**ORIGINAL ARTICLE** 



# The Effect of Whole-Body Vibration on Pulmonary Function and Cerebral Cortical Activity in Patients with Chronic Obstructive Pulmonary Disease

<sup>1</sup>Dae-Keun Jeong<sup>(D)</sup>, <sup>2</sup>Jong-Hyuk Yoon<sup>(D)</sup>, <sup>3</sup>Sam-Ho Park<sup>(D)\*</sup>

<sup>1</sup>Department of Physical Therapy, Sehan University, Yeongam-gun, Republic of Korea. <sup>2</sup>Department of Physical Therapy, Kunjang University, Gunsan-si, Republic of Korea.<sup>3</sup>Department of Rehabilitation Assistive Technology, National Rehabilitation Research Institute, National Rehabilitation Center, Seoul, Republic of Korea.

Submitted February 04, 2022; Accepted in final form April 15, 2022.

### ABSTRACT

**Background.** This study aimed to provide patients with chronic obstructive pulmonary disease (COPD) with an intervention based on whole-body vibration training (WBVT), examine pulmonary function and electroencephalograms (EEGs) to improve the physical capacity of these patients, and suggest an efficient approach to managing these patients in practice. **Methods.** A clinical sample of 22 patients with severe COPD was randomly assigned to either Experimental Group I (n=12), which performed squat exercises in combination with WBVT, or Experimental Group II (n=10), which served squat exercises alone. The intervention programs were administered over four weeks, with ten repetitions per set, three sets per session, one session per day, and three days per week. **Results.** In Experimental Group I, within-group changes pre-and post-intervention were significant for the alpha waves in Fp1, Fp2, F3, and F4, whereas no within-group changes in pulmonary function, EEG, or 6-minute walk test (6MWT) performance were observed in Experimental Group II. Significant between-group differences were observed in the alpha waves in Fp1, Fp2, and F4 (P<0.05). **Conclusion.** Exercise combined with WBVT was a safe and effective strategy to counteract the loss of musculoskeletal function in patients with COPD. Additional research is needed to develop protocols for combining WBVT and pulmonary function intervention programs.

**KEYWORDS:** Electroencephalograms, Proprioception, Pulmonary Disease, Pulmonary Function, Vibration.

### **INTRODUCTION**

Chronic obstructive pulmonary disease (COPD) is the third-leading cause of death worldwide, with an annual mortality rate of approximately 3 million (1). COPD is characterized by persistent airflow obstruction related to chronic lung inflammation. The symptoms include breathing difficulty, fatigue, and chronic cough due to excessive sputum production. The disease can decrease patients' physical activity and worsen the latent systemic symptoms of cardiovascular disease (2).

In COPD, airway stenosis and emphysema cause progressive chronic airflow obstruction, which leads to loss of alveolar attachments and parenchymal destruction. Thus, lung elasticity decreases, air resistance increases, and the inhaled air volume is greater than the exhaled air volume, thus blocking the small airways and trapping air in the lungs (3). Persistent respiratory symptoms and chronic airflow obstruction are linked to airway and alveolar abnormalities due to chronic inflammation in the airways and lung parenchyma (4). Musculoskeletal dysfunction is accompanied by respiratory symptoms, creating a vicious cycle of markedly reduced mobility and accelerated disease progression (5). COPD negatively affects the lungs and many other body systems through various factors causing muscle weakness, including decreased musculoskeletal activity, systemic inflammation, malnutrition, corticosteroid use, hypoxemia, aging, and smoking (6, 7).

Because muscle weakness and the consequent decrease in neural activity in COPD reduces mobility and gray matter density in the prefrontal area (7) and causes white matter lesions in pyramidal neurons, the level of excitation in the brain is likely not as high in patients with COPD as that in healthy people (8). In addition, the peak compound muscle action potential (CMAP) is delayed, and the amplitude is reduced in these patients, suggesting a problem in neuromuscular transmission in the motor neurons (9).

Exercise is essential for enhancing and maintaining physical health. It is one of the crucial components of pulmonary rehabilitation in patients with COPD (10). It may be an essential component aside from the most effective pharmaceutical therapies currently available (11). To improve endurance and muscle strength, linked to increased exercise tolerance and quality of life in patients with COPD, studies have investigated the effect of diverse exercise training programs and reported the benefits of various protocols to increase pulmonary function. However, most patients with COPD cannot typically perform activities due to difficulty breathing and fatigue, which deters their physical activity participation (12).

