

Dynamic hyperinflation and tolerance to interval exercise in patients with advanced COPD

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ABSTRACT: Dynamic hyperinflation (DH) contributes importantly to the limitation of constant-load exercise (CLE) in patients with chronic obstructive pulmonary disease (COPD). However, its role in the limitation of interval exercise (IE) remains to be explored.

The change (Δ) in inspiratory capacity (IC) was measured to reflect changes in DH in 27 COPD patients (forced expiratory volume in one second mean \pm SEM % predicted: 40 ± 3) at the end of a symptom-limited CLE test at 80% of peak work capacity (WR_{max}) and an IE test at 100% WR_{max} (30 s of work, alternated with 30 s of unloaded pedalling).

At the limit of tolerance in both IE and CLE, patients exhibited similar DH (Δ IC: 0.39 ± 0.05 L and 0.45 ± 0.05 L, respectively). However, exercise endurance time (t_{end}) for IE (32.7 ± 3.0 min) was significantly greater than for CLE (10.3 ± 1.6 min). The IE t_{end} correlated with resting IC, expressed as % pred normal. At 30 and 90% of total IE t_{end} , Δ IC (0.43 ± 0.06 and 0.39 ± 0.05 L, respectively) and minute ventilation (31.1 ± 1.6 and 32.7 ± 2.2 L·min⁻¹, respectively) were not significantly different.

Resting hyperinflation helps to explain the limitation of interval exercise. Implementation of interval exercise for rehabilitation should provide important clinical benefits because it prolongs exercise endurance time and allows sustaining higher stable ventilation.

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Recent studies have demonstrated the benefits of rehabilitative exercise training on exercise capacity, quality of life and utilisation of healthcare resources in patients with chronic obstructive pulmonary disease (COPD) [1]. Most rehabilitation programmes are based on constant-load exercise (CLE) training, consisting of sustained exercise for 30–40 min [1]. Generally, high-intensity training is argued to be needed for the improvement of exercise capacity [2]. Although patients with moderately severe COPD (mean forced expiratory volume in one second (FEV₁) >45% predicted) can tolerate high levels (80%) of their peak tolerance for several minutes [3, 4], patients with more severe disease are unable to tolerate such exercise intensities for sufficiently long periods [5, 6].

The factors that limit exercise tolerance in these patients are linked with the development of dynamic hyperinflation (DH) and the concurrent mechanical constraints on ventilation that contribute importantly to perceived respiratory discomfort. Secondary to DH and concomitant high mean intrathoracic pressure, cardiac performance and, hence, supply of oxygenated blood to the malfunctioning peripheral muscles are further compromised [7, 8]. This contributes to perceived leg discomfort and exercise intolerance. The importance of DH in exercise limitation in patients with advanced COPD arises from studies which demonstrated that alleviation of dyspnoea with acute bronchodilator therapy or oxygen

supplementation is due, in part, to decreased operating lung volumes [9–11]. Both interventions improved exercise endurance time (t_{end}), which, nonetheless, remained brief (typically ~8–10 min).

Interval exercise (IE) training, which consists of maximal-intensity exercise loads on peripheral muscles, has been used by the current authors as an equally effective alternative to CLE in patients with moderately severe COPD (mean FEV₁ 45% pred) [12]. Interestingly, the levels of dyspnoea in the IE group during the training sessions were significantly lower than in the CLE group. On the basis of the well-established mechanistic link between the intensity of dyspnoea and the degree of DH [13], the lower symptoms of dyspnoea during IE might reflect smaller increases in dynamic lung volumes as compared with CLE. However, there are no studies demonstrating the degree to which the behaviour of operating lung volumes during IE influences exercise tolerance in patients with severe COPD. Moreover, as IE consists of a sequence of on and off high-intensity muscular loading events, its tolerability in the context of perceived respiratory and peripheral muscle discomfort is still unknown.

Accordingly, the objectives of the current study were as follows: 1) to determine the range and pattern of change in the operating lung volume components during IE in patients with different degrees of airflow limitation; and 2) to investigate

whether IE could enable patients with advanced COPD to tolerate high-intensity exercise for sufficiently long periods of time.

