

# Exercise Training Decreases Ventilatory Requirements and Exercise-Induced Hyperinflation at Submaximal Intensities in Patients With COPD\*

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**Study objectives:** We hypothesized that endurance exercise training would reduce the degree of hyperinflation for a given level of exercise and thereby improve submaximal exercise endurance. **Methods:** Twenty-four patients with COPD (mean FEV<sub>1</sub>, 36.4 ± 8.5% of predicted [± SD]) undertook a high-intensity cycle ergometer exercise training program for 45 min, three times a week for 7 weeks. Before and after training, the patients performed both an incremental exercise test to maximum and a constant work rate (CWR) test on a cycle ergometer at 75% of the peak work rate obtained in the pretraining incremental test. Ventilatory variables were measured breath-by-breath, and inspiratory capacity (IC) was measured every 2 min to assess changes in end-expiratory lung volume.

**Results:** After training, the increase in peak oxygen uptake was not statistically significant; however, the peak work rate increased by 12.9 ± 10.3 W (p < 0.01). For the CWR test performed at the same work rate both before and after training, ventilation and breathing frequency (f) were lower after training (average, 1.97 L/min and 3.2 breaths/min, respectively; p < 0.01) and IC was greater (by an average of 133 mL, p < 0.05), signifying decreased hyperinflation. The increase in IC at the point of termination in the shortest CWR test for each individual (defined as isotime) correlated well with both the decreased f (r = 0.63, p = 0.001) and with the increase in CWR exercise endurance (average, 13.1 min, r = 0.46, p = 0.023).

**Conclusions:** Exercise training in patients with severe COPD dramatically improves submaximal exercise endurance. Decreased dynamic hyperinflation may, in part, mediate the improvement in exercise endurance by delaying the attainment of a critically high inspiratory lung volume.

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**Key words:** dynamic hyperinflation; endurance; exercise training; rehabilitation; respiratory rate

**Abbreviations:** CWR = constant work rate; EELV = end-expiratory lung volume; f = breathing frequency; IC = inspiratory capacity; Raw = airways resistance; TLC = total lung capacity; VCO<sub>2</sub> = carbon dioxide output; V̇E = minute ventilation; V̇O<sub>2</sub> = oxygen uptake

Exercise intolerance is one of the major complaints of patients with COPD. The cause is multifactorial. However, during exercise, patients with significant COPD and airflow limitation often increase their end-expiratory lung volume (EELV) as the demands for ventilation and expiratory airflow

increase.<sup>1–3</sup> This is termed *dynamic hyperinflation*. This increase in mean operating lung volume allows exercise ventilation to occur over a higher potential airflow range of the flow-volume curve. In addition, the more negative average intrathoracic pressure

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benefits venous return. However, as total lung capacity (TLC) is thought not to change during exercise,<sup>1,4,5</sup> dynamic hyperinflation constrains the potential for the tidal volume to increase. Tidal volumes that encroach on the upper portion of the thoracic compliance curve require marked increases in inspiratory muscle work, which can lead to fatigue and exacerbate the sensation of dyspnea.

Increased fractions of inspired oxygen have been shown to increase exercise tolerance in a high-intensity, constant-load cycle ergometer test in patients with COPD,<sup>6,7</sup> in part by reducing breathing frequency (*f*) at a given time and, consequently, the degree of hyperinflation.<sup>6</sup> We were therefore interested in determining the extent to which the previously demonstrated improvements in exercise tolerance that result from endurance training in patients with COPD<sup>8,9</sup> also involve a reduction in dynamic hyperinflation.

## MATERIALS AND METHODS

### Subjects

The 24 subjects participating in this study are a subgroup of the subjects previously described by Emtner et al.<sup>10</sup> This subgroup had had satisfactory EELV assessments that allowed us to focus, for what we believe is the first time, on the specific effects of endurance exercise training on EELV and its potential contribution to exercise intolerance in patients with COPD. These patients did not differ in any of their pulmonary function data from the rest of the original population. The original entry criteria included a clinical diagnosis of COPD, coupled with an FEV<sub>1</sub> < 40% of predicted, resting PaO<sub>2</sub> > 55 mm Hg, and pulse oximetry oxygen saturation > 88% during a high-intensity constant work rate (CWR) test. The Human Subjects Committee of the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center approved the protocol. All subjects provided written informed consent.

### Exercise Training

A 7-week endurance exercise training program was performed on electromechanically braked cycle ergometers (CatEye Ergociser, EC-1600; CatEye; Osaka, Japan) under investigator supervision. Training sessions were conducted three times per week for 7 weeks; they began with a 5-min loadless pedaling followed by the target training work rate for 35 min and then followed by a 5-min unloaded pedaling recovery phase. The training work rates were initially set at 75% of the peak work rate attained on the pretraining incremental test and then, as tolerated by the subjects, increased weekly.<sup>10</sup> During the training sessions only, a randomized subgroup of the subjects (*n* = 11) received, in a double-blinded manner, supplemental oxygen rather than compressed air (*n* = 13) via nasal cannula (3 L/min) to determine whether an even-greater posttraining improvement would be manifest in the oxygen-breathing exercise group.