Accordingly, exercises like whole-body vibration training (WBVT) have garnered interest as a method to enhance physical activity capacity in patients with severe COPD (13). WBVT is a training method that exercises on a vibrating platform that generates vertical sine waves. Vibration delivered to the body stimulates muscle spindles, eliciting the muscle contraction reflex in response to the tonic vibration reflex (14).

Gloeckl et al. (15) demonstrated the effectiveness of WBVT by improving exercise capacity without side effects in patients with COPD. WBVT can be used for therapeutic rehabilitation of pulmonary function by targeting neuromuscular function in patients with neuromuscular dysfunction. This training can stimulate and strengthen muscles by inducing muscle contraction (16). Accordingly, the present study aimed to enhance physical activity capacity in patients with COPD by applying a WBVT intervention and assessing pulmonary function and electroencephalogram (EEG); moreover, this study also suggested an efficient approach to managing these patients in practice.

### MATERIALS AND METHODS

Participants. This study was approved by the Institutional Review Board (SH-IRB 2021-71). The study participants were 22 male patients with COPD aged 50-70 who were admitted to H Hospital in Jeollanam-do between January and August 2020. They had been diagnosed with severe COPD (<50% forced expiratory volume in 1 s [FEV1]) according to the COPD diagnostic criteria in the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines. The study exclusion criteria were: a change in drug therapy such as antihypertensives in the last 12 weeks, cardiovascular diseases, orthopedic disorders, neurological disorders, use of drugs known to affect brain function (e.g., y-aminobutyric acid antidepressants, [GABA] agonists, selective serotonin/ adrenaline reuptake inhibitors, or opioid receptor agonists), lack of regular exercise in the last three months or more, and rapidly progressive COPD. The participants were informed about the purpose of the study, and they consented to participate in the study.

Procedures. Design. The clinical sample of 22 patients with severe COPD was randomly assigned to Experimental Groups I (n=12) or II (n=10). The former performed squat exercise combined with WBVT II (n=10), whereas the latter performed squat exercise alone. The intervention programs were administered for a total of 4 weeks, in which the participants completed the training in 10 repetitions per set, three sets per session, one session per day, and three days per week. Before the intervention, pulmonary function was assessed by spirometry, cortical electrical activities by EEG, and gait ability by a 6-minute walk test (6MWT). Four weeks post-intervention, the same tests were performed for comparison before and after the intervention.

Pulmonary Function. Pulmonary function was assessed using Chestgraph HI-701 (Chest, Japan). During the test, participants in a seated position placed a tube connected to the spirometer in their mouths. They then inhaled and exhaled as hard as they could. The lung capacity was measured for at least three trials, with the highest and the second-highest (if the difference from the highest was within 5% or 200 mL) values used in the analysis. (17)

EEG. EEG data were collected at a sampling rate of 256 Hz and a band-pass filter of 4–50 Hz. EEG was measured in a room without noise and with constant luminance and temperature. The participants were comfortably seated in a chair and informed of what to expect during the EEG measurements and precautions. After electrodes were placed on each participant's scalp, pre-testing was conducted to ensure no error in the EEG recording. A total of eight electrodes were identified according to the International 10-20 method of electrode placement in the following sites: left frontopolar1 (Fp1), right frontopolar 2 (Fp2), left frontal 3 (F3), correct frontal 4 (F4), left parietal 3 (P3), correct parietal 4 (P4), left occipital 1 (O1), and right occipital 2 (O2). Reference and ground electrodes were placed behind the right and left earlobes, respectively (Figure 1).

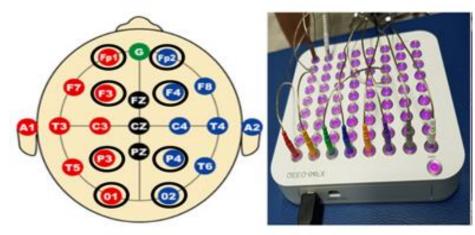


Figure 1. Measurement of Cortical Activity

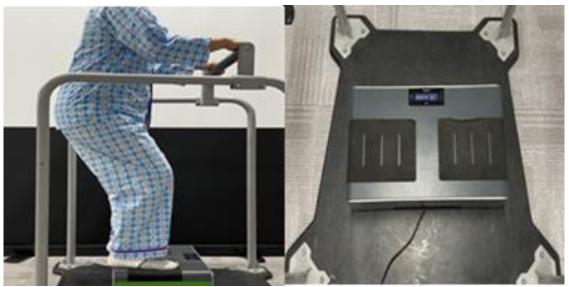


Figure 2. Whole Body Vibration Training

EEG Signal Analysis. EEG data were quantitatively analyzed by using an EEG analysis system, the Tele ScanTM program (Version 3.03, Laxtha Inc, Korea). To analyze the data, the noise was removed by examining the waveforms of the signals. The first and last 10 seconds of the original 3-min. Recorded data were excluded, while the remaining 160 seconds were included in the analysis. Because delta waves (0.5-4 HZ) are likely to be

