

Research Article

Effect of Expiration Muscle Exercise Using Positive Expiratory Pressure in Chronic Obstructive Pulmonary Disease

Nury Nusdwiningtyas^{1*}, Okta Hariza¹, Peggy Sunarjo¹, Kevin Triangto¹, Telly Kamelia² and Aria Kekalih³

¹Department of Physical Medicine and Rehabilitation, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia

²Department of Internal Medicine, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia

³Department of Community Medicine, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia

Abstract

In this COVID-19 pandemic era, it is important to obtain objective expiratory muscle strength measurement in Chronic Obstructive Pulmonary Disease patients (COPD). Previous studies have shown that exercise using a Positive Expiratory Pressure (PEP) device can improve expiratory muscle strength and clinical condition. The aim of this study was to assess the effectiveness of PEP expiratory muscle exercise in patients with COPD. This study utilized a one-group Pre-test-Post-test design, and all recruited subjects were COPD patients. Expiratory muscle exercise using the PEP device was carried out twice per day for 15 minutes per session as a home therapy program for eight weeks. The outcomes were Maximal Expiratory Pressure (MEP), Maximal Inspiratory Pressure (MIP), 6-minute walking distance (6 MWD) test, and St George Respiratory Questionnaire (SGRQ) total score; all tests were conducted before the intervention and then evaluated every two weeks. The data were analyzed using a paired sample t-test and Wilcoxon's test. Twelve male subjects with mean age of 63.33 ± 9.61 years were recruited for this study. Some significant improvement were observed in MIP ($P=0.01$), MEP ($P=0.04$), walking distance ($P=0.08$), and SGRQ total score ($P=0.012$) after the intervention, indicating that exercise using a PEP device can result in overall improvement in COPD symptoms. In particular, an improvement in expiratory and inspiratory muscle strength

***Corresponding author:** Nury Nusdwiningtyas, Department of Physical Medicine and Rehabilitation, Faculty of Medicine Universitas Indonesia/Dr. Cipto Mangunkusumo General Hospital, Jakarta, Indonesia, E-mail: nury_nus@yahoo.com

Citation: Nusdwiningtyas N, Hariza O, Sunarjo P, Triangto K, Kamelia T, Kekalih A (2021) Effect of Expiration Muscle Exercise Using Positive Expiratory Pressure in Chronic Obstructive Pulmonary Disease. J Phys Med Rehabil Disabil 7: 63.

Received: May 01, 2021; **Accepted:** May 14, 2021; **Published:** May 21, 2021

Copyright: © 2021 Nusdwiningtyas N, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

was attained even when resistance was focused only on expiratory muscles. In this COVID-19 pandemic era, home therapy programs with PEP devices may serve as alternatives to clinical programs for patients with COPD.

Keywords: Chronic obstructive pulmonary disease; Maximal expiratory pressure; Maximal inspiratory pressure; Positive expiratory pressure; Six-minute walking distance

Introduction

Chronic Obstructive Pulmonary Disease (COPD) currently imposes a substantial mortality and morbidity burden worldwide [1,2]. The estimates in 2010 were that 328 million people had COPD worldwide, with the majority of cases found in low- and middle-income countries [3]. In COPD, disorders of the airway or alveoli cause disruption to the expiratory flow, resulting in air trapping and the pathognomonic hyperinflation associated with COPD [1]. This arises because people with COPD experience dyspnea due to difficult expiration, so they do not have time to complete their exhalation. People with severe cases of COPD show elevated functional residual capacity as one of the spirometry characteristics. Consequently, they inhale more air than they exhale and, over time, they increase their end-expiratory lung volume in the process referred to as dynamic hyperinflation [4]. Some patients can perform Pursed Lips Breathing (PLB) on their own as a positive pressure breathing technique to overcome the hyperinflation, and numerous Positive Expiratory Pressures (PEP) devices (Flutter®, Acapella®, and RC Cornet®) have been developed recently [5,6]. PEP exercise is one breathing (expiration) exercise against resistance that can be performed either through a device or through pursed lips. This kind of exercise can be prescribed for a patient with a pulmonary disorder, a neurologic disorder, or a preoperative indication [5]. The objectives of using this type of assistive device are to improve ventilation, assist airway clearance, prevent recurring infections and atelectasis, improve pulmonary clearance mechanisms, and facilitate gas exchange, thereby lowering the impact of the disease progression [6]. The use of these devices has been widely accepted because of their clinical efficacy and the high level of acceptance and compliance by patients. These features make PEP devices very useful in home exercises, especially during this pandemic of COVID-19 [7-9].