### Pulmonary Function

Standard forced expiratory spirometry (FEV<sub>1</sub> and FVC)<sup>11</sup> and body plethysmography (residual volume, functional residual capacity, total lung capacity [TLC], and airways resistance [Raw]) were performed both before and after training<sup>12</sup> (Vmax 229 and Autobox 6200; SensorMedics; Yorba Linda, CA).

### Exercise Endurance

Peak exercise tolerance was assessed both before and after training using a standard 5 W/min or 10 W/min incremental, symptom-limited cycle ergometer test (Ergoline 800 Series; SensorMedics). After a recovery period of at least 45 min, a CWR test was conducted at the same work rate, both before and after training. The intensity chosen was 75% of the peak pretraining incremental work rate. During these tests, subjects breathed room air through a mouthpiece; ventilation, gas exchange, and heart rate were recorded breath-by-breath (Vmax 229, SensorMedics).

### Dynamic Hyperinflation

Assuming that TLC did not change during exercise,<sup>4,5,13</sup> changes in inspiratory capacity (IC) were used in assessing the level of dynamic hyperinflation. IC maneuvers were taken while

**Table 1—Demographic and Resting Pulmonary Function Data\***

Variables	Combined Group ( <i>n</i> = 24)		
	Before Training	After Training	Δ
Age, yr		66.5 ± 8.3	
Height, cm		170.8 ± 8.6	
Weight, kg		73.1 ± 15.6	
Male/female gender, No.		15/9	
FEV <sub>1</sub> , L	1.02 ± 0.27	1.16 ± 0.31	0.14 ± 0.18‡
FVC, L	2.65 ± 0.79	2.78 ± 0.79	0.13 ± 0.28†
FEV <sub>1</sub> /FVC, %	39.8 ± 9.3	43.0 ± 10.8	3.2 ± 4.6‡
Residual volume, L	4.32 ± 1.08	4.17 ± 1.04	− 0.15 ± 0.62
Functional residual capacity, L	5.12 ± 1.13	4.99 ± 1.1	− 0.13 ± 0.48
TLC, L	7.20 ± 1.35	7.20 ± 1.44	0.002 ± 0.45
Raw, cm H <sub>2</sub> O/L/min	3.79 ± 1.4	3.07 ± 1.1	− 0.72 ± 1.09‡

\*Data are presented as mean ± SD unless otherwise indicated.

†*p* < 0.05.

‡*p* < 0.01.

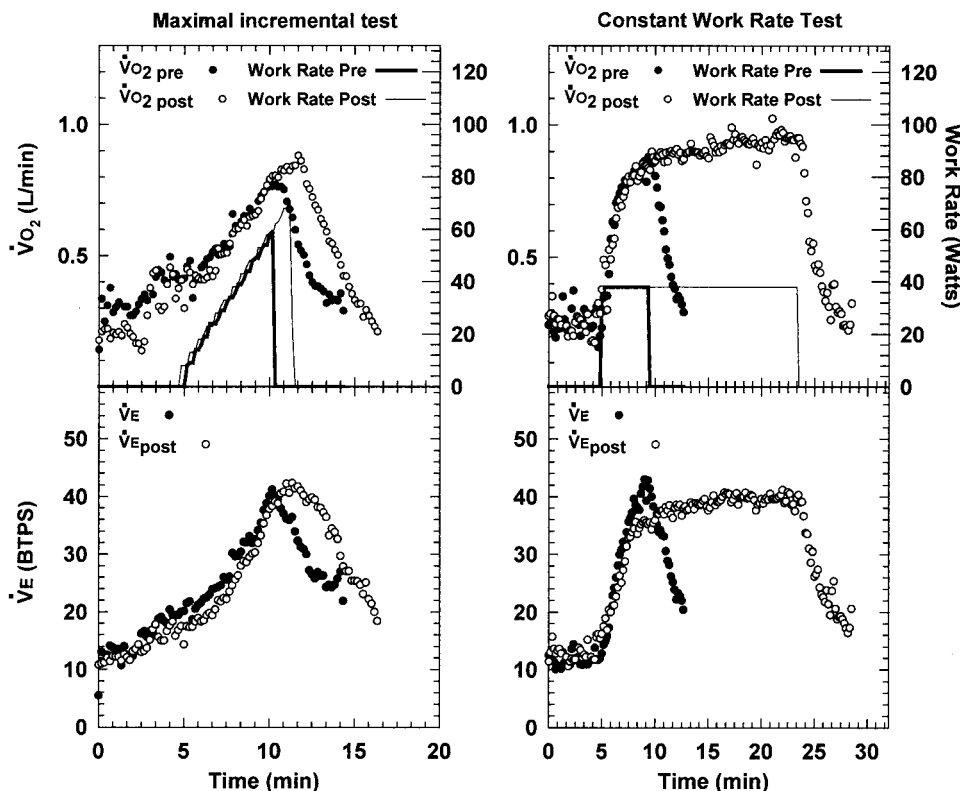


FIGURE 1. Typical  $\dot{V}O_2$  and  $\dot{V}E$  responses to incremental (left panels) and CWR (right panels) prior to (closed circles) and after (open circles) the endurance training program. Heavy continuous lines indicate work rate profile before training; thin continuous lines indicate work rate profile after training. BTPS = body temperature and pressure, saturated.

sitting at rest on the cycle ergometer and every second minute during exercise. The IC was the difference between the volume of maximal inspiratory effort and the stable EELV that was obtained by observing the volume-time plot through at least three breaths. The computer-determined value was overridden where either the automatically determined EELV or the volume of the consecutive IC was judged to be faulty by off-line examination of data. An investigator who was blinded as to the phase of the study determined the final values of the IC measurements.

