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Original Article

Effect of manual chest wall compression in participants with chronic obstructive pulmonary disease

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Abstract. [Purpose] Pulmonary rehabilitation is appropriate for most individuals with chronic obstructive pulmonary disease (COPD). Pulmonary rehabilitation consists of conditioning and exercise therapy. Conditioning includes relaxation, breathing exercises, and manual chest wall compression during expiration (CWC). CWC improves the symptoms in individuals with respiratory disease who have undergone mechanical ventilation. However, evidence supporting the effectiveness of CWC for COPD has been insufficient. This study aimed to determine physiological responses to CWC in participants with COPD. [Participants and Methods] Twenty-nine participants with COPD were included in the study. Manual CWC techniques were performed in a comfortable position chosen by the participants (sitting, forward-leaning (sitting), or semi-Fowler's). Ventilatory parameters, occlusion airway pressure ($P_{0.1}$), and dyspnea were assessed using a visual analog scale and were compared before and during CWC. [Results] During manual CWC, oxygen consumption, carbon dioxide production, end-tidal carbon dioxide concentration, and dyspnea were significantly decreased; however, $P_{0.1}$ was not affected. [Conclusion] Manual CWC for COPD had an immediate physiological effect, including a decrease in dyspnea that may have been facilitated by a reduced workload of the respiratory muscles. Thus, manual CWC may be effective for dyspnea by reducing oxygen consumption in the respiratory muscles.

Key words: Chronic obstructive pulmonary disease, Manual chest wall compression technique, Respiratory motor output

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INTRODUCTION

Pulmonary rehabilitation is appropriate for most individuals with chronic obstructive pulmonary disease (COPD). Pulmonary rehabilitation consists of conditioning and exercise therapy. Conditioning includes relaxation, breathing exercises, and manual chest wall compression during expiration (CWC). Exercise therapy primarily consists of exercise, including limb muscle strength training and endurance training via walking or ergometer[1, 2)]. Because dyspnea frequently observed in chronic respiratory disease is one of the limiting factors of exercise, the effect of exercise therapy can change significantly

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Table 1. Characteristics of participants

	Overall (n=29)	GOLD stage 1 (n=3)	GOLD stage 2 (n=11)	GOLD stage 3 (n=8)	GOLD stage 4 (n=7)
Age (years)	74.0 ± 8.7	59.7 ± 4.2	78.0 ± 6.0	75.5 ± 4.2	72.3 ± 11.3
Height (cm)	163.3 ± 8.5	172.3 ± 6.8	165.4 ± 7.4	162.8 ± 6.1	157.0 ± 9.9
Weight (kg)	58.7 ± 11.2	65.0 ± 4.4	64.6 ± 10.6	57.8 ± 9.2	47.9 ± 8.8
FVC (l)	2.69 ± 1.2	4.80 ± 0.6	3.22 ± 0.5	2.31 ± 0.6	1.40 ± 0.5
FEV_1 (l)	1.38 ± 0.8	3.29 ± 0.0	1.64 ± 0.3	0.99 ± 0.2	0.61 ± 0.2
FEV_1% (%)	50.6 ± 14.4	69.4 ± 8.8	51.6 ± 10.7	46.5 ± 14.1	45.8 ± 17.1
%FEV_1 (%)	52.6 ± 24.0	101.3 ± 4.0	65.7 ± 11.8	41.6 ± 10.0	30.1 ± 56.0
VC (l)	3.13 ± 1.0	5.19 ± 0.2	3.44 ± 0.6	2.66 ± 0.5	2.05 ± 0.6
PI_{max} (cmH_2O)	56.1 ± 23.3	75.0 ± 41.0	62.7 ± 20.4	51.0 ± 13.5	43.6 ± 24.3
PE_{max} (cmH_2O)	72.8 ± 31.5	103.7 ± 56.6	81.9 ± 23.2	63.8 ± 31.5	55.4 ± 20.1

Data presented as mean ± SD.
GOLD: Global Initiative for Chronic Obstructive Lung Disease; FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 s; FEV_1%: FEV_1/forced vital capacity (FVC) ratio; %FEV_1: FEV_1/$FEV_{1predicted}$; VC, vital capacity; PI_{max}: maximal inspiratory pressure; PE_{max}: maximal expiratory pressure.

