

Airflow limitation and control of end-expiratory lung volume during exercise

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Abstract

To test the hypothesis that the presence of airflow limitation (AFL) influences the control of end-expiratory lung volume (EELV) during exercise, 11 subjects with normal lung function, performed submaximal exercise (SM) on a cycle ergometer, with and without AFL. AFL was achieved during exercise by increasing the density of the air via a hyperbaric chamber, compressed to a depth of 3 atm (3 ATA; with AFL). Five subjects achieved AFL during SM exercise at 3 ATA while the remaining six subjects did not achieve AFL. SM exercise was performed with the same apparatus in the hyperbaric chamber at sea level pressure with none of the subjects achieving AFL (SL; no-AFL). EELV (% of TLC, BTPS), was significantly larger during exercise at 3 ATA than during exercise at SL for the AFL group (SL = $44 \pm 6\%$; 3 ATA–AFL = $51 \pm 9\%$, $P < 0.05$; but, was not for the no-AFL group (SL = $46 \pm 6\%$; 3 ATA–no AFL = $46 \pm 7\%$). End inspiratory lung volume was significantly elevated during exercise at 3 ATA compared with SL in the AFL group (SL = $80 \pm 6\%$; 3 ATA–AFL = $86 \pm 6\%$; $P = 0.01$) but not in the no-AFL group (SL = $82 \pm 4\%$; 3 ATA–no AFL = $84 \pm 4\%$). Tidal volume and ventilation were not different for any condition. These data suggest that the occurrence of AFL influences the control of EELV. © 2000 Elsevier Science B.V. All rights reserved.

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1. Introduction

During exercise, ventilation (\dot{V}_E) is elevated by increasing both the frequency of breathing (f) and

the magnitude of tidal volume (V_T). Tidal volume is expanded by increasing end inspiratory lung volume (EILV) and decreasing end expiratory lung volume (EELV) (Lind and Hesser, 1984; Younes and Kivinen, 1984; Henke et al., 1988; Babb and Rodarte, 1991). A reduction in EELV is proposed to be advantageous during exercise because it places the diaphragm in a better mechan-

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ical position to perform work and lowers the inspiratory work of breathing. Inspiratory work of breathing is reduced by recovering some of the work done by the expiratory muscles during the previous expiration (Druz and Sharp, 1981; Collett and Engel, 1986; Road et al., 1986; Henke et al., 1988; Johnson et al., 1991; Babb and Rodarte, 1992).

Although it is not clear how EELV is controlled during exercise, investigators have shown that EELV increases when tidal expiratory flow achieves maximal expiratory flow during exercise, defined here as airflow limitation (AFL) (Campbell et al., 1961; Grimby et al., 1971; Anthonisen et al., 1976; Jensen et al., 1980; Henke et al., 1988; O'Donnell et al., 1988). Studies have shown an increase in EELV during exercise in patients with severe chronic obstructive lung disease (COPD) (Grimby et al., 1973; Stubbing et al., 1980). Babb et al. (1991) also have seen small increases in EELV during exercise in subjects with mild-to-moderate chronic maximal expiratory airflow limitation. Increases in EELV also have been shown in young athletes and older active men with normal lung function, who are able to ventilate at rates high enough to achieve airflow limitation during exercise (Grimby et al., 1971; Johnson et al., 1991). The common factor among these patients and subjects appears to be that the increase in EELV coincides with the occurrence of airflow limitation (Jensen et al., 1980; Babb et al., 1991; Johnson et al., 1991). Pellegrino et al. (1993) investigated the influence of airflow limitation on the control of EELV by applying an external load and concluded that airflow limitation affects EELV, and dynamic compression of the airways, which occurs with airflow limitation, may be the mechanism responsible. It is unknown if the increase in EELV is an adaptive response to chronic AFL (at rest or during exercise) or whether subjects who have not previously encountered AFL during exercise would increase EELV with AFL. This has not formally been tested previously.

The present study tested whether airflow limitation, and indirectly dynamic compression of the airways, can result in an increased EELV during submaximal exercise (SM) in subjects with normal lung function and who do not achieve AFL dur-

ing exercise. The influence of airflow limitation on changes in EELV was tested directly by using increased air density under hyperbaric conditions to reduce maximal expiratory flow and thus achieve airflow limitation via pulmonary limits rather than external impositions. This allowed subjects with normal lung function, who had not previously encountered airflow limitation during exercise, to become airflow limited during moderate SM exercise. The hypothesis tested in this study was that EELV would increase during SM exercise, when airflow limitation is present at increased ambient pressure. This is in contrast to the response seen at normal sea level atmospheric pressure (SL), and at increased pressure when airflow limitation is absent.