#### Statistical Analysis

Values are expressed as mean  $\pm$  SD, unless otherwise noted. Significance of differences was tested by paired *t* test, and it was accepted at a level of  $p < 0.05$ . For correlation analysis, Pearson correlations were calculated. Statistical computations were performed (Excel 2000; Microsoft Corporation; Redmond, WA), and graphs were plotted and correlation analyses were performed (SigmaPlot 2000; SPSS; Chicago, IL). Isotime values for the respiratory variables (minute ventilation [ $\dot{V}E$ ], *f*, oxygen uptake [ $\dot{V}O_2$ ], carbon dioxide production [ $\dot{V}CO_2$ ], and IC) are defined at the point of termination of the shorter incremental or CWR test (this was the pretraining value in all but one case).

## RESULTS

Twenty-four subjects were involved in this study. Six of the 30 subjects in the report of Emtner et al<sup>10</sup>

were excluded because adequate IC measurements were not obtained. As there was no significant difference between the groups (*ie*, those receiving supplemental oxygen or air during the training) in terms of baseline pulmonary function, exercise tolerance, or ventilatory response, the groups were combined for further analysis (Table 1), although we utilized different symbols for the groups in the figures to better represent the study design.

#### Resting Pulmonary Function

Subjects manifested, on average, severe airways obstruction ( $FEV_1$ ,  $36.4 \pm 8.5\%$  of predicted<sup>11</sup>) with hyperinflation (TLC,  $124.9 \pm 18.8\%$  of predicted<sup>12</sup>). Small but significant increases in  $FEV_1$ , FVC, and decrease in Raw were seen after training. TLC did not change as a result of training, justifying the assumption inherent in our assessment of changes in hyperinflation by observing changes in IC (Table 1).

#### Exercise Tolerance and Ventilatory Response

Overall peak exercise tolerance increased by  $12.9 \pm 10.3$  W ( $p < 0.01$ ). The changes were  $11.1 \pm 6.0$  W ( $p < 0.01$ ) and  $14.5 \pm 13.5$  W

( $p < 0.01$ ) in the air training and oxygen training groups, respectively. There was no significant difference between the two groups. Overall, endurance time in the CWR test increased by  $11.6 \pm 8.1$  min ( $p < 0.01$ ) [ $9.9 \pm 7.7$  min in the air training group, and  $13.5 \pm 9.1$  min in the oxygen training group]. Again, the difference between these subgroups did not achieve statistical significance.

The metabolic and ventilatory responses of a representative subject to incremental and CWR tests are shown in Figure 1. Consistent with an increased peak work rate in the incremental test after training, the peak  $\dot{V}O_2$  was also higher in this subject. However, the group as a whole did not show a statistical increase in peak  $\dot{V}O_2$ . In the CWR, at isotime, the  $\dot{V}O_2$  response was identical before and after training. However, the peak  $\dot{V}O_2$  was higher after training. After training, the ventilatory response in the incremental test was lower at similar work rates, although peak ventilation was higher. For the group as a whole, ventilation at isotime in the CWR test was significantly lower by approximately 2 L/min but was not significantly different at the limit of endurance (Table 2), which increased after training from an average of 6 min to an average of 20 min.

All but one of the subjects (belonging to the oxygen training group) had an increased peak work rate after training (Fig 2, top left, A). The average increase, however, was moderate ( $12.9 \pm 10.3$  W;  $\dot{V}O_2$ ,  $70 \pm 200$  mL/min; Table 3). However, dramatic increases in endurance were noted in the CWR test ( $11.6 \pm 8.4$  min,  $p < 0.01$ ; Table 2, Fig 2, top right, B). In the pretraining CWR test, no subject could maintain the assigned work rate for as long as 15 min.

After training, not only did virtually all subjects improve their endurance but six of the subjects were in an apparent steady state; the investigators terminated the test at the predetermined time of 30 min (Fig 2, top right, B). Notably, five of these six patients trained with supplemental oxygen. The correlation between the change of endurance time in the CWR test and absolute change in the peak work rate in the incremental test was significant (Fig 2, bottom left, C). The correlation was not significant, however, when considered as percentage changes (Fig 2, bottom right, D). It was notable that a relatively small increase in peak work rate was often associated with a dramatic increase in endurance time in the CWR test.

In the posttraining CWR test, there were significant reductions in isotime values for  $\dot{V}E$  ( $-1.97 \pm 2.7$  L/min,  $p < 0.01$ ) and  $f$  ( $-3.2 \pm 3.2$  breaths/min,  $p < 0.01$ ). However, neither  $\dot{V}E$  nor  $f$  values were significantly different from pretraining values at the end of the CWR test (end-exercise).