influenced by artifacts such as eye blinking (2-4 Hz) and head movement due to postural instability (0.5–1 Hz), only signals between 4 and 50 Hz were analyzed. A fast Fourier transform (FFT) was performed to convert the original data into frequencies. FFT is an algorithm used to compute the contribution of individual spectral components in frequency domains. The results are displayed with the frequency spectrum on the x-axis and the power values on the y-axis, namely, the EEG power spectrum (power spectral analysis), which indicates the amplitudes of particular frequency bands. Relative power analysis was performed to examine relative alpha (8-13 Hz/4-50 Hz) and close beta (13-20 Hz/4-50 Hz) waves.

6MWT. In the 6MWT, the participants were instructed to walk a 20-meter-long straight walkway for 6 minutes repeatedly. An orange traffic cone was placed at the turning point at either end of the walkway, and the walkway was

marked at 2-meter intervals to measure the distance covered. Before the test, the participants were informed about the test's purpose and received instructions on performing the 6MWT while in a seated position, with no warm-up exercises. They were told to walk as long a distance as possible for 6 minutes, control their speed, and take rests according to their abilities. The total distance covered in 6 minutes was measured by counting the number of repetitions of walking the walkway and using the 2-meter markings (18).

Interventions. Squat exercise. Both groups of participants performed squats in 10 repetitions per set, three sets per day, three sessions per week, for a total of 4 weeks (Gloeckl et al., 2012). The participants were instructed to sit back to form an approximately 45-degree angle at the knees for 4 seconds (2 seconds each for concentric and eccentric phases) and to relax in a standing posture for 2 seconds between squats.

Items		Experimental group I		Experimental group II (n=10)	Р	
Age (year	s)	62.10±5.21		64.43±3.49	0.458	
Height (c	m)	$166.14 \pm 5.16$		167.57±6.23	0.795	
Weight (l	(g)	61.12±7.81		63.83±7.21	0.348	
Disease (y		8.74±2.41		7.71±2.61	0.819	
6MWT (i		389.15±55.42		352.39±49.55	0.455	
		Table ? Comparison of C	hango in Fynori	mental I Crown (Mean + SF)		
	Table 2. Comparison of Change in Experimental I Group (Mean ± SE)   Experimental I Group (n=11)					
		Pre-Test	Post-Test			
FEV1 (%	)	44.56±7.56	46.25±3.21	-2.143	0.084	
FEV1/FV		48.67±6.44	49.23±4.25	-1.347	0.224	
Fp1	. ,					
	α-wave	$0.19 \pm 0.05$	0.28±0.07	-9.140	0.001*	
	β-wave	0.13±0.03	0.17±0.05	-1.524	0.335	
Fp2						
	α-wave	0.2±0.06	0.32±0.07	-9.056	0.002*	
	β-wave	0.13±0.04	0.15±0.03	-2.104	0.285	
F3						
	α-wave	0.33±0.05	0.39±0.06	-5.755	0.006*	
	β-wave	0.23±0.06	$0.24\pm0.04$	-0.425	0.762	
F4						
	α-wave	0.32±0.06	0.42±0.05	-8.324	0.004*	
	β-wave	0.21±0.03	0.22±0.04	-0.784	0.726	
P3						
	α-wave	0.4±0.07	0.41±0.09	-0.857	0.684	
	β-wave	0.25±0.03	$0.26\pm0.08$	-0.952	0.658	
P4						
	α-wave	$0.37 \pm 0.08$	$0.38\pm0.04$	-0.842	0.693	
	β-wave	0.25±0.07	$0.24\pm0.08$	1.042	0.524	
01						
	α-wave	$0.48 \pm 0.05$	0.51±0.09	-1.254	0.481	
	β-wave	$0.37 \pm 0.08$	0.39±0.08	-0.855	0.688	
02						
	α-wave	$0.48\pm0.07$	$0.5\pm0.05$	-0.945	0.654	
	β-wave	$0.37 \pm 0.06$	$0.41 \pm 0.07$	-0.342	0.715	
6MWT(n	1)	387.45±57.28	427.45±37.2	8 28.282	0.008*	