2. Methods

2.1. Subject selection

Eleven men and women (7 male, 4 female) with normal lung function between the ages of 21 and 44 years were recruited for this study. Only subjects who had no history or evidence of heart disease, hypertension, asthma, or musculoskeletal impairment that would limit exercise, and a normal exercise ECG were accepted into the study. Normal lung function was defined as lung function values falling within the range of normal values as determined by the prediction equations of Knudson et al. (1976). Because moderate obesity can affect lung mechanics, a body weight (kg) to height (cm) ratio between 0.32 and 0.48 was considered acceptable for this study (Ray et al., 1983).

2.2. Pulmonary function screening

Pulmonary function testing was performed on the first visit to the exercise physiology lab and consisted of standard spirometry, maximal voluntary ventilation (MVV), lung volumes, and diffusing capacity, which were obtained in a pressure-corrected volume displacement body plethysmograph (SensorMedics 6200). Pulmonary function tests were performed according to the

American Thoracic Society guidelines (1987). All subjects met the established normal criteria.

2.3. Screening maximal exercise test

After the pulmonary function screening procedure, all subjects performed a graded maximal exercise test on an electrically braked cycle ergometer (Medical graphics, CPX). This test was used to exclude those subjects who may exhibit cardiovascular abnormalities during exercise. The test protocol consisted of a 3 min rest while seated on the ergometer, after which, exercise began at 20 or 30 W for 1 min, with 20 or 30 W increments (females and males, respectively) every minute until exhaustion. Oxygen uptake ($\dot{V}O_2$) was measured breath-by-breath using a Marquette 1100 mass spectrometer for analysis of expired gases, calibrated with known gases prior to each test. A VMM-2 volume turbine was used for volume measurements and was calibrated with a 3 L calibration syringe prior to each test (Hans Rudolph). Maximal exercise was determined by attaining two of the following criteria: a plateau in $\dot{V}O_2$ despite a further increase in work rate, respiratory exchange ratio (RER) in excess of 1.15, and reaching a heart rate (HR) within $\pm 10\%$ of age predicted maximal HR.

2.4. Inducing airflow limitation

Altering maximal expiratory flow in a subject with normal lung function was accomplished by increasing the density of the air via a hyperbaric chamber to 3 atm (3 ATA = 2280 mmHg). Work done by Hesser et al. (1981) using a hyperbaric chamber has shown that maximal expiratory flow is reduced by approximately 1/3 at 3 ATA over the first 3/4 of expiratory flow from total lung capacity (TLC). Therefore, the depth chosen for this study, based on Hesser's findings and in order to produce airflow limitation in subjects with normal lung function at moderate exercise levels, was 3 ATA (Wood and Bryan, 1969, 1978; Hesser et al., 1981). This depth was also chosen because of the additional concern of decompression time limits at this depth. At 3 ATA the decompression time limit is 50 min, after which mandatory de-

compression time is required. Testing at this depth restricted us to performing all necessary measurements in approximately 45 min, thus avoiding decompression time and additional risks to the subjects.

2.5. Breathing mechanics

Measurement of continuous inspiratory and expiratory flow was accomplished using a two-way breathing valve (Rudolph 2700) with inspiratory and expiratory pneumotachs (Fleisch # 3 and Celesco ± 2.0 cmH₂O pressure transducers) located upstream and downstream from the breathing valve. Maximal flow volume loops at rest and dynamic tidal flow-volume loops during exercise were determined with this same setup during all SL and 3 ATA tests. The resistance of the breathing system was less than 1.2 cmH₂O/L per sec up to 6 L/sec at sea level and was less than 2 cmH₂O/L per sec up to 6 L/sec at 3 ATA. Static flows were calibrated using a calibration flow meter (Gilmont # 6) at sea level and at 3 ATA (up to 8 and 6 L/sec, respectively). The inspiratory and expiratory flow signals were electronically summed and sampled at 100 HZ on a PC computer as were oral and transpulmonary pressures (PTP). Volume was obtained by digital integration of the summed flow signal.

PTP was measured as the differential pressure of mouth pressure and esophageal pressure. This was accomplished by placing the sample tubing from a port on the mouthpiece to the opposite side of the pressure transducer used to measure esophageal pressure. Pressure transducers were calibrated prior to each test using a water manometer. Esophageal pressure was measured with an esophageal balloon placed in the esophagus, 45 cm down from the nostril (Milic-Emili et al., 1964). Subjects were then instructed to blow through the mouthpiece, while a cork with a small orifice was held over the expiratory opening. If PTP remained constant in value while mouth pressure increased, then the balloon was considered to be in the esophagus and not in the stomach. Once the esophageal balloon was placed, it remained in the same position (without removal) for exercise testing at both SL and 3 ATA. Dynamic tidal

pressure–volume loops were also measured during exercise (pressure transducers, Celesco ± 100 cmH₂O).

