Immediate Effects of Thixotropy Conditioning of Inspiratory Muscles on Chest-Wall Volume in Chronic Obstructive Pulmonary Disease

Masahiko Izumizaki MD PhD, Fujiyasu Kakizaki PT PhD, Kazumasa Tanaka MD PhD, and Ikuo Homma MD PhD

INTRODUCTION:Thixotropy is a passive property of the skeletal muscle that depends on the muscle's immediate history of contraction and length change. Inspiratory-muscle thixotropy affects the end-expiratory position of the rib cage in normal subjects. OBJECTIVE: To determine whether a reduction in end-expiratory chest-wall volume occurs after thixotropy conditioning of inspiratory muscles in patients with chronic obstructive pulmonary disease. METHODS: Ten male subjects with chronic obstructive pulmonary disease (mean ± SD forced expiratory volume in the first second 70 ± 20% of predicted) showed an increased ratio of residual volume to total lung capacity (49 ± 4.7%). The subjects conducted inspiratory muscle thixotropy conditioning maneuvers at 3 different chest-wall volumes (end-expiratory volume of baseline breathing, residual volume plus 40% of expiratory reserve volume, and residual volume) and with 3 levels of inspiratory effort (0%, 30%, and 100% of maximal inspiratory mouth pressure at each volume), with airway-closure, in the sitting position. Using respiratory induction plethysmography, we measured the effect of effort-intensity and volume at the time of the conditioning maneuver on the end-expiratory chest-wall volume of the 5 respiratory cycles immediately following the conditioning maneuver. RESULTS: There was a reduction in end-expiratory chest-wall volume after the conditioning maneuver, except when conditioning was performed at end-expiratory baseline with 0% effort. The reduction increased as effort intensity increased ($p = 0.011$) and as volume decreased ($p < 0.001$), and the reduction was attained by rib-cage movement rather than abdominal movement. CONCLUSIONS: Thixotropy conditioning of inspiratory muscles, at a reduced chest-wall volume, decreased end-expiratory chest-wall volume in the 5 subsequent breaths in patients with chronic obstructive pulmonary disease. *Key words: chronic obstructive pulmonary disease, end-expiratory lung volume, hyperinflation, inspiratory muscles, thixotropy.* [Respir Care 2006;51(7):750–757. © 2006 Daedalus Enterprises]

Introduction

The passive response of a muscle to stretching is partly determined by its immediate history of muscle contraction and length change, depending on whether the muscle was contracted immediately beforehand at a long length (hold-long) or at a short length (hold-short).[1–4] This history-dependent property is referred to as thixotropy.[1–4] Stable cross-bridges, which are distinguishable from actively cycling bridges, are a primary source of this history-depen-

Masahiko Izumizaki MD PhD and Ikuo Homma MD PhD are affiliated with the Department of Physiology, Showa University School of Medicine, Tokyo, Japan. Fujiyasu Kakizaki PT PhD is affiliated with the Department of Physical Therapy, and Kazumasa Tanaka MD PhD is affiliated with the Department of Internal Medicine, Toyosu Hospital, Showa University, Tokyo, Japan.

Masahiko Izumizaki MD PhD presented a version of this report at the International Conference of the American Thoracic Society, held May 20–25, 2005, in San Diego, California.

This study was supported in part by a grant-in-aid for scientific research from the Ministry of Education, Culture, Sports, Science, and Technology of Japan (grant number 17790542).

Correspondence: Masahiko Izumizaki MD PhD, Department of Physiology, Showa University School of Medicine, 1-5-8 Hatanodai, Shinagawa-ku, Tokyo 142-8555, Japan. E-mail: masahiko@med.showa-u.ac.jp.

dent passive character of muscles.[5] Proske and colleagues proposed the hypothesis that stable cross-bridges can be detached by stretching or by a conditioning contraction, and after detachment the bridges are reformed at their length within a few seconds. If the muscle is shortened after stable cross-bridges have formed at a long length (hold-long conditioning), the fibers will be unable to absorb the length change and they will fall slack; if the muscle is lengthened after stable cross-bridges have formed at a short length (hold-short conditioning), no slack develops.[3,4]

Homma and colleagues showed that inspiratory-muscle conditioning based on the thixotropy principle affects end-expiratory rib-cage volume (V_{RC}).[6–8] Forceful contraction of inspiratory muscles at a deeply deflated lung volume with airway occlusion (ie, hold-long conditioning of inspiratory muscles) causes a subsequent reduction in end-expiratory V_{RC}; at a deeply inflated lung volume (ie, hold-short conditioning of inspiratory muscles), it causes a subsequent increase in end-expiratory V_{RC}.[6] Homma and colleagues proposed that history-dependent passive properties of inspiratory muscles are an important component of expiration, because expiratory movements need to stretch inspiratory muscles to reduce lung volume.[8]