Methods

Subjects

Subjects included 27 male patients with stable COPD who satisfied the following criteria: 1) postbronchodilator FEV₁ <50% pred and FEV₁/forced vital capacity <65% without significant reversibility (<12% change of the initial FEV₁ value); 2) optimised medical therapy; and 3) no clinical evidence of exercise-limiting cardiovascular or neuromuscular diseases.

Study design

Patients underwent three symptom-limited exercise tests on different days in the following order: 1) a ramp-incremental test to define the peak work rate (WR_{max}); 2) a CLE test at a work rate equivalent to 80% WR_{max}; and 3) an IE test at a work rate that corresponded to 100% WR_{max} with 30 s work, interspersed with 30 s of unloaded pedalling. All patients signed an informed consent and the protocol was approved by the current authors' hospital ethics committee.

Pulmonary function tests

Spirometry and lung diffusion capacity for carbon monoxide (DL_{CO}) were performed by a spirometer (Masterlab; Jaeger, Wurzburg, Germany) according to recommended techniques [14], whereas maximum voluntary ventilation (MVV) was directly measured (V_{max} 229; Sensor Medics, Anaheim, CA, USA). Arterial blood was drawn by puncture of the radial artery at rest, whilst breathing room air for the analysis of arterial oxygen tension (Pa,O₂), carbon dioxide tension (Pa,CO₂) and pH (ABL330; Radiometer, Copenhagen, Denmark).

Exercise testing

All tests were performed on an electromagnetically braked cycle ergometer (Ergoline 800; Sensor Medics), with the subjects maintaining a pedalling frequency of 60 rpm. Tests were preceded by a 2-min rest period, followed by 3 min of unloaded pedalling. The following pulmonary gas exchange and ventilatory variables were recorded breath-by-breath (V_{max} 229; Sensor Medics): oxygen uptake (V'O₂), carbon dioxide output (V'CO₂), respiratory exchange ratio, minute ventilation (V'E), tidal volume (VT), and breathing frequency. Cardiac frequency (fC) and percentage oxygen saturation measured by pulse oximetry were determined using the R-R interval from a 12-lead online electrocardiogram (Marquette Max; Marquette Hellige GmbH, Freiburg, Germany) and a pulse oximeter (Nonin 8600; Nonin Medical, Plymouth, MN, USA), respectively. The modified Borg Scale was used to rate the magnitude of perceived dyspnoea and leg discomfort every 3 min throughout and upon cessation of exercise [15]. During the ramp-incremental test (increments of 5–10 W), the anaerobic threshold (AT) was determined *via* the V-slope technique [16]. The peak V'O₂ values were compared with those of JONES [17].

During exercise tests, changes in operational lung volumes were evaluated from measurements of dynamic inspiratory

capacity (IC), assuming that total lung capacity (TLC) remained constant during exercise [18], thus reflecting changes in end-expiratory and end-inspiratory lung volumes (EILV). By subtracting VT from the coinciding IC, changes in inspiratory reserve volume (IRV) were calculated. Prior to exercise testing, patients were familiarised with the IC manoeuvre, where they were instructed to make 3–5 maximal efforts according to previously described methods, *i.e.* "at the end of the next normal expiration, take a deep breath all the way in", followed by verbal encouragement to make a maximal effort before relaxing [18, 19]. Throughout exercise testing, IC was measured every 3 min and at the end of exercise. During the IE tests, IC measurements were carried out during the 30-s work phases. Arterial blood for the determination of Pa,O₂, Pa,CO₂, pH, alveolar–arterial oxygen pressure difference, arterial–end tidal carbon dioxide pressure difference and arterial lactate concentration was drawn before and at the end of the tests.

Data analysis

Data were presented as mean±SEM. A statistical significance of 0.05 was used for all analyses, with appropriate Bonferroni corrections for multiple comparisons. During IE, temporally matched (at 30, 60 and 90% of the total exercise time) measurements for V'O₂, fC, and V'E, corresponding to successive 30-s intervals of work and unloaded pedalling, were analysed by a two-way analysis of variance (ANOVA) with repeated measures and the appropriate *post hoc* analysis. Similarly, changes in IC and rates of perceived dyspnoea and leg discomfort across the different work phases were assessed by ANOVA with repeated measures. Within and between group comparisons were performed using paired and unpaired t-tests, respectively. Linear regression analysis was performed using the least square method. When this analysis was carried out using IE *t*_{end} as a dependent variable, the independent variables included the resting pulmonary function and IE measurements. The strongest significant contributors to *t*_{end} were selected using stepwise multiple regression analysis.