An inspiratory capacity (IC) maneuver was performed during all exercise tests at SL and at 3 ATA from which EELV was determined. An IC was performed after attaining the SM work rate and ventilation required for that test, which marks the beginning of the measurement sequence. The second IC was then performed at the end of the measurement sequence, which lasted approximately 1.5 min. EELV was then determined by subtracting the IC from TLC. End-inspiratory lung volume (EILV) was equal to EELV plus V_T . Previous studies have shown that subjects have no trouble performing the IC maneuver and that this method of determining EELV is accurate when monitoring maximal inspiratory pressure to assure a maximal inspiratory effort (Babb et al., 1991). It is possible that performance of an IC maneuver may temporarily alter breathing pattern and EELV during exercise. Therefore, the breaths chosen for determination of EELV, were selected either prior to an IC maneuver or at least six breaths after an IC maneuver. Upon examination of each ventilatory pattern after an IC, EELV either had not changed or had returned to the same level as that prior to the IC.

2.6. Airflow limitation

Airflow limitation during exercise was determined in the following manner. SM exercise tidal pressure–volume loops that met or exceeded the critical pressure range (the range of pressure where additional effort does not result in additional flow) were used as evidence of airflow limitation. Briefly, once maximal expiratory flow has been attained at lung volumes less than 80% of TLC, any additional expiratory pressure generated by the respiratory muscles does not result in additional airflow. Thus, the minimum PTP necessary to generate maximal flow is termed the critical pressure for maximal flow (Pcrit). Pcrit was measured from graded effort loops performed in the body box prior to exercise and on the exercise system at 3 ATA

prior to exercise. From these graded loops, isovolume pressure flow diagrams were constructed (Olafsson et al., 1969). Pcrit was determined at 75, 50, and 25% of FVC at both SL and 3 ATA. However, because we were constrained by the number of graded loops that could be completed in the time allowed at 3 ATA, the isovolume pressure flow diagrams produced a less defined leveling off of flow at a discrete pressure. Therefore, we used a Pcrit range to determine airflow limitation rather than Pcrit itself. This technique has been used by others for the determination of airflow limitation during exercise (Johnson et al., 1992).

As an additional indicator of airflow limitation, maximal flow volume loops were obtained prior to and immediately after exercise on the dual pneumotach system during both the SL and 3 ATA conditions. A maximal flow volume loop obtained in the pressure-corrected volume displacement body plethysmograph prior to exercise served as the compression corrected maximal loop in which exercise tidal flow volume loops collected at sea level were placed. Graded effort flow volume loops from TLC were performed during the 3 ATA condition to obtain a maximal expiratory flow volume curve that approximates a gas compression corrected curve for 3 ATA (Ingram and Schilder, 1966; Olafsson et al., 1969). This compression corrected curve served as the maximal loop in which the exercise tidal flow volume loops collected at 3 ATA were placed as an additional indicator of airflow limitation. SM exercise tidal pressure volume curves that met or exceeded Pcrit range AND flow volume curves that touched or exceeded the maximal flow volume loop during the SL or 3 ATA condition were considered airflow limited. This method of determining airflow limitation is commonly used in the literature (Stubbing et al., 1980; Babb et al., 1991; Johnson et al., 1991; Babb and Rodarte, 1992). If exercise flow–volume loops met or exceeded the maximal flow–volume loop, but the pressure–volume loops did not achieve or exceed the range for Pcrit, then airflow limitation was deemed not to have occurred. This technique is very conservative in determining airflow limitation.

2.7. Submaximal exercise protocol

Determination of the work rate to be used for both SL and 3 ATA SM tests was accomplished by reducing the subject's maximal expiratory flow, obtained at sea level in the plethysmograph, by 33%. This was the expected reduction in maximal expiratory flow at 3 ATA, as determined by Hesser et al. (1981). Tidal flow volume loops from every stage of the subjects' maximal exercise test, performed during screening, were then superimposed on this reduced maximal expiratory flow volume loop. As ventilation increased with work rate, the exercise tidal flow volume loops that first impinged on this reduced expiratory loop was designated as the ventilation rate necessary to achieve airflow limitation at 3 ATA. The work rate was then noted for the stage where the tidal flow volume loops impinged on the reduced maximal expiratory loop. This work rate was the work rate used during the SL phase of SM testing. At 3 ATA, the work rate began at the work rate used for SL testing and was adjusted as necessary to match the ventilation obtained during SL exercise.

All subjects underwent SM exercise testing at sea level and then at 3 ATA. SM exercise then consisted of cycling at approximately 20–30 W for 30 sec then slowly increasing the load until the pre-determined work rate was attained (approximately an additional 2 min). This work rate was adjusted as necessary to achieve the desired ventilation for that subject (approximately an additional 60 sec).

After attainment of the desired ventilation during the SM sea level tests, the subject performed an IC maneuver and pedaled for approximately an additional 60 sec while breathing normally, after which another IC was performed. Total measurement time was approximately 1 min and 20 sec, (1.34 + 0.21 min), and total SM exercise time was approximately 5 min (5.0 + 0.3 min).

