change was observed in BODE index in group C (P > 0.05).  $\Delta$ BODE index: Significant decrease (P < 0.01) was present in  $\Delta$ BODE index of groups A and B compared with that of group C, with no statistical differences shown between groups A and B (P > 0.05) (**Tables 2**, **3**).

### Discussion

PR is an evidence-based, multidisciplinary, and comprehensive intervention for patients with chronic respiratory diseases that are symptomatic and often have decreased daily life activities. Comprehensive PR programs include patient assessment, exercise training, education, nutritional intervention, and psychosocial support. Integrated into the individualized treatment of patients, PR was designed to reduce symptoms, optimize functional status, increase participation, and reduce health-care costs. PR guidelines [4] treat exercise training as the core content of the entire PR plan. In PR treatment, respiration training is one of the important components. It is simple.

In previous evidence-based review documents, the guideline [4] panel concluded that the highest strength of evidence. They supported the recommendation for including lower and upper extremity exercise training as a key component of PR for patients with COPD. However, the effects of respiration training remain controversial and require more comprehensive research in the future. Empirical respiration training on COPD patients is not quality-controlled. The clinical efficacy lacks the basis of a multicenter, large sample, and randomized controlled trial study.

The self-designed novel breathing training use in this study is based on expiratory airflow limitation and impaired inspiratory muscle function in COPD patients with rapid deep inspiration and prolonged expiration (alleviate dynamic hyperinflation during breathing training). A prospective, randomized, and controlled study was conducted to compare the efficacy of these two breathing training methods (novel breathing training and traditional DB).

Exercise tolerance in patients with COPD is limited by impaired ventilatory capacity, partially due to the mechanical disadvantage of inspiratory muscles. It has been proposed that respiration training may improve ventilatory capacity of COPD patients and increase exercise performance in patients with COPD [10]. In the present study, 6-MWD increased significantly after 8 weeks, compared to baseline values in groups A and B, with no statistical differences between group A and B. Results suggest that both methods have good effects for improvement in exercise endurance. In most previous studies [11-14], it was found that FEV, was a poor predictor of exercise capacity. Recently, however, inspiratory capacity (IC) has been found to be more closely related to exercise tolerance than FEV<sub>1</sub>. This study demonstrates that the two training methods could improve IC. Thus, IC may play an important role in evaluating and improving exercise capacity in COPD patients. Moreover, it has been shown that exercise tolerance is correlated with the function of respiratory muscles and limb muscles. Wijkstra and co-workers [15] have shown that MIP was an important variable in determining exercise capacity in COPD patients with severe airway obstruction. This suggests that the function of respiratory muscles is related to exercise capacity. In this study, it was shown that respiratory muscle strength was improved in the training groups. Therefore, improvement of respiratory muscle function is one of the main reasons for increased exercise tolerance.

Many COPD patients are limited in their physical activity by dyspnea. Some COPD patients show decreased MIP, indicating respiratory muscle weakness. This weakness may contribute to the perception of dyspnea. Some studies have shown that dyspnea may be improved as a result of respiratory muscle training [16]. In the present study, mMRC scale declined significantly after 8 weeks, compared to baseline values in groups A and B. Results show that these two methods could improve the dyspnea symptom in COPD patients. Mechanisms behind this observation can be explained from two aspects: 1) Reducing dynamic hyperinflation (DH) and improving gas exchange ability.

In COPD patients, there may exist DH which acts as an inspiratory threshold load. In addition, the performance of the inspiratory pump is compromised by unfavorable length-tension properties of the inspiratory muscles. It follows that, to maintain ventilation, drive to the inspiratory muscles should be increased. Yan and co-workers [17] found that IC was more closely related to exercise tolerance and dyspnea than FEV<sub>1</sub> and forced vital capacity (FVC). The present results indicate that, in COPD patients, there was a greater increase of IC (reduced DH) after training in groups A and B, which closely correlates with the improvement in dyspnea sensation at rest. Furthermore, an increase in IC after bronchodilator administration implies a reduction in DH, as with breathing training [18].

2) Improving respiratory muscle function.