It seems likely that hold-long conditioning of inspiratory muscles also reduces end-expiratory V_{RC} and, thus, chest-wall volume (V_{CW}) in patients with chronic obstructive pulmonary disease (COPD). However, it is unclear whether this effect can be detected in these patients, because changes in structure and function of the respiratory system, such as air trapping, thwart inspiratory muscle lengthening for hold-long conditioning.[9] The aim of the present study was to explore whether thixotropy conditioning of inspiratory muscles at a reduced V_{CW} (hold-long conditioning) reduces end-expiratory V_{CW} in COPD patients who have an elevated ratio of residual volume (RV) to total lung capacity (TLC). We examined the effect of the strength of inspiratory-muscle contraction and the length of inspiratory muscles (estimated by V_{CW}) at which conditioning was performed, on end-expiratory V_{CW} of the 5 subsequent breathing cycles. We also analyzed the breathing pattern after conditioning, because an altered breathing pattern (particularly a change in expiratory time [T_E]) is a possible contributing factor to a change in end-expiratory lung volume.[10]

Methods

This study was approved by the ethics committee of Showa University, and all the subjects provided written informed consent for their participation.

Patients

Ten male patients (age range 58–81 years) with COPD took part in the study. COPD was diagnosed on the basis of clinical history, exposure to risk factors such as cigarette smoking, and pulmonary function tests showing airflow obstruction (ratio of forced expiratory volume in the first second to forced vital capacity $< 70\%$ of predicted). Lung volume was determined via the helium-dilution method. Table 1 shows the anthropometric data and resting-lung-function data. All the subjects had air trapping (RV/TLC $> 35\%$).

Table 1. Patient Characteristics*

Variable	Mean ± SD
Age (y)	72 ± 8
BMI (kg/m^2)	22 ± 3
FEV_1 (L, % pred)	1.5 ± 0.3, 70 ± 20%
FEV_1/FVC (%)	50 ± 11
FRC (L, % pred)	3.9 ± 0.7, 107 ± 15%
RV (L (% pred)	2.9 ± 0.5, 179 ± 31%
TLC (L, % pred)	6.0 ± 0.6, 116 ± 12%
RV/TLC (%)	49 ± 4.7

*n = 10
BMI = body mass index
FEV_1 = forced expiratory volume in the first second
FVC = forced vital capacity
FRC = functional residual capacity
RV = residual volume
TLC = total lung capacity

Equipment

We measured respiration with a respiratory-induction plethysmograph (Respitrace System, Ambulatory Monitoring, Ardsley, New York) and a respiratory flow meter (RF-2, Minato Medical, Osaka, Japan), and we estimated the cross-sectional areas of the rib cage and the abdomen with the plethysmograph operated in direct-current (DC) mode. The bands of coiled Teflon-insulated wire were positioned just below the axillae and above the iliac crest. Rib-cage and abdominal movements during respiration change the inductance of the bands, and the changes in inductance are converted into proportional voltage changes. The plethysmograph was calibrated via the least-squares method,[11] which is based on the assumption that the respiratory system can be considered as a simple physical system with 2 degrees of freedom of motion; V_{CW} changes are the sum of the V_{RC} and the abdominal volume (V_{AB}) changes.[12] The subjects breathed in sitting and semi-recumbent positions for the calibration, so that the different relative contributions of the rib cage and abdominal movements were identified. The subjects breathed into a mouthpiece that houses a transducer (AR-601G, Nihon Kohden, Tokyo, Japan) attached to the pressure gauge. The data were fed into a computerized analysis system (PowerLab, ADInstruments, Castle Hill, Australia). During the trials,

the V_{CW} signal was monitored online to determine when the airway was closed, and a display of the mouth pressure enabled the subject to adjust to the target inspiratory pressure. We gave the subjects verbal encouragement to continue the effort during conditioning.

Protocol

The inspiratory-muscle conditioning maneuvers were conducted with 3 different levels of inspiratory effort and at 3 different V_{CW}, with airway-closure, in the sitting position. Using the plethysmograph traces, we measured the after-effects of the conditioning maneuver on end-expiratory V_{CW}, relative to the different inspiratory-effort intensities and the different V_{CW} at which the conditioning maneuvers were performed.

During the trials, each subject was seated on a chair, with his nose clipped, and he was breathing quietly. A magnetically driven mouthpiece shutter connected to the flow meter was manually triggered to close the airway. At the start of the experiment we measured inspiratory capacity and expiratory reserve volume from the V_{CW} trace, and maximal inspiratory mouth pressure (P_{Imax}) at 3 levels of V_{CW}: end-expiratory V_{CW} of baseline breathing; RV plus 40% of expiratory reserve volume; and RV.

All the tests were preceded by preconditioning maneuvers at an inflated position in which the inspiratory muscles were shortened. Because the resting tension and passive stiffness of striated muscles depend on the immediate history of muscle movements and contractions, we found it necessary to place the muscles in a defined state before the start of the experiments.[4] Before each trial, inspiratory muscles were contracted with the chest wall inflated (end-expiratory V_{CW} during baseline breathing plus 60% of inspiratory capacity) at a mouth pressure of -5 cm H_2O for 2 s, and then relaxed for 2 s. The airway was then reopened and the subject resumed quiet breathing. The plethysmograph traces were maintained in a semi-steady state for at least 2 min before the start of each trial.