2.8. Data analysis

Data were analyzed using a 2 way ANOVA, repeated on one factor. Significance was set at a P value less than or equal to 0.05. Significant main effects were further analyzed with follow up post-

hoc tests conducted using a Duncan procedure at a P value less than 0.05. For comparisons between the two groups only, an independent t -test was used. All data are expressed as mean \pm SD.

3. Results

3.1. Airflow limitation

No subjects were airflow limited during SL exercise. However, the threefold increase in air density effectively reduced maximal expiratory flow and five subjects were airflow limited during the pre-selected exercise level at 3 ATA. This was based on tidal expiratory pressure–volume curves meeting or exceeding P_{crit} range and tidal flow–volume curves impinging on maximal expiratory flow curves. We then divided the subjects into two groups based on whether or not they achieved airflow limitation during the 3 ATA testing. There were no significant differences in subject characteristics, lung function or exercise capacity between the two groups with the exception of age ($P < 0.05$) (Tables 1 and 2). Also, there were no significant differences in rest and SM exercise ventilatory variables between the two groups, Table 3. As one would expect, all measured variables in Table 3 were significantly different during SM exercise when compared with rest.

3.2. Lung volume changes

At rest, EELV was increased in both groups at 3 ATA compared with SL ($P = 0.007$; Fig. 1). During exercise at 3 ATA, the airflow limitation group (AFL group) did not have a significantly lower EELV during exercise compared with rest as they did at SL ($P > 0.05$). The no airflow limitation group (no AFL group) did have a significantly lower EELV during exercise compared with rest at both SL and 3 ATA ($P < 0.05$). Subjects with airflow limitation had a significantly larger EELV during exercise at 3 ATA than during exercise at SL ($P = 0.008$; Fig. 1). Subjects with no airflow limitation had no significant difference in EELV during exercise between SL and 3 ATA ($P > 0.05$; Fig. 1). Also, unlike SL, EELV

Table 1
Subject characteristics and maximal exercise test results for the no AFL group^a

Variable	Subject 1	Subject 2	Subject 3	Subject 4	Subject 5	Subject 6	Mean ± SD
Sex	Female	Male	Male	Male	Male	Female	
Age (years)	44	38	38	44	36	32	39 ± 5
Height (cm)	170	183	168	178	175	165	173 ± 7
Weight (kg)	60	82	69	80	83	70	74 ± 9
FVC (L)	5.85	7.26	5.30	5.71	4.98	3.82	5.49 ± 1.13
FVC (% PRED)	165	136	125	119	102	106	126 ± 23
FEV ₁ (L)	4.33	5.36	3.91	4.29	4.10	3.22	4.20 ± 0.70
FEV ₁ (% PRED)	149	125	111	111	104	105	118 ± 17
TLC (L)	7.53	8.69	6.83	7.33	6.15	4.69	6.87 ± 1.36
TLC (% PRED)	134	116	113	106	91	88	108 ± 17
RV (L)	1.68	1.94	1.41	1.62	0.96	0.87	1.41 ± 0.42
RV (% PRED)	86	91	82	77	51	52	73 ± 17
DLCO (ml/min per mmHg)	23.9	na	27.2	29.9	28.4	20.0	25.9 ± 4.0
$\dot{V}O_2$ max (L/min)	2.60	3.45	1.90	3.29	4.03	2.23	2.92 ± 0.81
$\dot{V}E$ max (L/min)	107	194	128	135	146	100	135 ± 34
W, max	200	300	180	240	300	160	230 ± 60
fH, max (beats/min)	na	na	210	179	181	183	188 ± 15
RER, max	1.14	1.33	1.56	1.40	1.21	1.33	1.33 ± 0.15

^a FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 sec; TLC, total lung capacity; RV, residual volume; DLCO, diffusion capacity of the lung for carbon monoxide; $\dot{V}O_2$ max, maximal O₂ uptake; $\dot{V}E$ max, maximal minute ventilation; RER, respiratory exchange ratio; fH, heart rate; na, not available.

Table 2
Subject characteristics and maximal exercise test results for the AFL group^a

