

Effect of Artificial Respiratory Muscle Training in Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Chronic obstructive lung disease (COPD) is a chronic lung pathology that leads to respiratory muscle weakness and decreased function capacity. Patients need to have pulmonary rehabilitation to increase respiratory muscle strength. The aim of the study was to assess the effect of artificial respiratory muscle training (ARMT) on respiratory muscle function and exercise performance in chronic obstructive pulmonary disease (COPD). Thirty patients in the mild to moderate COPD stage were randomly classified into an ARMT (n = 10), a control group (n = 10), and a standard respiratory muscle training group (SRMT; n = 10) by following the blind procedure. The control group received no training. The training groups, however, were trained at home for 30 min per day, every day, for 6 weeks. The measurement analyses included spirometry, an inspiratory muscle strength examination, and an exercise performance test. Exercise performance was evaluated by a 6 min walk test (SWT). The results showed that the maximal inspiratory pressure (P_{imax}) and the maximal expiratory pressure (P_E_{max}) were observed to have significantly increased in both the ARMT group and the SRMT group compared with the control group ($p < 0.05$). Moreover, the ARMT group was found to have significantly increased the 6 min walking distance in comparison with the control group. However, the ARMT group and the SRMT group did not differ significantly in those parameters. We conclude that it would be possible for the ARMT group among COPD patients to have improved respiratory muscle strength and increased capacity to walk.

Keywords: Chronic obstructive lung disease (COPD), inspiratory muscle training, exercise performance, lung function, 6 min walk test (SWT)

Introduction

Chronic obstructive pulmonary disease (COPD) ranks fifth among the causes of death worldwide. Emphysema and chronic bronchitis [1] cause characteristic pathologic changes in the lungs of individuals with the disease, including chronic airflow limitation, resistance to airflow, hyperinflation, and the associated inflammatory response of lungs (central airways, peripheral airways, lung parenchyma, and pulmonary vasculature). COPD decreases the respiratory muscle force, which leads to ventilation insufficiency and decreased oxygenation [2]. The main risk factor of COPD is tobacco smoking; other risk factors include inhalation of noxious particles and gases [3,4]. The imbalance of proteinases and antiproteinases leads to inflammation and oxidative stress, which leads to COPD pathology [5]. The physiological changes with regard to abnormality are mucous, hypersecretion, gas exchange, and

ventilation abnormalities [6]. Some studies have shown that the respiratory muscle has decreased maximal respiratory pressure [7]. Patients with COPD have respiratory muscle weakness and peripheral muscle weakness, which lead to dyspnea and reduced functional performance [8]. Therefore, respiratory training of patients is needed to improve muscle functions and reduce dyspnea. Several studies have shown that adequate respiratory muscle training stimulates functional performance [9-11]. The most proven effective respiratory muscle training (RMT) has been seen in resistance breathing to reduce the severity of breathlessness and to enhance the respiratory muscle function in patients with moderate-to-severe COPD [12,13].

Several studies have demonstrated that inspiratory muscle training increases the endurance and strength of the inspiratory muscle [14,15]. The most common technique for RMT is inspiratory muscle training, which helps muscle strength upon dyspnea in COPD. It promotes benefits such as improved pulmonary function and respiratory muscle strength, and helps in the reduction of dyspnea severity; it also affects improved exercise tolerance. However, it has its limitations, with regard to the cost of RMT; therefore, rural patients may find it hard to afford. Hence, the focus of interest of this study is on a new RMT instrument called artificial respiratory muscle training (ARMT), as shown in **Figure 1**, which is easy to use and is made from polyvinyl chloride.

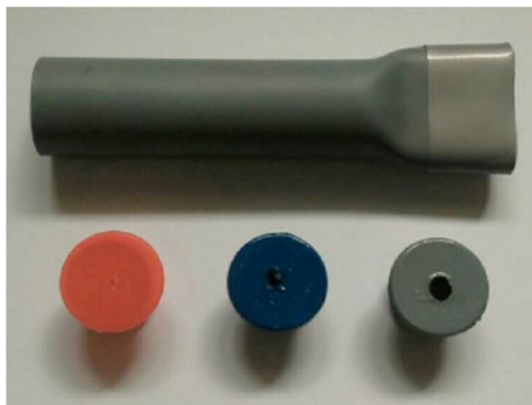


Figure 1 Artificial respiratory muscle strength (ARMT).