### Dynamic Hyperinflation

The time course of the change in IC during the CWR test is shown for an individual subject in Figure 3, where isotime points are connected with dashed arrows. Note the large decrease in IC early in exercise in the pretraining but not the posttraining study (left, A), and that there is a close relationship between the rise in  $f$  and the decrease in IC (right, B). In the posttraining study, the appreciable decrease in  $f$  was associated with a dramatic increase in IC (Fig 3, right, B). In the whole group, there was a

**Table 2—Effect of Training on Endurance Time, Ventilation, and Metabolic Parameters Obtained at the Same Submaximal CWR in Patients With COPD\***

Variables	CWR Test		
	Before Training	After Training	$\Delta$
Endurance time, min	$6.6 \pm 2.9$	$18.2 \pm 9.4$ §	$11.6 \pm 8.4$ ‡
Isotime $\dot{V}E$		$30.3 \pm 8.1$	$-1.97 \pm 2.7$ ‡
End-exercise $\dot{V}E$	$32.3 \pm 8.4$	$33.5 \pm 9.0$	$1.15 \pm 3.9$
Isotime $\dot{V}O_2$		$0.81 \pm 0.24$	$-0.08 \pm 0.10$ ‡
End-expiratory $\dot{V}O_2$	$0.89 \pm 0.27$	$0.87 \pm 0.23$	$-0.01 \pm 0.1$
Isotime $\dot{V}CO_2$		$0.76 \pm 0.24$	$-0.10 \pm 0.12$ ‡
End-exercise $\dot{V}CO_2$	$0.86 \pm 0.29$	$0.83 \pm 0.25$	$-0.03 \pm 0.11$
Isotime respiratory exchange ratio		$0.94 \pm 0.08$	$-0.03 \pm 0.08$
End-exercise respiratory exchange ratio	$0.96 \pm 0.07$	$0.95 \pm 0.07$	$-0.02 \pm 0.09$
Isotime $f$		$26.0 \pm 4.4$	$-3.2 \pm 3.2$ ‡
End-exercise $f$	$29.1 \pm 4.9$	$28.9 \pm 4.8$	$-0.17 \pm 3.4$
Isotime IC		$1.7 \pm 0.4$	$0.133 \pm 0.29$ †
End-exercise IC	$1.5 \pm 0.4$	$1.6 \pm 0.3$	$0.05 \pm 0.27$

\*Data are presented as mean  $\pm$  SD.

† $p < 0.05$ .

‡ $p < 0.01$ .

§The endurance of six patients on posttraining CWR test reached 30 min, of which five patients trained on supplemental oxygen (ceiling effect).

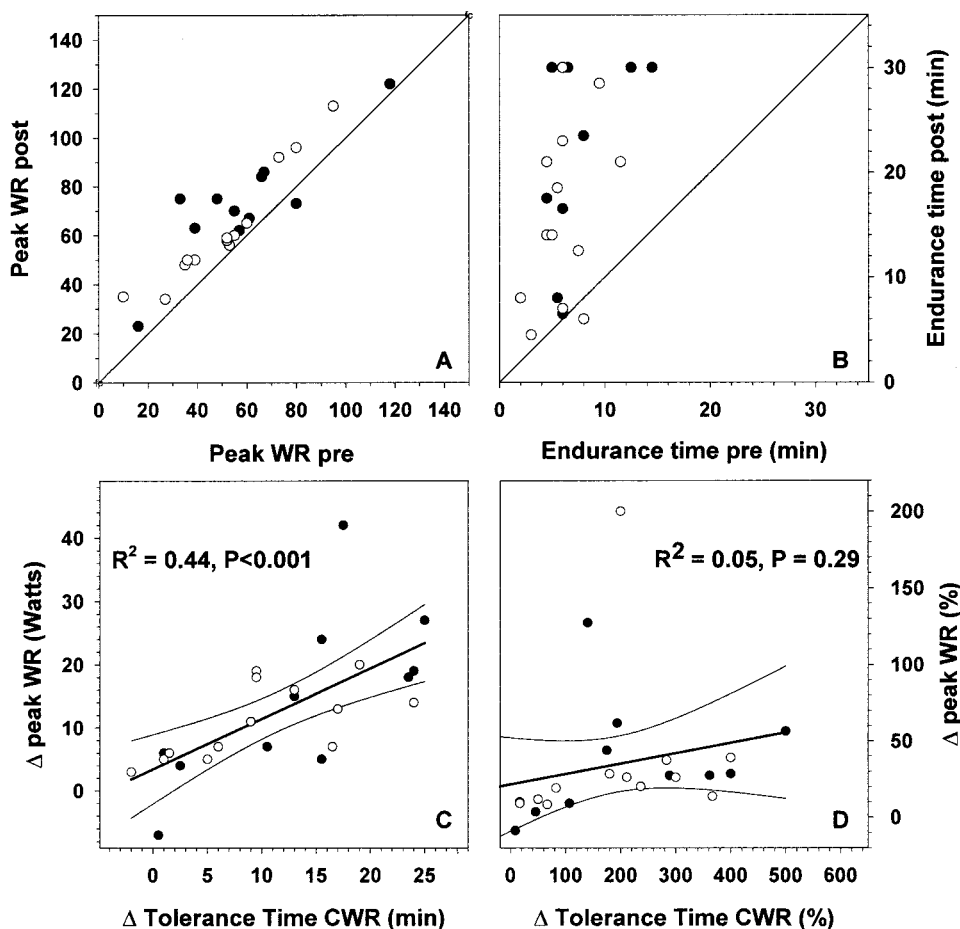


FIGURE 2. Change in peak work rate (WR) [top left, A], CWR endurance time (top right, B) and the relationship between changes in endurance time and peak work rate in absolute terms (bottom left, C) and as a percentage (bottom right, D) in response to endurance training. Closed circles indicate oxygen trained group; open circles indicate air trained group. Top panels: Lines indicate identity. Bottom panels: Lines indicate linear regressions with 95% confidence limits.

significantly lower  $\dot{V}E$ ,  $f$ , and greater IC at isotime but not at the limit of exercise tolerance in the CWR test (Table 2, Fig 4).