To the authors' knowledge, this is the first study conducted in Indonesia, a developing country with an increasing number of COPD cases. Indonesia has unique geographical characteristics that create difficulties in access to health facilities. The aim of this study was to demonstrate the effectiveness of home exercise by adding PEP to the training regimen COPD cases. The findings presented here are also expected to guide readers in other developing countries with high populations and difficult access to the health facilities to choose assistive devices for breathing exercises. The authors believe that the use of a simple yet inexpensive device to train expiratory muscles would be practical solution for reducing disability in patients with COPD.

Materials and Methods

The study was set up as a one-group Pretest-Post-test Design to analyze the effect of PEP by comparing the expiratory muscle strength,

using the 6-minute walking distance (6MWD) test, and St George Respiratory Questionnaire (SGRQ) scores, before and after the intervention. The subjects were patients with COPD being treated at the Cipto Mangunkusumo General Hospital outpatient clinic. The subjects were recruited using a purposive sampling method. The study was approved by Ethical Committee Faculty Medicine of Universities Indonesia no. 0374/UN2.F1/ETIK/2018. The inclusion criteria for the subjects were (1) age ≥ 40 years old; (2) meeting the diagnosis criteria based on Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2020; (3) ability to correctly perform breathing exercises using PEP with a routine that can be seen in their exercise diary; and (4) no other exercise program. The exclusion criteria were (1) a cardiac disease, asthma, or uncontrolled metabolic disorder (based on anamnesis and physical examination); (2) a risk of pneumothorax or a rib fracture; (3) pain in a lower extremity with a visual analog scale score ≥ 7 ; (4) limited range of motion and leg length discrepancy; (5) a history of unstable angina pectoris or myocardial infarction in the last 2 months; (6) systolic blood pressure > 180 mmHg; (7) diastolic blood pressure > 100 mmHg; and [8] resting heart rate > 120 beats/minute. The intervention of exercise using a PEP assistive device was prescribed as a home program therapy. To perform this exercise, the subjects sit upright with their elbows resting on a table to maintain the over distention. The exercise can be started by slow inspiration until the tidal capacity has been reached, and then the subjects perform a breath hold for 2-3 seconds. The dosage of resistance is an inspiration to expiration ratio of 1:3; the subjects are then asked to perform huffing and coughing to expel the mucus. This exercise can be repeated for 10-15 repetitions in normal respiration. The subjects are then asked to rest for 5-10 expirations before starting the next cycle. The frequency of the exercise is twice a day for 15 minutes for eight weeks. Follow-up was performed every two weeks in the Respiratory Rehabilitation Clinic, with the dosage of resistance adjusted to the present state and re-evaluated every two weeks. Initially, the subjects were examined using spirometry to diagnose the lung function. Expiratory muscle strength was measured with Micro RPM. The final two procedures namely 6MWD was done to measure functional capacity, and SGRQ were performed to evaluate quality of life. All the data were analyzed using the Statistical Package for Social Sciences (SPSS) version 20.0. Any comparison was regarded as statistically significant when $p < 0.05$.