There were 9 different types of conditioning maneuver. The subject was instructed to produce an inspiratory effort at one of 3 levels of V_{CW} (end-expiratory V_{CW} during baseline breathing, RV plus 40% of expiratory reserve volume, and RV) at one of 3 levels of mouth pressure (0%, 30%, and 100% of P_{Imax} at each V_{CW}). Each conditioning maneuver was performed once, in random order. Muscle contractions were maintained for 2 s, with subsequent relaxation for 2 s, with the airway closed. After each conditioning maneuver, the shutter was reopened and the subject resumed quiet breathing. At a mouth pressure of 0%, no respiratory effort was made for 4 s at each of the volumes before the airway was released. Trials were separated by a resting period of at least 3 min, and a preconditioning maneuver was performed prior to each trial.

For quantitative analysis, the mean end-expiratory volume of the 5 breaths taken immediately before each conditioning maneuver was defined as the zero level of each plethysmograph trace. Differences in end-expiratory volume between the zero line and after each conditioning were measured from each plethysmograph trace. With each subject we averaged the end-expiratory-volume differences over the 5 respiratory cycles after each conditioning. Inspiratory time (T_I), T_E, and expiratory tidal volume (V_T) were also analyzed.

Analysis

Results are expressed as mean ± standard deviation. Statistical analysis was via 2-way analysis of variance for repeated measures to test for the within-factor (effort intensity and V_{CW} at the time of conditioning) effects and interactions between those 2 effects. Differences were considered statistically significant when $p < 0.05$.

Results

Table 2 shows the results for inspiratory-effort intensity, estimated from mouth pressure, and V_{RC}, V_{AB}, and V_{CW} positions at the time of conditioning. P_{Imax} increased as the conditioning volume decreased, and deflation of the chest wall for conditioning at RV was achieved largely by V_{RC} reductions, rather than by V_{AB} reductions.

Figure 1 shows typical traces of V_{RC}, V_{AB}, and V_{CW} after 3 conditionings, performed by a 61-year-old subject with moderate COPD. Figure 1D represents the conditioning schedule. Conditioning consisted of a 2-s inspiratory effort and a 2-s subsequent breath-holding period at the target volume, with airway occlusion. In Figure 1A, one conditioning, consisting of 2-s inspiratory effort at end-expiratory V_{CW} during baseline breathing with 100% P_{Imax}, is followed by a few end-expiratory volume changes in the 3 traces. Figure 1B shows the after-effects of another conditioning at RV without inspiratory effort. We found small reductions in end-expiratory volume. End-expiratory volume reductions were most obvious after conditioning at RV with 100% P_{Imax}, as shown in Figure 1C.

Analysis of the pooled data verified these end-expiratory volume reductions in COPD patients. Figure 2 shows the after-effects of all conditionings on the averaged end-expiratory volume of the V_{RC}, V_{AB}, and V_{CW} traces. Reductions of end-expiratory V_{CW} were most prominent after conditioning at RV with 100% P_{Imax}, and these were attained by V_{RC} rather than V_{AB}. We found a significant effect of V_{CW}, where conditioning occurred, on end-expiratory volume in V_{RC} ($p = 0.011$), V_{AB} ($p = 0.003$), and V_{CW} ($p < 0.001$) traces, which showed that a greater reduction in end-expiratory volume occurred after conditioning maneuvers conducted at lower V_{CW}. The signifi-

Table 2. Inspiratory Effort and Volume of Rib Cage, Abdomen, and Chest Wall at the Time of Thixotropy Conditioning

Conditioning Position	Inspiratory Effort (mean ± SD)		Change in Volume (mean ± SD)*		
	% P_{Imax}	Mouth Pressure (cm H_2O)	Rib Cage (L)	Abdomen (L)	Chest Wall (L)
EEB	0	0.2 ± 2.6	−0.01 ± 0.08	0.01 ± 0.03	0.00 ± 0.08
	30	−10.2 ± 5.5	0.01 ± 0.06	0.00 ± 0.03	0.01 ± 0.07
	100	−26.6 ± 17.6	−0.02 ± 0.06	0.00 ± 0.06	−0.02 ± 0.06
RV + 40% ERV	0	2.5 ± 3.0	−0.22 ± 0.12	−0.22 ± 0.14	−0.42 ± 0.16
	30	−12.6 ± 7.8	−0.26 ± 0.16	−0.19 ± 0.13	−0.42 ± 0.14
	100	−30.8 ± 17.3	−0.25 ± 0.14	−0.23 ± 0.10	−0.45 ± 0.14
RV	0	3.4 ± 4.7	−0.44 ± 0.23	−0.31 ± 0.16	−0.71 ± 0.26
	30	−10.9 ± 6.2	−0.49 ± 0.20	−0.30 ± 0.17	−0.75 ± 0.26
	100	−36.3 ± 16.1	−0.49 ± 0.20	−0.27 ± 0.17	−0.73 ± 0.26

*Volume measured with a Respitrace respiratory induction plethysmograph
% P_{Imax} = percent of maximal inspiratory mouth pressure at conditioning position
EEB = end-expiratory chest-wall volume during baseline breathing
RV + 40% ERV = residual volume plus 40% of expiratory reserve volume

cant effect of the strength of inspiratory effort in the V_{RC} ($p = 0.041$) and V_{CW} ($p = 0.012$) traces suggests that greater inspiratory effort enhanced the subsequent reductions in end-expiratory volume in these 2 traces, whereas inspiratory-effort intensity, estimated by mouth pressure, was not a factor that influenced reductions in end-expiratory V_{AB}.