Respiratory muscle weakness contributes to the breathing task (PI/PImax) and increases the sensation of respiratory effort. According to previous studies [19], inspiratory muscle training may improve inspiratory muscle strength and lower the PI/PImax, thus probably diminishing the sensation of respiratory effort. Present results showed that changes in MIP ( $\Delta$ MIP) were positively associated with  $\Delta$ mMRC in group A (data not shown). This suggests that novel breathing training may result in the reduction in dyspnea by improvement of respiratory muscle function.

Gosker and co-workers [20] have demonstrated the involvement of increased proportions of hybrid I/IIA and IIA/IIX fiber types in the fibertype shift from I to IIX in the vastus lateralis of COPD patients. Another study [12] has shown that the external intercostal muscles of patients with COPD have the capacity to express structural remodeling after specific inspiratory training. Both the proportion of type I fibers and sizes of type II fibers were found to increase after training. These structural adaptations could partially explain functional improvements observed in trained muscles (increased inspiratory muscle strength and endurance) after specific training. In the present study, MIP and MEP increased significantly after 8 weeks, compared to baseline values in group A and B. Accordingly, both respiration training methods

(novel breathing training and traditional DB) can improve respiratory muscle function.

The basic principles of respiratory muscle training are overloaded specificity and reversibility. The novel breathing training, used in the present study, rested on a training incentive of sufficient intensity to produce a training effect (overload). The training used the same training modality (specificity). The reversibility principle states that the effects of conditioning decline after a training program. Hence, when patients finish in the training program, it is recommended that they continue performing breathing training regularly to maintain the obtained improvements.

No changes were observed for pulmonary function parameters (FEV<sub>1</sub>, FEV<sub>1</sub>%pre, FEV<sub>1</sub>/FVC), as has been the case in similar studies [16, 19, 21, 22]. Presence of lung hyperinflation is a frequent occurrence in patients with COPD, one that is easily recognized on the physical exam by the presence of barrel-shaped chest. Resting IC performed during pulmonary function testing mirrors the end-expiratory lung volume (EELV). Its decrease is taken to represent increased EELV. Significant increase was present in  $\Delta$ IC of groups A and B. Results demonstrate that both training methods can reduce EELV.

To guarantee optimal lung deposition of the medication, it is necessary to generate a certain inspiratory flow through the inhaler. The degree of the optimal flow depends on the internal airflow resistance of various DPIs. An inspiratory flow of 30 L/min [23] is enough for an optimal deposition of the drug in patient lungs, while an inspiratory flow of 60 L/min [24] is necessary to guarantee optimal deposition with the Turbuhaler.

Weiner and Weiner [25] found that inspiratory muscle training may improve inspiratory muscle strength as well as PIF in COPD patients. In the present research, significant increase was present in  $\Delta$ PIF of group A. Therefore, only novel breathing training could increase PIF, leading to adequate lung deposition of the drugs.

After training, COPD patients experienced an important improvement in their HRQL. SGRQ total scores and each category (symptoms, activity, and impact score) decreased significantly after 8 weeks in groups A and B, with no statistical differences shown between groups A and B. Therefore, results prove that both two breathing training skills could improve HRQL. These findings are consistent with previous studies [19, 26].

Although COPD is primarily characterized by the presence of airflow limitation, many systemic manifestations that accompany this disease can effectively signal an increased risk for mortality. Recognizing and quantifying these manifestations provides a more comprehensive assessment of disease severity and helps elucidate prognosis. Next, this paper will discuss the ability of the BODE multidimensional index, composed of body mass index (B), degree of airflow obstruction (O), level of functional dyspnea (D), and exercise capacity (E), to better stage COPD severity and monitor and assess its response to therapeutic interventions and to exacerbations [9]. Although PR has minimal effects on lung function, it improves dyspnea, exercise capacity, health status, and healthcare resource utilization. Two of these outcomes, dyspnea and exercise capacity, are components of the BODE index. Thus, the BODE index could be used to evaluate the effects of PR. Cote [20] defined one unit change in BODE as being clinically significant because it implies a change in any of its component of a magnitude large enough to influence clinical outcomes. Indeed, one-unit change in the mMRC predicts mortality. Likewise, one-unit change in the 6MWD of the BODE score far exceeds the 50m considered to be clinically significant changes for this test [27]. In the present study, BODE index declined significantly after 8 weeks, compared to baseline values in groups A and B. Similarly, COPD patients participating in breathing training improved the BODE index. This finding suggests that BODE is a valid tool to evaluate the integrated response to interventions.