Results

Twenty-five subjects were involved in this study. Nine subjects dropped out because of the distance from the hospital to their residences. The remaining 16 subjects consisted of 12 males and 4 females, and all finished all the sessions. Because of the differences in body height and the small sample of female subjects (4 subjects) versus male subjects, the authors only analyzed the data obtained from the male subjects. Table 1 illustrates the descriptive data; where most of the subjects were elderly with a normal body mass index. The mean expiratory muscle strength was $69.83 (\pm 29.88)$ cm H₂O. The mean walking distance was 324.25 ± 112.66 meters. The mean SGRQ score was 47.05 ± 21.11 for the symptoms, 57.72 ± 29.33 for the activity, 37.29 ± 23.34 for the impact, and 44.98 ± 23.07 for the total. Expiratory muscle strength is illustrated in table 2, and highlights the effect of PEP exercise over the eight-week period. An improvement in the expiratory muscle strength was evident even after two weeks of intervention. The mean expiratory muscle strength before the intervention was $69.83 (\pm 29.88)$ cm H₂O and this increased to highest mean expiratory muscle strength of 99.00 ± 36.99 cm H₂O after 8 weeks of intervention; this increase was statistically significant ($P = 0.004$).

Subjects Characteristics	n = 12
Age (years)	63.33 \pm 9.61
Body Weight (kg)	67.44 \pm 12.98
Body Height (cm)	162.66 \pm 5.19
Body Mass Index (BMI)	25.65 \pm 5.34
FEV1 percent prediction	57.34 \pm 25.20
FVC percent prediction	59.07 \pm 17.46
FEV1 percent	73.26 \pm 14.82
Maximal Expiratory Pressure (cm H ₂ O)	69.83 \pm 29.88
Six Minute Walking Distance (meter)	324.25 \pm 112.66
SGRQ	
- Symptom	47.05 \pm 21.11
- Activity	57.72 \pm 29.33
- Impact	37.29 \pm 23.34
Total	44.98 \pm 23.07

Table 1: Subjects Characteristics.

Maximum Expiratory Pressure (CmH ₂ O)	n	Mean \pm SD	P Value
Pre-	12	69.83 \pm 29.88	
2 weeks post intervention	12	81.92 \pm 25.69	0.035
4 weeks post intervention	12	85.42 \pm 23.69	0.027
6 weeks post intervention	12	88.58 \pm 34.41	0.036
8 weeks post intervention	12	99.00 \pm 36.99	0.004

Table 2: Maximum Expiratory Pressure.

Conversely, table 3 shows the impact of the exercise on inspiratory muscle strength. Similar significant improvements were seen to those observed for the expiratory muscle strength. The baseline inspiratory strength was 52.17 ± 21.91 cm H₂O, and this improved to 60.75 ± 22.06 cm H₂O after two weeks. The final measurement after eight weeks was 68.92 ± 21.63 cm H₂O, and the difference was statistically significant compared to the baseline ($p < 0.05$).

Maximum Inspiratory Pressure (CmH ₂ O)	n	Mean \pm SD	P Value
Pre-	12	52.17 \pm 21.91	
2 weeks post intervention	12	60.75 \pm 22.06	0.035
4 weeks post intervention	12	60.17 \pm 20.84	0.027
6 weeks post intervention	12	66.58 \pm 24.92	0.036
8 weeks post intervention	12	68.92 \pm 21.63	0.004

Table 3: Maximum Inspiratory Pressure.

Functional capacity as evaluated based on the 6MWD results (Table 4). Improvement in the walking distance was noted every two weeks after the intervention. The mean walking distance before the intervention was $324.25 (\pm 112.66)$ meters, and after eight weeks of the intervention, the mean walking distance was $396.10 (\pm 107.19)$ meters. Statistical analyses showed significant differences in the mean walking distances at every two-week evaluation. Health-related quality of life (HRQL) using the SGRQ is shown in table 5. All values clearly indicate improvement from the baseline, and the differences were statistically significant.

Six Minute Walking Distance	n	Mean ± SD	P-Value	ΔWalking Distance (meters)
Pre-	12	324.25 ± 112.66		
2 weeks post intervention	12	369.3 ± 102.60	0.049	45.05
4 weeks post intervention	12	389.5 ± 83.27	0.016	65.25
6 weeks post intervention	12	350.6 ± 138.64	0.259	26.35
8 weeks post intervention	12	396.1 ± 107.19	0.005	71.85

Table 4: Six Minute Walking Distance.