depending on success in controlling dyspnea. CWC, in positions such as semi-Fowler's, forward-leaning sitting with pillow, or forward-leaning sitting with supporting elbow on knee, is often used to improve dyspnea before, during, and after exercise. Using the manual CWC technique, patients exhale their own breath to a lower than functional residual capacity facilitated by pressure from a therapist's hand; their thorax subsequently expands by its own elastic recoil. This reduces workload on the inspiratory muscles and increases tidal volume (VT). It appears that these interventions reduce dyspnea due to improved breathing efficiency and a reduction in the consumption of oxygen in respiratory muscles. There have been reports of the effects of CWC in COPD and symptomatic controls[3]. However, evidence supporting the effectiveness of this technique has been insufficient, despite the frequency of use of this maneuver in Japan. Accordingly, the aim of this study was to experimentally verify the effects of manual CWC from a physiological perspective.

PARTICIPANTS AND METHODS

A total of 29 ambulatory participants (25 males, 4 females) with COPD (Global Initiative for Chronic Obstructive Lung Disease [GOLD] stage 1 [n=3]; stage 2 [n=11]; stage 3 [n=8]; stage 4 [n=7]), who did not require home oxygen therapy, were recruited from the Kirigaoka Tsuda Hospital (Fukuoka, Japan). None of the participants had severe orthopedic, cardiovascular, or central nervous system disorder(s), and all had locomotor abilities with/without cane (Table 1). The advantages and disadvantages of participating in this study were explained to all participants before informed written consent was obtained from each. This study was approved by the Kyorin University institutional ethics committee (approval no. 24-22 in 2014).

Vital capacity (VC), FEV_1, FEV % in 1 s ($FEV_{1\%}$), and FVC were measured using spirometry (HI-801, CHEST MI, Inc., Tokyo, Japan). Maximum inspiratory mouth pressure (PImax) was measured using a respiratory muscle strength device (0100, Micro Medical, Rochester Kent, UK).

Occlusion airway pressure ($P_{0.1}$) was evaluated as an alternative index for respiratory motor output[4–6]. An airway occlusion system (model 9326, Hans Rudolph, Shawnee Mission, KS, USA) was used to measure $P_{0.1}$ during exercise (dead space 48.9 ml). A differential pressure transducer (DP-10, Validyne, CA, USA) was used to measure airway pressure, and a metabolic gas analyzer (AE-300S, Minato Medical Science, Osaka, Japan) was used to measure ventilatory parameters. A hot-wire flow transducer was connected to the outlet of the airway occlusion system, and a mask (MAS0215, Minato Medical Science, Osaka, Japan) was connected to the oral side port. To measure airway pressure, a differential pressure transducer was connected to the airway occlusion system via a tube (diameter 4 mm) (Fig. 1). The inlet of the airway occlusion system was occluded using a balloon with manual manipulation at the end of expiration, and held until the beginning of inspiration. Oral pressure was measured 100 ms after beginning expiration and defined as $P_{0.1}$[7, 8]. $P_{0.1}$ was measured randomly five times, and the mean value calculated from 4 stable measurements was recorded[8]. Electrocardiography (WEP-7202, Nihonkoden, Tokyo, Japan) was used to measure heart rate. Analog signals from raw flow pressure and electrocardiography were downloaded into a personal computer via an AD converter (PowerLab 16/30, ADInstruments, Sydney, Australia) at a sampling frequency of 1,000 Hz. These signals were analyzed using commercially available software (Chart 5.3, ADInstruments, Sydney, Australia) to calculate VT, minute ventilation ($\dot{V}E$), oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}CO_2$), end-tidal carbon dioxide concentration ($ETCO_2$), breathing frequency, heart rate, and $P_{0.1}$. A 10 cm visual analog scale was used to measure dyspnea. Because COPD is characterized by weakness in respiratory muscle strength, $P_{0.1}$ was corrected to PImax ($P_{0.1}$/PImax)[9].