Variable	Subject 7	Subject 8	Subject 9	Subject 10	Subject 11	Mean ± SD
Sex	Male	Male	Female	Male	Female	
Age (years)	37	25	23	27	37	29 ± 7
Height (cm)	178	180	152	185	178	175 ± 13
Weight (kg)	81	63	58	86	64	70 ± 12
FVC (L)	6.43	6.19	4.24	6.27	4.79	5.58 ± 1.00
FVC (% PRED)	126	113	133	103	120	119 ± 12
FEV ₁ (L)	4.97	4.75	3.44	5.02	3.45	4.33 ± 0.81
FEV ₁ (% PRED)	118	103	123	100	106	110 ± 10
TLC (L)	7.77	7.87	5.21	7.55	6.91	7.06 ± 1.10
TLC (% PRED)	112	104	114	96	110	107 ± 7
RV (L)	1.42	1.65	0.76	1.24	2.02	1.42 ± 0.47
RV (% PRED)	71	89	64	61	95	76 ± 15
DLCO (ml/min per mmHg)	34.0	35.4	21.9	29.8	23.6	28.9 ± 6.0
$\dot{V}O_2$ max (L/min)	3.22	3.42	2.28	3.18	2.47	2.90 ± 0.50
$\dot{V}E$ max (L/min)	175	135	99	116	100	125 ± 32
W, max	270	300	160	240	220	238 ± 53
fH, max (beats/min)	178	201	na	na	178	186 ± 13
RER, max	1.22	1.16	1.25	1.22	na	1.21 ± 0.04

^a FVC, forced vital capacity; FEV₁, forced expiratory volume in 1 s; TLC, total lung capacity; RV, residual volume; DLCO, diffusing capacity of the lung for carbon monoxide; $\dot{V}O_2$ max, maximal O₂ uptake; $\dot{V}E$ max, maximal minute ventilation; RER, respiratory exchange ratio; fH, heart rate; na, not available.

Table 3
Rest to SM exercise test results at SL and 3 ATA^a

Variables	SL	3 ATA	SL	3 ATA
	Rest	Rest	Exercise	Exercise
AFL group				
\dot{V}_E (L/min)	14.6 ± 10.3	13.9 ± 7.40	76.6 ± 12.9	69.1 ± 17.1
V_T (% TLC)	18.9 ± 17.7	16.9 ± 6.40	36.2 ± 5.50	34.9 ± 6.10
fR (breaths/min)	11.7 ± 2.00	11.2 ± 4.10	30.3 ± 3.10	28.1 ± 2.20
V_T/TE (L/sec)	0.40 ± 0.27	0.41 ± 0.25	2.47 ± 0.50	2.37 ± 0.64
Peak tidal expiration flow (L/sec)	0.82 ± 0.54	0.82 ± 0.52	3.70 ± 0.88	3.37 ± 1.04
TE (sec)	3.12 ± 0.61	3.37 ± 0.96	1.04 ± 0.15	1.05 ± 0.08
No AFL group				
\dot{V}_E (L/min)	9.20 ± 2.4	11.2 ± 3.50	65.2 ± 23.4	63.0 ± 24.9
V_T (% TLC)	14.6 ± 5.9	16.9 ± 11.1	36.7 ± 8.20	37.3 ± 4.07
fR (breaths/min)	9.90 ± 2.9	10.6 ± 4.60	29.4 ± 17.5	25.6 ± 11.0
V_T/TE (L/sec)	0.41 ± 0.3	0.43 ± 0.24	2.21 ± 0.92	2.14 ± 0.90
Peak tidal expiration Flow (L/sec)	0.72 ± 0.3	0.80 ± 0.28	3.20 ± 1.06	3.45 ± 1.44
TE (sec)	3.92 ± 1.3	3.84 ± 1.39	1.39 ± 0.65	1.35 ± 0.52

^a \dot{V}_E , minute ventilation; V_T , tidal volume; fR, breathing frequency; V_T/TE , mean expiratory flow; TE, expiratory time. There were no significant differences in any variable between SL and 3 ATA, at rest or during exercise ($P > 0.05$). All Variables were significantly different from rest to exercise ($P < 0.05$). + $P \leq 0.05$, between groups.

for the AFL group was significantly larger than the no-AFL group during exercise at 3 ATA (Fig. 1).

EILV was larger during rest at 3 ATA for the no AFL group ($P = 0.01$), but not for the AFL group ($P > 0.05$; Fig. 2). EILV was not different during exercise between SL and 3 ATA in the group with no AFL, ($P > 0.05$; Fig. 2), but was larger at 3 ATA for the AFL group ($P \leq 0.05$; Fig. 2). EILV was not different between groups during exercise at SL or at 3 ATA ($P > 0.05$).

Flow and pressure volume loops denoting changes in EELV and EILV from rest to exercise are shown in Figs. 3 and 4 for one subject in the AFL group. The top panel in Fig. 3 shows a tidal flow volume loop during SM exercise with no airflow limitation at SL, while the bottom panel shows a pressure–volume loop for the same breath during exercise. This figure shows that without airflow limitation, PTP remains negative, and well below the Pcrit range for SM tidal breathing. Fig. 4 shows the reduction in the maximal flow–volume loop achieved at 3 ATA as well as the occurrence of airflow limitation during SM exercise for the same subject shown in Fig. 3. Fig.

4 also shows that expiratory PTP is significantly higher, and well beyond the Pcrit range during exercise at 3 ATA, due to airflow limitation.