Results

Patient characteristics

As shown in table 1, patients were characterised by severe airflow limitation, moderate hypoxaemia and a substantially reduced DL_{CO} with considerable alveolar ventilation/perfusion inequality, as reflected by the high physiological dead space (VD)/VT. Mean resting IC was reduced below normal limits (<80% pred) at 1.98±0.09 L or 67±3% of the predicted normal; predicted normal values for IC were calculated as pred TLC–pred functional residual capacity [13, 18]. The 95% confidence interval (CI) for resting IC measurements was ±0.20 L or ±6.9% pred. Exercise capacity was severely compromised because of ventilatory limitation, as peak exercise V'E approached the maximal ventilatory capacity, *i.e.* mean V'E/MVV was 90±3% (table 2). The latter constitutes one of the criteria when patient effort is usually considered to be maximal [20]. At the limit of tolerance, patients' EILV closely approached their TLC, whereas IRV was reduced to 0.28±0.03 L or 4.4±0.8% pred TLC. The lowest IRV value that was achieved at the peak of symptom-limited incremental exercise test was defined as minimal IRV [13]. At the limit of tolerance, the change (Δ) in IC from its resting value amounted to -0.52±0.06 L or -17.6±2.0% pred, which was

well beyond the 95% CI of the resting value. The AT could be identified in 22 out of 27 patients.

Table 1. – Physical and baseline pulmonary function characteristics of patients

Age yrs	67±1
Height cm	170±1
Weight kg	76±3
BMI kg·m ⁻²	25.8±0.8
FEV ₁ L	1.14±0.07
FEV ₁ % pred	39.7±2.6
FVC L	2.44±0.13
FVC % pred	65.7±3.8
FEV ₁ /FVC % pred	47.3±2.0
DL _{CO} % pred	52.2±3.6
Pa _a O ₂ mmHg	71.0±1.7
Pa _a CO ₂ mmHg	42.6±1.0
pH	7.42±0.04
Arterial lactate conc. mMol·L ⁻¹	1.3±0.1
V _D L	0.36±0.03
V _D /V _T %	44±2
IC L	1.98±0.09
IC % pred	67±3
MVV L·min ⁻¹	46±4

Data are presented as mean±SEM. BMI: body mass index; FEV₁: forced expiratory volume in one second; % pred: percentage of predicted value; FVC: forced vital capacity; DL_{CO}: transfer factor for carbon monoxide; Pa_aO₂: arterial oxygen tension; Pa_aCO₂: arterial carbon dioxide tension; conc.: concentration; V_D: physiological dead space; V_T: tidal volume; IC: inspiratory capacity; MVV: maximum voluntary ventilation. 1 mmHg=0.1 kPa.

Table 2. – Peak responses to the ramp-incremental exercise test

WR W	76±5
WR % pred	51±3
V _O ₂ L·min ⁻¹	1.09±0.07
V _O ₂ % pred	54±3
V _{CO} ₂ L·min ⁻¹	1.10±0.08
R	1.01±0.03
V _E L·min ⁻¹	40.0±2.1
V _E /MVV %	90±3
BR L·min ⁻¹	6.4±3.9
V _E /V _O ₂	37.9±1.4
V _E /V _{CO} ₂	38.6±1.4
V _T L	1.18±0.06
f breaths·min ⁻¹	34±1
fC beats·min ⁻¹	126±4
fC % pred	83±2
AT L·min ⁻¹	0.74±0.04
SP _O ₂ %	90±2
IC L	1.46±0.10
IC % pred	49.5±3.1
ΔIC from rest L	-0.52±0.06
ΔIC from rest % pred	-17.6±2.0
V _T /IC %	80.8±1.7
IRV L	0.28±0.03
IRV % pred TLC	4.4±0.8
Dyspnoea Borg	4.7±0.3
Leg discomfort Borg	5.0±0.3

Data are presented as mean±SEM. WR: work rate in watts; % pred: percentage of predicted value; V_O₂: oxygen uptake; V_{CO}₂: carbon dioxide output; R: respiratory exchange ratio; V_E: minute ventilation; MVV: maximum voluntary ventilation; BR: breathing reserve; V_E/V_O₂: ventilatory equivalent for V_O₂; V_E/V_{CO}₂: ventilatory equivalent for V_{CO}₂; V_T: tidal volume; f: breathing frequency; fC: cardiac frequency; AT: anaerobic threshold (identified in 22 out of 27 patients); SP_O₂: arterial oxygen saturation measured by pulse oximetry; IC: inspiratory capacity; ΔIC from rest: change in IC from rest; IRV: inspiratory reserve volume; TLC: total lung capacity.