SGRQ	Mean ± SD	P value
Symptoms		
Pre	47.05 ± 21.11	0.001
Post	28.67 ± 13.41	
Activity		
Pre	57.72 ± 29.32	0.019
Post	43.62 ± 28.03	
Impact		
Pre	37.29 ± 23.34	0.028
Post	24.01 ± 19.65	
Total		
Pre	44.98 ± 23.07	0.01
Post	30.73 ± 18.80	

Table 5: St. George Respiratory Questionnaire (SGRQ).

Discussion

In the early analyses, the data for the male and female subjects were compared. The body heights between male and female subjects were significantly different. The outcome of this study was the 6MWD score, which is influenced by walking speed. Walking speed is related to age, height, lower limb muscular force, balance ability, and lower extremity joint disorders. Therefore, the walking speed can be expected to show a reduction in individuals of greater age and of lesser height and lower extremity muscle strength [10,11]. The lung volume also influences the expiration muscle strength because the increase in the expiratory volume can promote a greater inspiratory volume [12]. Due to the small number of only four female subjects, we have excluded them from further analyses, and only males were included.

This study successfully showed that the addition of a PEP device significantly increased both the MEP and MIP in subjects with COPD. The main pathology in the COPD subjects was clearly hyperinflation, which resulted from narrowing of the airways caused by muscle spasms, mucosal inflammation, mucus hyper secretion, an unstable airway, or the deterioration of the lung recoil elasticity from destruction of the lung parenchyma. The narrowing of the airway lumen diameter pathologically increases the expiratory resistance, leading to airway collapse at normal levels of Functional Residual Capacity (FRC) [13].

All the pathological processes mentioned above would cause a decrease in the expiratory flow, leading to insufficient expiration and air trapping and ultimately causing dynamic hyperinflation in the thorax cavity [1,5]. Although this study did not measure the breathing volume directly, but instead relied on indirect measurement of the breathing volume through the expiratory muscle strength, the improvement in expiratory muscle function can reduce hyperinflation [14,15]. Ultimately, an improvement in respiratory muscle strength would reduce hyperinflation more effectively by opening the airway.

This study subjects had a mean age of 63.33 (± 9.61) years, and the morbidity databases in GOLD 2020 show that the morbidity due to COPD increases with age. Hence, our study findings are in line with the majority of other COPD studies, where 62% of the investigated patients were over 40 years of age, with a particular focus on those aged between 40 and 64 years [2,16,17]. A previous study of the COPD prevalence in Indonesia and Vietnam also showed that the mean age of the subjects with COPD in Indonesia was 52 years [2,16,17]. Similarly, the subjects in the present study had mean body weight 67.74 (± 12.98) kg and a mean height of 162.66 (± 5.19) cm, with a mean body mass index of 25.65 (± 5.34) kg/m². These values were in line with those published by Susanto et al., who showed that 80% of the subjects with COPD had a body mass index ≤ 25 kg/m² [18].

In line with previous studies, this study evaluated the changes occurring every two weeks and found a steady increase in the baseline mean MEP from 65.23 cmH₂O to 85.15 cmH₂O at the final evaluation. Table 3 shows a constant improvement in the inspiratory muscle strength, which reached the highest value at the eighth week. These improvements were in line with those reported by Mosa, et al., who compared a PEP exercise group and control group of patients with COPD. The control group was given chest physiotherapy and other group was given the PEP exercise, and the PEP group showed a significant increase in MEP from 70.3 ± 8.7 cmH₂O to 84.35 ± 9.76 cm H₂O whereas the control group showed only a small increase, from 76.6 ± 13.22 cmH₂O to 77.12 ± 12.11 cm H₂O (19). Routine PEP exercises could therefore significantly increase MEP by more than 10 cmH₂O, which would have clinical benefits in subjects with COPD. Interestingly, a study from Italy also showed a beneficial effect of Temporary Positive Expiratory Pressure (TPEP) used either as a home exercise, in the hospital, and without physical exercise. The number of exacerbation events decreased after one month and three months of exercise at home (5.7% after one month of intervention and 14.3% after three months of intervention) and in hospital (8.8% after one month of intervention and 14.7% after three months of intervention) when compared to a control group (28.7% after one month and 38.7% after three months) [19]. The same study also revealed an improvement in inspiratory muscle strength in all the TPEP groups compared to their controls [9]. These earlier studies strengthen the findings of the present study regarding MIP improvement with the PEP device, whereas only one report, to our knowledge, has reported similar findings [20]. Hence, although the PEP is a device designed to strengthen the MEP, biomechanical configuration has allowed both inspiratory and expiratory muscle to be strengthened. One plausible reason would be that good expiration requires adequate inflation of the lungs, as assisted by diaphragm being the primary inspiratory muscle. This would then promote long-lasting effects of the PEP exercise, whether administered at home or in the hospital.

