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ORIGINAL ARTICLE

A COMPARISON BETWEEN POSITIVE AND NEGATIVE PRESSURE OSCILLATION IN AIRWAY CLEARANCE CHEST PHYSIOTHERAPY FOR OBESE PATIENTS UNDER MECHANICAL VENTILATION: A CROSS-SECTIONAL STUDY

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Introduction: Airway clearance chest physiotherapy for patients under mechanical ventilation can use positive pressure oscillation (PPO) or negative pressure oscillation (NPO) therapy. This study compared these two therapies for obese patients. **Methods:** Eight patients with body mass index ≥ 25 , under mechanical ventilation, and suffering from retained airway secretions were included. In this crossover trial, the subjects were randomly assigned to receive either PPO or NPO therapy for 30 min; after six h, each subject received the other therapy. **Measurements and main results:** Both therapies significantly improved the arterial oxygen tension/inspired oxygen fraction (P/F) ratio (PPO: 276.2 (24.4) to 305.2 (21.3), $P = 0.014$; NPO: 273.5 (21.0) to 277.5 (18.2), $P = 0.039$) and tidal volume (Vt) (PPO: 439.5 (28.8) to 457.6 (28.3) mL, $P = 0.008$; NPO: 456.6 (24.7) to 461.9 (24.5) mL, $P = 0.021$). PaCO₂ decreased significantly with PPO (43.2 (2.3) to 41.8 (2.1) mmHg, $P = 0.008$). Compared to NPO, PPO improved more in the P/F ratio (10.9% vs. 4.5%, $P = 0.028$), Vt (5.4% vs. 1.3%, $P = 0.038$) and PaCO₂ (2.7% vs. 0.8%, $P = 0.036$). **Conclusions:** Airway clearance chest physiotherapy with PPO is more effective for obese

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INTRODUCTON

In an acute care setting, patients who require mechanical ventilation are at a risk of retained secretions. This can lead to significant problems in those critically ill undergoing mechanical ventilation¹ and is associated with significantly higher mortality and morbidity, because the retained secretions and mucus can occlude the airways and cause atelectasis and gas exchange impairment, as well as being a sequestered growth medium for bacteria^{2,3}. These problems are even more crucial for obese patients at risk of expiratory flow limitation and airway obstruction due to increased respiratory and airway system resistance^{4,5}.

There are several chest physiotherapy (CPT) techniques for clearing retained secretions during mechanical ventilation⁶. One of these techniques is high frequency oscillation therapy (HFO)⁶, that occur in two different ways: by oscillating the airway directly through generating positive transrespiratory pressure, and oscillating the airway indirectly via the chest wall through negative changes in transrespiratory pressure. A currently available HFO-CPT technique for positive pressure oscillation (PPO) uses an intrapulmonary percussive ventilator (IPV) to create positive transrespiratory pressure by injecting short, rapid inspiratory flow pulses directly into the airway at a high frequency. This makes airway pressure oscillate (described as percussive oscillation), and airway walls to vibrate in synchrony with these oscillations. During the intrapulmonary percussive ventilation, percussive oscillation opens the airways and enhances airway secretion mobilization and drainage from the lung periphery to the larger airways^{7,8}. The other type of HFO-CPT technique that uses negative pressure oscillation (NPO) can be achieved with high frequency chest wall oscillation (HFCWO) applied with a rigid chest cuirass connected to a compressor that can deliver negative pressures to the chest wall and generate negative changes in transrespiratory pressure at a high frequency. These oscillations reduce the secretion viscosity⁹, improving its mobilization. Previous studies have suggested that treatment with HFCWO is as effective as conventional CPT in patients with cystic fibrosis^{10,11}.

Until now, no direct comparison has been made on the effectiveness of PPO-CPT and NPO-CPT for airway clearance, and so it remains unclear whether positive or

negative oscillation therapy should be the choice for first-line therapy in obese ventilated patients. Therefore, the aim of this study was to compare the differences between the two types of HFO-CPT for mechanically ventilated obese patients with excessive airway secretions.

METHODS

This study was approved by the local Human Ethics Committee of the Hokkaido University Hospital and a written informed consent was obtained from each patient's more close relative (IRB number 100514). The study was conducted between April 2010 and March 2011.