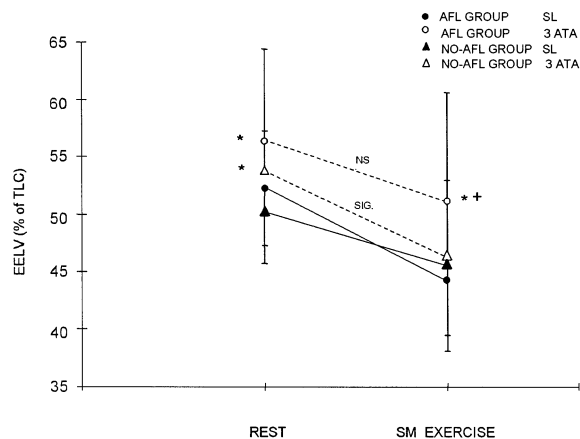


Fig. 1. Changes in EELV (% of TLC) at rest and during SM exercise, at SL and at 3 ATA (AFL). Symbols denote significant differences. * SL versus 3 ATA; + group differences, $P \leq 0.05$. Note the normally significant reduction in EELV with exercise at SL and at 3 ATA in the no AFL group; there was no significant reduction in EELV during exercise in the AFL group while airflow limited at 3 ATA.

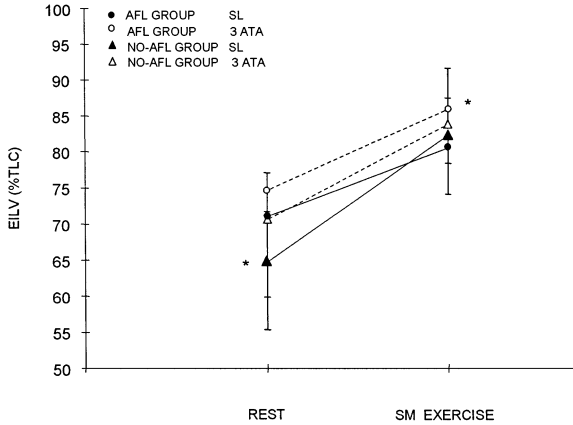


Fig. 2. Changes in EILV (% of TLC) at rest and during SM exercise, at SL and at 3 ATA (AFL). Symbols denote significant differences. *SL versus 3 ATA; + group differences, $P \leq 0.05$.

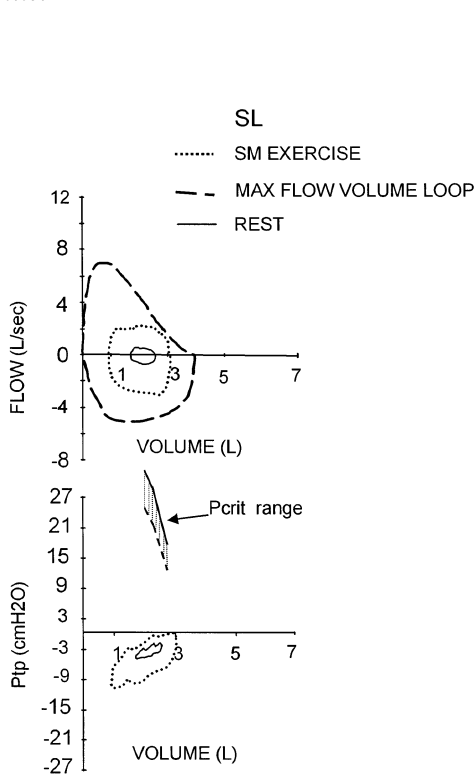


Fig. 3. Flow and PTP pressure volume curves during SM SL (non-AFL) exercise for a typical subject (subject 3). Pcrit is the minimum pressure necessary to generate maximal flow at a given lung volume; A Pcrit range is noted by the hatched area in which AFL is deemed to have occurred. PTP remains lower than Pcrit range without AFL.

3.3. Respiratory pressures

Peak expiratory PTP was higher during exercise at 3 ATA when compared with SL in the AFL group ($P = 0.04$; Fig. 5), due to airflow limitation. Thus, the significantly higher expiratory PTP, that met or exceeded the Pcrit range, combined with the flow volume loop criterion, confirmed the presence of airflow limitation. Peak expiratory PTP was not different during exercise at 3 ATA when compared with SL in the no AFL group ($P > 0.05$; Fig. 5). Thus, when not airflow limited, expiratory PTP remained more negative. There were no differences in peak expiratory transpulmonary pressure between groups at SL, but the groups were different during exercise at 3 ATA.

