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Does dynamic hyperinflation contribute to dyspnoea during exercise in patients with COPD?

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ABSTRACT

Dynamic hyperinflation (DH) during exercise occurs in most but not all patients with advanced COPD. It is not known whether the presence or absence of DH has implications for dyspnoea and exercise tolerance. Therefore, we compared detailed ventilatory and sensory responses to exercise in hyperinflators and non-hyperinflators with moderate to severe COPD.

Non-hyperinflators (n=65) were retrospectively identified from a sample of 427 patients and case-matched to a group of hyperinflators (n=65) based on sex, age, body mass index and %predicted forced expiratory volume in 1 second. Resting pulmonary function and constant work rate cycle exercise responses were compared.

Hyperinflators decreased inspiratory capacity (IC) from rest to peak exercise by 0.46±0.24L whereas the non-hyperinflators increased IC by 0.10±0.15L (P<0.0001). There were no significant group differences in endurance time (9.11±5.98 vs. 8.87±5.24min) or dyspnoea intensity for any given time or ventilation. An inflection in tidal volume versus ventilation occurred in the majority of non-hyperinflators (n=61) and hyperinflators (n=62) at a similar time and ventilation. Mechanical constraints on tidal volume expansion and the attendant rise in dyspnoea intensity were similar in both groups.

Dyspnoea intensity during exercise was associated with progressive mechanical constraints on tidal volume expansion regardless of the presence of DH.

Key Words: inspiratory capacity, inspiratory reserve volume, chronic obstructive pulmonary disease

INTRODUCTION

In patients with chronic obstructive pulmonary disease (COPD), dyspnoea (or breathing discomfort) arises in any situation where there is a disparity between the central drive to breathe and the mechanical response of the respiratory system, i.e., neuromechanical uncoupling [1-3]. Resting lung hyperinflation and reduced inspiratory capacity (IC) predispose to critical mechanical constraints on tidal volume (V_T) expansion as ventilatory requirements increase during exercise. An inflection or plateau in the V_T response to exercise, when expressed as a function of increasing ventilation, occurs at a minimal dynamic inspiratory reserve volume (IRV) of 0.5-1.0L. This mechanical event marks the beginning of a progressive disparity between respiratory muscle effort (i.e., tidal oesophageal pressure relative to maximum inspiratory pressure) and the corresponding V_T response (relative to vital capacity) [3]. This increasing neuromechanical uncoupling is associated with an abrupt increase in dyspnoea intensity which is predominantly perceived as unsatisfied inspiration [1, 3]. The smaller the IC, the lower the V_E during exercise at which the V_T reaches its plateau and the earlier the onset of intolerable dyspnoea [2].

Traditionally, dynamic hyperinflation (DH) refers to the variable and temporary increase in end-expiratory lung volume (EELV) above its baseline value that occurs when ventilatory demand is acutely increased. This is usually measured by serial inspiratory capacity (IC) manoeuvres which accurately reflect changes in EELV provided that total lung capacity (TLC) remains unaltered. This is to be distinguished from changes in end-inspiratory lung volume (EILV) which represents the combination of change in EELV and expansion of V_T, and is therefore not a measure of DH. The specific contribution of DH and the consequent progressive erosion of dynamic IC to dyspnoea causation during exercise is unclear and is the main focus of this study. In population samples of patients with moderate to severe COPD, a decrease in rest to peak IC was reported in the majority of patients (80-85%) [4, 5]. Smaller studies employing optoelectronic plethysmography have identified

varied behaviour of end-expiratory chest wall motion during exercise and have designated subgroups of COPD as non-hyperinflators ("euvolemics") [6] and; "early" and "late" hyperinflators [7].

The mechanical consequences of DH during exercise are complex. In many patients the largest increase in dynamic EELV occurs within the first few minutes of exercise where dyspnoea ratings are generally only in the mild to moderate range [3]. DH at these lower exercise intensities attenuates expiratory flow limitation which helps to preserve neuromechanical coupling of the respiratory system [3]. However, it is also possible that progressive erosion of dynamic IC during exercise in hyperinflators will force an earlier V_T plateau with attendant increase in dyspnoea at a lower V_E than in non-hyperinflators. Moreover, it is known that further acute-on-chronic lung hyperinflation has other potentially negative pulmonary and cardiovascular consequences as recently reviewed [8].