Figure 3 shows the after-effects of conditioning on the breathing pattern. The significant effect of V_{CW}, where conditioning occurred, on T_I ($p = 0.013$) shows that conditioning maneuvers performed at a deflated volume were followed by a prolonged T_I. There was no significant difference in T_E between conditionings. Although V_T increased after conditioning at RV in the V_{RC} ($p = 0.047$), V_{AB} ($p = 0.009$), and V_{CW} ($p = 0.024$) traces, the intensity of inspiratory effort did not affect the magnitude of V_T.

Discussion

In the present study, immediate effects of thixotropy conditioning of inspiratory muscles on end-expiratory V_{CW} were detected in COPD patients who had an increased RV/TLC ratio. In these patients, end-expiratory V_{CW} decreased after conditioning maneuvers comprising inspiratory-muscle contraction with airway occlusion at deflated chest-wall volumes.

We found that V_{CW} at the time of conditioning influenced the magnitude of the reductions of end-expiratory volume in the V_{RC}, V_{AB}, and V_{CW} traces. This observation is in line with previous papers concerning inspiratory-muscle thixotropy, which found that the V_{RC} at which the conditioning occurs is a major determinant of the direction in which subsequent end-expiratory V_{RC} will move and to what extent the end-expiratory V_{RC} will change.[6,8] Our results suggest that changes in the length of inspiratory muscles for conditioning promote thixotropy of the muscles, even in COPD patients with increased RV/TLC. We also found larger reductions in end-expiratory V_{RC} and V_{CW} after greater inspiratory-muscle contractions in COPD patients.

Muscle contraction produces thixotropy after-effects in limb muscles.[3] In a 1985 study of upper-limb muscles, Hagbarth et al found that stiffness of the muscles is reduced not only by a large passive stretch of the muscles, but also by voluntary lengthening contractions of the muscle.[2] Gregory et al,[13] in 1987, and Hagbarth et al,[14] in 1995, proposed that muscle contractions effectively break preexisting cross-bridges and rapidly establish new bridges. The effects of muscle contraction on thixotropic behavior of respiratory muscles are also substantial in normal subjects.[6,8] In patients with COPD, inspiratory-effort intensity also contributed to the magnitude of reduction in end-expiratory V_{RC}, and thus V_{CW}, after conditioning. In contrast, the aftereffects of inspiratory-effort intensity on end-expiratory V_{AB} were not significant. However, this lack of effort-dependence may have resulted from our methods. The magnitude of mouth pressure may not represent the intensity of diaphragmatic contraction in patients with COPD.[15] Measurements of pleural pressure, gastric pressure, and the difference between those pressures (transdiaphragmatic pressure) may be useful to assess the intensity of inspiratory-muscle contraction, because the mouth pressure may not give a reasonable approximation of alveolar pressure and, thus, pleural pressure in patients with COPD, and because mouth pressure is derived from a complex set of interactions within and between muscles and the chest wall and its contents.[15] However, because mouth pressure