However, the main goals of pulmonary rehabilitation (PR) are to decrease the symptoms and to improve exercise performance [16]. Therefore, respiratory training is needed to enhance respiratory muscle function in order to improve function tolerance. It has been shown that respiratory training stimulates and adequately improves the capacity to exercise. In this study, we compare the effects of artificial inspiratory respiratory muscle training (ARMT) and standard RMT in the short term of a randomized controlled study in COPD subjects with a control group.

Materials and methods

Subjects

Patients of both sexes (15 men and 15 women) with mild to moderate and stable COPD, diagnosed by spirometry according to the American Thoracic Society [17], were included in this study, recruited from the outpatient Pulmonary clinic of Sansai hospital. They were all older than 40 years. The subjects who agreed to participate were in a clinically stable state, with no recent infective exacerbation or drugs. We had them randomly assigned to an RMT group or a control group. All were randomized into 3 groups, with the control group receiving breathing exercises, and the other groups receiving standard respiratory muscle training (SRMT) and ARMT. They were all observed during 6 weeks of run-in period. The

ARMT group began using the gray 6 mm instrument within the 1st to 2nd weeks, the blue 4 mm within the 3rd to 4th weeks, and the red 2 mm within the 5th to 6th weeks. In the paper, disease severity was defined according to the GOLD guidelines [18]. Studies that included individuals with additional comorbidities that would contribute to dyspnea, such as other lung diseases or heart dysfunction, and individuals using assisted ventilation, were excluded from this review. Patients with heart diseases, poor compliance, a requirement for supplemental oxygen therapy or CO₂ retention, or neurological or visual disorders, as well as patients who did not agree to participate in the study, were excluded [19,20]. Calculation was based on the study of G.power 3.0.10 in F-test (ANOVA repeated measurement within-between interaction) that determines clinically significant difference for P_{Imax} by considering the calculations performed by a previous study [21]; the results showed the effect size = 0.972 and power = 0.95, assuming an alpha error of 0.05 and a sample size of 9 subjects.

Their characteristics are summarized in **Table 1**. The results of the individual pulmonary function tests respiratory muscle strength and 6 min walk test are summarized in **Table 2**.

Table 1 General characteristic of patients.

Characteristics	Control group	SRMT group	ARMT group	p value
	n=10	n=10	n=10	
Sex				
M	5	5	5	NS
F	5	5	5	NS
Age (yr)	62.5±8.6	63.7±3.5	64.6±6.6	NS
Weight (kg)	59.4±15.1	52.9±11.4	52.7±16.0	NS
High (m)	1.64±0.1	1.55±0.1	1.59±0.1	NS
BMI (kg/m ²)	22.20±6.12	22.09±4.63	20.72±5.17	NS
FEV1 % predicted	62.22±4.47	62.68±4.31	62.64±2.67	NS

Note: Data has been checked with the Shapiro–Wilk test and showed normal distribution.

*Values are given as mean±SD. M=male; F=female; N.S.=not significant.

Table 2 Values of maximal expiratory pressure, maximal inspiratory pressure, lung function, and 6 min walking distance training before and at 4th and 6th week after standard respiratory muscle (SRMT) and artificial respiratory muscle training (ARMT).

Weeks	Control group (n=10)			ARMT group (n=10)			SRMT group (n=10)		
	0	4	6	0	4	6	0	4	6
PI _{max} ,cmH ₂ O	56.1±7.8	57.5±7.82	59.1±8.5	57.7±6.6	60.6±6.3	91.1±5.6*	56.1±6.4	59.9±6.2	92.4±3.1*
PE _{max} ,cmH ₂ O	83.7±6.4	83.3±7.4	85.4±6.6	84.6±4.4	86.9±5.3	104.4±5.5*	85.8±6.6	87.8±4.1	105.2±5.9*
FEV1/FVC%	61.7±3.7	62.9±4.12	62.3±4.7	61.5±2.1	62.7±3.6	67.0±1.1*	61.9±2.5	62.2±3.3	66.9±1.1*
6-min WD,m	289.5±19.5	284.2±17.4	285.6±19.3	287.7±25.7	299.1±21.9	375±24.5*	282.2±15.6	289.2±8.4	383.1±23.7*