Given the variable mechanical consequences of DH, its specific contribution to perceived respiratory discomfort during physical activity in COPD is difficult to predict. For example, improvement in dyspnoea ratings after bronchodilator therapy is more closely associated with reductions in absolute lung volumes (or increase in V_T and inspiratory reserve volume (IRV)) than with reduction of DH which is often unaffected or, in some cases, may even increase modestly [9-11].

The main purpose of this study was to determine the direct contribution of DH to dyspnoea and exercise intolerance in COPD. We therefore compared breathing pattern, time to the V_T plateau/minimal IRV, dyspnoea/IRV relationships and endurance time in hyperinflators and non-hyperinflators matched for severity of airway obstruction, age, sex, and body mass index. We reasoned that the finding of an earlier onset of critical mechanical constraints on V_T expansion and corresponding increase in dyspnoea in hyperinflators would support the notion that DH of itself has important negative sensory consequences in COPD.

METHODS

Subjects and Study Design

This study is a retrospective analysis of exercise data from a large group (n=427) of COPD patients that participated in two multicentre clinical trials examining the effects of tiotropium on exercise tolerance [12, 13]. It does not overlap with previous analyses of the same data set [2, 14, 15]. Ethical approval was obtained by all research sites and patients gave informed written consent prior to participation. The Research Ethics Board of Queen's University and Affiliated Teaching Hospitals approved the use of this data (DMED-1424-11).

Original inclusion criteria were as follows: 40-75 years of age, cigarette smoking history > 10 pack-years, plethysmographic functional residual capacity > 120% predicted and a forced expiratory volume in 1 second (FEV_1) ≤ 65% predicted. Subjects were excluded if they had a history of asthma, allergic rhinitis or atopy, any contraindication to clinical exercise testing and/or participation in a COPD rehabilitation program within 6 weeks prior to the screening visit.

Subjects were required to refrain from using long-acting bronchodilators for a minimum of 1 week prior to and throughout the duration of the study. Short-acting anticholinergics were withdrawn a minimum of 1 day prior to the screening visit and were not used throughout the study. Salbutamol was given as rescue medication during the study but was withdrawn ≥ 6 hours prior to each visit.

Detailed pulmonary function testing and an incremental symptom-limited cycle exercise test were performed during a screening visit which was followed by two run-in visits whereby subjects performed pulmonary function tests and a symptom-limited constant work rate cycle test. Exercise and pulmonary function data analysis were based upon the second run-in visit. DH was defined as a decrease in IC from rest of more than 150 ml or 4.5% predicted at any time point during exercise [4].

O'Donnell et al [4] previously demonstrated that the 95% confidence interval for the resting IC measurement was ± 0.14 L or ± 4.5% predicted in patients with COPD, indicating that reproducibility criteria of within 150 ml is appropriate for testing IC in this population. Importantly, the 95% CI for peak exercise IC was similar. Subjects were then divided into two subgroups based on the presence or absence of DH. After identifying all non-hyperinflators (n=65), experimenters systematically matched them to 65 of the remaining 362 hyperinflators based on sex, percent predicted FEV_1, age, and BMI while remaining blinded to all other measurements. Matching was randomly determined if more than one hyperinflator was a suitable match to a non-hyperinflator.

Pulmonary Function

Spirometry and body plethysmography were performed according to established guidelines and values are expressed as percentages of predicted normal values. Predicted IC was calculated as predicted total lung capacity minus predicted functional residual capacity since there are no current equations for predicting normal IC. Maximal ventilatory capacity (MVC) was estimated by multiplying FEV_1 by 35 [16].

Exercise Tests

Details regarding the incremental cycle test have been described elsewhere [12]. The constant work rate exercise test involved a steady-state rest period and a 1 minute warm up at 0W followed immediately by an increase in work rate corresponding to 75% of the peak incremental work rate until symptom limitation. Time from the onset of this work rate to symptom limitation was defined as the endurance time. Metabolic and ventilatory parameters were measured on a breath-by-breath basis using various commercially available systems. Intensity of dyspnoea and leg discomfort were assessed using the modified Borg scale [17]. Borg ratings and IC maneuvers were performed at rest, throughout exercise, and at symptom limitation. IC maneuvers were used to examine operating lung volumes and

DH as previously described [18]. Data are presented as 30 second averages during rest, the last 30 seconds of each second minute during exercise, and at peak exercise. The inflection point of V_T relative to V_E during exercise was also determined for each subject using the 30 second averaged data at each time point [19].