Physiological responses during interval exercise

Average *tend* (32.7±3.0 min) was significantly longer compared with the mean *tend* recorded for CLE (10.3±1.6 min) in the present study (table 3). The time course of changes in V_O₂, V_{CO}₂, V_E and IC during the IE protocol in two representative patients is shown in figure 1. ANOVA with repeated measures revealed that measurements of V_O₂, V_{CO}₂ and V_E did not differ significantly between work and unloaded pedalling phases in either of the temporally matched measurements that were taken at time points corresponding to 30, 60 and 90% of the total duration during IE (table 4). Similarly, IC did not differ significantly across the different work phases (table 4).

Measurements of operational lung volumes

At the end of symptom-limited IE, IC was significantly reduced from its baseline value by 0.39±0.05 L; this corresponded to a mean ΔIC of -20±4% or -13±2% pred, which was well beyond the 95% CI for IC. IE produced significant volume constraints on V_T expansion, indicated by the higher reduction in IRV in the current authors' COPD population than in normal populations (table 3) [13]. However, at the end of IE, the IRV value (8.9±0.8% pred TLC) was significantly higher compared to the minimal IRV that was recorded at the limit of tolerance during the ramp-incremental and CLE tests (tables 2 and 3).

Table 3. – Responses to constant-load exercise (CLE) and interval exercise (IE) protocols

	End of CLE	End of IE
Exercise time min	10.3±1.6	32.7±3.0 [#]
V _O ₂ L·min ⁻¹	0.94±0.07	0.81±0.05 [#]
V _{CO} ₂ L·min ⁻¹	0.95±0.07	0.75±0.04 [#]
R	1.00±0.02	0.95±0.02 [#]
V _E L·min ⁻¹	38.4±2.2	33.1±1.5 [#]
V _E /MVV %	85±3	76±4 [#]
V _T L	1.14±0.06	1.01±0.05 [#]
f breaths·min ⁻¹	34±1	33±1
fC beats·min ⁻¹	128±5	123±5
IC L	1.53±0.08	1.59±0.08 [¶]
IC % pred	51.9±3.0	53.9±2.6 [¶]
ΔIC L	-0.45±0.05	-0.39±0.05 [¶]
ΔIC % pred	-15.2±2.4	-13.3±1.5 [¶]
V _T /IC %	75.2±1.7	66.4±2.0 ^{#,¶}
IRV L	0.38±0.03	0.58±0.06 ^{#,¶}
IRV % pred TLC	5.9±0.5	8.9±0.8 ^{#,¶}
Pa _a O ₂ mmHg	66.7±2.6	68.7±2.5
Pa _a CO ₂ mmHg	45.4±1.2	44.0±1.3 ^{#,+}
pH	7.34±0.07	7.38±0.06 ^{#,+}
V _D L	0.53±0.02	0.48±0.02 ^{#,+}
V _D /V _T %	46±6	47±8 ⁺
Arterial lactate conc. mMol·L ⁻¹	5.81±0.41	3.89±0.36 ^{#,+}
Dyspnoea Borg	4.8±0.3	4.3±0.3
Leg discomfort Borg	4.9±0.4	4.6±0.5

Data are presented as mean±SEM. V_O₂: oxygen uptake; V_{CO}₂: carbon dioxide output; R: respiratory exchange ratio; V_E: minute ventilation; MVV: maximum voluntary ventilation; V_T: tidal volume; f: breathing frequency; fC: cardiac frequency; IC: inspiratory capacity; ΔIC: change in IC from rest; IRV: inspiratory reserve volume; IRV % pred TLC: IRV as a percentage of the predicted value for total lung capacity; Pa_aO₂: arterial oxygen tension; Pa_aCO₂: arterial carbon dioxide tension; V_D: physiological dead space; conc.: concentration. [#]: significant differences between IE and CLE; [¶]: significant differences between the incremental exercise test (table 2) and the terminal point of the IE test; ⁺: significant differences between baseline and the terminal point of the IE test. 1 mmHg=0.1 kPa.