The study by Tapan, et al. showed an improvement in the maximum expiratory pressure from 98.2 ± 5.7 cm H₂O to 109.3 ± 6.7 cm H₂O after using a nasal continuous positive airway pressure (nCPAP) device for eight weeks. This study, conducted in 31 patients with Obstructive Sleep Apnea Syndrome (OSAS), demonstrated an improvement in the maximum inspiratory pressure, maximum expiratory pressure, VO₂ max, and maximal heart rate after the intervention [21]. Consequently, this confirms that strengthening of the expiratory muscles is always accompanied by improvement in the inspiratory muscles, and this phenomenon is not exclusive to individuals with COPD [21]. The applicable theory would be that enhancement of the thoracic inflation as an individual tries to blow air against a resistance could improve the length-tension relationship of the diaphragm, which in turn would train the diaphragm to act as the primary inspiratory muscle. The current study utilized a PEP as the assistive device, since PEPs are more practical and more comfortable for the patient compared to nCPAP devices.

Table 4 shows the improvement in walking distance based on the 6 MWD test results evaluated every two weeks. The average walking distance was improved except at six weeks of intervention, and we speculate this may have reflected the inability of one subject to perform the test due to musculoskeletal thigh pain, which would be a contraindication for performing the 6MWD test. This finding is in line with a larger study that showed a significant difference in the walking distance of a patient with COPD after PEP exercise compared to exercise without the PEP exercise. The subjects were assigned either to the PEP exercise group or groups without PEP exercise. The improvement in walking distance was from 232.46 to 294.22 meters in the PEP exercise group versus 262.44 meters to 265.67 meters in the control group [22]. The Minimal Clinically Important Difference (MCID) of the 6 MWD test for functional capacity assessment is 26 ± 2 meters for patients with severe COPD, whereas PEP exercise provided a robust clinical improvement in the 6MWD test (≥ 70 meters after eight weeks, compared to baseline) [23,24].

The final measured outcome was the SGRQ, which is a questionnaire that assesses and evaluates the quality of life of patients with COPD [25]. The sum score of SGRQ represents the quality of life, with lower values indicating better quality, and this value showed a direct correlation with the severity of COPD [26]. Improvement in the SGRQ score after PEP exercise in this study is summarized in table 5, where the symptoms subscale score was reduced from 47.47 to 27.24, the activity subscale score from 58.17 to 43.67, the impact subscale score from 34.78 to 21.00, and the total score from 44.02 to 28.90 by the PEP exercise. The MCID of SGRQ in COPD is 4 units, whereas a difference of 15.12 was noted at eight weeks in the present study, classifying this as an important clinical improvement [25].

Although great differences were seen throughout the eight weeks of PEP exercise, a control group with pursed lip breathing exercise without any device should be planned for future comparison studies. Larger samples including both genders should also be proposed in order to determine the confounding factors that promote improvement. Other possible classifications could be made using the BMI, as several studies have also classified an emphysematous group as having cachexic COPD, while patients with obesity show to bronchitis COPD [27]. These pathognomonic differences would also correlate with muscular weakness, and thus may also reflect different effects of respiratory muscle exercise.

Conclusion

This study showed that exercise using a PEP device provides an overall improvement in breathing by patients with COPD. In particular, an improvement in both expiratory and inspiratory muscle strength was attained even though the resistance exercise was focused only on the expiratory muscles. In this COVID-19 pandemic era, home therapy programs with PEP devices may serve as safer alternatives for patients with COPD, as well as providing longer lasting benefits on their endurance and quality of life.