The magnitude and time course of the training-induced change in IC was highly variable among subjects (Fig 5, left, A). Only seven subjects had similar changes to those shown in Figure 3. In fact, nine of the subjects actually had decreased IC following training. There was a proportional relationship between the change in isotime IC and the increase in endurance ( $r = 0.46$ ) and the reduction in isotime  $f$  ( $r = 0.62$ ), respectively (Fig 5). The fact that the IC is increased at isotime but not at end of exercise suggests that hyperinflation may have been delayed after training leading to at least some of the dramatic improvement in endurance.

Since Raw is an important contributor to the mechanical time constant(s) of the lung, and since Raw showed a small but significant decrease after

training (Table 1), we considered a possible link of the decrease in Raw to the increase in CWR isotime IC and/or increase in tolerance time. However, as shown in Figure 6, we could demonstrate no such relationship for either variable. A similar analysis failed to demonstrate significant correlation with change in FEV<sub>1</sub> or Borg scale change (data not shown). We further conducted a multiple linear regression analysis to determine the relative ability of the training-associated changes in IC, Raw, and FEV<sub>1</sub> to predict the change in CWR exercise tolerance. Only the change in IC contributed significantly to the change in exercise tolerance ( $p < 0.023$ ).

## DISCUSSION

In this article, we demonstrate that after exercise training, there is a marked increase in constant work



**Table 3—Effect of Endurance Training on Ventilatory and Pulmonary Gas Exchange Indexes During Maximal Incremental Exercise in Patients With COPD\***

Variables	Incremental Exercise Test		
	Before Training	After Training	$\Delta$
Peak work rate, W	54.5 $\pm$ 24.3	67.3 $\pm$ 23.6	12.9 $\pm$ 10.3‡
Isotime $\dot{V}_E$		32.5 $\pm$ 8.4	- 1.2 $\pm$ 4.1
End-exercise $\dot{V}_E$	34.3 $\pm$ 8.94	38.6 $\pm$ 9.38	3.93 $\pm$ 5.9‡
Isotime $\dot{V}_{O_2}$		0.81 $\pm$ 0.22	- 0.07 $\pm$ 0.11‡
End-exercise $\dot{V}_{O_2}$	0.88 $\pm$ 0.26	0.95 $\pm$ 0.27	0.07 $\pm$ 0.20
Isotime $\dot{V}_{CO_2}$		0.79 $\pm$ 0.23	- 0.08 $\pm$ 0.10‡
End-exercise $\dot{V}_{CO_2}$	0.87 $\pm$ 0.28	0.97 $\pm$ 0.28	0.10 $\pm$ 0.20†
Isotime respiratory exchange ratio		0.97 $\pm$ 0.08	- 0.02 $\pm$ 0.09
End-expiratory respiratory exchange ratio	0.99 $\pm$ 0.09	1.02 $\pm$ 0.07	0.04 $\pm$ 0.09‡

\*Data are presented as mean  $\pm$  SD. End-exercise refers to the time of exercise termination. Isotime refers to the time of exercise termination in the pretraining incremental test. Therefore, in the pretraining incremental test, isotime is the same as end-exercise.

†p < 0.05.

‡p < 0.01.

endurance (almost 300% longer than pretraining; Table 2). This is associated with reduced dynamic hyperinflation during CWR exercise in the majority of subjects. Further, the reduction in dynamic hyperinflation was shown to be correlated with the reduced  $f$ . This is not surprising, as an acute effect of oxygen inhalation has been shown to reduce  $f$  and also to reduce dynamic hyperinflation.<sup>6</sup> However, to our knowledge, this is the first demonstration that a reduction in  $f$  through exercise training reduces and delays the development of dynamic hyperinflation. The reduction is significant at isotime but disappears at end-exercise. The extent to which this reduction in dynamic hyperinflation plays a role in the dramatic improvement in endurance is unclear, but we believe that it may have a role.