This study had some limitations, however. First, few females were included. Thus, the findings from the current study may not be applicable to both sexes. Similar studies with a large group of females may be needed before conclusions can be extended to both sexes. Second, the duration of this study was not long enough to define the roles of breathing training.

In conclusion, this study demonstrates that breathing training could improve dyspnea, exer-

cise capacity, respiratory muscle function, and quality of life in patients with moderate to severe COPD. There were no significant differences between the novel breathing training and diaphragmatic breathing training. Results prove that novel breathing training is an effective rehabilitation method. It is easy for the patients to learn and seems appropriate for the physiological abnormalities of COPD patients and long-term home rehabilitation.

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### Disclosure of conflict of interest

None.

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### References

- [1] Vogelmeier CF, Criner GJ, Martinez FJ, Anzueto A, Barnes PJ, Bourbeau J, Celli BR, Chen R, Decramer M, Fabbri LM, Frith P, Halpin DM, Lopez VM, Nishimura M, Roche N, Rodriguez-Roisin R, Sin DD, Singh D, Stockley R, Vestbo J, Wedzicha JA and Agusti A. Global Strategy for the diagnosis, management, and prevention of chronic obstructive lung disease 2017 report: GOLD executive summary. Am J Respir Crit Care Med 2017; 195: 557-582.
- [2] Gosselink R, Troosters T and Decramer M. Peripheral muscle weakness contributes to exercise limitation in COPD. Am J Respir Crit Care Med 1996; 153: 976-980.
- [3] Bernard S, LeBlanc P, Whittom F, Carrier G, Jobin J, Belleau R and Maltais F. Peripheral muscle weakness in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1998; 158: 629-634.

- [4] Alison JA, McKeough ZJ, Johnston K, McNamara RJ, Spencer LM, Jenkins SC, Hill CJ, Mc-Donald VM, Frith P, Cafarella P, Brooke M, Cameron-Tucker HL, Candy S, Cecins N, Chan AS, Dale MT, Dowman LM, Granger C, Halloran S, Jung P, Lee AL, Leung R, Matulick T, Osadnik C, Roberts M, Walsh J, Wootton S and Holland AE; Lung Foundation Australia and the Thoracic Society of Australia and New Zealand. Australian and New Zealand pulmonary rehabilitation guidelines. Respirology 2017; 22: 800-819.
- [5] Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, Crapo R, Enright P, van der Grinten CP, Gustafsson P, Jensen R, Johnson DC, MacIntyre N, McKay R, Navajas D, Pedersen OF, Pellegrino R, Viegi G and Wanger J. Standardisation of spirometry. Eur Respir J 2005; 26: 319-338.
- [6] Jones PW, Quirk FH and Baveystock CM. The St George's respiratory questionnaire. Respir Med 1991; 85 Suppl B: 25-31, 33-37.
- [7] Celli BR and MacNee W. Standards for the diagnosis and treatment of patients with COPD: a summary of the ATS/ERS position paper. Eur Respir J 2004; 23: 932-946.
- [8] ATS statement: guidelines for the six-minute walk test. Am J Respir Crit Care Med 2002; 166: 111-117.
- [9] Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Mendez RA, Pinto Plata V and Cabral HJ. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med 2004; 350: 1005-1012.
- [10] Gosselink R, De Vos J, van den Heuvel SP, Segers J, Decramer M and Kwakkel G. Impact of inspiratory muscle training in patients with COPD: what is the evidence? Eur Respir J 2011; 37: 416-425.
- [11] Bauerle O, Chrusch CA and Younes M. Mechanisms by which COPD affects exercise tolerance. Am J Respir Crit Care Med 1998; 157: 57-68.
- [12] Murariu C, Ghezzo H, Milic-Emili J and Gautier H. Exercise limitation in obstructive lung disease. Chest 1998; 114: 965-968.
- [13] Diaz O, Villafranca C, Ghezzo H, Borzone G, Leiva A, Milic-Emil J and Lisboa C. Role of inspiratory capacity on exercise tolerance in COPD patients with and without tidal expiratory flow limitation at rest. Eur Respir J 2000; 16: 269-275.
- [14] Guenette JA, Chin RC, Cory JM, Webb KA and O'Donnell DE. Inspiratory capacity during exercise: measurement, analysis, and interpretation. Pulm Med 2013; 2013: 956081.
- [15] Wijkstra PJ, TenVergert EM, van der Mark TW, Postma DS, Van Altena R, Kraan J and Koeter