Selection Criteria

Patients undergoing mechanical ventilation in the Intensive Care Units (ICU) of the Hokkaido University Hospital with copious secretions were enrolled in this study. The following inclusion criteria were applied: acute respiratory failure [arterial oxygen tension (P_{aO_2})/inspired oxygen fraction (F_{iO_2}) ratio (P/F ratio) < 300] diagnosis; intubation and mechanical ventilation for at least 48 hours prior to enrollment; body mass index (BMI) ≥ 25 ; age of 20 years or more; airway secretion retention diagnosed by clinical evaluation (auscultation, the presence of consolidation in the chest X-ray, the number of suctioning procedures needed, episodes of airway occlusion, and a Miller and Jones classification for P2 or P3 sputum). The exclusion criteria were as it follows: the presence of acute exacerbation of COPD; asthma; interstitial lung disease; pneumothorax; pulmonary thromboembolism; P/F ratio < 100; hemodynamic instability; patients who have experienced thoracotomy or laparotomy within the previous 5 days; suctioning by bronchofiberscope within the previous 24 hours; pregnancy; and receiving percutaneous cardiopulmonary support and extracorporeal membrane oxygenation. The exit criteria were as it follows: deterioration in the patient's general condition and the presence of hemodynamic instability because of PPO or NPO (e.g., changes in blood pressure and heart rate $\geq 20\%$, a decrease in percutaneous oxygen saturation $\geq 10\%$, or an increase in end-tidal $CO_2 \geq 20\%$); or development of one of the exclusion criteria during the study period.

Design

The cross-sectional study was conducted as it follows. Subjects were randomly assigned to receive either PPO therapy or NPO therapy for 30 min. After a washout period of 6 hours, the subject received the other therapy for 30 min as a crossover trial (Figure 1).

HFO-CPT Devices and Settings

Two advanced HFO-CPT devices were used: the Intrapulmonary Percussive Ventilator (IPV2C; Percussionaire Corp., Bird Space Technology, Sandpoint, ID, USA) and the Biphasic Cuirass Ventilator (RTX respirator; United Hayek Industries, London, United Kingdom). IPV was used throughout the trial with the following settings: frequency 4–5 Hz, inspiratory/expiratory (IE) ratio 1:1, and percussive pressure span 30–35 psi (2.1–2.46 kg/cm²) for 30 min⁸. The IE ratio was matched with the RTX setting. The IPV was in-lined conventional ventilator circuits. The frequency and duration were set as described previously⁸. The IPV frequency was set at 4–5Hz, a frequency between that for optimal ventilatory and percussive effects, because the subjects were not only retaining secretions but were also in acute respiratory failure. One of the preset modes of the RTX, the airway clearance mode, delivers two types of oscillation: a period of high frequency/low-amplitude chest wall oscillation (the HFCWO mode), followed by a period of high-amplitude pressure at low frequency with a shortened expiratory ratio (the cough mode). The cough mode was not used in this study. Only the high-frequency period was used to compare the oscillation effects, based on the following settings: frequency 10 Hz, IE ratio 1:1, and cuirass pressure –25 to –30 cm H₂O for 30 min.^{12,13}

Protocol

During the study period, the subjects were ventilated with an EC ventilator (GE Healthcare, Madison, WI, USA) with a COVX-module (GE Healthcare, Helsinki, Finland). The subjects were initially ventilated using a synchronized-intermittent mandatory ventilation mode (with pressure control) with a tidal volume (Vt) of 8 mL/kg ideal body weight, an IE ratio of 1:2, the respiratory rate adjusted to achieve normocapnia, and appropriate levels of positive end-expiratory pressure. During the study period, the subjects were ventilated with mandatory breathing under deep sedation (Richmond Agitation Sedation Scale –5) and no spontaneous breathing. No muscle relaxant was used.

The cough reflex was very poor. This protocol is illustrated in Figure 1. Each subject underwent two therapy sessions of 30 min. The IPV (or HFCWO) was added and superimposed on the conventional ventilation without changing the conventional ventilator settings. When the IPV or HFCWO finished after 30 min, airway suctioning was performed again, followed by a recruitment maneuver, using the sustained inflation method (continuous positive airway pressure at 45 cm H₂O × 20 s) to prevent alveolar collapse from the suctioning¹⁴. The subjects remained in a recumbent position while receiving each therapy, except during the washout period. Supine position was applied for all patients during the washout period for all.

Data Collection and Analysis

In a clinical study on airway clearance therapy for mechanically ventilated and intubated patients, it is difficult to set the volume of discharged secretion as an end point because there is no established method to precisely quantify the amount of secretions clinically^{15,16}. Considering the retained secretions and mucus can occlude airways and cause atelectasis and gas exchange impairment, in this study, we used P/F ratio, VCO₂, PaCO₂, and Vt as substitute endpoints to obtain airway clearance, as seen on previous studies^{15,17}. Arterial blood gas analysis and Vt measurements were made 5 min before and 10 min after each treatment (Figure 1).