Note: Definition of abbreviations: PE_{max}=maximal expiratory pressure, PI_{max} = maximal inspiratory pressure, FEV1 = forced expiratory volume 1, FVC = forced vital capacity, and 6-min WD = 6 min walking distance. The values are expressed as mean±SD. *p-value < 0.05. *The p-value was less than 0.05 when compared with the intragroup initial value.

Spirometry test

Standard forced expiratory spirometry was performed according to the American Thoracic Society guidelines, using an electronic spirometer (CHEST GRAPH HI-101, Tokyo, Japan). Spirometry was performed to obtain the effort (the best of 3) parameters having a percentage of forced expiratory volume in 1 s (FEV1), forced vital capacity (FVC), and the relation FEV1/FVC; these were measured 3 times.

Respiratory muscle strength

Respiratory muscle strength was assessed using the maximal inspiratory pressure (P_Imax) and the maximal expiratory pressure (P_Emax) by respiratory muscle strength scaled in cmH₂O (0 - 300 cmH₂O). The value obtained from the best of at least 3 efforts was used.

Six-min walk test

The distance that the patient was able to walk in 6 min was determined in a measured corridor. The 6MWT followed the recommendations from the American Thoracic Society guidelines [22]. The patients were given standardized instructions to walk as fast as possible for 6 min without running. The test was performed twice, and the results of the better distance walked were reported.

Training program

The subjects were trained daily, every day, with each session consisting of 30 min, for 6 weeks. All the groups received breathing exercise and coughing exercise training. ARMT and SRMT groups were trained for specific respiratory muscle strength using artificial respiratory training and standard respiratory training, respectively. They were tested by following parameters that included spirometry, respiratory muscle strength, and 6 MWT before, at 4 weeks, and at 6 weeks. On the first day, subjects received correct and clear training from experts in a hospital setting and then exercised by themselves at home following these training protocol. The researcher followed up by telephone and requested the subjects to record their adherence to this exercise in their log-book.

Data analysis

The values are expressed as mean±SD. The baseline and the post-training data were compared within the groups using the nonparametric (Wilcoxon) tests. Statistical analysis was carried out by repeated measure ANOVA and was followed by Post Hoc Dunnett's test. The level of significance was taken as $p \leq 0.05$.

Ethical approval

This study was approved by the Ethics Committee of the Faculty of Associated Medical Sciences, Chiang Mai University, in Thailand, with reference No. AMSEC-59EX-009.

Results and discussion

There were no significant differences between the 3 groups in terms of age and BMI at the start of the study. The general characteristics are shown in **Table 1**. The pulmonary function was performed by spirometry. The FVC and the FEV1 were measured 3 times, and the results of the best trial were reported. The results showed that after the study period at 4th weeks, there were no significant differences in the spirometry results compared with the control group (**Figure 2**). However, both ARMT and SRMT increased significantly in lung function compared with the control group. ARMT showed no significant difference in lung function compared with SRMT. These data suggested that ARMT improved lung function. Respiratory muscle strength was assessed by measuring the maximal inspiratory pressure (P_Imax) and the maximal expiratory pressure (P_Emax) at residual volume and total lung capacity, respectively, as previously described by Black and Hyatt [23]. The value obtained from the best of at least 3 efforts was used. In the artificial respiratory muscle training group, the peak P_Imax increased from 57.7±6.6 to 91.1±5.6 cmH₂O, and P_Emax increased from 84.6±4.4 to 104.4±5.5 cmH₂O after training ($p < 0.05$) and was significantly different from that of the control group (**Figure 3**). However, it was not

different from the standard RMT. The differences between the 2 groups after the training were significant ($p < 0.05$), as shown by the mean values. These data suggested that ARMT increased inspiratory muscle strength. The distance test was for the distance covered in walking for 6 min (6 min walk test). The test was performed twice, and the best result was reported. There was no significant difference between the 3 groups in 2 and 4 weeks as compared to the observations before the study. However, in 6 weeks, it was found that there was a significant increase in the mean walking distance in 6 min in the SRMT and ARMT compared with the control and before the study, while the control group was found to show no changes. The results are presented in **Figure 4**; there was no statistically significant difference between the ARMT and the SRMT groups.