Table 1. General Characteristics of the Participants (Mean ± SE)

		Experimental II group (n=10)		t	Р
		Pre-Test	Post-Test		
FEV1 (%)		42.77±4.31	43.85±4.84	-1.846	.122
FEV1	/FVC (%)	46.23±5.18	47.13±4.85	-1.561	.148
Fp1					
	α-wave	0.19±0.04	0.23±0.03	-2.913	.086
	β-wave	0.16±0.04	0.18±0.05	-1.857	.284
Fp2					
	α-wave	$0.18\pm0.05$	0.22±0.07	-3.952	.058
	β-wave	$0.14 \pm 0.07$	0.15±0.05	742	.703
F3					
	α-wave	$0.33 \pm 0.05$	0.37±0.05	-3.742	.074
	β-wave	0.23±0.07	0.23±0.08	254	.881
F4	·				
	α-wave	$0.32 \pm 0.06$	0.37±0.06	-3.855	.068
	β-wave	0.21±0.04	0.22±0.07	915	.634
P3	·				
	α-wave	$0.41 \pm 0.11$	$0.4\pm0.09$	.317	.786
	β-wave	$0.24 \pm 0.04$	0.23±0.08	.842	.598
P4	,				
	α-wave	$0.35 \pm 0.07$	0.39±0.1	-3.342	.098
	β-wave	$0.24 \pm 0.06$	$0.24\pm0.08$	251	.864
01					
	α-wave	0.47±0.05	0.49±0.08	-1.428	.306
	β-wave	0.38±0.07	$0.4\pm0.08$	-1.254	.284
02	,				
	α-wave	0.47±0.05	0.48±0.07	341	.792
	β-wave	$0.38 \pm 0.07$	$0.42\pm0.05$	-2.175	1.584
6MW		348.85±48.41	368.1±37.18	18.254	.041*

Table 3. Comparison of Change in Experimental II Group (Mean ± SE)

The length of time taken to perform the 10 repetitions was measured. If necessary, the participant's posture was adjusted. After the exercise, the participants rested in a seating position for 5 minutes. The extent of breathing difficulty during exercise was quantified using a dyspnea scale, with the score ranging from 0 ("breathing was not difficult at all") to 10 ("breathing was too difficult to continue exercising") (Figure 2) (15). The participants in Experimental Group I performed the same squat exercise in parallel with WBVT, whereas those in Experimental Group II performed only the squat exercise.

Squat Exercise Combined with WBVT. WBVT was applied to Experimental Group 1 using a vertically vibrating platform (Apsuninc, Wellengang, Korea). Before the intervention, the participants in this group practiced for 2 minutes while a therapist adjusted their squat form and timing. The squat exercise in combination with WBVT was performed at 20 Hz and a peak-topeak displacement of 7 mm (a typical setting in WBVT experiments with patients with COPD). The same protocol used in Experimental Group II was used in this group.

Data Analysis. Data were analyzed using IBM SPSS Statistics for Windows, version 20.0. To analvze the participants' general characteristics, normality was tested by Shapiro-Wilk tests, while the homogeneity of the variances was tested using Levene's test. Paired ttests were used to assess within-group pre-post change in pulmonary function, EEG, and 6MWT performance. Between-group differences in postintervention scores were evaluated by analysis of covariance (ANCOVA) using the preintervention scores as covariance to control for pre-intervention differences between groups. The significance level was set at.05.

#### RESULTS

General Characteristics of the Study Participants. Experimental Groups I (n=12) and II (n=10) did not differ significantly in age, height, weight, duration of disease, and 6MWT performance. Thus, the two groups were equivalent (Table 1).

Within-Group Changes in Experimental Group I. In Experimental Group I, significant pre-post changes were observed in alpha waves in Fp1, Fp2, F3, and F4 (P<0.01) (Table 2).

Within-Group Changes in Experimental Group II. In Experimental Group II, no significant pre-post changes were observed in pulmonary function, EEG, or 6MWT performance (Table 3).

**Between-Group Comparisons.** The between-group comparison showed significant differences in alpha waves in Fp1, Fp2, and F4 between the two groups (P<0.05) (Table 4).