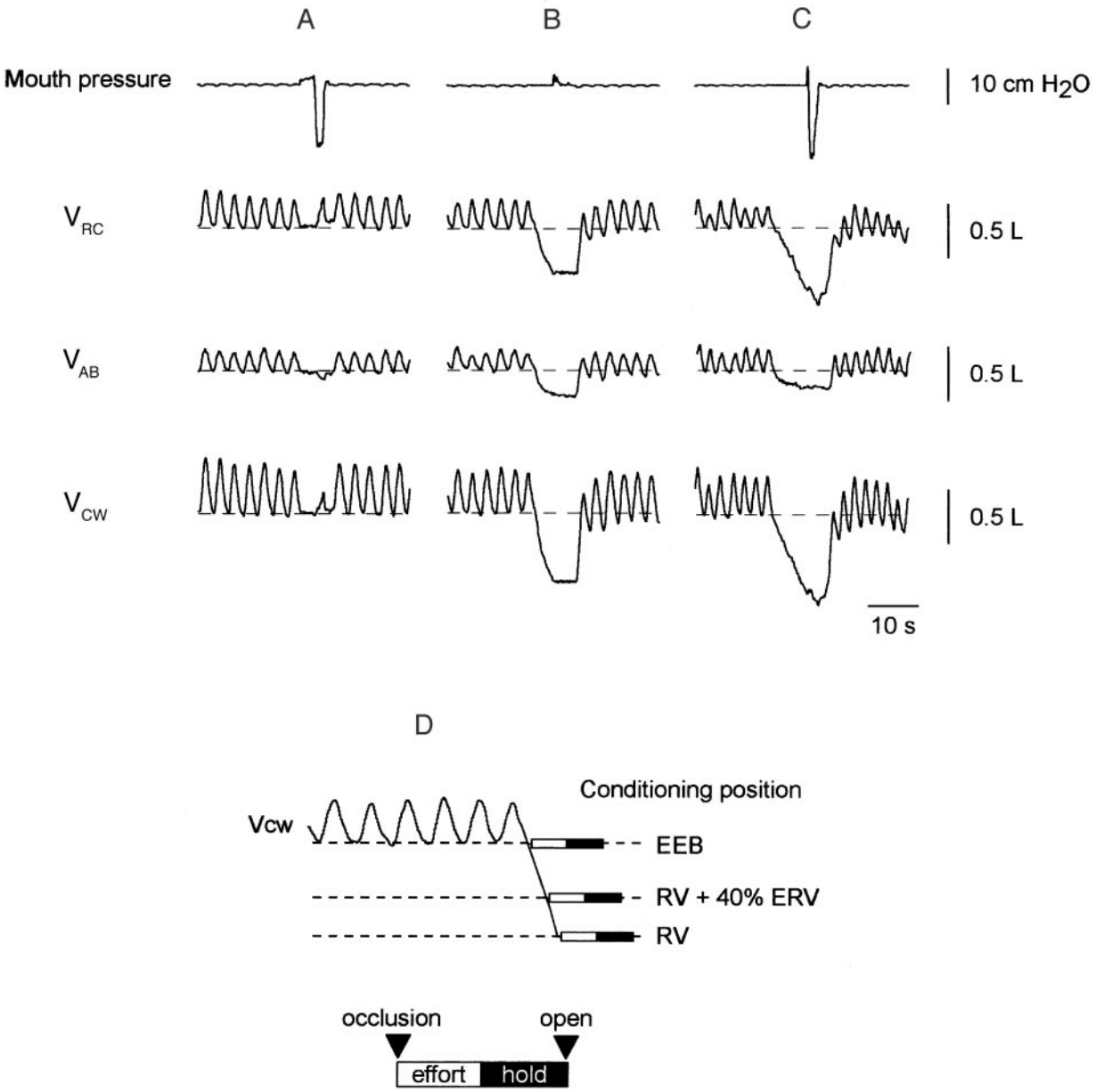

Fig. 1. Typical examples of the effects of inspiratory-muscle thixotropy conditioning performed by a subject with chronic obstructive pulmonary disease. Three inspiratory-muscle-conditioning efforts are represented: A: Conditioning performed at end-expiratory volume of the baseline breathing with forceful inspiratory effort produced little change in end-expiratory volume of the subsequent 5 breathing cycles. B: Conditioning performed at residual volume without inspiratory effort is followed by small reductions in end-expiratory volume. C: Conditioning performed at residual volume with forceful inspiratory effort produced obvious reduction in end-expiratory volume. From top to bottom, the rows of traces represent: mouth pressure, rib-cage volume (V_{RC}), abdominal volume (V_{AB}), and chest-wall volume (V_{CW}). The change in V_{CW} is the sum of the change in V_{RC} and V_{AB}. Downward deflections in the mouth-pressure trace and upward deflections of the V_{CW}, V_{RC}, and V_{AB} traces correspond to inspiratory movements. D: Schematic of the conditioning maneuver, which consisted of a 2-s inspiratory effort and a 2-s subsequent breath-holding period at the target volume with airway occlusion. EEB = end-expiratory V_{CW} during baseline breathing. RV = residual volume. ERV = expiratory reserve volume.

is easy to measure, estimation of inspiratory effort from mouth pressure seems advantageous for use in thixotropy conditioning in clinical settings.

Breath-holding during conditioning may affect breathing via central and peripheral chemoreceptors, leading to chemoreflex-mediated changes in the breathing pattern. In the present study we found no significant changes in T_E, regardless of which conditioning preceded. Therefore, a prolonged T_E could not explain greater reductions in end-expiratory volume after conditioning with strong inspira-