This study shows that home-based RMT with ARMT and SRMT improved respiratory muscle function and exercise performance with significant difference in COPD patients. COPD rehabilitation is important in COPD patients for improving respiratory muscle strength by respiratory training [24]. Our results in the COPD mild stage show that home-based ARMT significantly improved lung function, respiratory muscle strength, and exercise performance compared with the control group. In addition, in this study, ARMT was studied in COPD patients who were diagnosed to be in the mild stage and who were not different in characteristics such as sex, age, and BMI, as demonstrated in **Table 1**, and lung volume (FEV1 and FEV1/FVC ratio), as presented in **Figure 2**. The baseline characteristics of the 3 groups were similar. The SRMT results show no significant difference in the results of ARMT in the parameters, including lung function, respiratory muscle strength, and exercise performance. In accordance with the findings of the study of Ramirez-Sarmiento *et al.* [20], it was observed that SRMT increased specific inspiratory muscle training strength and lung function. SRMT is the common standard for respiratory muscle strength training, but it is expensive. Therefore, people in rural areas find it difficult to afford. There have been several studies in SRMT that have shown that SRMT was a part of the training done by COPD patients over 4 weeks, 5 weeks, and 8 weeks, at 3 - 7 times per week [25-27]. It could be useful in improving lung function, respiratory muscle activity, and exercise performance [24,28]. Moreover, in the present study, it was observed that, at 0 - 4 weeks, the results were not different when compared with the other groups. However, the ARMT group showed improved lung function and muscle strength at 6 weeks. Decrease in lung function and respiratory muscle strength leads to decrease in exercise performance [29]. In the study by Weiner and coworkers [30], COPD patients were found to have increased P_{Imax}, which was significantly greater in the respiratory muscle training group than in the control group. In addition, this shows that the ARMT group specifically improved the respiratory muscle strength associated with increased exercise performance. However, the pulmonary function parameters were found to be similar in the studies. They assumed the thesis utilized in this study. In the trained device group, increased P_{Imax} was observed, and the control demonstrated no effect of the training on its P_{Imax} values. Regarding the clinical significant of the function main outcome, the improvement shown in the 6 min walk test also reached the minimal clinical important difference (MCID) of greater than 30.5 meters. It supported meaningful change in the clinical situation of a COPD clinical trial [31].

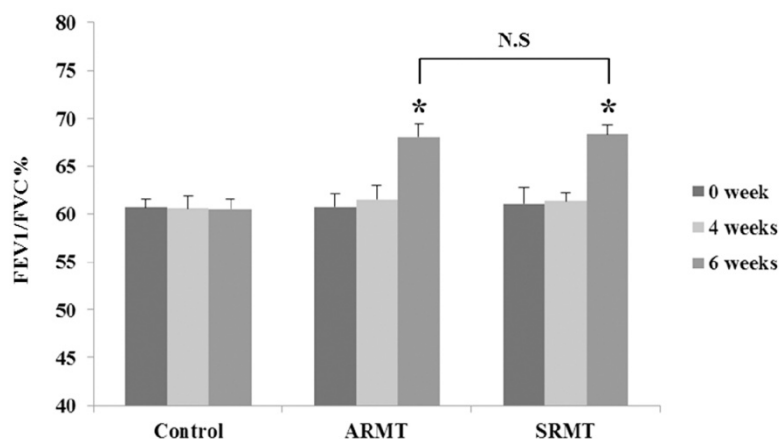


Figure 2 Lung function, as assessed by spirometry, before and following the training period over 4 and 6 weeks. *The *p*-value was less than 0.05 when compared with the intragroup initial value; “N.S” refers to non-significant difference between groups.