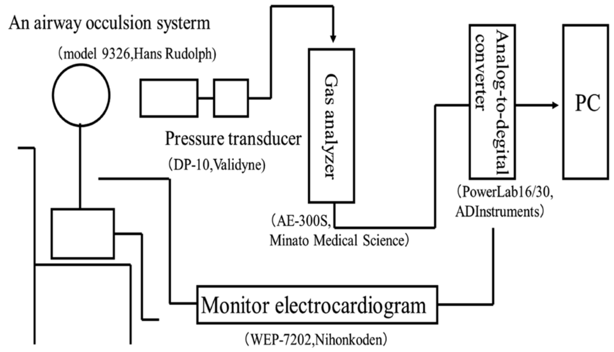

Fig. 1. Measuring equipment.
The airway occlusion system used to measure $P_{0.1}$. A pressure transducer was connected to the side port of the airway occlusion system to measure mouth pressure, while a hot-wire flow transducer from the gas analyzer was connected to the expiratory port. The analog signal from the gas analyzer, as well as measurements from the pressure transducer, were continuously recorded using an analog-to-digital converter. PC: Personal computer.

Table 2. The most comfortable breathing position selected by participants

GOLD stage	Sitting	Forward leaning sitting	Semi-Fowler's position
1	1 (0.6)	1 (0.4)	1 (−1.0)
2	3 (1.5)	1 (−1.3)	7 (−0.2)
3	0 (−1.1)	0 (−1.7)	8* (2.8)
4	0 (−1.0)	4* (2.6)	3 (−1.6)
Total	4	6	19

Data presented as n (adjusted residual). χ^2 p=0.03; effect size (φ)=0.03. GOLD: Global Initiative for Chronic Obstructive Lung Disease.
*Statistically significant.

Participants were first asked to place themselves in a sitting, forward-leaning (sitting), and semi-Fowler's position, and asked to choose for themselves the most comfortable position for breathing. These positions are described as follows: sitting position (sitting on a chair with a backrest, with feet touching the floor; forward-leaning sitting position (body bent forward with a pillow); semi-Fowler's position (lying on a bed with head at a 30° and knees slightly bent). A senior physical therapist performed manual CWC by way of pressing on the bilateral lower rib cage during expiration. The strength of rib cage compression was adjusted to one in which the participants were most comfortable based on interview feedback.

Participants were asked to place themselves in their chosen position; ventilation and HR were measured for 5 min thereafter. They then received manual CWC from a therapist while remaining in the same position. Manual CWC was continued for 5 min, after which $P_{0.1}$ measurements were repeated five times at 1 min intervals. Finally, dyspnea before/after manual CWC was assessed according to a visual analog scale.

SPSS version 21.0 (IBM Corporation, Armonk, NY, USA) was used for statistical analysis. The correlation between GOLD stage and respiratory function was determined using Pearson correlation analysis. The χ^2 test was used to compare GOLD stage and positioning. The Paired t-test and Wilcoxon signed-rank tests were used to compare values before and after manual breathing assistance. All values are expressed as mean ± standard deviation, and statistical significance was set at $p<0.05$.

RESULTS

The positioning selected by the participants is summarized in Table 2. Chosen positioning differed according to individual GOLD stage: the semi-Fowler's position was most frequently chosen by participants in GOLD stage 3; the forward-leaning sitting position was chosen most by those in GOLD stage 4 (p=0.03). Among all participants, 19 (65.5%) chose the semi-Fowler's position. Changes in ventilation index before and after breathing assistance are summarized in Tables 3 and 4. $\dot{V}O_2$, $\dot{V}CO_2$, $ETCO_2$, and visual analog scale decreased after manual breathing assistance (p=0.003, p=0.003, p<0.001, p<0.001, respectively) although VT, $P_{0.1}$, and $P_{0.1}$/PImax were not affected.

DISCUSSION

In our study, the most comfortable breathing position chosen by participants with COPD differed according to their GOLD stage. The reason for reduced dyspnea based on positioning is explained by ventilatory mechanics. When supine, the abdominal viscus presses the diaphragm into the rib cage compared with the upright position[10]. Therefore, although elevation of the diaphragm is supported by these pressures during expiration, stronger contractions are needed to move the diaphragm. The tension-length relationship of the diaphragm is improved by its movement into the rib cage in the supine position[11]. These effects, however, are altered to the contrary in the upright position. The semi-Fowler's position confers benefits from both the effect of gravity and improvement in length-tension relationship because it is intermediary between lying and upright. Furthermore, the semi-Fowler's position is equivalent to the lying position given that the entire body is supported by an external surface. Oxygen consumption may be lower because of low skeletal muscle activity while in the semi-Fowler's position.