Statistical Analysis

Data are presented as means ± SD unless otherwise specified. Reasons for stopping exercise were analyzed as frequency statistics and compared using the Fisher's exact test. Between group comparisons (non-hyperinflators vs. hyperinflators) for descriptive characteristics and exercise responses at standardized times were performed using unpaired *t*-tests. Statistical significance was set at $P < 0.05$.

RESULTS

Subject Characteristics

Sixty-five out of 427 (15%) subjects were identified as non-hyperinflators. Characteristics of the non-hyperinflators and the matched hyperinflators (n=65) are shown in Table 1. By design, both groups were closely matched for FEV_1 (% predicted and liters), age, BMI, and sex. The hyperinflators had a larger forced vital capacity (FVC) resulting in a slightly lower FEV_1/FVC ratio. Hyperinflators also had greater percent predicted values for total lung capacity (TLC) and functional residual capacity compared with the non-hyperinflators. There were no significant differences between groups in peak incremental work rate and oxygen consumption (VO_2).

Exercise Responses

Physiological and perceptual responses at the V_T inflection point and at peak exercise are summarized in Table 2. Both groups were well matched for absolute work rate during the constant work rate cycling test with no significant differences in cycle endurance time or peak VO_2.

The change in dynamic IC from rest to peak exercise (i.e., the inverse magnitude of DH) was -0.46±0.24L in the hyperinflators and 0.10±0.15 L in the non-hyperinflators (Figure 1A, Table 2). IC in the hyperinflators decreased rapidly (by 0.34±0.23 L) within the first 2 minutes of exercise and continued to decrease, albeit less abruptly, until symptom limitation (Figure 1). In contrast, the non-hyperinflators increased IC modestly (by 0.10±0.28 L) at the onset of exercise and then maintained this level throughout exercise.

Selected exercise responses are shown in Figure 2. There were no significant differences between groups for VO_2, V_E, breathing frequency or V_T at any given time throughout exercise. An inflection point in the relation between V_T and V_E occurred in the majority of non-hyperinflators (61/65) and hyperinflators (62/65). This inflection point occurred at a similar time, VO_2, V_E, V_T, and inspiratory reserve volume (IRV) in each group (Table 2). After the V_T/V_E inflection point where IRV had reached a critically reduced level in both groups, there was no further change in V_T during exercise, i.e., there was a plateau (Figure 3).

Exertional Dyspnoea

The main reasons for stopping constant work rate exercise were similar in both groups: dyspnoea was selected as the primary reason, either alone or in combination with leg discomfort, in 51/65 and 53/65 of non-hyperinflators and hyperinflators, respectively. No significant differences in dyspnoea intensity were observed at any given exercise time or V_E during constant work rate cycling (Figure 4). Likewise, no differences in dyspnoea intensity were observed at the V_T inflection point (Table 2). Dyspnoea intensity increased linearly as IRV decreased in both groups up to an inflection point (corresponding to the V_T/V_E inflection point) where subjects reported "moderate" exertional dyspnoea. Beyond this point, and irrespective of the presence of DH, dyspnoea as a function of IRV increased

steeply to intolerable levels where patients reported "very severe" dyspnoea at the symptom-limited endpoint (Figure 4C).

A secondary analysis comparing the non-hyperinflators (n=65) to all hyperinflators (n=362) whereby groups were not systematically matched for any baseline characteristics, revealed similar results for our primary outcomes (i.e., no group differences in dyspnea or cycle endurance time).

DISCUSSION

The main findings of this study are as follows: *1*) patients who acutely increased EELV during exercise did not experience higher exertional dyspnoea ratings or greater exercise intolerance compared with FEV_1-matched patients who did not increase dynamic EELV; *2*) hyperinflators and non-hyperinflators reached critical constraints on V_T expansion at a similarly reduced dynamic IRV and at a similar time and V_E during constant work rate cycle exercise; 3) dyspnoea/IRV and dyspnoea/V_E relationships were not altered by the presence of DH.