	Table 4. Comparison of Changes between Groups (Mean ± SE)						
		Experimental g	Experimental group I (n=11)		Experimental group II (n=10)		Р
		pre-test	post-test	pre-test	post-test		
FEV1		44.56±7.56	46.25±3.21	42.77±4.31	43.85±4.84	1.925	.248
FEV1/	/FVC (%)	48.67±6.44	49.23±4.25	46.23±5.18	47.13±4.85	1.725	.213
Fp1							
	α-wave	$0.19 \pm 0.05$	0.28±0.07	$0.19\pm0.04$	0.23±0.03	3.248	.031*
	β-wave	0.13±0.03	$0.17 \pm 0.05$	$0.16\pm0.04$	$0.18\pm0.05$	.854	.482
Fp2							
	α-wave	$0.2\pm0.06$	$0.32\pm0.07$	$0.18\pm0.05$	$0.22 \pm 0.07$	2.847	.043*
	β-wave	0.13±0.04	0.15±0.03	$0.14\pm0.07$	$0.15 \pm 0.05$	.324	.614
F3							
	α-wave	0.33±0.05	0.39±0.06	0.33±0.05	0.37±0.05	2.289	.062
	β-wave	0.23±0.06	$0.24\pm0.04$	0.23±0.07	0.23±0.08	.212	.785
F4							
	α-wave	0.32±0.06	$0.42\pm0.05$	0.32±0.06	0.37±0.06	3.214	.032
	β-wave	0.21±0.03	0.22±0.04	0.21±0.04	0.22±0.07	.197	.824
P3							
	α-wave	$0.4\pm0.07$	0.41±0.09	0.41±0.11	0.4±0.09	.241	.724
	β-wave	0.25±0.03	0.26±0.08	$0.24\pm0.04$	0.23±0.08	.489	.541
P4							
	α-wave	0.37±0.08	0.38±0.04	0.35±0.07	0.39±0.1	.332	.607
	β-wave	$0.25 \pm 0.07$	0.24±0.08	0.24±0.06	$0.24 \pm 0.04$	.128	.814
01							
	α-wave	$0.48 \pm 0.05$	0.51±0.09	0.47±0.05	$0.49 \pm 0.08$	.224	.704
	β-wave	0.37±0.08	0.39±0.08	0.38±0.07	$0.4\pm0.08$	.348	.619
02							
	α-wave	$0.48\pm0.07$	$0.5\pm0.05$	$0.47 \pm 0.05$	$0.48 \pm 0.07$	.434	.524
	β-wave	0.37±0.06	$0.41 \pm 0.07$	0.38±0.07	0.42±0.05	.567	.495
6MW	<b>Γ</b> ( <b>m</b> )	$387.45 \pm 57.28$	427.45±37.28	$348.85 \pm 48.41$	368.1±37.18	2.427	.138

#### DISCUSSION

Patients with COPD experience limitations in daily life and poor physical status due to compromised respiratory function, in which oxygen supply to the tissues is decreased and physical fatigue is easily triggered. Recently, interventions to improve physical function in patients with COPD in combination with WBVT have been described. Accordingly, this study examined the effects of the combination of squat exercises and WBVT on changes in pulmonary function, EEG, and 6MWT performance in patients with COPD.

Pulmonary dysfunction and musculoskeletal weakening frequently occur in patients with COPD, resulting in poor health status. In this context, WBVT has been used as an alternative to respiratory rehabilitation in these patients. In a study including 60 patients with COPD assigned to one of WBVT, neuromuscular electrical stimulation, and control groups, Abdel-fattah and Abdel-aziem (19) examined the changes in pulmonary function and

quadriceps muscle strength and reported no significant between-group differences in pulmonary function. Samir et al. (20) compared two groups of participants (a total of 32 patients with COPD) who performed squats on a vibrating or flat platform, reporting enhanced exercise capacity and quality of life in both groups, with a significant between-group difference in ventilatory function. The present study also observed no significant between-group differences in pulmonary function. In their metaanalysis of the effects of interventions combined with WBVT on pulmonary function, lower body strength, and functional mobility in patients with COPD, Berner et al. (21) reported that WBVT for <12 weeks was not effective in improving pulmonary function. Thus, the length of intervention may be important in improving respiratory muscle strength and lung capacity weakened due to reduced airflow.