Table 3. Comparison of ventilatory parameters and heart rate (HR) before and after breathing assistance

Parameter	Before	After	p value (ES)
V_T (l)	0.63 ± 0.15	0.65 ± 0.20	0.906
$\dot{V}_E$ (l/min)	10.2 ± 2.63	9.86 ± 3.27	0.188
Mean flow (ml/s)	0.29 ± 0.09	0.28 ± 0.11	0.242
$\dot{V}O_2$ (l/min)	0.22 ± 0.07	0.19 ± 0.06	0.003* (0.53)
$\dot{V}CO_2$ (l/min)	0.17 ± 0.04	0.15 ± 0.05	0.003* (0.52)
$ETCO_2$ (%)	3.98 ± 0.63	3.70 ± 0.62	0.001* (0.65)
f (breaths/min)	16.2 ± 4.17	15.7 ± 4.13	0.331
HR (beats/min)	74.3 ± 7.31	75.3 ± 5.88	0.600

Data presented as mean ± SD. VT: tidal volume; $\dot{V}E$: minute ventilation; Mean flow: mean expiratory flow rate; $\dot{V}O_2$: oxygen consumption; $\dot{V}CO_2$: carbon dioxide production; $ETCO_2$: end-tidal carbon dioxide concentration; f: breathing frequency; ES: effect size.
*Statistically significant.

Table 4. Comparison of respiratory motor output and visual analog scale between before and after breathing assist

Parameter	Before	After	p value (ES)
$P_{0.1}$ (cmH_2O)	2.70 ± 1.0	2.69 ± 1.1	0.963
$P_{0.1}$/PImax (%)	5.61 ± 3.1	5.84 ± 4.3	0.519
Visual analog scale (cm)	1.22 ± 1.3	0.82 ± 1.3	0.001* (0.72)

Data presented as mean ± SD.
$P_{0.1}$: airway-occlusion pressure 0.1 s after the start of inspiratory flow; $P_{0.1}$/PImax: airway-occlusion pressure 0.1 s after the start of inspiratory flow/maximal inspiratory pressure; PImax: maximal inspiratory pressure; ES: Effect size.
*Statistically significant.

Only participants in GOLD stage 4 chose the forward-leaning sitting position instead of the semi-Fowler's position. The forward leaning posture has been shown to be highly effective and is probably the body position most adopted by patients with lung disease[12–14]. The effectiveness of this position does not appear to be related to the severity of airway obstruction, changes in $\dot{V}E$, or improved oxygenation. Hyperinflation and paradoxical abdominal movement were, in fact, reported to be related to the relief of dyspnea in the forward-leaning position. Alternatively, forward leaning has been associated with a significant reduction in electromyographic activity of the scalene and sternomastoid muscles under transdiaphragmatic pressure[12]. From these studies, it was concluded that the subjective improvement of dyspnea in patients with COPD was the result of a more favorable position of the diaphragm with regard to its length-tension curve. In addition, forward leaning with arm support enables accessory muscles (pectoralis minor and major) to significantly contribute to rib cage elevation. The same holds true for the forward leaning position with head support, enabling the accessory neck muscles to assist inspiration. The forward-leaning sitting position facilitates increases in the diameter or circumference of the rib cage and lung volume; consequently, individuals in this position experience improved dyspnea[15–17]. These facts may be the reason that forward-leaning sitting was chosen as most comfortable position in patients in GOLD stage 4. Postures in which participants were most comfortable differed according to disease severity. Therefore, we chose to perform our evaluations from among sitting, forward-leaning, and semi-Fowler's positioning in our study.

Several studies have also reported that manual CWC during expiration increases expiratory flow rates, improves removal of airway secretions, gas exchange, and pulmonary mechanics in patients on mechanical ventilation[18–20], and those with cystic fibrosis[21], COPD[22], and asthma[23]. The physiological effects of CWC have been studied in patients with COPD[3]. During CWC, the COPD group demonstrated significantly higher peak expiratory and inspiratory flow rates, VT, inspiratory capacity, inspiratory and expiratory times, and the ratio of VT to inspiratory time, than during quiet breathing, but not $\dot{V}_{50}$ and $\dot{V}_{25}$[3]. These results suggest that CWC may reduce hyperinflation in COPD. In fact, CWC has been used as a technique to reduce dyspnea by reducing hyperinflation[24].