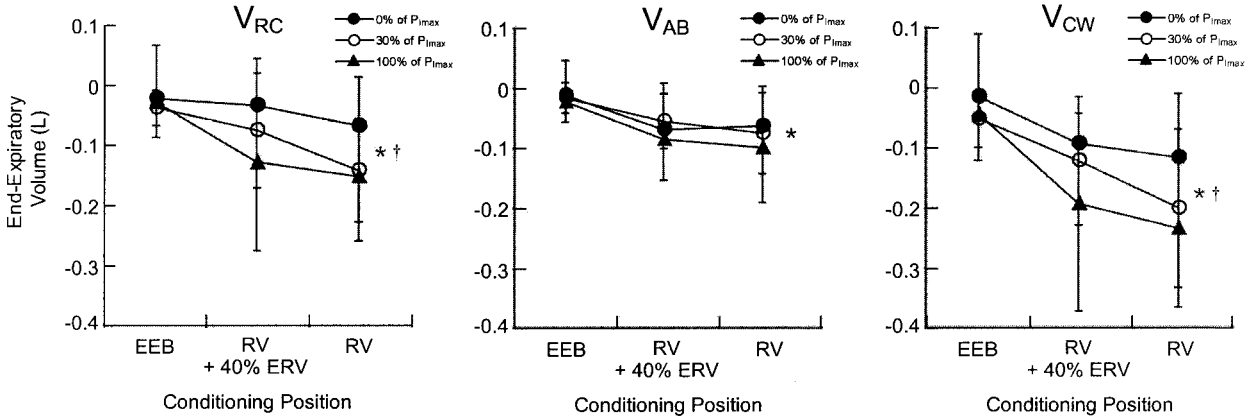

Fig. 2. The effects of inspiratory effort and chest-wall volume (V_{CW}) on (mean ± SD) end-expiratory V_{CW} of the following 5 breathing cycles, with 3 different thixotropy conditioning V_{CW}: end-expiratory V_{CW} during baseline breathing (EEB); residual volume plus 40% of expiratory reserve volume (RV + 40% ERV); and RV. The closed circles are data points from conditioning with 0% of maximal inspiratory mouth pressure (P_{Imax}) at each V_{CW}. The open circles are data points from conditioning with 30% of P_{Imax}. The black triangles are data points from conditioning with 100% of P_{Imax}. * Significant effect for V_{cw} at the time of conditioning ($p < 0.05$). † Effort-intensity had a significant effect ($p < 0.05$). V_{RC} = end-expiratory rib-cage volume. V_{AB} = abdominal volume.

tory efforts; however, if the conditioning time is prolonged, the breathing-control systems may affect these reductions because of an increase in respiratory drive with asphyxia. On the other hand, we found that T_I was prolonged with a reduction in the V_{CW} at which conditioning was performed. In 1980, Homma found an inspiratory inhibitory reflex caused by chest-wall vibrations, which suggests that nonvagal afferents from rib-cage muscles affect the off-switch mechanism of respiration.[16] Deep expiratory movements may reduce such nonvagal afferents, regardless of the presence or absence of conditioning, leading to an increase in T_I.

Expiratory-muscle activation following conditioning might contribute to thoracic-volume deflation. End-expiratory V_{CW} is a continuous variable that fluctuates widely, particularly during exercise in flow-limited patients.[17,18] In 2004, Aliverti et al measured V_{AB} and V_{RC} changes during exercise with optoelectronic plethysmography in patients with COPD.[19] They found that in most of their subjects, end-expiratory V_{CW} increased with exercise, but, in a substantial number of subjects, end-expiratory V_{CW} decreased. Optoelectronic plethysmography clearly showed that this end-expiratory V_{CW} reduction was due to an end-expiratory V_{AB} reduction with higher abdominal pressure. Accordingly, if expiratory-muscle recruitment played a major part in reducing V_{CW} following thixotropy conditioning, reduction in V_{AB} would account for a large part of the V_{CW} reduction. In the present study, however, reduction in end-expiratory V_{CW} could be explained mainly by a reduction in end-expiratory V_{RC}. Thus, expiratory-muscle recruitment does not seem to be a primary cause of end-expiratory V_{CW} reduction after conditioning. Nevertheless, we cannot entirely rule out this possibility, because Kikuchi et al found that inspiratory effort at baseline functional residual capacity with airway occlusion is followed by a reduction in functional residual capacity, with an increased surface electromyogram signal from electrodes placed over the seventh intercostal spaces.[20]

The present study suggests a therapeutic role for thixotropy conditioning of inspiratory muscles for ameliorating lung hyperinflation in COPD. Lung hyperinflation progresses dynamically during exercise because of limited airflow, which contributes to dyspnea and limits exercise capacity of patients with COPD.[17,18] Pharmacologic bronchodilation can reduce, but not eliminate, lung hyperinflation,[21–24] and a therapy readily available to patients with lung hyperinflation is needed. Although inspiratory-muscle thixotropy conditioning is promising, further research is necessary before it can be recommended for clinical use. In particular, we need to determine how long the thixotropic after-effect lasts; the present study only measured the after-effects in the subsequent 5 respiratory cycles. Hagbarth et al found that in upper limb muscles the thixotropy effect continues for more than 10 min, unless subsequent muscle contractions or stretch occurs.[2] Thus, for inspiratory-muscle thixotropy there is the possibility that respiratory movements following conditioning attenuate the thixotropy effect. It is essential to determine the effect of age,[25] chest-wall configuration,[26] and static inspiratory muscle strength (including nutritional factors[27] and steroid use[28]) on the response. All of those factors potentially affect the thixotropic behavior of the chest wall, primarily because of a reduction in inspiratory muscle strength, which is a factor that determines after-effects of thixotropy conditioning.[8]