Author's Contribution

The main author N.N. had the most contributions in providing research ideas, and leading the research team. The full article writing and study operations were completed by O.H., P.S. and K.T.

Finally, expert consultations were provided by T.K., and A.K. Despite the various categories, all these authors have equal contributions towards the final accomplishments to this study.

Acknowledgment

We would extend our gratitude to all the involved faculties in this study. Lastly, we acknowledge the participants for their continuous and enthusiastic participation in the investigation.

References

1. GOLD (2017) Global Initiative for Chronic Obstructive Lung Disease : Pocket Guide To COPD Diagnosis, Management, and Prevention, A Guide for Health Care Professionals. Gold 1-48.
2. GOLD (2020) Global Initiative for Chronic Obstructive Lung Disease. Gold 1-141.
3. Quaderi SA, Hurst JR (2018) The unmet global burden of COPD. *Glob Heal Epidemiol Genomics* 3: 9-11.
4. Sherwood L (2018) Human Physiology.9th edition. Boston: Cengage Learning, USA.
5. Olsén MF, Lannefors L, Westerdahl E (2015) Positive expiratory pressure - Common clinical applications and physiological effects. *Respir Med* 109: 297-307.
6. Clini E (2009) Positive expiratory pressure techniques in respiratory patients: old evidence and new insights. *Breathe* 6: 153-159.
7. Venturelli E, Crisafulli E, Debiase A, Righi D, Berrighi D, et al. (2013) Efficacy of temporary positive expiratory pressure (TPEP) in patients with lung diseases and chronic mucus hypersecretion. the UNIKO® project: A multicentre randomized controlled trial. *Clin Rehabil* 27: 336-46.
8. Nicolini A, Mollar E, Grecchi B, Landucci N (2014) Comparación de la respiración con presión positiva intermitente y la presión espiratoria positiva temporal en pacientes con enfermedad pulmonar obstructiva crónica grave. *Arch Bronconeumol* 50: 18-24.
9. Mascardi V, Grecchi B, Barlascini C, Banfi P, Nicolini A (2016) Effectiveness of temporary positive expiratory pressure (T-PEP) at home and at hospital in patients with severe chronic obstructive pulmonary disease. *J Thorac Dis* 8: 2895-2902.
10. Bohannon RW (1997) Comfortable and maximum walking speed of adults aged 20-79 years: Reference values and determinants. *Age Ageing* 26: 15-19.
11. Ito H, Nagasaki H, Maruyama H, Hashizume K, Nakaruma R (1989) Age related changes of the walking cycle during fastest walking in healthy male subjects. *Igakkai Zasshi* 26: 347-52.
12. Padkao T, Boonla O (2020) Relationships between respiratory muscle strength, chest wall expansion, and functional capacity in healthy non-smokers. *J Exerc Rehabil* 16: 189-196.