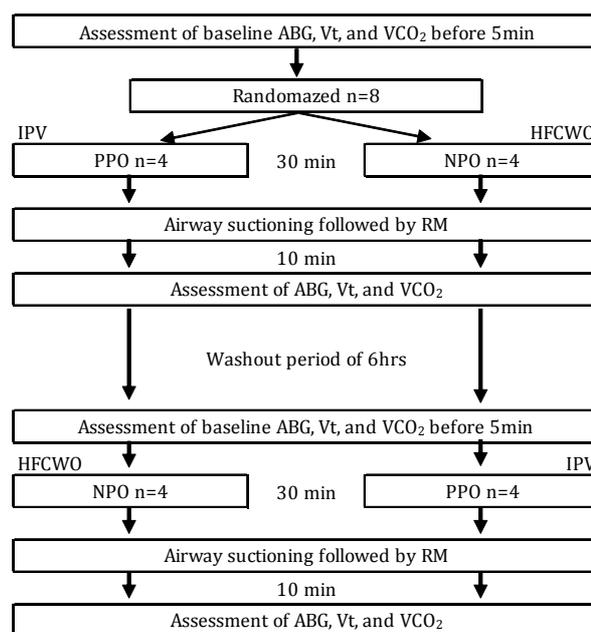


Figure 1. Protocol for the study: The study contained two therapy arms and patients were randomized to one of the

two therapy arms. PPO (IPV) and NPO (HFCWO) therapy session was applied 30 minutes in each, with an interval of 6hrs between PPO and NPO. Collection of the arterial blood gas samples, tidal volume and VCO_2 were performed 5 minutes before and 10 minutes after the PPO or NPO. Airway suctioning and recruitment maneuver were conducted after the termination of PPO or NPO. PPO, positive pressure oscillation; NPO, negative pressure oscillation; IPV, intrapulmonary percussive ventilation; HFCWO, high frequency chest wall oscillation; ABG, arterial blood gases; V_t , tidal volume; RM, recruitment maneuver; VCO_2 , volumetric exhaled carbon dioxide;

At the same time points, a CO_2 production (VCO_2) procedure available in the ventilator was performed based on the washout/washin method with a F_iO_2 step change of 0.1, as previously described¹⁸. The P/F ratio was calculated from the arterial blood gas sample and the mean of two VCO_2 values was taken. To assess the effects of the two HFO therapies on the airway secretions, the P/F ratio, VCO_2 , P_aCO_2 , V_t , and the relative changes of each parameter were compared between PPO-CPT and NPO-CPT.

Statistical Analysis

The Wilcoxon signed-rank test was used to compare the parameters before and after each treatment, and the Mann-Whitney U test was used to compare the PPO-CPT and the NPO-CPT. Data from these interventions are presented as median (standard error: SE). A P -value <0.05 was considered statistically significant. The statistical analysis was performed using the Graphpad 5.0 software package (Graphpad Software Inc., San Diego, CA, USA).

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RESULTS

Eight patients were enrolled in the study. Their demographic data, and their underlying conditions and initial respiratory parameters, are presented in Table 1.

Table 1. Characteristics of the patients

Age (years)	61.4	(16.4)
Sex (male/female)	4/4	
Body mass index (kg/m)	27.1	(1.8)
APACHE II score	25.6	(6.2)
P/F ratio	239.8	(68)
Respiratory rate	21	(8)
Positive end-expiratory pressure (cmH)	8.5	(2.4)
Peak inspiratory pressure (cmH)	18.5	(4.2)
ICU days before study's enrollment (days)	7.9	(4.1)
Diagnosis		
Pneumonia	6	
Trauma	1	
Burn	1	

We presented data as mean (SD) or n. APACHE II score, Acute Physiology and Chronic Health Evaluation II score; P/F ratio, a ratio of particle pressure of oxygen (P_aO_2) to fractional concentration of oxygen ($F_{I}O_2$); ICU Intensive Care Unit.

The subjects had BMIs between 25.06 and 30.08, and six (75%) of them had pneumonia. Before the therapy sessions, there were no statistically significant differences

between the trial arms regarding P/F ratio (PPO: 276.2 (24.4) vs. NPO: 273.5 (21.0), *P* = 0.879), VCO_2 (PPO: 184.8 (12.1) vs. NPO: 173.1 (6.3) mL, *P* = 0.505), P_aCO_2

(PPO: 43.2 (2.3) vs. NPO: 41.2 (2.2) mmHg, $P = 0.674$), or Vt (PPO: 439.5 (28.8) vs. NPO: 456.6 (24.7) mL, $P = 0.721$) (Figure 2).