Exercise performance was found to have increased in the ARMT group for the mild stage COPD patients because it may have helped to improve daily activity performance and the quality of life [32]. Short periods (6 - 9 weeks) increase the maximum inspiratory muscle [33] in inspiratory muscle training, which is evident in the ARMT group as compared to the control group. Lisboa and coworkers [26] reported that the results after training using SRMT demonstrated that there was significant increase in the P_Imax value and in the 6 min walking distance. In a study by Beaumont and coworkers [34], the COPD subjects were found to have increased P_Imax after training using SRMT. In this study, it was shown that the P_Imax value in both the SRMT group and the ARMT group increased significantly when compared with the control group. These data present that ARMT could be helpful in improving respiratory muscle performance. Moreover, the training group was found to increase significantly in P_Emax value, by an amount much greater than that of the control group. This may be because of improved expiratory muscle strength. Furthermore, it also clearly demonstrated that ARMT can be useful in improving lung function, respiratory muscle strength, and exercise performance. The 6 min walking distance increased in the ARMT group and was significant in comparison with the control group. This study has shown that ARMT allows respiratory muscle strength training by improving the respiratory muscle and exercise performance in COPD patients. Evidence shows that respiratory muscle weakness in COPD leads to dyspnea and limits exercise tolerance significantly in COPD patients [35]. In the present study, ARMT was also found to increase exercise performance. The 6 min walking distance of the ARMT group increased significantly in comparison with the control group. Scherer and coworkers [27] reported that home-based respiratory muscle training significantly improves the 6 min walking distance.