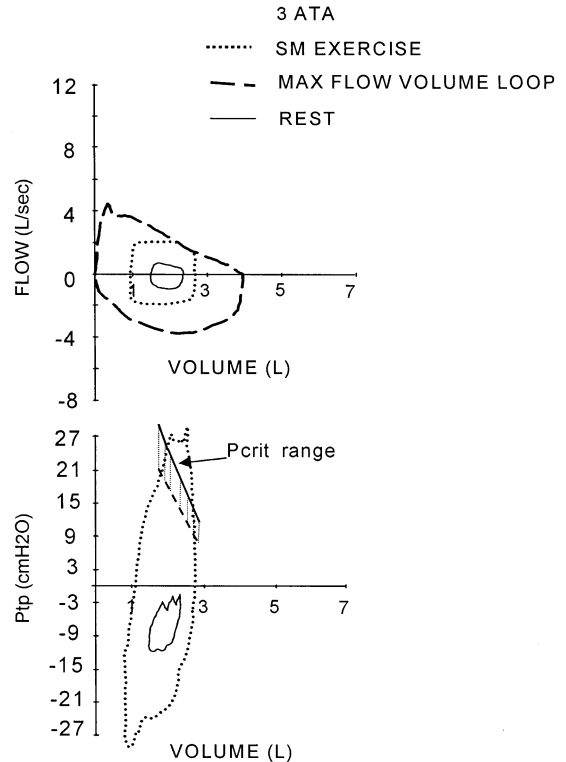


Fig. 4. Flow and PTP pressure volume curves during SM 3 ATA (AFL) exercise for the same typical subject (subject 3). Pcrit is the minimum pressure necessary to generate maximal flow at a given lung volume; A Pcrit range is noted by the hatched area in which AFL is deemed to have occurred. PTP is elevated beyond Pcrit range over the tidal volume that impinges on the maximal flow curve.

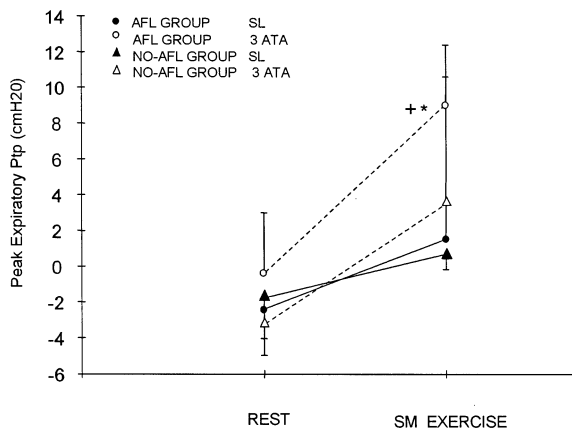


Fig. 5. Changes in peak expiratory PTP during rest and SM exercise, at SL and at 3 ATA. Symbols denote significant differences. * SL versus 3 ATA; + group differences, $P \leq 0.05$.

4. Discussion

The major finding of this study was that airflow limitation increased EELV during SM exercise in subjects with normal lung function who have probably never previously encountered airflow limitation during exercise, which to our knowledge has not previously been tested. Subjects with airflow limitation had a significantly larger EELV during SM exercise at 3 ATA compared with SL exercise, while subjects with no AFL had no change in EELV. Similar findings have been reported by others in the literature with subjects who chronically achieve airflow limitation during maximal exercise (Campbell et al., 1961; Grimby et al., 1971; Hesser et al., 1981; Henke et al., 1988). The subjects in these studies included patients with chronic obstructive pulmonary disease (COPD), elderly athletes and subjects with normal lung function, but who nevertheless achieve airflow limitation during exercise.

The common link between these studies and ours is that EELV is increased during exercise in subjects who achieve airflow limitation. This would support the hypothesis that the occurrence of airflow limitation influences EELV during exercise in subjects with normal lung function as suggested by Pellegrino et al. (1993). However, unlike Pellegrino et al. (1993) who imposed an

external load to reduce tidal expiratory flow and the amount of airflow limitation, we imposed flow limitation internally (within the airways) with increased ambient pressure in subjects who normally do not encounter airflow limitation at SM levels. When airflow limitation occurs, as it does in this case, compression of the airways results, which may result in an increased EELV (Pellegrino et al., 1993). The differences in EELV and expiratory Ptp between our two groups during exercise at 3 ATA demonstrates that in subjects with normal lung function, who have probably never encountered airflow limitation during exercise, EELV can become larger with the imposition of airflow limitation. This would suggest that dynamic airway compression may be the mechanism by which an increase in EELV occurs (Pellegrino et al., 1993).

The hyperbaric environment has been previously used to elicit airflow limitation. However, these studies differ in reported effects on EELV during exercise (Hesser; 81, 84, 90). For example, Hesser et al. (1981) found an increase in EELV during maximal exercise under hyperbaric conditions, while in 1984 and 1990, they found no changes in EELV during exercise in contrast to our data. In these studies however, Hesser et al. used maximal expiratory curves measured at the mouth (no thoracic compression correction) as their only criteria to determine airflow limitation. They did not use Pcrit to determine airflow limitation, as we have, and use of flow–volume loops alone is not necessarily indicative of airflow limitation.