$\dot{V}O_2$ and $\dot{V}CO_2$ were significantly decreased, in addition to dyspnea, in our study. It appeared that decreases in $\dot{V}O_2$ and $\dot{V}CO_2$ reflected decreasing respiratory muscle mechanical activity and respiratory muscle metabolism. Respiratory muscle oxygen uptake and consumption were also possibly decreased by CWC. Furthermore, substantial alveolar ventilation increased when considering decreasing $ETCO_2$, although it did not decrease and VT did not increase, despite our predicted results. These results appear to reflect the physiological effect of manual CWC on the respiratory muscles.

We used $P_{0.1}$ as an alternative respiratory motor output measure because it has been intimately connected with dyspnea, and could be evaluated objectively[7, 25]. In patients with COPD, $P_{0.1}$ is clearly higher than in healthy participants[26, 27], and higher with increasing severity[28]. However, both $P_{0.1}$ and $P_{0.1}$/PImax were not different before/after manual CWC. Manual CWC is a maneuver in which lung volume is decreased below functional residual capacity (FRC) by forced expirations. When the lung volume is lowered by FRC at initial inspiration, $P_{0.1}$ is strongly affected by thoracic elastic recoil. Therefore, the resulting $P_{0.1}$ value reflects inspiratory effort added to thoracic elastic recoil. Although $P_{0.1}$ was not decreased by manual CWC in our study, we do not believe it increased respiratory motor output.

This study had limitations that should be addressed. Some short-term effects of manual CWC were clearly visible from a physiological perspective; however, we could not examine whether it had a measurable benefit for exercise (i.e., prolonged exercise endurance time, increased $\dot{V}O_2$ max, or aerobic threshold). Furthermore, we considered decreased dyspnea to be related to decreased respiratory muscle activity or respiratory motor output; however, these differences were not reflected in the $P_{0.1}$ values. This requires direct evaluation of neuromuscular activity (e.g., using electromyography on respiratory muscle, or performing near-infrared spectroscopy on the brain) to clarify supportive evidence. In conclusion, the present study investigated the physiological effects of CWC in participants with COPD. Manual CWC that was administered in positions most comfortable for the participants improved oxygen consumption, respiratory rate, and dyspnea. We conclude that manual CWC may lead to decreased dyspnea in individuals experiencing respiratory failure, and that the physical responses were directly related to the technique.

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Conflict of interest

The authors declare no conflict of interest associated with this manuscript.

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REFERENCES

1) Nici L, Donner C, Wouters E, et al. ATS/ERS Pulmonary Rehabilitation Writing Committee: American Thoracic Society/European Respiratory Society statement on pulmonary rehabilitation. Am J Respir Crit Care Med, 2006, 173: 1390–1413. [Medline] [CrossRef]
2) Ries AL, Bauldoff GS, Carlin BW, et al.: Pulmonary rehabilitation: Joint ACCP/AACVPR evidence-based clinical practice guidelines. Chest, 2007, 131: 4S–42S. [Medline] [CrossRef]
3) Nozoe M, Mase K, Ogino T, et al.: Effects of chest wall compression on expiratory flow rates in patients with chronic obstructive pulmonary disease. Braz J Phys Ther, 2016, 20: 158–165. [Medline] [CrossRef]
4) Killian KJ, Gandevia SC, Summers E, et al.: Effect of increased lung volume on perception of breathlessness, effort, and tension. J Appl Physiol, 1984, 57: 686–691. [Medline] [CrossRef]
5) Manning HL, Schwartzstein RM: Pathophysiology of dyspnea. N Engl J Med, 1995, 333: 1547–1553. [Medline] [CrossRef]
6) Milic-Emili J, Whitelaw WA, Derenne JP: New tests to assess lung function: occlusion pressure—a simple measure of the respiratory center’s output. N Engl J Med, 1975, 293: 1029–1030. [Medline] [CrossRef]
7) Whitelaw WA, Derenne JP: Airway occlusion pressure. J Appl Physiol 1985, 1993, 74: 1475–1483. [Medline] [CrossRef]
8) Kera T, Aihara A, Inomata T: Reliability of airway occlusion pressure as an index of respiratory motor output. Respir Care, 2013, 58: 845–849. [Medline]
9) Nemer SN, Barbas CS, Caldeira JB, et al.: Evaluation of maximal inspiratory pressure, tracheal airway occlusion pressure, and its ratio in the weaning outcome. J Crit Care, 2009, 24: 441–446. [Medline] [CrossRef]
10) Agostoni E, Mognoni P, Torri G: Relation between changes of rib cage circumference and lung volume. Appl Physiol, 1965, 20: 1179–1186. [CrossRef]
11) Druz WS, Sharp JT: Activity of respiratory muscles in upright and recumbent humans. J Appl Physiol, 1981, 51: 1552–1561. [Medline] [CrossRef]
12) Sharp JT, Drutz WS, Moisan T, et al.: Postural relief of dyspnea in severe chronic obstructive pulmonary disease. Am Rev Respir Dis, 1980, 122: 201–211. [Medline]
13) Druz WS, Sharp JT: Electrical and mechanical activity of the diaphragm accompanying body position in severe chronic obstructive pulmonary disease. Am Rev Respir Dis, 1982, 125: 275–280. [Medline]
14) Banzett RB, Topulos GP, Leith DE, et al.: Bracing arms increases the capacity for sustained hyperpnea. Am Rev Respir Dis, 1988, 138: 106–109. [Medline] [CrossRef]
15) Dean E: Effect of body position on pulmonary function. Phys Ther, 1985, 65: 613–618. [Medline] [CrossRef]
16) Ogino T, Mase K, Nozoe M, et al.: Effects of arm bracing on expiratory flow limitation and lung volume in elderly COPD subjects. Respir Care, 2015, 60: 1282–1287. [Medline] [CrossRef]
17) Prandi E, Couture J, Bellemare F: In normal subjects bracing impairs the function of the inspiratory muscles. Eur Respir J, 1999, 13: 1078–1085. [Medline]