Figure 2 shows the changes in the P/F ratio, VCO_2 , P_aCO_2 , and Vt. Both types of CPT significantly improved the P/F ratio (PPO: from 276.2 (24.4) to 305.2 (21.3), $P = 0.014$; NPO: from 273.5 (21.0) to 277.5 (18.2), $P = 0.039$) and Vt (PPO: from 439.5 (28.8) to 457.6 (28.3), $P = 0.008$; NPO: from 456.6 (24.7) to 461.8 (24.5) mL, $P = 0.021$). P_aCO_2 decreased significantly with PPO-CPT therapy (from 43.2 (2.3) to 41.8 (2.1) mmHg, $P = 0.008$). We observed no

changes in VCO_2 after both therapies. The comparison between the two CPTs improved more with PPO than with NPO in the P/F ratio (10.9 (4.7) % vs. 4.5 (2.6) %, $P = 0.028$), Vt (5.4 (2.1) % vs. 1.3 (0.8) %, $P = 0.038$) and P_aCO_2 (2.7 (0.4)% vs. 0.8 (0.6) %, $P = 0.036$) (Figure 3). We found no statistically significant difference between the two therapies in the change in VCO_2 (12.0 (7.5) % vs. 13.2 (6.1) %, $P = 0.879$). All subjects tolerated both treatments and we observed no harmful adverse effects during the study period.