Recently, interest has increased not only in pulmonary function but also in EEG associated with hypoxia in the evaluation of patients with

COPD. The pathway by which respiratory signals are delivered to the cortex originates in the respiratory muscles, passes through the brainstem and medulla oblongata, and projects primarily to the ventroposterior thalamus area. From this area, thalamocortical projections ascend to the primary and secondary somatosensory cortices (22). Ide and Secher (23) reported increased oxygenation and blood flow in the prefrontal cortex in response to increased mobility, while Higashimoto et al. (24) reported that prefrontal cortical activity was correlated with exercise-induced breathing difficulty. Herigstad et al. (25) used functional magnetic resonance imaging (fMRI) to compare patients with COPD (n=40) and healthy adults (n=41), reporting higher prefrontal activity in patients with COPD than in the control group. Finally, Gaurav et al. (26) reported that a change in breathing led to hypoxemia, which is directly linked to the cortical activity to excite and inhibit different cortical areas. Moreover, changes in breathing not only altered cardiac activity but also caused hypoxemia and hypercarbia, eventually affecting cortical electrical activities. Alpha waves are produced when a person is highly alert and the body and mind are in harmony; thus, they are dominant when the body and mind are relaxed and comfortable so that consciousness is moved to the brain. Kokodoko et al. (27) reported decreased alpha waves and increased slow-wave activity in 65% of patients with COPD who did not manifest clinically noticeable neurological signs or symptoms. Gaurav et al. (26) reported that during a rest period, the alpha waves showed the highest amplitude primarily in the back of the head, particularly the occipital region, and that the alphawave amplitude was greater than the beta wave amplitude in the front of the head. Likewise, in the present study, EEG analysis by region showed the highest alpha-wave activity in the occipital region, O1, and O2, among all regions and that the alphawave amplitudes were greater than the beta-wave amplitude in all regions. Because the combination of squat and WBVT helped improve physical functioning in patients with COPD, the alpha waves may have been more dominant than the beta waves.

The 6MWT is used to assess exercise and functional mobility capacities in patients with COPD. Braz et al. (28) reported that the combination of squat and WBVT significantly increased 6MWT performance and quality of life in a random group of 11 patients with COPD. Greulich et al. (29) reported significantly improved 6MWT performance in the experimental group of 40 patients with COPD who underwent WBVT. In the current study, 6MWT performance was also significantly improved in both Experimental Groups I and II, a finding that supports those previously reported. Thus, as a safe and effective strategy to counteract the loss of musculoskeletal function in patients with COPD, squat exercise improved 6MWT performance by helping in the recovery of skeletal muscle function.

A limitation of this study was that the participants were patients with COPD treated at a single healthcare institution; thus, caution must be exercised while generalizing the findings to all patients with COPD. Another limitation was that it was difficult to control the daily lives of the study participants.

### CONCLUSION

To improve physical functioning among patients with COPD, the participants in this study performed a combination of squats and WBVT. Although lung capacity decreased due to airflow reduction and did not improve in the short-term, EEG analysis by region showed higher alphawave amplitude in the occipital region, O1, and O2, compared to the other regions and dominance of alpha waves over beta waves in all regions. Hence, we confirmed that the combination of squat and WBVT helped improve physical function. Exercise combined with WBVT was a safe and effective strategy to offset the loss of musculoskeletal function in patients with COPD. Studies are needed to develop a variety of protocols for pulmonary function intervention programs incorporating WBVT.

#### **APPLICABLE REMARKS**

• The findings reported in this study suggest that exercise combined with WBVT was a safe and effective strategy to counteract the loss of musculoskeletal function in patients with COPD patients.

#### **AUTHORS' CONTRIBUTIONS**

Study Concept and Design: Dae-Geun Jeong, Jong-Hyuk Yoon, Sam-Ho Park. Acquisition of data: Dae-Geun Jeong. Analysis and interpretation of data: Sam-Ho Park. Drafting of the manuscript: Dae-Geun Jeong, Jong-Hyuk Yoon. Critical revision of the manuscript for important information: Sam-Ho Park. Statistical analysis: Dae-Geun Jeong, Jong-Hyuk Yoon. Administrative, technical, and material support: Dae-Geun Jeong. Study supervision: Sam-Ho Park.

### ACKNOWLEDGEMENTS

This paper was supported by the Sehan University Research Fund in 2022.

## **CONFLICTS OF INTEREST**

No potential conflict of interest relevant to this article was reported.