13. Ramos FL, Krahnke JS, Kim V (2014) Clinical issues of mucus accumulation in COPD. *Int J COPD* 9: 139-150.
14. Casaburi R, Porszasz J (2006) Reduction of hyperinflation by pharmacologic and other interventions. *Proc Am Thorac Soc* 3:185-189.
15. Mota S, Güell R, Barreiro E, Solanes I, Ramirez-Sarmiento A, et al. (2007) Clinical outcomes of expiratory muscle training in severe COPD patients. *Respir Med* 101: 516-524.
16. Raheison C, Girodet PO (2009) Epidemiology of COPD. *Eur Respir Rev* 18: 213-221.
17. Nguyen Viet N, Yunus F, Nguyen Thi Phuong A, Dao Bich V, Damayanti T, et al. (2015) The prevalence and patient characteristics of chronic obstructive pulmonary disease in non-smokers in Vietnam and Indonesia: An observational survey. *Respirology* (2015) 20: 602-611.
18. Susanto AD, Antono W, Yunus F (2020) Prevalensi Penyakit Paru Obstruktif Kronik Pada Penyapu Jalan Raya di Jakarta. *J Indo* 70: 100-109.
19. Mosa MS, El Aziz AA, Mohamed AR, Shaban MM (2017) Response of expiratory muscle training to positive end expiratory pressure in Chronic Obstructive Pulmonary Disease. *Int J Physiother Res* 5: 2344-2348.
20. Sheng TF, Jao WC, Ho shu chuan, Chen L, Wang C, et al. (2013) Positive expiratory pressure therapy improves inspiratory capacity and physical activity in patients with chronic obstructive pulmonary disease. *Eur Respir J* 42: 1834.
21. Tapan ÖO, Sevinç C, İtil BO, Öztura İ, Kayatekin BM, et al. (2016) Effect of nasal continuous positive airway pressure therapy on the functional respiratory parameters and cardiopulmonary exercise test in obstructive sleep apnea syndrome. *Turk Toraks Derg* 17: 1-6.
22. Nicolini A, Merliak F, Barlascini C (2013) Use of positive expiratory pressure during six minute walk test: Results in patients with moderate to severe chronic obstructive pulmonary disease. *Multidiscip Respir Med* 8: 19.
23. Jones PW, Beeh KM, Chapman KR, Decramer M, Mahler DA, et al. (2014) Minimal clinically important differences in pharmacological trials. *Am J Respir Crit Care Med* 89: 250-255.
24. Polkey MI, Spruit MA, Edwards LD, Watkins ML, Pinto-Plata V, et al. (2013) Six-minute-walk test in chronic obstructive pulmonary disease: Minimal clinically important difference for death or hospitalization. *Am J Respir Crit Care Med* 187: 382-386.
25. Wiyono WH, Riyadi J, Yunus F, Ratnawati A, Prasetyo S (2006) The benefit of pulmonary rehabilitation against quality of life alteration and functional capacity of chronic obstructive pulmonary disease (COPD) patient assessed using St George's respiratory questionnaire (SGRQ) and 6 minutes walking distance test. *Med J Indones* 15: 165-172.
26. Naito A, Honma T, Sekizawa K (2012) Quality of life in COPD patients. *Respir Circ* 61: 281-289.
27. Voica AS, Oancea C, Tudorache E, Crisan AF, Fira-Mladinescu O, et al. (2016) Chronic obstructive pulmonary disease phenotypes and balance impairment. *Int J Chron Obstruct Pulmon Dis* 11: 919-925.