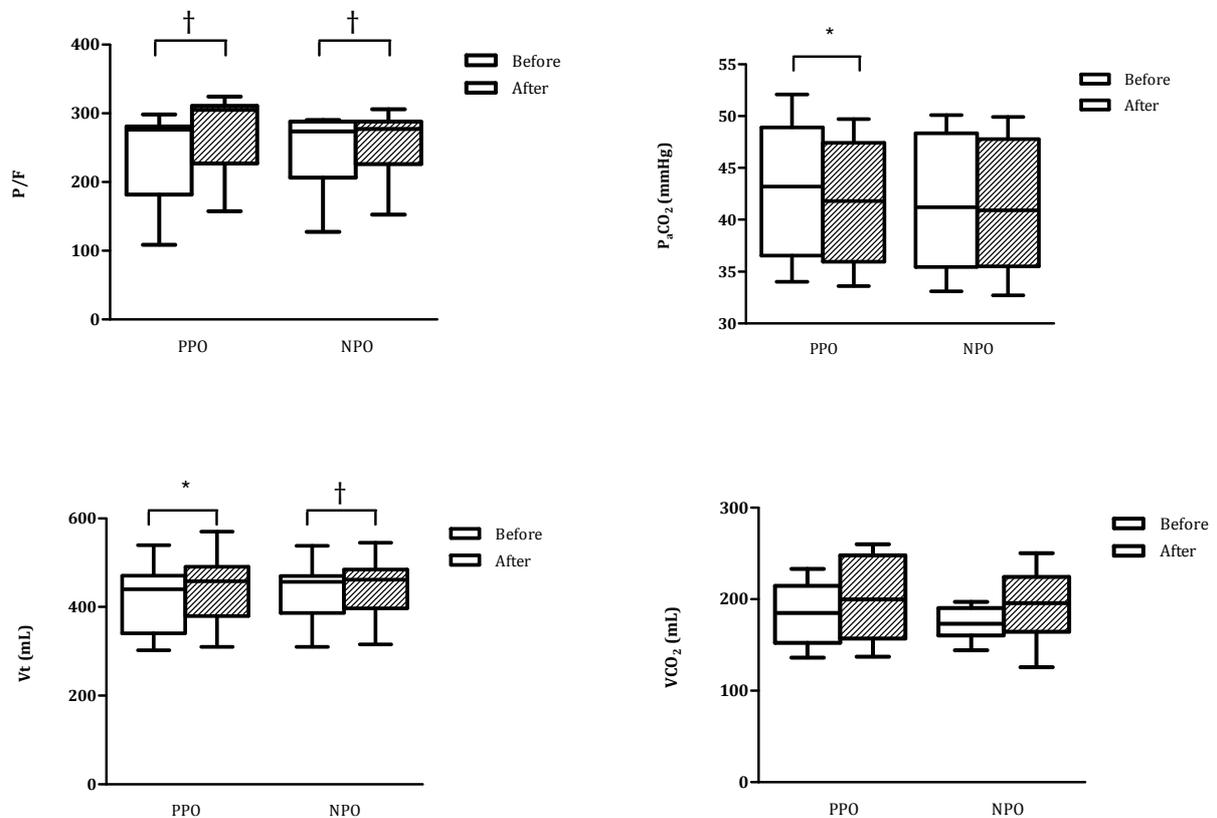


Figure 2. The comparison of P/F ratio, P_aCO_2 , VCO_2 , and Vt of the both HFO: Data are presented as median (standard error: SE). PPO, positive pressure oscillation; NPO, negative pressure oscillation; P/F ratio, a ratio of partial pressure of oxygen (P_aO_2) to fractional concentration of oxygen (F_iO_2); VCO_2 , volumetric exhaled carbon dioxide; P_aCO_2 , partial pressure of arterial carbon dioxide; Vt, tidal volume. * $P < 0.01$, Before vs. After. † $P < 0.05$, Before vs. After.

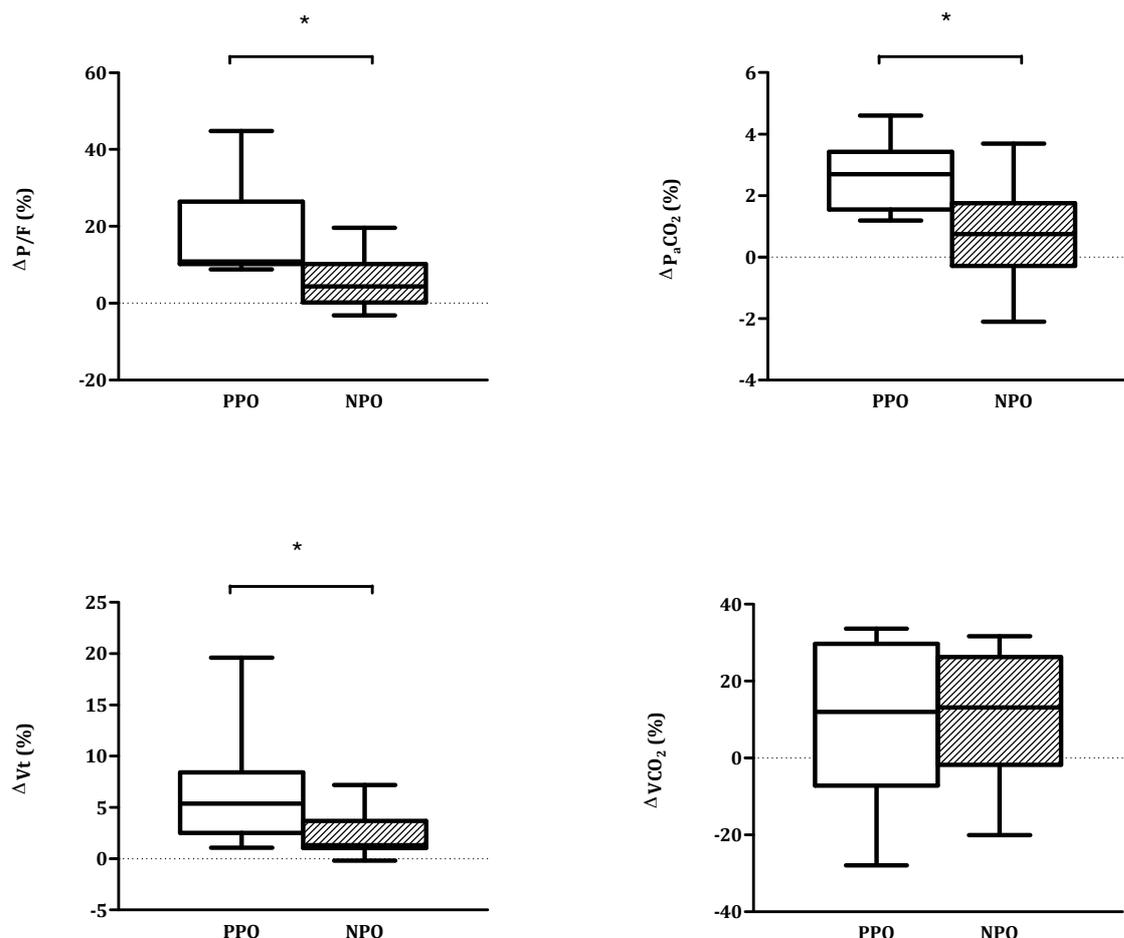


Figure 3. Relative change rate of P/F ratio, P_aCO_2 , VCO_2 , and V_t of the both HFO: Relative changes of each parameter are expressed percentage values. Data are presented as median (standard error: SE). PPO, positive pressure oscillation; NPO, negative pressure oscillation; P/F ratio, a ratio of partial pressure of oxygen (P_aO_2) to fractional concentration of oxygen (F_iO_2); VCO_2 , volumetric exhaled carbon dioxide; P_aCO_2 , partial pressure of arterial carbon dioxide; V_t , tidal volume. * $P < 0.05$, IPV vs. HFCWO.