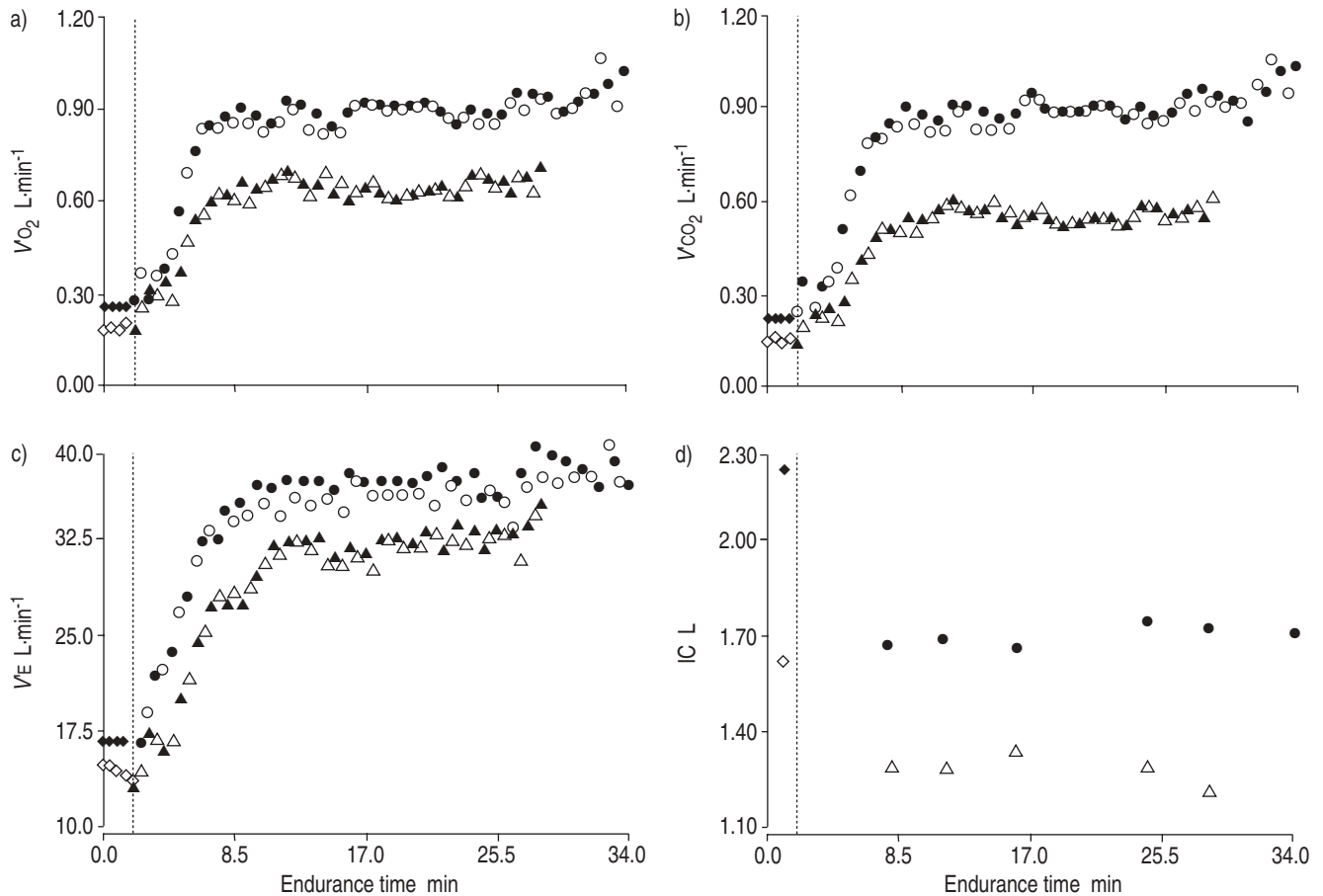


Fig. 1. – Time course of a) oxygen uptake ($V'\text{O}_2$), b) carbon dioxide output ($V'\text{CO}_2$), c) minute ventilation ($V'\text{E}$) and d) inspiratory capacity (IC) in a patient with CO_2 retention (arterial carbon dioxide tension >45 mmHg; \blacktriangle and \triangle) and a patient without CO_2 retention (\bullet and \circ) during the interval exercise protocol. Gas exchange values are 30-s average measurements of baseline (\blacklozenge and \circlozenge), unloaded pedalling phases (open symbols) and interval exercise loaded phases (closed symbols). Dashed lines represent the onset of interval exercise.