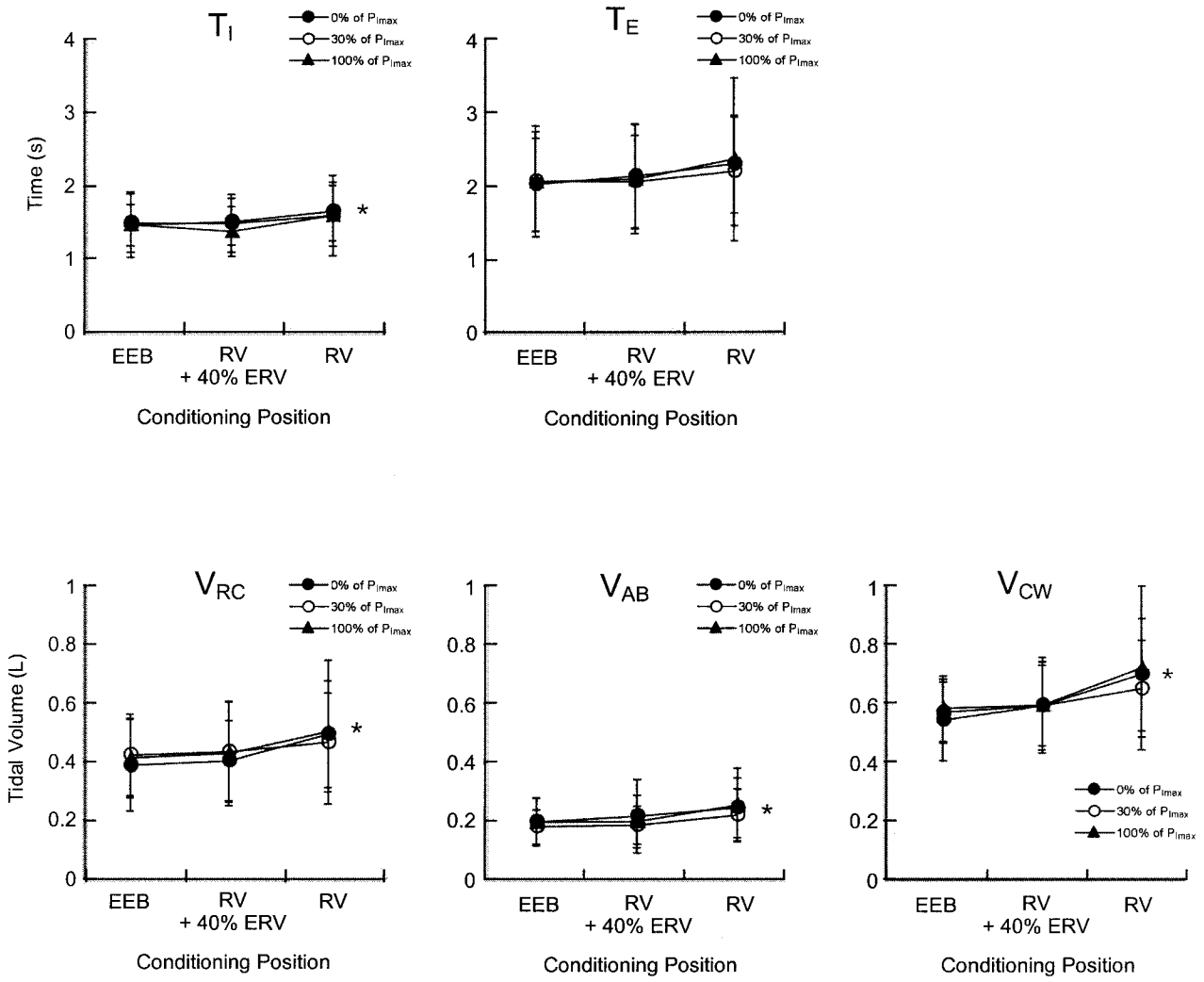

Fig. 3. The effects of inspiratory effort and the chest-wall volume (V_{CW}) at which the effort was made on (mean ± SD) inspiratory time (T_I), expiratory time (T_E), and tidal volume of the following 5 breathing cycles. * Significant effect for V_{CW} at the time of conditioning ($p < 0.05$).

It is important to consider whether limitations in our methods influenced our results. We used a respiratory-induction plethysmograph to quantify shifts in end-expiratory V_{CW}. In 1984, Hudgel et al found that respiratory-induction-plethysmography measurements of changes in end-expiratory V_{CW} are less accurate than those of V_T in patients with COPD, though it is possible to obtain the direction of change and a quantitative estimate of the change.[29] In addition, movement of the bands or a change in body position that affects calibration can occur during conditioning.[15] These problems raise the concern that some of the volume shifts we found might have been artifactual. It could also be argued that our use of a small group of subjects who had a relatively wide range of ages and forced expiratory volume in the first second makes it difficult to extrapolate the results to the general COPD population.

Conclusions

Thixotropy conditioning of inspiratory muscles, consisting of an inspiratory effort at a reduced V_{CW} with airway-closure, reduced end-expiratory V_{CW} of the next 5 respiratory cycles in COPD patients with increased RV/TLC. The data suggest that inspiratory-muscle conditioning, based on the principles of muscle thixotropy, has the possibility to reduce lung hyperinflation.