DISCUSSION

This is the first report to compare the effects of airway clearance CPT on positive pressure oscillation via the airway and negative pressure oscillation via the chest wall in obese patients undergoing mechanical ventilation in the ICU. For these patients, both therapies improved the P/F ratio and V_t , and PPO also improved P_aCO_2 . A comparison between the two therapies showed that P/F ratio, P_aCO_2 , and V_t improved more with PPO than with NPO.

We infer that improvements in blood gas and V_t values after both treatments were due to improvements in atelectasis or collapsed alveoli and in the peripheral airway, a result of airway clearance by oscillation¹⁹⁻²¹. There are two possible reasons for airway clearance being different in

PPO and NPO: 1) the influence of the subject's body type, and 2) not using the "cough mode" with NPO-CPT. The pressure conduction efficiency to the peripheral airways and lungs may have differed between the two therapies because the subjects were obese. PPO (IPV) involves transtracheal pressurization, whereas NPO (HFCWO) uses transthoracic pressurization; therefore, the generated pressure at the NPO cuirass could be absorbed or obstructed in the subcutaneous adipose tissue of the thoraco-abdominal region (in general, the subcutaneous adipose tissue acts as a absorber or cushion against the external pressure²²). If so, the pressure generated at the cuirass would not be enough at the pleural space or at the

airways and lungs²³. This detrimental effect would increase for thicker subcutaneous adipose tissue. The subjects in this study were obese, with BMI 25–30; considering they had thick subcutaneous adipose tissue, the oscillating pressure of NPO may not get to their peripheral airways and lungs sufficiently. This hypothesis is according to the differences in HFCWO efficacy among obese adult and children with neuromuscular disease who are not obese. Despite both having low chest compliance, only the latter can receive HFCWO²³⁻²⁵. The difference between obese adult and children with neuromuscular disease is that the primary cause of low chest compliance in obese is the thick subcutaneous adipose tissue. Moreover, the great effectiveness of HFCWO requires high thoracic tissue elasticity²⁶. The elasticity of adipose tissue is inferior when compared to the one of the muscle tissue²⁷. Nevertheless, PPO can transmit generated positive pressure directly to the airway and, consequently, to the peripheral airways and lungs²⁸, less influenced by the thickness of the subcutaneous adipose tissue. Thus, the transpulmonary pressure (P_L) generated in the lungs and peripheral airways may have differed a lot when comparing both therapies^{29,30}. We based these considerations on the data from a clinical study conducted by Scholz SE et al²³. They showed that HFCWO failed at improving the arterial oxygenation in obese patients. However, their study also improved blood gas value when adding positive pressure (via airway) to HFCWO. Consequently, NPO may not have generated sufficient oscillations in the peripheral airways compared to PPO, not properly optimizing the HFO mechanisms for airway clearance, such as airway wall radial displacement and expiratory bias flow with secretion^{31,32}. However, obesity could work positively for PPO-CPT. When added to normal compliance airways in a low compliance thorax, PPO increased expiratory bias flow and airway wall radial displacement achieved their maximum effect³³. The results of this study support this: the subjects were obese patients, without airway diseases such as COPD, who had increased lung–thorax elastance. Thus, elastic recoil and its bias might have increased and enhanced during PPO. In addition, obesity may have worked against NPO, as described above, resulting in a significant difference between the two therapies³⁴.

This study only focused on the effect of oscillation type, and the cough mode; we did not use one of the component factors of the HFCWO secretion mode to allow this comparison. The cough mode adds high pressure to increase expiratory airflow. Chari et al.¹⁹ used the cough mode with the high-frequency mode and showed the effect of airway clearance for patients with a BMI of 30. Another case report also included successful use of the cough mode¹³. Fink et al.^{35,36} described the key to success in airway clearance as positive pressure generated by the device during expiration. When applying NPO-CPT for obese patients, the authors suggested that the cough mode should be an indispensable factor.