The results of this study coupled with those of others [4, 5, 20] suggest that approximately 15-20% of patients with moderate to severe COPD do not consistently increase EELV during exercise. Out of 427 patients in the present study, we identified 65 patients who did not meet our conservative definition of DH [4]. After carefully matching subgroups of hyperinflators and non-hyperinflators for disease severity, age, sex, and BMI, we observed that those who did not increase dynamic EELV during exercise had a slightly higher FEV_1/FVC ratio and less resting lung hyperinflation suggesting less airway dysfunction than the group who hyperinflated (Table 1). Given that ventilatory demand and the volume and timing components of breathing during exercise were similar in both groups, we can assume that differences in EELV behaviour during exercise primarily reflected unmeasured differences in mechanical time constants for lung emptying.

The fact that patients in each group were well matched for several key parameters that influence respiratory mechanics allowed us to evaluate the role of DH in contributing to dyspnoea and exercise intolerance in COPD. We found that, contrary to our original hypothesis, the presence of DH was not associated with increased dyspnoea ratings or greater exercise intolerance. Aliverti *et al.* [6] recently measured operating lung volumes by optoelectronic plethysmography in patients with moderate to severe COPD. As in the current study, dyspnoea ratings during a symptom-limited incremental cycle test were similar in 8 non-hyperinflators and 12 hyperinflators who were not matched for spirometric or anthropometric parameters. However, despite having better baseline spirometry, and in contrast to our results, the non-hyperinflators had diminished exercise performance. This discrepancy in results between the current and previous studies is likely related to differences in methods of measurement of DH and in exercise protocols.

The relative importance of DH in contributing to the intensity and quality of dyspnoea during exercise in COPD has been difficult to determine. Previous studies have shown that besides increased dynamic EELV, several indices of dynamic mechanical constraint have correlated, albeit variably, with dyspnoea intensity during exercise including increases in EILV and the V_T/IC ratio and decreases in dynamic IRV, as recently reviewed [21]. In addition to correlative evidence, specific therapeutic interventions can be used to manipulate DH and its mechanical consequences. For example, low level continuous positive airway pressure therapy, which is thought to counterbalance the negative effects of the inspiratory threshold load, has been shown to reduce dyspnoea and improve exercise endurance in selected patients with COPD [22, 23]. Similarly, improvement in dyspnoea and endurance time following helium-oxygen therapy has been associated with a reduction in the rate of DH [24, 25]. In contrast, dyspnoea reduction following bronchodilator therapy, hyperoxia, and exercise training have been shown to occur in the absence of a reduced rate of DH confirming the multifactorial nature of this symptom [9-11, 26-28]. It is possible that other mechanical improvements following these

interventions such as reduced absolute lung volumes with a delay in reaching critical ventilatory constraints are more important in explaining dyspnoea relief than small or inconsistent reductions in the rate of DH. It is also noteworthy that increases in EELV in the hyperinflator group tended to occur early during high intensity constant work rate exercise: 69% of hyperinflators showed an average decrease in IC of 0.2 L in the first 2 min of exercise where perceived dyspnoea intensity was only 'slight' at 2.4 Borg units.

In keeping with previous studies, a discernable inflection or plateau in the V_T/V_E relation during exercise occurred in nearly all (~95%) of our study patients. This occurred regardless of whether they hyperinflated or not (Figure 3A). Beyond this V_T inflection (at a minimal IRV of 0.5-1 L), dyspnoea rose sharply to intolerable levels (Figure 4C). We have previously proposed that the magnitude of the resting IC and the decrease in dynamic IRV during exercise importantly influence the evolution of dyspnoea in COPD [1, 2]. The current study suggests that dyspnoea rises as V_T expands to reach a minimal IRV regardless of whether IC remains stable (non-hyperinflators) or diminishes (hyperinflators) during exercise. Thus, the regulation of end-inspiration relative to TLC likely provides a more proximate measure of the critical mechanical constraints during exercise relevant to dyspnoea provocation than the behaviour of EELV *per se*. For example, the difference in IC from rest to peak exercise between the two groups was 0.56 L; change in EELV in excess of 0.5 L would be expected to increase inspiratory threshold loading of the inspiratory muscles and, of itself, may have negative sensory consequences [23]. The results of the current study suggest other mechanical factors are more important. In both groups EILV from the V_T/V_E inflection to peak was in excess of 90% of TLC (Table 2). Breathing at this high EILV is difficult to sustain given the associated increased elastic loading and functional respiratory muscle weakness [29]. This is further compounded by increased velocity of shortening of the inspiratory muscles and decreased dynamic lung compliance. At this point, central neural drive has reached near maximal levels as a result of metabolic and possibly