Patients with COPD are disadvantaged with re-

spect to meeting the ventilatory demands of muscular exercise in several respects. The physiologic dead space fraction of the breath is typically high.<sup>14,15</sup> Further, lactic acidosis often occurs at low exercise levels, providing an additional ventilatory stimulus.<sup>16,17</sup> Hypoxia also may play a role in selected patients. These factors and the often-reduced set point level of  $P_{aCO_2}$ <sup>14</sup> increase the  $\dot{V}_E$  required to provide the adequate alveolar ventilation needed for acid-base regulation. The increased  $R_{aw}$  and reduced lung recoil pressure reduce the potential for expiratory airflow at any lung volume. This is manifested as an increased mechanical time constant of the lung both as a whole and regionally. Consequently, to return the thorax to its previous EELV within the time set for the next inspiration by the ventilatory control system, expiratory airflow needs

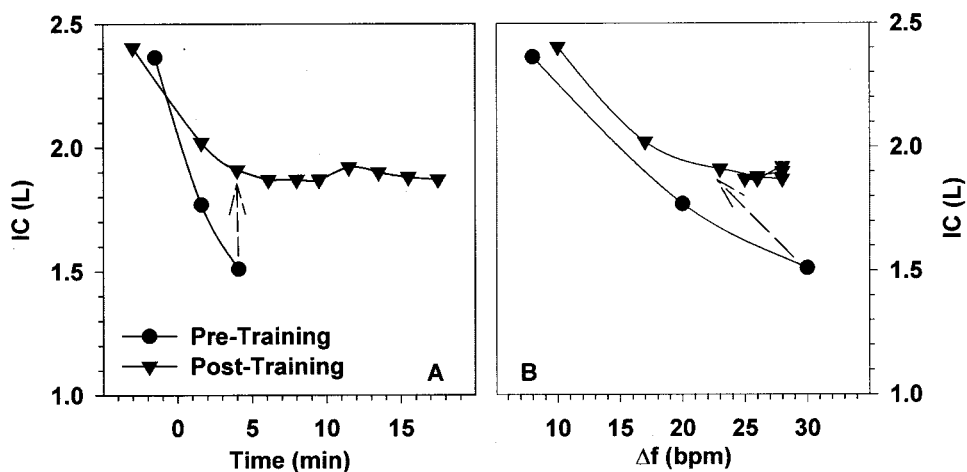


FIGURE 3. Changes in IC as a function of time (left, A) and of  $f$  (right, B) during CWR exercise prior to and after the training program in a representative subject. The dashed arrows connect the isotime values.

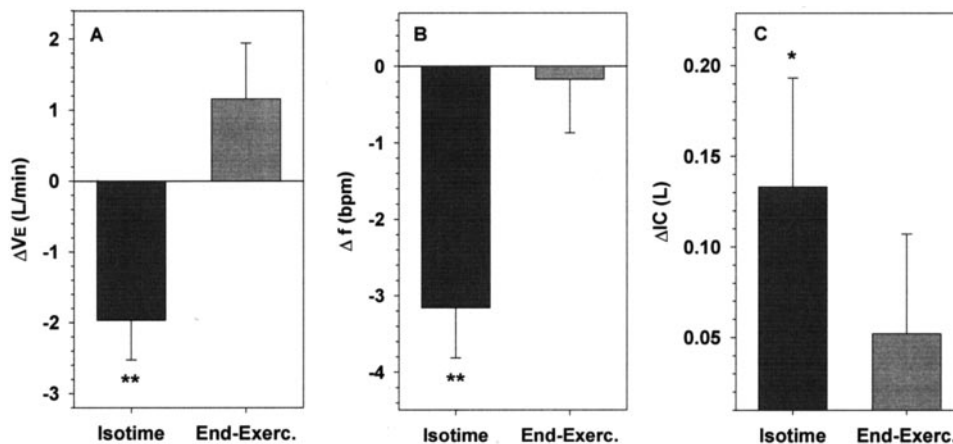


FIGURE 4. Training-induced differences ( $\Delta$ ) in  $\dot{V}_E$  (left, A),  $f$  (center, B), and IC (right, C) at isotime and end-exercise for the CWR test. Error bars indicate  $\pm$  SE. End-exerc = value at end-exercise; bpm = breaths per minute. \* $p < 0.05$ ; \*\* $p < 0.01$ .

to be increased. This is achieved with both a reduction of inspiratory muscle restraint<sup>18</sup> and increased expiratory muscle drive.<sup>19</sup> But the resulting positive intrapleural pressure predisposes to dynamic airway compression and even regional collapse as lung volume decreases.<sup>20,21</sup> Consequently, EELV typically increases (dynamic hyperinflation) during strenuous aerobic exercise in patients with COPD.<sup>6,21,22</sup> This is in contrast to the decrease in EELV seen in most normal subjects, although EELV can also increase at high work rates in some normal elderly subjects in whom lung recoil is somewhat reduced.<sup>23</sup> While this higher lung volume improves the scope for airflow generation, it reduces the potential for inspiratory tidal volume increase as

inspiratory muscle work increases markedly as EELV approaches TLC, a region termed *minimum inspiratory reserve volume* by O'Donnell et al.<sup>24</sup> In this region, dynamic hyperinflation begins to constrain increases in tidal volume; further increases in ventilation can only be accomplished by increases in  $f$ , which further exacerbates dynamic hyperinflation; the result is reduced exercise tolerance.