REFERENCES

1. Lakie M, Walsh EG, Wright GW. Resonance at the wrist demonstrated by the use of a torque motor: an instrumental analysis of muscle tone in man. J Physiol 1984;353:265–285.
2. Hagbarth KE, Hagglund JV, Nordin M, Wallin EU. Thixotropic behaviour of human finger flexor muscles with accompanying changes

in spindle and reflex responses to stretch. J Physiol 1985;368:323–342.
3. Proske U, Morgan DL, Gregory JE. Thixotropy in skeletal muscle and in muscle spindles: a review. Prog Neurobiol 1993;41(6):705–721.
4. Gregory JE, Wise AK, Wood SA, Prochazka A, Proske U. Muscle history, fusimotor activity and the human stretch reflex. J Physiol 1998;513(Pt 3):927–934.
5. Whitehead NP, Gregory JE, Morgan DL, Proske U. Passive mechanical properties of the medial gastrocnemius muscle of the cat. J Physiol 2001;536(Pt 3):893–903.
6. Homma I, Hagbarth KE. Thixotropy of rib cage respiratory muscles in normal subjects. J Appl Physiol 2000;89(5):1753–1758.
7. Shibata M, Izumizaki M, Homma I. The activation of muscle spindles enhances the thixotropic behavior of rib cage respiratory muscles. Jpn J Physiol 2003;53(3):243–246.
8. Izumizaki M, Shibata M, Homma I. Factors contributing to thixotropy of inspiratory muscles. Respir Physiol Neurobiol 2004;140(3): 257–264.
9. Singh B, Eastwood PR, Finucane KE. Volume displaced by diaphragm motion in emphysema. J Appl Physiol 2001;91(5):1913–1923.
10. Pride NB, Macklem PT. Lung mechanics in disease. In: Fishman AP, editor. Handbook of physiology, Section 3: The respiratory system, Vol. III: Mechanics of breathing, part 2. Bethesda: American Physiological Society; 1986: 659–692.
11. Tobin MJ, Guenther SM, Perez W, Mador MJ. Accuracy of the respiratory inductive plethysmograph during loaded breathing. J Appl Physiol 1987;62(2):497–505.
12. Konno K, Mead J. Measurement of the separate volume changes of rib cage and abdomen during breathing. J Appl Physiol 1967;22(3): 407–422.
13. Gregory JE, Morgan DL, Proske U. Changes in size of the stretch reflex of cat and man attributed to aftereffects in muscle spindles. J Neurophysiol 1987;58(3):628–640.
14. Hagbarth KE, Nordin M, Bongiovanni LG. After-effects on stiffness and stretch reflexes of human finger flexor muscles attributed to muscle thixotropy. J Physiol 1995;482(Pt 1):215–223.
15. ATS/ERS Statement on respiratory muscle testing. Am J Respir Crit Care Med 2002;166(4):518–624.
16. Homma I. Inspiratory inhibitory reflex caused by the chest wall vibration in man. Respir Physiol 1980;39(3):345–353.
17. O'Donnell DE, Webb KA. Exertional breathlessness in patients with chronic airflow limitation: the role of lung hyperinflation. Am Rev Respir Dis 1993;148(5):1351–1357.
18. O'Donnell DE, Revill SM, Webb KA. Dynamic hyperinflation and exercise intolerance in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2001;164(5):770–777.
19. Aliverti A, Stevenson N, Dellaca RL, Lo Mauro A, Pedotti A, Calverley PM. Regional chest wall volumes during exercise in chronic obstructive pulmonary disease. Thorax 2004;59(3):210–216.
20. Kikuchi Y, Hida W, Chonan T, Shindoh C, Sasaki H, Takishima T. Decrease in functional residual capacity during inspiratory loading and the sensation of dyspnea. J Appl Physiol 1991;71(5):1787–1794.
21. Newton MF, O'Donnell DE, Forkert L. Response of lung volumes to inhaled salbutamol in a large population of patients with severe hyperinflation. Chest 2002;121(4):1042–1050.
22. Celli B, ZuWallack R, Wang S, Kesten S. Improvement in resting inspiratory capacity and hyperinflation with tiotropium in COPD patients with increased static lung volumes. Chest 2003;124(5):1743–1748.
23. O'Donnell DE, Voduc N, Fitzpatrick M, Webb KA. Effect of salmeterol on the ventilatory response to exercise in chronic obstructive pulmonary disease. Eur Respir J 2004;24(1):86–94.
24. O'Donnell DE, Fluge T, Gerken F, Hamilton A, Webb K, Aguilaniu B, et al. Effects of tiotropium on lung hyperinflation, dyspnoea and exercise tolerance in COPD. Eur Respir J 2004;23(6):832–840.
25. Chan ED, Welsh CH. Geriatric respiratory medicine. Chest 1998; 114(6):1704–1733.
26. Orozco-Levi M. Structure and function of the respiratory muscles in patients with COPD: impairment or adaptation? Eur Respir J Suppl 2003;46:41s–51s.
27. Schols AM, Soeters PB, Mostert R, Pluymers RJ, Wouters EF. Physiologic effects of nutritional support and anabolic steroids in patients with chronic obstructive pulmonary disease: a placebo-controlled randomized trial. Am J Respir Crit Care Med 1995;152(4 Pt 1): 1268–1274.
28. Decramer M, Lacquet LM, Fagard R, Rogiers P. Corticosteroids contribute to muscle weakness in chronic airflow obstruction. Am J Respir Crit Care Med 1994;150(1):11–16.
29. Hudgel DW, Capehart M, Johnson B, Hill P, Robertson D. Accuracy of tidal volume, lung volume, and flow measurements by inductance vest in COPD patients. J Appl Physiol 1984;56(6):1659–1665.