Another method used in the literature to determine the control of EELV during exercise is use of a heliox air mixture to eliminate airflow limitation during exercise. These studies show differing results or report that no relationship exists between airflow limitation and EELV (McClaran et al., 1998, 1999; Mota et al., 1999). However, they also have methodological problems. For example, McClaran et al., 1998, used only a maximal flow volume loop, measured at the mouth to determine airflow limitation. They did not account for any thoracic gas compression artifact and did not use Pcrit as an indicator of airflow limitation, as we have done in our study. Also, in their study, they

used the inspiratory capacity technique to determine EELV, which is reliable during exercise when using peak inspiratory esophageal pressure as an indicator of maximal inspiratory effort. Since they did not measure esophageal pressure, this verification was not possible.

Our data incorporated Pcrit as our primary indicator of airflow limitation with use of tidal flow volume loops meeting the maximal expiratory flow as an additional indicator, which others have not done. While we attempted to minimize limitations to our methods, we acknowledge that our measurement of Pcrit and flow–volume loops may not account entirely for compression artifact in these measures. Nevertheless, our techniques have been shown to be acceptable in the literature (Mota et al., 1999).

Occurrence of airflow limitation was further substantiated in our study, by the significantly greater peak expiratory Ptp during exercise at 3 ATA in subjects who were airflow limited compared with their SL values and with the peak pressures of subjects who were not airflow limited, both at SL and 3 ATA (Fig. 5). Subjects who were not airflow limited had similar peak expiratory pressures during exercise at SL and 3 ATA. The significantly different EELV response, to SM exercise at 3 ATA between subjects with airflow limitation and those without airflow limitation, demonstrates that when subjects were airflow limited, they did not reduce EELV to the level they could achieve if they were not airflow limited. Thus, it was concluded that the occurrence of airflow limitation caused airway compression and a larger EELV to occur during exercise at 3 ATA.

EILV also was larger to a similar degree as EELV during exercise at 3 ATA in the AFL group, resulting in a V_T that was not different from SL. This maintained a ventilation that also was not different from SL. The subjects with no airflow limitation did not have a larger EILV during exercise at 3 ATA compared with SL. Physiologically this would mean that airflow limited subjects chose to maintain their V_T and breathe at a higher lung volume, possibly incurring greater work of breathing, rather than incur greater airflow limitation at a lower lung volume (Druz and Sharp, 1981; Collett and Engel, 1986;

Johnson et al., 1991). EILV was increased to the upper portion of the compliance curve of the respiratory system for the AFL group in order to maintain V_T and \dot{V}_E . Thus, it would seem that it was more important to limit the amount of airflow limitation and possibly incur more inspiratory work near TLC. Since the diaphragm is more fatigue resistant than the expiratory muscles, perhaps incurring more work with the inspiratory and accessory muscles is preferable to expiratory muscle work, or as in the hypothesis tested here, airflow limitation causes airway compression and results in an increased EELV at the expense of the work of breathing.

Our data also revealed a significantly larger EELV during rest at 3 ATA when compared with rest at SL for both groups, which has not been reported before (Fig. 1). The larger EELV at rest may be explained by the increased air density and thus resistance in the airways, which may have altered the functional residual capacity (FRC) equilibrium point during rest. Because during rest expiration is passive, expired airflow is dependent on the recoil of the respiratory system to overcome airway resistance to airflow. In this respect the resistance acts like an external resistive load at rest and could result in a larger EELV depending on the recoil of the respiratory system and airway resistance. This makes resting measures more susceptible to changes in EELV. Alternatively, it is also possible that behavioral effects of the pressurized chamber on the subjects resulted in an elevated EELV during rest, but not during exercise, at 3 ATA. This may be more likely since Pkpe was not significantly changed at 3 ATA except with the occurrence of AFL.

Therefore, we believe that the mechanism altering EELV during rest and exercise was different and thus the increase seen at rest did not influence EELV during exercise. Furthermore, during exercise, expiration is active and possibly less influenced by increased levels of airway resistance on EELV. In support of this conclusion, data from the no-AFL group also showed a significantly larger EELV at rest between SL and 3 ATA, however, during exercise at 3 ATA this group reduced EELV to a level not different from that seen during SL exercise, for either group (Fig. 1).

This demonstrates that even though EELV was larger at rest, subjects who were not airflow limited at 3 ATA reduced EELV to the same level observed during SL exercise, as our hypothesis would predict. If the same mechanism that resulted in a larger EELV at rest was responsible for the larger EELV during exercise then it would have been expected that the EELV during exercise in the group without airflow limitation would not be different from the EELV in the AFL group, but they were.

In conclusion, the occurrence of airflow limitation in subjects with normal lung function, under hyperbaric conditions, does appear to influence the control of EELV during exercise. The subjects in this study had a larger EELV in response to the occurrence of airflow limitation during exercise, while subjects without airflow limitation did not have a larger EELV.

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