[CrossRef]
18) Gonçalves EC, Souza HC, Tambascio J, et al.: Effects of chest compression on secretion removal, lung mechanics, and gas exchange in mechanically ventilated patients: a crossover, randomized study. Intensive Care Med, 2016, 42: 295–296. [Medline] [CrossRef]
19) Martí JD, Li Bassi G, Rigol M, et al.: Effects of manual rib cage compressions on expiratory flow and mucus clearance during mechanical ventilation. Crit Care Med, 2013, 41: 850–856. [Medline] [CrossRef]
20) Naue WS, Forgiarini Junior LA, Dias AS, et al.: Chest compression with a higher level of pressure support ventilation: effects on secretion removal, hemodynamics, and respiratory mechanics in patients on mechanical ventilation. J Bras Pneumol, 2014, 40: 55–60. [Medline] [CrossRef]
21) McCarren B, Alison JA: Physiological effects of vibration in subjects with cystic fibrosis. Eur Respir J, 2006, 27: 1204–1209. [Medline] [CrossRef]
22) Kolaczkowski W, Taylor R, Hoffstein V: Improvement in oxygen saturation after chest physiotherapy in patients with emphysema. Physiother Can, 1989, 41: 18–23.
23) Fisher MM, Whaley AP, Pye RR: External chest compression in the management of acute severe asthma—a technique in search of evidence. Prehosp Disaster Med, 2001, 16: 124–127. [Medline] [CrossRef]
24) Yoshimi K, Ueki J, Seyama K, et al.: Pulmonary rehabilitation program including respiratory conditioning for chronic obstructive pulmonary disease (COPD): improved hyperinflation and expiratory flow during tidal breathing. J Thorac Dis, 2012, 4: 259–264. [Medline]
25) Whitelaw WA, Derenne JP, Milic-Emili J: Occlusion pressure as a measure of respiratory center output in conscious man. Respir Physiol, 1975, 23: 181–199. [Medline] [CrossRef]
26) Erbland ML, Ebert RV, Snow SL: Interaction of hypoxia and hypercapnia on respiratory drive in patients with COPD. Chest, 1990, 97: 1289–1294. [Medline] [CrossRef]
27) Marin JM, Montes de Oca M, Rassulo J, et al.: Ventilatory drive at rest and perception of exertional dyspnea in severe COPD. Chest, 1999, 115: 1293–1300. [Medline] [CrossRef]
28) Montes de Oca M, Celli BR: Mouth occlusion pressure, CO2 response and hypercapnia in severe chronic obstructive pulmonary disease. Eur Respir J, 1998, 12: 666–671. [Medline] [CrossRef]