Correlates of interval exercise tolerance

The t_{end} (32.7 ± 3.0 min) correlated with resting IC, expressed as % pred normal ($r=0.46$, $p<0.01$), and, additionally, with the $P_{\text{a,CO}_2}$ ($r=-0.44$, $p<0.02$) and the $V\text{T}$ ($r=0.43$, $p<0.01$), both recorded at the limit of tolerance during IE. Using stepwise multiple regression analysis, t_{end} was best described by the combination of $V\text{T}$ and IC % pred recorded at the terminal point of IE ($r=0.55$, $p<0.02$). In turn, IC % pred and $V\text{T}$ at the limit of tolerance during IE correlated strongly with the end exercise $P_{\text{a,CO}_2}$ ($r=-0.64$, $p<0.0001$ and

$r=-0.58$, $p<0.001$, respectively) and $P_{\text{a,O}_2}$ ($r=0.55$, $p<0.001$ and $r=0.44$, $p<0.02$, respectively).

Exertional symptoms

During IE, symptoms of dyspnoea and leg discomfort increased significantly across the temporally matched time points (table 4). At the limit of tolerance, symptoms were not significantly different compared with those recorded at the end of the incremental (table 2) and the CLE (table 3) protocols.

Table 4. – Responses to interval exercise at temporally matched time points between work and unloaded pedalling phases

	30% total time		60% total time		90% total time	
	Work phase	Unloaded phase	Work phase	Unloaded phase	Work phase	Unloaded phase
$V'\text{O}_2$ L·min ⁻¹	0.74±0.04	0.74±0.04	0.77±0.05	0.77±0.05	0.78±0.04	0.78±0.05
$V'\text{E}$ L·min ⁻¹	31.1±1.6	31.0±1.5	32.0±1.8	32.0±2.0	32.7±2.2	32.3±2.0
$f\text{C}$ beats·min ⁻¹	113±5	114±6	118±5 [#]	118±7	120±4 [#]	120±5
IC L	1.55±0.08		1.61±0.08		1.59±0.08	
Dyspnoea Borg	2.9±0.2		3.3±0.3 [#]		4.3±0.4 [#]	
Leg discomfort Borg	3.1±0.3		3.6±0.4 [#]		4.6±0.5 [#]	

Data are presented as mean±SEM. $V'\text{O}_2$: oxygen uptake; $V'\text{E}$: minute ventilation; $f\text{C}$: cardiac frequency; IC: inspiratory capacity. [#]: significant differences between the work phases of the temporally matched time points recorded at 30% of the total exercise time and those recorded at 60 and 90% of the total exercise time.

Arterial blood gases, arterial lactate concentration and anaerobic threshold

At the limit of tolerance during IE, there was a significant increase in P_{a,CO_2} and $\dot{V}D$ from rest (table 3). Arterial lactate concentration was significantly higher, and arterial pH was lower, at the end of IE compared to baseline. Compared to the terminal point of CLE (table 3), arterial lactate concentration, P_{a,CO_2} and $\dot{V}D$ were significantly lower, and arterial pH was higher, at the end of IE. $\dot{V}'O_2$ at the AT ($0.74 \text{ L}\cdot\text{min}^{-1}$) was not significantly different to the mean $\dot{V}'O_2$ ($0.78 \text{ L}\cdot\text{min}^{-1}$) sustained during IE in the 22 patients whose AT was identified.

Discussion

The principal aim of the present study was to evaluate the influence of DH on IE tolerance in patients with severe airflow limitation. Additionally, it was examined whether IE would enable such patients to tolerate high-intensity exercise for a sufficient time to achieve physiological training effects. The main findings were as follows: 1) the total exercise duration during IE was significantly greater than at CLE; 2) IE was associated with stable metabolic and ventilatory responses as the mean exercise $\dot{V}'O_2$ was slightly above the patients' AT; this, in turn, allowed patients to exercise for a prolonged period of time before symptoms limited the exercise endurance capacity; and 3) symptom-limited IE t_{end} correlated with resting hyperinflation.