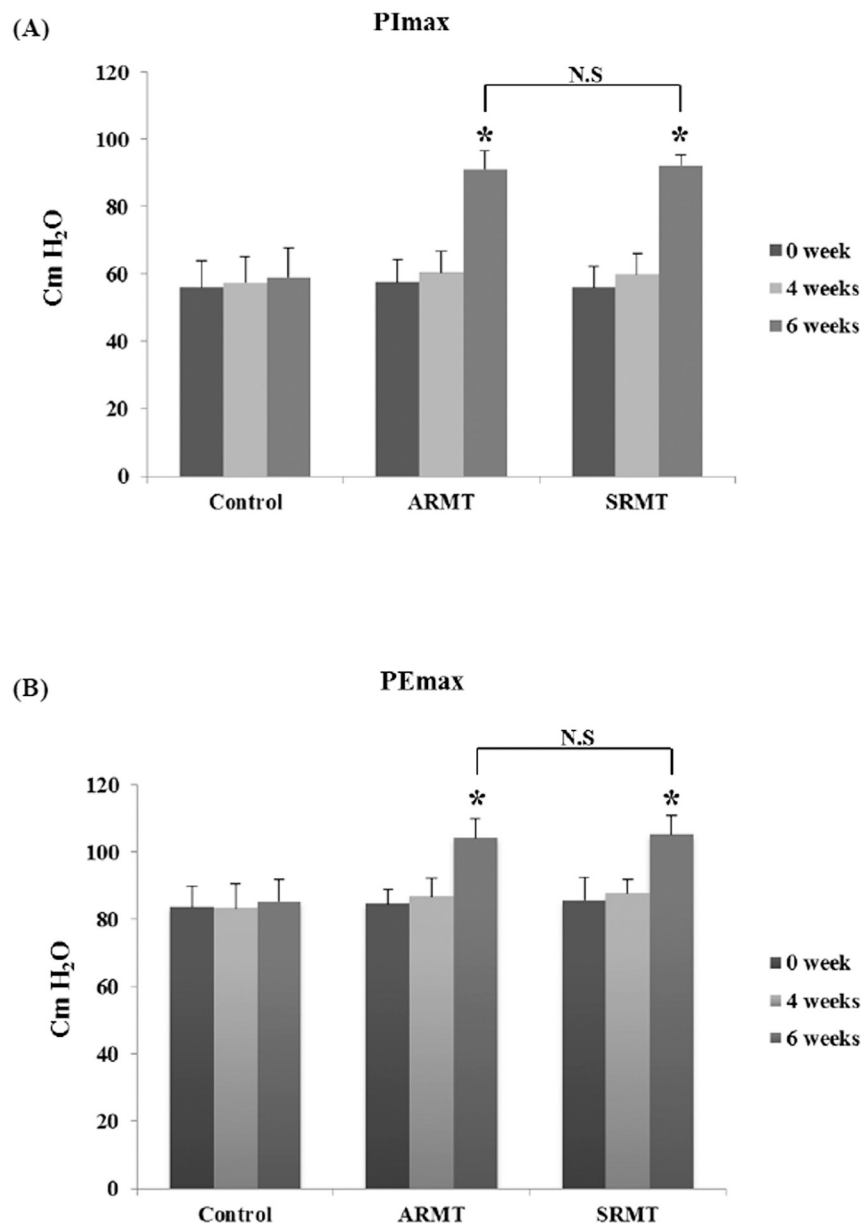


Figure 3 Respiratory muscle strength, as assessed by PEmax (A) and PImax (B), before and following the training period over 4 and 6 weeks. *The *p*-value was less than 0.05 when compared with the intragroup initial value; “N.S.” refers to non-significant difference between groups.

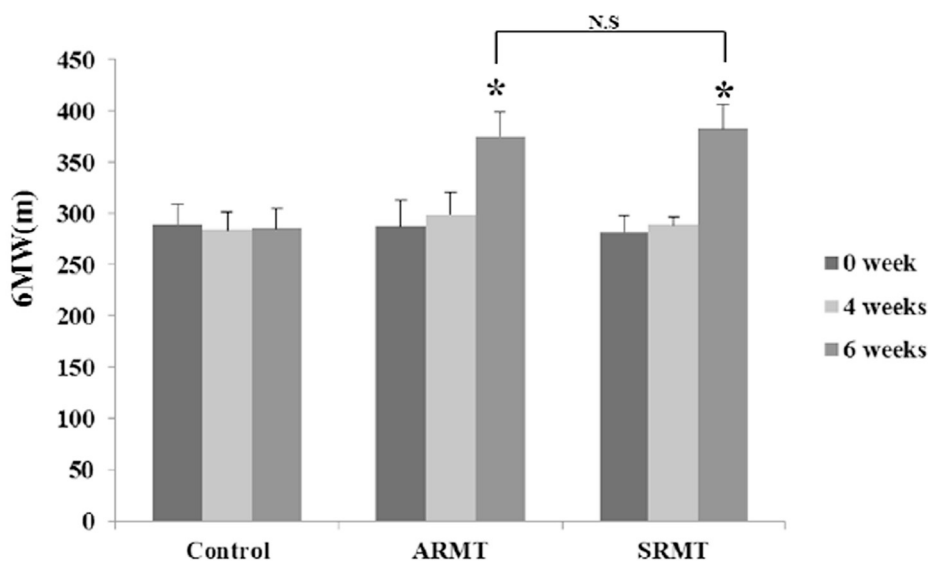


Figure 4 Distance walked in 6 min before and following the training period over 4 and 6 weeks; 6 MW = 6 min walk. *The *p*-value was less than 0.05 when compared with the intragroup initial value; “N.S” refers to non-significant difference between groups.

Conclusions

In the present study, it has been shown that ARMT training can be specifically used to train the respiratory muscle in COPD patients by increasing respiratory muscle strength, similar to SRMT. Respiratory muscle strength was observed to have increased the 6 min walking distance significantly in comparison with the control group. Therefore, ARMT allows respiratory muscle strength training by improving the respiratory muscle, and exercise performance in COPD patients. A new portable training device was used in the study. It is recommended that ARMT be considered in pulmonary rehabilitation programs in order to improve respiratory muscle strength.