STUDY LIMITATIONS

In a clinical study on airway clearance therapy for mechanically ventilated, intubated patients, it is difficult to set the volume of discharged secretion as an end point, as there is no established method to precisely quantify the amount of secretions clinically. In this study, we used P/F ratio, VCO_2 , P_aCO_2 , and V_t as substitute end points for airway clearance^{16,17}. We inferred that differences in transmission efficiency of pressure oscillation contributed to differences in the effects of both therapies, which still needs to confirmation by P_L measurement. However, we were not able to measure this because of the difficulty in carrying out such procedure in a clinical environment and because of the inaccuracy of the values obtained during the body's high frequency oscillation. At the present, the only NPO-CPT device applicable in a clinical setting is the RTX, as it can not deliver NPO to the whole body, only administering negative pressure to the front surface of the rib cage, which we needed to consider when interpreting the effects of NPO in this study. With the indications of ventilation, there was no statistically significant difference, but the value before HFCWO showed a better trend than IPV. Consequently, we can not completely discard the possibility of influence by previously conducted IPV. Despite small sample size limiting the generalization from these findings, this study may partially provide useful information for CPT in clinical settings.

CONCLUSION

CPT with positive pressure oscillations via the airway is an effective and feasible therapy to enhance the physiological effects of airway clearance therapy in obese patients undergoing mechanical ventilation. These results suggest that positive pressure oscillation CPT should be the choice for first-line airway clearance therapy in patients about to undergo negative pressure oscillation CPT; however, there is need for further studies to confirm these effects.

REFERENCES

1. Branson RD. Secretion management in the mechanically ventilated patient. *Respir Care.* 2007;52(10):1328-1342; discussion 1342-1327.
2. Konrad F, Schreiber T, Brecht-Kraus D, et al. Mucociliary transport in ICU patients. *Chest.* 1994;105(1):237-241.
3. Rogers DF. The role of airway secretions in COPD: pathophysiology, epidemiology and pharmacotherapeutic options. *Copd.* 2005;2(3):341-353.
4. Zerah F, Harf A, Perlemuter L, et al. Effects of obesity on respiratory resistance. *Chest.* 1993;103(5):1470-1476.
5. Salome CM, King GG, Berend N. Physiology of obesity and effects on lung function. *J Appl Physiol.* 2010;108(1):206-211.
6. Gosselink R, Bott J, Johnson M, et al. Physiotherapy for adult patients with critical illness: recommendations of the European Respiratory Society and European Society of Intensive Care Medicine Task Force on Physiotherapy for Critically Ill Patients. *Intensive Care Med.* 2008;34(7):1188-1199.
7. Salim A, Martin M. High-frequency percussive ventilation. *Crit Care Med.* 2005;33(3 Suppl):S241-245.
8. Susumu Nakahashi MH, Kenichi Katabami, Takeshi Wada, Atsushi Sawamura, Takehiko Ishikawa, Satoshi Gando. Effects of intrapulmonary percussive ventilation for acute respiratory failure. *J Jpn Soc Intensiv Care Med.* 2012;19(2):191-196.
9. King M, Phillips DM, Gross D, et al. Enhanced tracheal mucus clearance with high frequency chest wall compression. *Am Rev Respir Dis.* 1983;128(3):511-515.
10. Arens R, Gozal D, Omlin KJ, et al. Comparison of high frequency chest compression and conventional chest physiotherapy in hospitalized patients with cystic fibrosis. *Am J Respir Crit Care Med.* 1994;150(4):1154-1157.
11. Burnett M, Takis C, Hoffmeyer B. Comparative efficacy of manual chest physiotherapy and a high frequency chest compression vest in inpatient treatment of cystic fibrosis. *Am Rev Respir Dis.* 1993;147(4(suppl)):A30.
12. Phillips GE, Pike SE, Jaffe A, et al. Comparison of active cycle of breathing and high-frequency oscillation jacket in children with cystic fibrosis. *Pediatr Pulmonol.* 2004;37(1):71-75.
13. Scherer TA, Barandun J, Martinez E, et al. Effect of high-frequency oral airway and chest wall oscillation and conventional chest physical therapy on expectoration in patients with stable cystic fibrosis. *Chest.* 1998;113(4):1019-1027.
14. Dyhr T, Bonde J, Larsson A. Lung recruitment manoeuvres are effective in regaining lung volume and oxygenation after open endotracheal suctioning in acute respiratory distress syndrome. *Crit Care.* 2003;7(1):55-62.
15. Clini EM, Antoni FD, Vitacca M, et al. Intrapulmonary percussive ventilation in tracheostomized patients: a randomized controlled trial. *Intensive Care Med.* 2006;32(12):1994-2001.
16. Macchione M, Guimaraes ET, Saldiva PH, et al. Methods for studying respiratory mucus and mucus clearance. *Braz J Med Biol Res.* 1995;28(11-12):1347-1355.
17. Takeda S, Nakanishi K, Takano T, et al. The combination of external high-frequency oscillation and pressure support ventilation in acute respiratory failure. *Acta Anaesthesiol Scand.* 1997;41(6):670-674.
18. Olegard C, Sondergaard S, Houltz E, et al. Estimation of functional residual capacity at the bedside using standard monitoring equipment: a modified nitrogen washout/washin technique requiring a small change of the inspired oxygen fraction. *Anesth Analg.* 2005;101(1):206-212, table of contents.
19. Chari S, King J, Rajesh PB, et al. Resolution of left lower lobe collapse postesophagectomy using the Medivent RTX respirator, a novel noninvasive respiratory support system. *J Cardiothorac Vasc Anesth.* 2004;18(4):482-485.
20. Reper P, van Looy K. Chest physiotherapy using intrapulmonary percussive ventilation to treat persistent atelectasis in hypoxic patients after smoke inhalation.