Historically, the rationale for IE training has been the ability to impose very high power outputs to peripheral muscles without overloading the cardiorespiratory capacity [21]. Classical studies [21] have shown that the metabolic response during IE is very similar to continuous moderate exercise and, thus, is associated with a stable pattern of cardiorespiratory responses and low lactate concentration in the muscle throughout the relatively long exercise and recovery periods. This was shown in the present study by the fact that IE was associated with a relatively stable metabolic and ventilatory response, *i.e.* $\dot{V}'O_2$ and $\dot{V}'E$ changed very little throughout the exercise and unloaded pedalling phases, and corresponded to values typically seen during CLE at markedly lower intensity (50–70% WR_{max}) in patients with similar degrees of airflow limitation [22, 23]. Interestingly, in spite of the fact that mean symptom-limited $\dot{V}'O_2$ was slightly above the patients' AT, the t_{end} was relatively long, which was not the case during CLE (table 3) above the AT [3]. Moreover, the small increase in arterial lactate concentration to the terminal point of exercise further supports the notion that IE closely resembled steady-state exercise. The capacity to reload myoglobin stores during the recovery phases, allowing a more oxidative degradation of glycogen and, hence, a partially reduced demand, has been proposed as the principal mechanism for the slowed glycolysis observed during IE [21]. As lactic acidosis puts particular stress on the ventilatory system, the small increase in arterial lactate concentration observed during IE as compared to CLE (table 3) appeared to be beneficial to the COPD patients by reducing some of the acid stimulus to breathe [4], thereby maintaining ventilation and dyspnoea at sustainable levels for a prolonged period of time.

This is the first study to document DH during IE in COPD patients. Patients were dynamically hyperinflated throughout the IE test, as shown by the significant reduction in IC from baseline, which averaged $\sim 0.40 \text{ L}$ or 13% of IC pred normal. This is similar to the values reported by O'DONNELL and colleagues [9, 22, 23] during CLE in patients with a

comparable degree of severity and close to the value (0.45 L) recorded during the CLE protocol in the present study (table 3). An interesting feature of the present study was that IC did not change significantly throughout IE in contrast to CLE [9, 23]. In spite of DH, the current authors' patients were able to sustain bouts of maximal-intensity loads for a period of time that was several times longer compared to the present and other CLE protocols [3, 4, 9, 10, 11, 22, 23]. Whilst facing steady metabolic and ventilatory demands during IE, patients were able to sustain levels of pulmonary ventilation averaging 76% MVV at the terminal point of exercise for a prolonged period. This is further supported by the finding that, even at the limit of tolerance, the patients' IRV was significantly higher ($p=0.01$) than the IRV attained at the end of the incremental and CLE tests ($0.58\pm 0.06 \text{ L}$ versus $0.28\pm 0.03 \text{ L}$ and $0.38\pm 0.03 \text{ L}$, respectively).

In agreement with previous studies [6, 9, 10, 23, 24], it was found that, at the limit of interval exercise tolerance, IC and $\dot{V}T$ were the most important contributors to t_{end} . This is not surprising as the dynamic IC has been shown to reflect the operating limits for $\dot{V}T$ expansion during incremental [13, 24] and CLE protocols [9, 10, 23]. The P_{a,CO_2} also emerged as a significant contributory variable to endurance capacity, confirming previous findings that the propensity to develop CO_2 retention during exercise reflects ventilatory constraints due to prolonged hyperinflation [6–26]. In turn, IC % pred normal and the curtailed $\dot{V}T$ response at the limit of IE tolerance were strongly correlated with changes in P_{a,CO_2} and P_{a,O_2} from baseline, thus reflecting the effects of worsening alveolar ventilation/perfusion inequalities.

In summary, it has been shown that, in severely disabled chronic obstructive pulmonary disease patients, interval exercise is associated with stable metabolic demands, minute ventilation and rates of dynamic hyperinflation, and that the total exercise duration is much greater than at constant-load exercise. Hence, the application of this method in the rehabilitation setting has the potential to convey important clinical benefits, as it allows the application of intense loads on peripheral muscles for sufficiently long periods of time in order to obtain the desired physiological training effects. Interval exercise may, therefore, provide a good alternative to constant-load rehabilitative exercise training in order to improve compliance with high-intensity exercise and, thus, the effectiveness of this treatment.

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