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References

- [1] DE O'Donnell, P Hernandez, A Kaplan, S Aaron, J Bourbeau, D Marciniuk, M Balter, G Ford, A Gervais, Y Lacasse, F Maltais, J Road, G Ricker, D Sin, T Sinuff and N Voduc. Canadian thoracic society recommendations for management of chronic obstructive pulmonary disease: 2008 update - highlights for primary care. *Can. Respir. J.* 2008; **15**, 1A-8A.
- [2] H Sahin, Y Varol, I Naz, N Aksel, F Tuksavul and A Ozsoz. The effect of pulmonary rehabilitation on COPD exacerbation frequency per year. *Clin. Respir. J.* 2018; **12**, 165-74.
- [3] R Rodriguez-Roisin and W MacNee. Pathophysiology of chronic obstructive pulmonary disease. *Eur. Respir. Mono.* 1998; **3**, 107-26.
- [4] GOLD. From the Global Strategy for the Diagnosis, Management and Prevention of COPD. Global Initiative for Chronic Obstructive Lung Disease, Available at: <http://www.goldcopd.org>, accessed April 2017.
- [5] RM Tuder and I Petrache. Pathogenesis of chronic obstructive pulmonary disease. *J. Clin. Invest.* 2012; **122**, 2749-55.
- [6] JE Repine, A Bast and I Lankhorst. Oxidative stress in chronic obstructive pulmonary disease. Oxidative stress study group. *Am. J. Respir. Crit. Care Med.* 1997; **156**, 341-57.
- [7] HJ Kabitz, S Walterspacher, D Walker and W Windisch. Inspiratory muscle strength in chronic obstructive pulmonary disease depending on disease severity. *Clin. Sci.* 2007; **113**, 243-9.
- [8] J Singer, EH Yelin, PP Katz, G Sanchez, C Iribarren, MD Eisner and PD Blanc. Respiratory and skeletal muscle strength in chronic obstructive pulmonary disease: Impact on exercise capacity and lower extremity function. *J. Cardiopulm. Rehabil. Prev.* 2011; **31**, 111-9.
- [9] H Chen, R Dukes and BJ Martin. Inspiratory muscle training in patients with chronic obstructive pulmonary disease. *Am. Rev. Respir. Dis.* 1985; **131**, 251-5.
- [10] R Gosselink, J De Vos, SP van den Heuvel, J Segers, M Decramer and G Kwakkel. Impact of inspiratory muscle training in patients with COPD: What is the evidence? *Eur. Respir. J.* 2011; **37**, 416-25.
- [11] A Marques, C Jácome, J Cruz, R Gabriel and D Figueiredo. Effects of a pulmonary rehabilitation program with balance training on patients with COPD. *J. Cardiopulm. Rehabil. Prev.* 2015; **35**, 154-8.
- [12] G Sturdy, D Hillman, D Green, S Jenkins, N Cecins and P Eastwood. Feasibility of high-intensity, interval-based respiratory muscle training in COPD. *Chest* 2003; **123**, 142-50.
- [13] JI Kang, DK Jeong and H Choi. The effects of breathing exercise types on respiratory muscle activity and body function in patients with mild chronic obstructive pulmonary disease. *J. Phys. Ther. Sci.* 2016; **28**, 500-5.
- [14] D Nikolettou, WD Man, N Mustfa, J Moore, G Rafferty, RL Grant, L Johnson and J Moxham. Evaluation of the effectiveness of a home-based inspiratory muscle training programme in patients with chronic obstructive pulmonary disease using multiple inspiratory muscle tests. *Disabil. Rehabil.* 2016; **38**, 250-9.
- [15] FD Dias, LM Sampaio, GA da Silva, ÉL Gomes, ES do Nascimento, VL Alves, R Stirbulov and D Costa. Home-based pulmonary rehabilitation in patients with chronic obstructive pulmonary disease: A randomized clinical trial. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2013; **8**, 537-44.
- [16] L Nici and R ZuWallack. Chronic obstructive pulmonary disease-evolving concepts in treatment: Advances in pulmonary rehabilitation. *Semin. Respir. Crit. Care Med.* 2015; **36**, 567-74.
- [17] American Thoracic Society. Standard for the diagnosis and care of patients with COPD. *Am. J. Respir. Crit. Care Med.* 1995; **152**, 78-121.
- [18] Global Initiative for Chronic Obstructive Lung Disease, Inc. Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease, Available at: http://www.goldcopd.org/uploads/users/files/GOLD_Report_2013_Feb20.pdf, accessed May 2013.
- [19] HS Riera, TM Rubio, FO Ruiz, PC Ramos, DDC Otero, TE Hernandez and JC Gomez. Inspiratory muscle training in patients with COPD: Effect on dyspnea, exercise performance, and quality of life. *Chest* 2001; **120**, 748-56.