### REFERENCES

- 1. Rabe KF, Calverley PMA, Martinez FJ, Fabbri LM. Effect of roflumilast in patients with severe COPD and a history of hospitalisation. *Eur Respir J*. 2017;**50**(1). **doi:** 10.1183/13993003.00158-2017 **pmid:** 28679611
- Halbert RJ, Natoli JL, Gano A, Badamgarav E, Buist AS, Mannino DM. Global burden of COPD: systematic review and meta-analysis. *Eur Respir J.* 2006;28(3):523-532. doi: 10.1183/09031936.06.00124605 pmid: 16611654
- 3. Barnes PJ. The cytokine network in chronic obstructive pulmonary disease. *Am J Respir Cell Mol Biol*. 2009;**41**(6):631-638. **doi:** 10.1165/rcmb.2009-0220TR **pmid:** 19717810
- Goncalves PA, Dos Santos Neves R, Neto LV, Madeira M, Guimaraes FS, Mendonca LMC, et al. Inhaled glucocorticoids are associated with vertebral fractures in COPD patients. *J Bone Miner Metab*. 2018;36(4):454-461. doi: 10.1007/s00774-017-0854-3 pmid: 28766137
- Rabinovich RA, Vilaro J. Structural and functional changes of peripheral muscles in chronic obstructive pulmonary disease patients. *Curr Opin Pulm Med.* 2010;16(2):123-133. doi: 10.1097/MCP.0b013e328336438d pmid: 20071991
- Choudhury G, Rabinovich R, MacNee W. Comorbidities and systemic effects of chronic obstructive pulmonary disease. *Clin Chest Med.* 2014;35(1):101-130. doi: 10.1016/j.ccm.2013.10.007 pmid: 24507840
- Jaitovich A, Barreiro E. Skeletal Muscle Dysfunction in Chronic Obstructive Pulmonary Disease. What We Know and Can Do for Our Patients. *Am J Respir Crit Care Med.* 2018;198(2):175-186. doi: 10.1164/rccm.201710-2140CI pmid: 29554438
- Zhang J, Chu S, Zhong X, Lao Q, He Z, Liang Y. Increased expression of CD4+IL-17+ cells in the lung tissue of patients with stable chronic obstructive pulmonary disease (COPD) and smokers. *Int Immunopharmacol.* 2013;15(1):58-66. doi: 10.1016/j.intimp.2012.10.018 pmid: 23127823
- 9. Agrawal D, Vohra R, Gupta PP, Sood S. Subclinical peripheral neuropathy in stable middle-aged patients with chronic obstructive pulmonary disease. *Singapore Med J*. 2007;**48**(10):887.
- 10. Andrianopoulos V, Wagers SS, Groenen MT, Vanfleteren LE, Franssen FM, Smeenk FW, et al. Characteristics and determinants of endurance cycle ergometry and six-minute walk distance in patients with COPD. *BMC Pulm Med.* 2014;14:97. doi: 10.1186/1471-2466-14-97 pmid: 24885117
- 11.Bourbeau J, Tan WC, Benedetti A, Aaron SD, Chapman KR, Coxson HO, et al. Canadian Cohort Obstructive Lung Disease (CanCOLD): Fulfilling the need for longitudinal observational studies in COPD. COPD. 2014;11(2):125-132. doi: 10.3109/15412555.2012.665520 pmid: 22433011
- 12. Van Remoortel H, Raste Y, Louvaris Z, Giavedoni S, Burtin C, Langer D, et al. Validity of six activity monitors in chronic obstructive pulmonary disease: a comparison with indirect calorimetry. *PLoS One*. 2012;**7**(6):e39198. **doi:** 10.1371/journal.pone.0039198 **pmid:** 22745715
- 13.Spielmanns M, Boeselt T, Gloeckl R, Klutsch A, Fischer H, Polanski H, et al. Low-Volume Whole-Body Vibration Training Improves Exercise Capacity in Subjects With Mild to Severe COPD. *Respir Care*. 2017;62(3):315-323. doi: 10.4187/respcare.05154 pmid: 27923937
- 14.Cochrane DJ. Vibration exercise: the potential benefits. *Int J Sports Med.* 2011;**32**(2):75-99. doi: 10.1055/s-0030-1268010 pmid: 21165804
- 15.Gloeckl R, Heinzelmann I, Baeuerle S, Damm E, Schwedhelm AL, Diril M, et al. Effects of whole body vibration in patients with chronic obstructive pulmonary disease--a randomized controlled trial. *Respir Med*. 2012;**106**(1):75-83. **doi:** 10.1016/j.rmed.2011.10.021 **pmid:** 22104540
- 16.Gloeckl R, Heinzelmann I, Kenn K. Whole body vibration training in patients with COPD: A systematic review. *Chron Respir Dis*. 2015;**12**(3):212-221. doi: 10.1177/1479972315583049 pmid: 25904085