respiratory acidosis in some and V_T expansion is critically constrained. We have argued that this progressive neuromechanical uncoupling of the respiratory system after reaching maximal EILV provokes intolerable dyspnea which, in many patients with COPD, is the proximate cause of exercise limitation. Other factors such as respiratory muscle fatigue and central inhibition of neural drive may also contribute to exercise intolerance but their precise role is inconclusive at this time [29-32].

Methodological Considerations

The underlying mechanism for the different behaviour of EELV between the groups could not be determined. By exclusion, differences in expiratory flow limitation and mechanical time constants for lung emptying which could not be measured in this study are likely important. Our patients had a reasonably well preserved resting IC (75-78 % predicted) and results may not be generalizable to patients with a smaller resting IC.

Accurate assessment of dynamic hyperinflation using the IC is based on the assumption that TLC remains constant and that patients are able to inspire to TLC throughout exercise. Stability of TLC during exercise could not be evaluated in this study. However, previous work has confirmed that TLC remains constant during exercise in healthy subjects [33] and in COPD [34]. Studies have also shown that patients with COPD can consistently generate similar peak inspiratory oesophageal pressures during serial IC manoeuvres throughout exercise, despite progressive reduction of the latter as a result of DH [35, 36]. Moreover, patients are capable of maximal diaphragm activation during inspiratory efforts to TLC [29, 37] even when dyspneic at peak exercise [29]. These observations coupled with recent evidence that IC during cycle exercise is highly reproducible in a large patient population which included the current study sample [5], support our approach for detecting dynamic hyperinflation.

In conclusion, we have shown that differences in the behaviour of dynamic EELV during exercise in FEV_1-matched groups with COPD did not appear to influence exertional dyspnoea intensity or exercise

endurance time during high intensity constant work rate cycle exercise. This study has shown for the first time that critical constraints on V_T expansion occur at a similar time and V_E in patients with moderate to severe COPD irrespective of the presence of DH during exercise. These results support the idea that the prevailing IC and the mechanical constraints on V_T as the IRV approaches its minimal value strongly influence dyspnoea intensity and exercise tolerance in COPD, independent of the presence of acute-on-chronic DH during exercise.

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Table 1. Subject characteristics

Subject Characteristics	Non-Hyperinflators (n = 65)	Hyperinflators (n = 65)
Males : Females (n)	44 : 21	44 : 21
Age (years)	60 ± 7	62 ± 7
Height (cm)	171 ± 8	170 ± 9
Mass (kg)	73.5 ± 18.4	74.6 ± 15.6
BMI (kg/m^2)	25.1 ± 5.6	25.7 ± 4.2
Smoking history (pack-years)	48.1 ± 23.5	48.9 ± 25.3
Duration of COPD (years)	9.8 ± 8.0	7.8 ± 6.4
FEV_1 (L)	1.41 ± 0.45	1.38 ± 0.47
FEV_1 (% predicted)	50 ± 14	50 ± 13
FVC (L)	2.78 ± 0.79	2.96 ± 0.79
FVC (% predicted)	70 ± 16	76 ± 15 *
FEV_1/FVC (%)	51.1 ± 10.9	46.7 ± 11.1 *
FEV_1/FVC (% predicted)	71 ± 16	66 ± 15.3 *
FEF_{25-75} (L/sec)	0.61 ± 0.37	0.52 ± 0.29
FEF_{25-75} (% predicted)	21 ± 12	18 ± 9
IC (L)	2.16 ± 0.62	2.22 ± 0.68
IC (% predicted)	75 ± 18	78 ± 20
IC/TLC	30.6 ± 7.5	29.9 ± 7.6
TLC (L)	7.08 ± 1.17	7.50 ± 1.52 ‡
TLC (% predicted)	115 ± 15	122 ± 16 *
FRC (L)	4.92 ± 1.00	5.27 ± 1.28 ‡
FRC (% predicted)	151 ± 30	161 ± 33 †
RV (L)	4.12 ± 1.00	4.29 ± 1.20
RV (% predicted)	196 ± 48	201 ± 49
Raw (cmH_2O/L/sec)	5.58 ± 2.72	5.46 ± 2.04
Raw (% predicted)	425 ± 215	413 ± 155
Wpeak (W)	81 ± 28	86 ± 32
Wpeak (% predicted)	55 ± 20	58 ± 17
VO_2peak (L/min)	1.25 ± 0.41	1.27 ± 0.47
VO_2peak (mL/kg/min)	17.2 ± 4.9	16.9 ± 4.8
VO_2peak (% predicted)	65 ± 23	67 ± 18