There have been several approaches to improving exercise tolerance in patients with COPD. These have included  $\beta$ -agonists and anticholinergics,<sup>25,26</sup> dyspnea suppressants,<sup>27</sup> hyperoxic inspirates to reduce hypoxemic and any metabolic-acidemic peripheral chemoreceptor stimulation,<sup>28</sup> and endurance exercise training.<sup>8,9</sup> These have proved successful to

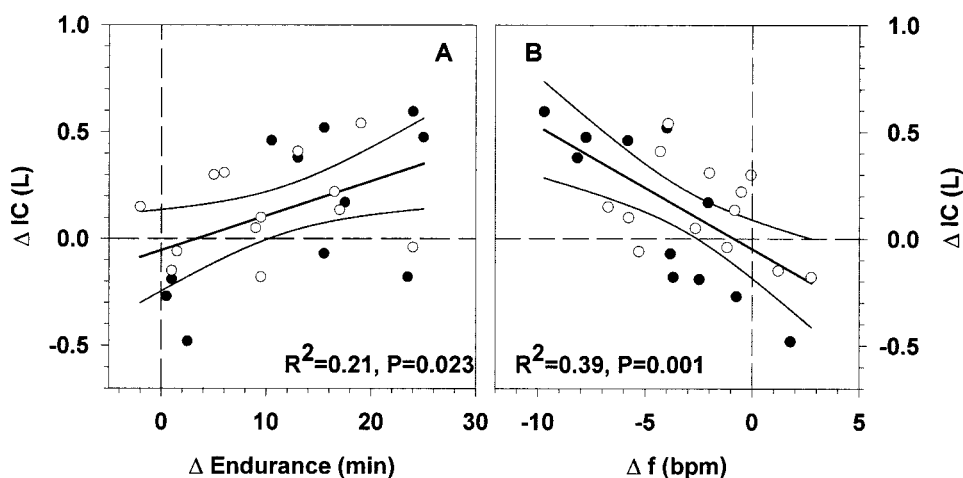


FIGURE 5. Correlation between the change in isotime IC and change in endurance (left, A), and change in  $f$  (right, B). Closed circles indicate group trained while breathing oxygen; open circles indicate group trained while breathing air. Lines are results of linear regression  $\pm$  95% confidence limits. See Table 4 for expansion of abbreviation.

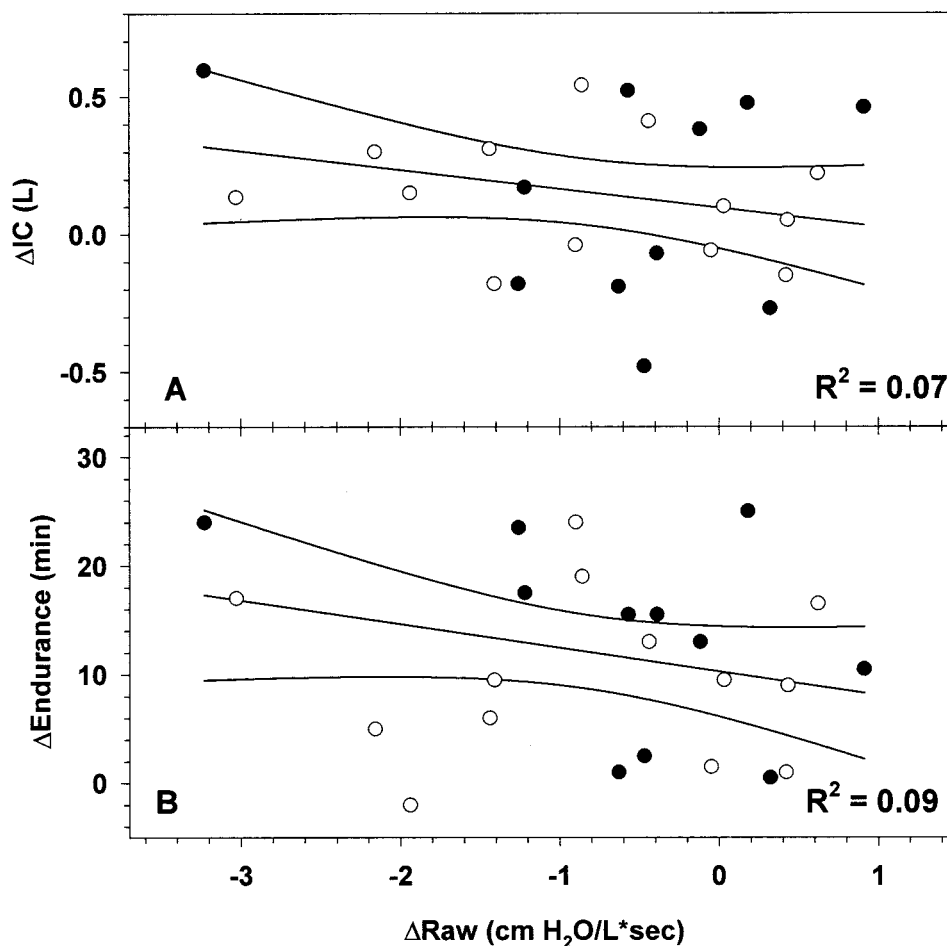


FIGURE 6. The effect of endurance training on the relationship between isotime ( $\Delta\text{IC}$ ) [top, A] and endurance time (bottom, B) in the CWR test as a function of Raw ( $\Delta\text{Raw}$ ) measured at rest. In neither case is the correlation significantly different from zero. Closed circles indicate group trained while breathing oxygen; open circles indicate group trained while breathing air. Lines are results of linear regression  $\pm$  95% confidence limits.

a varying degree. For example, it has been shown that long- and short-acting anticholinergic drugs (tiotropium, ipratropium) decrease dynamic hyperinflation and appreciably increase exercise endurance.<sup>22</sup> This effect has also been shown with  $\beta$ -agonist and combination drugs as well.<sup>25</sup> Hyperoxic inspirates can reduce  $f$  and decrease the ventilatory demand, leading to reduction in dynamic hyperinflation and a profound effect on exercise endurance, even in patients who do not meet the usual criteria for oxygen supplementation.<sup>6,7</sup> However, unlike the previously demonstrated beneficial effects of acute interventions on dynamic hyperinflation and exercise endurance, those consequent to training are likely to continue to benefit spontaneous activities in patients with COPD in the long term.