- 17. Kang JI, Jeong DK, Park SK, Park SK, Lee JH. Effects of chest resistance exercise on forced expiratory volume in one second and fatigue in patients with COPD. *J Kor Phys Ther*. 2011;**23**(2):37-43.
- 18.Fulk GD, Echternach JL, Nof L, O'Sullivan S. Clinometric properties of the six-minute walk test in individuals undergoing rehabilitation poststroke. *Physiother Theory Pract.* 2008;24(3):195-204. doi: 10.1080/09593980701588284 pmid: 18569856
- 19.Gloeckl R, Richter P, Winterkamp S, Pfeifer M, Nell C, Christle JW, et al. Cardiopulmonary response during whole-body vibration training in patients with severe COPD. *ERJ Open Res.* 2017;3(1). doi: 10.1183/23120541.00101-2016 pmid: 28326310
- 20. Fattah A, Sayed M, Abdel-aziem AA. "Benefits of neuromuscular electrical stimulation versus vibration training to chronic obstructive pulmonary disease patients.". *J Phys Ther Heal Promot*. 2017;**5**:10-17. **doi:** 10.18005/PTHP0501002
- 21.Samir AA, Weaam SH, Salfeldeen AR, Eman R. "Effect of Whole Body Vibration on Exercise Capacity and Quality ofLife in Obstructive Lung Disease.". *Med J Cairo Univ.* 2021;**89**:47-52.
- 22. Berner K, Albertyn SCS, Dawnarain S, Hendricks LJ, Johnson J, Landman A, et al. The effectiveness of combined lower limb strengthening and whole-body vibration, compared to strengthening alone, for improving patient-centred outcomes in adults with COPD: A systematic review. *S Afr J Physiother*. 2020;**76**(1):1412. doi: 10.4102/sajp.v76i1.1412 pmid: 32671277
- 23. Higashimoto Y, Honda N, Yamagata T, Sano A, Nishiyama O, Sano H, et al. Exertional dyspnoea and cortical oxygenation in patients with COPD. *Eur Respir J*. 2015;**46**(6):1615-1624. **doi:** 10.1183/13993003.00541-2015 **pmid:** 26493791
- 24.Ide K, Secher NH. Cerebral blood flow and metabolism during exercise. *Progress Neurobiol*. 2000;**61**(4):397-414. **doi:** 10.1016/S0301-0082(99)00057-X
- 25. Higashimoto Y, Honda N, Yamagata T, Matsuoka T, Maeda K, Satoh R, et al. Activation of the prefrontal cortex is associated with exertional dyspnea in chronic obstructive pulmonary disease. *Respiration*. 2011;**82**(6):492-500. **doi:** 10.1159/000324571 **pmid:** 21474913
- 26. Herigstad M, Hayen A, Evans E, Hardinge FM, Davies RJ, Wiech K, et al. Dyspnea-related cues engage the prefrontal cortex: evidence from functional brain imaging in COPD. *Chest.* 2015;**148**(4):953-961. **doi:** 10.1378/chest.15-0416 **pmid:** 26134891
- 27.Gaurav S, Meenakshi S, Jayshri G, Ramanjan S. Effect of alterations in breathing patterns on EEG activity in normal human subjects. *Int J Curr Res Med Sci.* 2016;2:38-45. doi: 10.22192/ijcrms.2016.02.12.007
- 28. Kokodoko AD, Pasquino C, Satta A, Neri M, Galli M. Quantitative evaluation of the brain electrical activity of patients suffering from chronic obstructive bronchopneumonopathy (COPD). *Schweiz Arch Neurol Psychiatr.* 1992;**143**(5):473-479.
- 29. Braz Junior DS, Dornelas de Andrade A, Teixeira AS, Cavalcanti CA, Morais AB, Marinho PE. Wholebody vibration improves functional capacity and quality of life in patients with severe chronic obstructive pulmonary disease (COPD): a pilot study. *Int J Chron Obstruct Pulmon Dis*. 2015;10:125-132. doi: 10.2147/COPD.S73751 pmid: 25624756