Burns. 2013;39(1):192-193.

21. Tonan M, Hashimoto S, Kimura A, et al. Successful treatment of severe asthma-associated plastic bronchitis with extracorporeal membrane oxygenation. *J Anesth.* 2012;26(2):265-268.

22. Kudo S, Osawa Y, Momiyama H. Effects of Fat Thickness at The Hip and Seating Positions on The Distribution of Pressure in a Wheelchair, Using Three Types of Cushions *Bulletin of College of Allied Medical Science, Akita University.* 2000;8(1):67-73.

23. Scholz SE, Sticher J, Haufler G, et al. Combination of external chest wall oscillation with continuous positive airway pressure. *Br J Anaesth.* 2001;87(3):441-446.

24. Keating JM, Collins N, Bush A, et al. High-frequency chest-wall oscillation in a noninvasive-ventilation-dependent patient with type 1 spinal muscular atrophy. *Respir Care.* 2011;56(11):1840-1843.

25. Toyoshima M, Maeoka Y, Kawahara H, et al. Pulmonary atelectasis in patients with neurological or muscular disease; gravity-related lung compression by the heart and intra-abdominal organs on persistent supine position. *No To Hattatsu.* 2006;38(6):419-424.

26. Hayek Z, Peliowski A, Ryan CA, et al. External high frequency oscillation in cats. Experience in the normal lung and after saline lung lavage. *Am Rev Respir Dis.* 1986;133(4):630-634.

27. Inoue M, Fukuda O, Tsubai M, et al. Automated Discrimination Method of Muscular and Subcutaneous Fat Layers Based on Tissue Elasticity. *JSICE.* 2010;46:401-407.28. Dellamonica J, Louis B, Lyazidi A, et al. Intrapulmonary percussive ventilation superimposed on conventional ventilation: bench study of humidity and ventilator behaviour. *Intensive Care Med.* 2008;34(11):2035-2043.

29. Borelli M, Benini A, Denkewitz T, et al. Effects of continuous negative extrathoracic pressure versus positive end-expiratory pressure in acute lung injury patients. *Crit Care Med.* 1998;26(6):1025-1031.

30. Loring SH, Banzett RB. Whole-body "negative-pressure" ventilation: is it really different? *Am J Respir Crit Care Med.* 2008;178(5):542; author reply 542-543.

31. Freitag L, Kim CS, Long WM, et al. Mobilization of mucus by airway oscillations. *Acta Anaesthesiol Scand Suppl.* 1989;90:93-101.

32. Soland V, Brock G, King M. Effect of airway wall flexibility on clearance by simulated cough. *J Appl Physiol.* 1987;63(2):707-712.

33. Toussaint M, De Win H, Steens M, et al. Effect of intrapulmonary percussive ventilation on mucus clearance in duchenne muscular dystrophy patients: a preliminary report. *Respir Care.* 2003;48(10):940-947.

34. Tsuruta R, Kasaoka S, Okabayashi K, et al. Efficacy and safety of intrapulmonary percussive ventilation superimposed on conventional ventilation in obese patients with compression atelectasis. *J Crit Care.* 2006;21(4):328-332.

35. Fink JB. Positive pressure techniques for airway clearance. *Respir Care.* 2002;47(7):786-796.

36. Fink JB, Mahlmeister MJ. High-frequency oscillation of the airway and chest wall. *Respir Care.* 2002;47(7):797-807.