Quantifying improvement in exercise tolerance, however, is not straightforward. In laboratory testing, the peak work rate or peak  $\dot{V}\text{O}_2$  achieved in an incre-

mental cycle-ergometer or treadmill test is often used for this purpose. The physiologic (and pathophysiologic) factors that would allow these findings to be transferred to a useful prediction for the more directly relevant ability to sustain a constant work rate task are poorly understood at present, especially in patients with chronic diseases such as COPD.

In our study, virtually every subject increased the peak work rate in the incremental test and increased the tolerance time in the high-intensity CWR test (Fig 2). The magnitudes of the changes are instructive. The peak work rate increased by an average of  $37 \pm 53\%$ , while the CWR tolerance time increased by an average of  $192 \pm 147\%$ . It is also notable that the variation among patients in increase in CWR endurance time was wide, presumably reflecting the different position on the subject's individual power-duration relationship imposed by 75% of the subject's initial (pretraining) peak incremental work rate.<sup>9,29,30</sup>



Endurance training decreased  $\dot{V}_E$  at isotime during the CWR test, thereby allowing exercise to continue until the subject reached approximately the same maximum level of ventilation at the limit of tolerance (Table 2; Figs 1 and 4). As we previously demonstrated with hyperoxic inhalates,<sup>6</sup> the reduced  $\dot{V}_E$  was associated with a reduced  $f$  (in all but four of the subjects in this study), which was significantly correlated with a reduction in the degree of hyperinflation. The conclusion that less hyperinflation is associated with a reduced  $f$  rather than a reduced  $\dot{V}_E$  is justified on the basis of the measured increase in posttraining IC at isotime (Table 2, Fig 4) and the fact that TLC, measured at rest by body plethysmography (Table 1), was not altered. This is further supported by the increase in tidal volume both at isotime and end-exercise (inherent in Table 3) after training.

Despite the consistent increase in tolerance time (Fig 5) after training, not all subjects manifested a reduced degree of dynamic hyperinflation. Further, the improvement in endurance time for those with increased IC ( $12.9 \pm 7.2$  min) was not statistically different from those subjects without increased IC ( $8.7 \pm 9.9$  min). However, only four of these latter subjects evidenced an appreciable increase in endurance time. Thus, these results demonstrate that improved dynamic hyperinflation is not required to obtain an improved tolerance time in response to endurance training in patients with COPD. This is not surprising, as not all patients with COPD are limited by ventilation at the limit of exercise tolerance, some being limited by muscle fatigue or various combinations.<sup>31–33</sup> Further, the training-based improvement in metabolic and acid-base status of the exercising muscle can also reduce ventilatory drive and requirements. The reduced  $\dot{V}_{O_2}$  and  $\dot{V}_{CO_2}$  at isotime (Tables 2 and 3) and the reduction in  $\dot{V}_E$  are consistent with this notion. However, we believe that dynamic hyperinflation is often an important factor in many patients with severe COPD.

We were surprised to find a small, but significant, increase in  $FEV_1$  and a lower plethysmographically determined  $R_{aw}$  after training. Although this is not the first observation of this phenomenon even in our laboratory,<sup>8,10</sup> we do not think that this is a direct consequence of exercise training *per se*; rather, it is a result of a “better maintenance” of lung function in a more consistent way throughout the duration of rehabilitation. It is generally accepted that training (or rehabilitation) itself does not improve lung function.<sup>27</sup> However, this could conceivably, in and of itself, reduce the work of breathing or reduce the degree of dynamic hyperinflation during exercise by allowing greater expiratory flow rates for a given degree of expiratory driving pressure. However,

neither the improvements in IC at isotime nor the improvement in endurance time were significantly correlated to the change of  $R_{aw}$  (Fig 6). Therefore, we conclude that training-induced reduction in ventilatory drive and  $f$  is the predominant factor allowing a lesser degree of hyperinflation and improving submaximal exercise endurance time.

In summary, we found that high-intensity endurance exercise training can reduce hyperinflation at a given level of exercise in patients with severe COPD. Our findings provide evidence that training, through its  $f$ -reducing effect, often leads to a lesser degree of hyperinflation and contributes to dramatic improvement in submaximal exercise endurance. Although the training-induced improvement in metabolic function, with its consequent reduction in  $\dot{V}_E$  and related variables, would in itself be expected to improve endurance time, reduction in dynamic hyperinflation may also play a significant role. Our findings further demonstrate and help to explain the profound benefits of rehabilitative exercise on “quality of life” for patients with advanced COPD.

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