BMI = body mass index; FEV_1 = forced expiratory volume in 1 second; FVC = forced vital capacity; $FEF_{25-75\%}$ = forced expiratory flow between 25 and 75% of FVC; IC = inspiratory capacity; TLC = total lung capacity; FRC = functional residual capacity; RV = residual volume; Raw = airways resistance; Wpeak = peak incremental cycle work rate; VO_2peak = peak oxygen consumption obtained during an incremental cycle test. Values are means ± SD. * Significantly different between groups ($P<0.05$); † $P=0.05$; ‡ $P=0.08$.

Table 2. Measurements during exercise at the tidal volume/ventilation inflection point and at symptom-limited peak

	V_T/V_E Inflection		Peak	
	Non-Hyperinflators (n=61)	**Hyperinflators (n=62)**	**Non-Hyperinflators (n=65)**	**Hyperinflators (n=65)**
Work rate (W)	63 ± 21	66 ± 25	63 ± 21	66 ± 25
Time (min)	2.81 ± 1.41	2.47 ± 1.29	9.11 ± 5.98	8.87 ± 5.24
IC (L)	2.13 ± 0.59	1.99 ± 0.59	2.10 ± 0.57	1.87 ± 0.57 *
ΔIC from rest (L)	0.14 ± 0.34	-0.34 ± 0.26 *	0.10 ± 0.15	-0.46 ± 0.24 *
IC/TLC (%)	30 ± 7	27 ± 7 *	30 ± 8	25 ± 7 *
V_T/IC (%)	72 ± 16	73 ± 12	72 ± 16	77 ± 12 *
EELV (%TLC)	70 ± 7	73 ± 7 *	70 ± 8	75 ± 7 *
EILV (%TLC)	91 ± 5	92 ± 4	91 ± 6	94 ± 4 *
V_E (L/min)	35.8 ± 11.4	35.1 ± 10.8	44.4 ± 14.1	44.9 ± 14.1
V_E/MVCpred (%)	76 ± 24	78 ± 21	94 ± 27	98 ± 24
VO_2 (L/min)	1.10 ± 0.36	1.08 ± 0.38	1.25 ± 0.40	1.26 ± 0.44
V_T (L)	1.50 ± 0.47	1.43 ± 0.44	1.48 ± 0.45	1.41 ± 0.40
*F*b (breaths/min)	24.8 ± 6.4	25.2 ± 5.3	30.9 ± 7.0	32.2 ± 6.2
IRV (L)	0.62 ± 0.41	0.56 ± 0.32	0.61 ± 0.40	0.46 ± 0.31 *
IRV (%TLC)	9 ± 5	8 ± 4	9 ± 6	6 ± 4 *
Dyspnoea (Borg)	3.5 ± 1.5	3.1 ± 1.7	6.8 ± 2.1	6.5 ± 2.3
SpO_2 (%)	94 ± 3	94 ± 3	93 ± 5	94 ± 4
ΔSpO_2 from rest (%)	-1.6 ± 2.4	-1.7 ± 2.2	-2.4 ± 3.5	-2.5 ± 3.4