- [20] A Ramirez-Sarmiento, M Orozco-Levi, R Guell, E Barreiro, N Hernandez, S Mota, M Sangenis, JM Broquetas, P Casan and J Gea. Inspiratory muscle training in patients with chronic obstructive pulmonary disease: Structural adaptation and physiologic outcomes. *Am. J. Respir. Crit. Care Med.* 2002; **166**, 1491-7.
- [21] R Magadle, AK McConnell, M Beckerman and P Weiner. Inspiratory muscle training in pulmonary rehabilitation program in COPD patients. *Respir. Med.* 2007; **101**, 1500-5.
- [22] ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories. ATS statement: Guidelines for the six-minute walk test. *Am. J. Respir. Crit. Care Med.* 2002; **166**, 111-7.
- [23] LF Black and RE Hyatt. Maximal respiratory pressures: Normal values and relationship to age and sex. *Am. Rev. Respir. Dis.* 1969; **99**, 696-702.
- [24] F Lötters, B van Tol, G Kwakkel and R Gosselink. Effects of controlled inspiratory muscle training in patients with COPD: A meta-analysis. *Eur. Respir. J.* 2002; **20**, 570-6.
- [25] AV Ovechkin, DG Sayenko, EN Ovechkina, SC Aslan, T Pitts and RJ Folz. Respiratory motor training and neuromuscular plasticity in patients with chronic obstructive pulmonary disease: A pilot study. *Respir. Physiol. Neurobiol.* 2016; **229**, 59-64.
- [26] C Lisboa, V Munoz, T Beroiza, A Leiva and E Cruz. Inspiratory muscle training in chronic airflow limitation: Comparison of two different training loads with a threshold device. *Eur. Respir. J.* 1994; **7**, 1266-74.
- [27] TA Scherer, CM Spengler, D Owassapian, E Imhof and U Boutellier. Respiratory muscle endurance training in chronic obstructive pulmonary disease: Impact on exercise capacity, dyspnea, and quality of life. *Am. J. Respir. Crit. Care Med.* 2000; **162**, 1709-14.
- [28] P Weiner, R Magadle, M Beckerman, M Weiner and N Berar-Yanay. Comparison of specific expiratory, inspiratory, and combined muscle training programs in COPD. *Chest* 2003; **124**, 1357-64.
- [29] RL Pardy and DE Leith. Ventilatory muscle training. *RespirCare* 1984; **29**, 278-84.
- [30] P Weiner and A McConnell. Respiratory muscle training in chronic obstructive pulmonary disease: Inspiratory, expiratory, or both? *Curr. Opin. Pulm. Med.* 2005; **11**, 140-4.
- [31] RW Bohannon and R Crouch. Minimal clinically important difference for change in 6-minute walk test distance of adults with pathology: A systematic review. *J. Eval. Clin. Pract.* 2017; **23**, 377-81.
- [32] ES do Nascimento, LM Sampaio, FS Peixoto-Souza, FD Dias, EL Gomes, FR Greiffo, AP Ligeiro de Oliveira, R Stirbulov, RP Vieira and D Costa. Home-based pulmonary rehabilitation improves clinical features and systemic inflammation in chronic obstructive pulmonary disease patients. *Int. J. Chron. Obstruct. Pulmon. Dis.* 2015; **10**, 645-53.
- [33] LM Romer and AK McConnell. Specificity and reversibility of inspiratory muscle training. *Med. Sci. Sports Exerc.* 2003; **35**, 237-44.
- [34] M Beaumont, P Mialon, C Le Ber-Moy, C Lochon, L Péran, R Pichon, C Gut-Gobert, C Leroyer, C Morelot-Panzini and F Couturaud. Inspiratory muscle training during pulmonary rehabilitation in chronic obstructive pulmonary disease: A randomized trial. *Chron. Respir. Dis.* 2015; **12**, 305-12.
- [35] DF Rochester and NT Braun. Determinants of maximal inspiratory pressure in chronic obstructive pulmonary disease. *Am. Rev. Respir. Dis.* 1985; **132**, 42-7.