- Advances In Industrial Biotechnology | ISSN: 2639-5665
- Advances In Microbiology Research | ISSN: 2689-694X
- Archives Of Surgery And Surgical Education | ISSN: 2689-3126
- Archives Of Urology
- Archives Of Zoological Studies | ISSN: 2640-7779
- Current Trends Medical And Biological Engineering
- International Journal Of Case Reports And Therapeutic Studies | ISSN: 2689-310X
- Journal Of Addiction & Addictive Disorders | ISSN: 2578-7276
- Journal Of Agronomy & Agricultural Science | ISSN: 2689-8292
- Journal Of AIDS Clinical Research & STDs | ISSN: 2572-7370
- Journal Of Alcoholism Drug Abuse & Substance Dependence | ISSN: 2572-9594
- Journal Of Allergy Disorders & Therapy | ISSN: 2470-749X
- Journal Of Alternative Complementary & Integrative Medicine | ISSN: 2470-7562
- Journal Of Alzheimers & Neurodegenerative Diseases | ISSN: 2572-9608
- Journal Of Anesthesia & Clinical Care | ISSN: 2378-8879
- Journal Of Angiology & Vascular Surgery | ISSN: 2572-7397
- Journal Of Animal Research & Veterinary Science | ISSN: 2639-3751
- Journal Of Aquaculture & Fisheries | ISSN: 2576-5523
- Journal Of Atmospheric & Earth Sciences | ISSN: 2689-8780
- Journal Of Biotech Research & Biochemistry
- Journal Of Brain & Neuroscience Research
- Journal Of Cancer Biology & Treatment | ISSN: 2470-7546
- Journal Of Cardiology Study & Research | ISSN: 2640-768X
- Journal Of Cell Biology & Cell Metabolism | ISSN: 2381-1943
- Journal Of Clinical Dermatology & Therapy | ISSN: 2378-8771
- Journal Of Clinical Immunology & Immunotherapy | ISSN: 2378-8844
- Journal Of Clinical Studies & Medical Case Reports | ISSN: 2378-8801
- Journal Of Community Medicine & Public Health Care | ISSN: 2381-1978
- Journal Of Cytology & Tissue Biology | ISSN: 2378-9107
- Journal Of Dairy Research & Technology | ISSN: 2688-9315
- Journal Of Dentistry Oral Health & Cosmesis | ISSN: 2473-6783
- Journal Of Diabetes & Metabolic Disorders | ISSN: 2381-201X
- Journal Of Emergency Medicine Trauma & Surgical Care | ISSN: 2378-8798
- Journal Of Environmental Science Current Research | ISSN: 2643-5020
- Journal Of Food Science & Nutrition | ISSN: 2470-1076
- Journal Of Forensic Legal & Investigative Sciences | ISSN: 2473-733X
- Journal Of Gastroenterology & Hepatology Research | ISSN: 2574-2566
- Journal Of Genetics & Genomic Sciences | ISSN: 2574-2485
- Journal Of Gerontology & Geriatric Medicine | ISSN: 2381-8662
- Journal Of Hematology Blood Transfusion & Disorders | ISSN: 2572-2999
- Journal Of Hospice & Palliative Medical Care
- Journal Of Human Endocrinology | ISSN: 2572-9640
- Journal Of Infectious & Non Infectious Diseases | ISSN: 2381-8654
- Journal Of Internal Medicine & Primary Healthcare | ISSN: 2574-2493
- Journal Of Light & Laser Current Trends
- Journal Of Medicine Study & Research | ISSN: 2639-5657
- Journal Of Modern Chemical Sciences
- Journal Of Nanotechnology Nanomedicine & Nanobiotechnology | ISSN: 2381-2044
- Journal Of Neonatology & Clinical Pediatrics | ISSN: 2378-878X
- Journal Of Nephrology & Renal Therapy | ISSN: 2473-7313
- Journal Of Non Invasive Vascular Investigation | ISSN: 2572-7400
- Journal Of Nuclear Medicine Radiology & Radiation Therapy | ISSN: 2572-7419
- Journal Of Obesity & Weight Loss | ISSN: 2473-7372
- Journal Of Ophthalmology & Clinical Research | ISSN: 2378-8887
- Journal Of Orthopedic Research & Physiotherapy | ISSN: 2381-2052
- Journal Of Otolaryngology Head & Neck Surgery | ISSN: 2573-010X
- Journal Of Pathology Clinical & Medical Research
- Journal Of Pharmacology Pharmaceutics & Pharmacovigilance | ISSN: 2639-5649
- Journal Of Physical Medicine Rehabilitation & Disabilities | ISSN: 2381-8670
- Journal Of Plant Science Current Research | ISSN: 2639-3743
- Journal Of Practical & Professional Nursing | ISSN: 2639-5681
- Journal Of Protein Research & Bioinformatics
- Journal Of Psychiatry Depression & Anxiety | ISSN: 2573-0150
- Journal Of Pulmonary Medicine & Respiratory Research | ISSN: 2573-0177
- Journal Of Reproductive Medicine Gynaecology & Obstetrics | ISSN: 2574-2574
- Journal Of Stem Cells Research Development & Therapy | ISSN: 2381-2060
- Journal Of Surgery Current Trends & Innovations | ISSN: 2578-7284
- Journal Of Toxicology Current Research | ISSN: 2639-3735
- Journal Of Translational Science And Research
- Journal Of Vaccines Research & Vaccination | ISSN: 2573-0193
- Journal Of Virology & Antivirals
- Sports Medicine And Injury Care Journal | ISSN: 2689-8829
- Trends In Anatomy & Physiology | ISSN: 2640-7752

Submit Your Manuscript: <https://www.heraldopenaccess.us/submit-manuscript>