Tidal volume (V_T) inflection data are from subjects with a detectable V_T inflection and peak data are from all subjects. IC = inspiratory capacity; TLC = total lung capacity; V_T = tidal volume; EELV = end expiratory lung volume; EILV = end inspiratory lung volume; V_E = minute ventilation; MVCpred = predicted maximal ventilatory capacity based on forced expiratory volume in 1 second multiplied by 35; VO_2 = oxygen uptakes; *F*b = breathing frequency; IRV = inspiratory reserve volume; SpO_2 = pulse oximetry derived oxygen saturation. Values are means ± SD. * Significantly different between groups (P<0.05).

FIGURE LEGEND

Figure 1. Change in inspiratory capacity from rest (ΔIC) and operating lung volumes are plotted against constant work rate exercise time in hyperinflators and non-hyperinflators. Dashed lines are from the last standardized measurement time to peak exercise. Total lung capacity in the hyperinflators and non-hyperinflators were 122 and 115% predicted, respectively. EELV, end-expiratory lung volume; EILV, end-inspiratory lung volume. Shaded region represents tidal volume in the non-hyperinflators. Data are presented as mean ± SE. * $P<0.05$ significant difference between groups at a given time point.

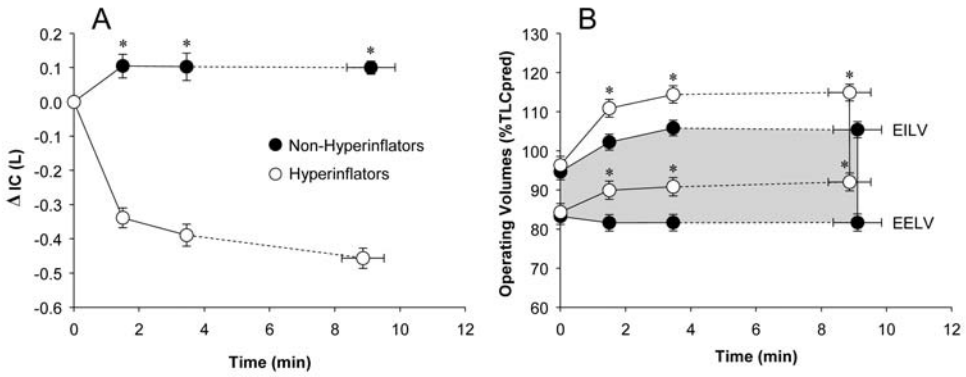


Figure 2. Ventilation (V_E), oxygen consumption (VO_2), tidal volume (V_T), and breathing frequency (*F*b) versus constant work rate exercise time in hyperinflators and non-hyperinflators. Dashed lines are from the last standardized measurement time to peak exercise. Data are presented as mean ± SE.