GH. Relation of lung function, maximal inspiratory pressure, dyspnoea, and quality of life with exercise capacity in patients with chronic obstructive pulmonary disease. Thorax 1994; 49: 468-472.

- [16] Lisboa C, Villafranca C, Leiva A, Cruz E, Pertuze J and Borzone G. Inspiratory muscle training in chronic airflow limitation: effect on exercise performance. Eur Respir J 1997; 10: 537-542.
- [17] Yan S, Kaminski D and Sliwinski P. Reliability of inspiratory capacity for estimating end-expiratory lung volume changes during exercise in patients with chronic obstructive pulmonary disease. Am J Respir Crit Care Med 1997; 156: 55-59.
- [18] Di Marco F, Milic-Emili J, Boveri B, Carlucci P, Santus P, Casanova F, Cazzola M and Centanni S. Effect of inhaled bronchodilators on inspiratory capacity and dyspnoea at rest in COPD. Eur Respir J 2003; 21: 86-94.
- [19] Sánchez Riera H, Montemayor Rubio T, Ortega Ruiz F, Cejudo Ramos P, Del Castillo Otero D, Elias Hernandez T, Castillo Gomez J. Inspiratory muscle training in patients with COPD: effect on dyspnea, exercise performance, and quality of life. Chest 2001; 120: 748-756.
- [20] Cote CG and Celli BR. Pulmonary rehabilitation and the BODE index in COPD. Eur Respir J 2005; 26: 630-636.
- [21] Ramirez-Sarmiento A, Orozco-Levi M, Guell R, Barreiro E, Hernandez N, Mota S, Sangenis M, Broquetas JM, Casan P and Gea J. Inspiratory muscle training in patients with chronic obstructive pulmonary disease: structural adaptation and physiologic outcomes. Am J Respir Crit Care Med 2002; 166: 1491-1497.

- [22] Weiner P, Magadle R, Beckerman M, Weiner M and Berar-Yanay N. Maintenance of inspiratory muscle training in COPD patients: one year follow-up. Eur Respir J 2004; 23: 61-65.
- [23] Frijlink HW and De Boer AH. Dry powder inhalers for pulmonary drug delivery. Expert Opin Drug Deliv 2004; 1: 67-86.
- [24] Engel T, Heinig JH, Madsen F and Nikander K. Peak inspiratory flow and inspiratory vital capacity of patients with asthma measured with and without a new dry-powder inhaler device (Turbuhaler). Eur Respir J 1990; 3: 1037-1041.
- [25] Weiner P and Weiner M. Inspiratory muscle training may increase peak inspiratory flow in chronic obstructive pulmonary disease. Respiration 2006; 73: 151-156.
- [26] Hill K, Jenkins SC, Philippe DL, Cecins N, Shepherd KL, Green DJ, Hillman DR and Eastwood PR. High-intensity inspiratory muscle training in COPD. Eur Respir J 2006; 27: 1119-1128.
- [27] Redelmeier DA, Bayoumi AM, Goldstein RS and Guyatt GH. Interpreting small differences in functional status: the six minute walk test in chronic lung disease patients. Am J Respir Crit Care Med 1997; 155: 1278-1282.