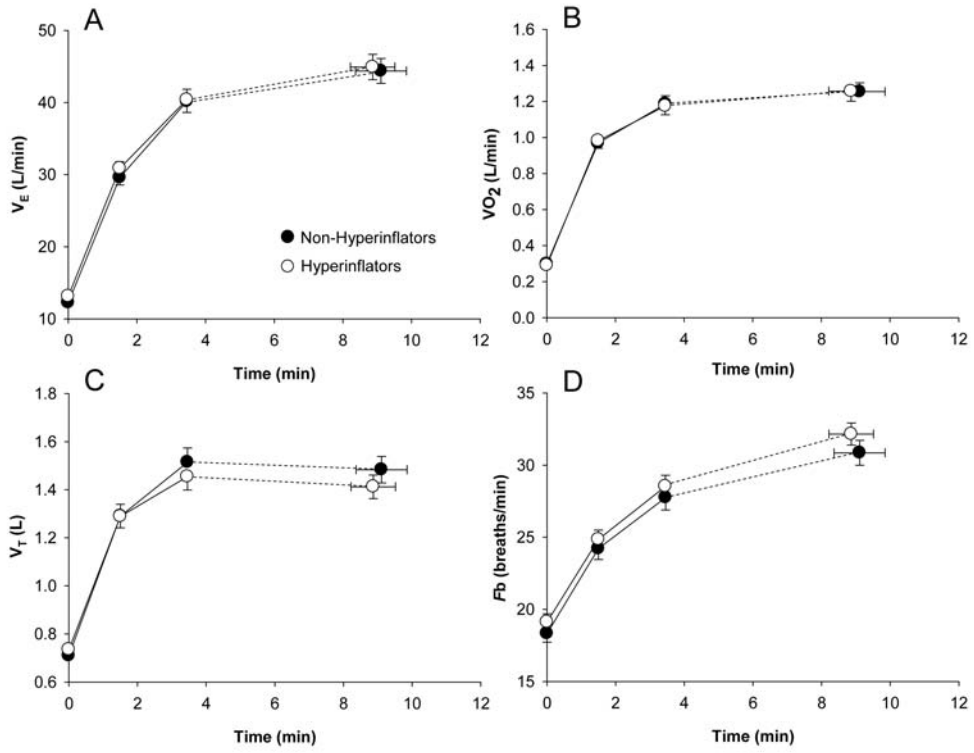


Figure 3. Tidal volume (V_T) and inspiratory reserve volume (IRV) versus ventilation (V_E) in hyperinflators and non-hyperinflators. Dashed lines are from the last standardized measurement time to peak exercise. Triangles represent data at the V_T/V_E inflection. TLC, total lung capacity. Data are presented as mean ± SE. * $P<0.05$.

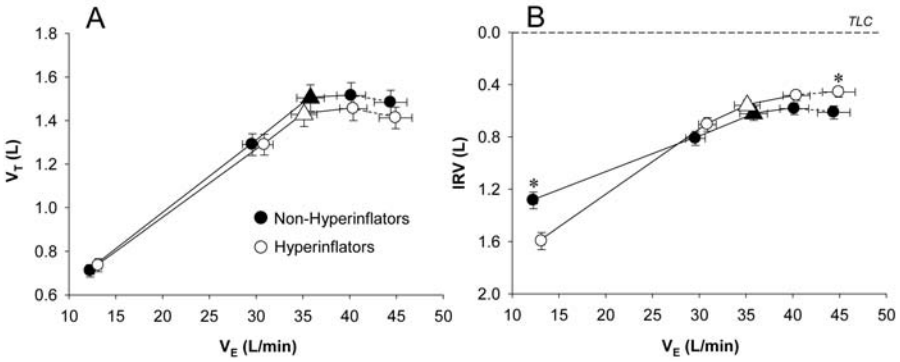
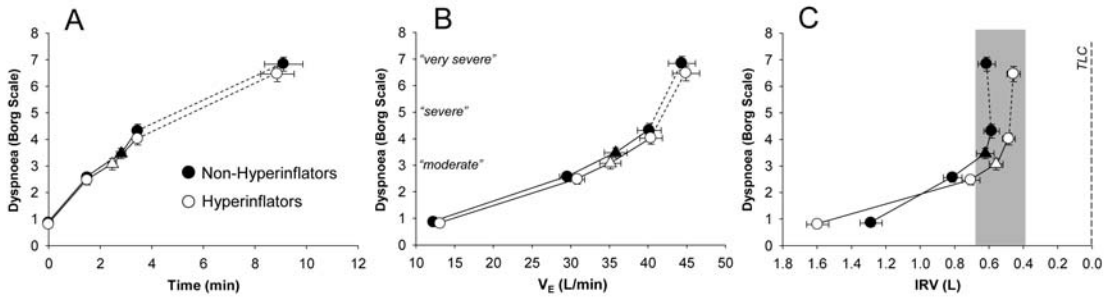


Figure 4. Dyspnoea versus constant work rate exercise time, ventilation (V_E), and inspiratory reserve volume (IRV) in hyperinflators and non-hyperinflators. Dashed lines are from the last standardized measurement time to peak exercise. Triangles represent data at the tidal volume inflection point. TLC, total lung capacity. Shaded region represents the critical or minimal IRV where dyspnoea intensity ratings deviate from linearity and increase vertically. Data are presented as mean ± SE.


A
B
C
Dyspnoea (Borg Scale)
Time (min)
Non-Hyperinflators
Hyperinflators
"very severe"
"severe"
"moderate"
V_E (L/min)
IRV (L)
TLC