



ELSEVIER

respiratoryMEDICINE

Interval training compared with continuous training in patients with COPD

Ragnheiður Harpa Arnardóttir^{a,*}, Gunnar Boman^{a,1}, Kjell Larsson^b,
Hans Hedenström^{c,2}, Margareta Emtner^{a,3}

^aDepartment of Medical Sciences, Respiratory Medicine and Allergology, Uppsala University, Uppsala, Sweden

^bLung and Allergy Research, National Institute of Environmental Medicine, Karolinska Institute, SE-171 77 Stockholm, Sweden

^cDepartment of Medical Sciences, Clinical Physiology, Uppsala University, Uppsala, Sweden

Received 22 July 2006; accepted 8 November 2006

Available online 26 December 2006

KEYWORDS

Chronic obstructive pulmonary disease;
Continuous training;
Endurance training;
Health-related quality of life;
Interval training;
Rehabilitation

Summary

The aim of this study was to compare the effects of interval training (3-min intervals) with continuous training on peak exercise capacity (W peak), physiological response, functional capacity, dyspnoea, mental health and health-related quality of life (HRQoL) in patients with moderate or severe COPD.

Sixty patients exercised twice weekly for 16 weeks after randomisation to interval- or continuous training. Target intensity was $\geq 80\%$ of baseline W peak in the interval group (I-group) and $\geq 65\%$ in the continuous group (C-group). Patients were tested by spirometry, ergometer cycle test, cardiopulmonary test and a 12 min walk test. Dyspnoea was measured by the dyspnoea scale from Chronic Obstructive Disease Questionnaire (CRDQ), mental health by Hospital Anxiety and Depression scale (HAD) and HRQoL by the Medical Outcomes Survey Short Form 36 (SF-36).

After training, W peak, peak oxygen uptake (VO_2 peak) and exhaled carbon dioxide (VCO_2 peak) increased significantly in both groups, no significant differences between the groups. Minute ventilation (V_E peak) increased only in the C-group. At identical work rates (isotime) VO_2 , VCO_2 and V_E were significantly more decreased in the I-group than in the C-group ($p < 0.05$). Functional capacity, dyspnoea, mental health, and HRQoL improved significantly in both groups, no difference between the groups.

*Corresponding author. Physiotherapy Unit, Fjórðungssjúkrahúsid, IS-600 Akureyri, Iceland. Tel.: +354 4630100; fax: +354 4631340.

E-mail address: harpa.arnardottir@medsci.uu.se.

¹Enheten för lungmedicin och allergologi, Akademiska sjukhuset, SE-751 85 Uppsala, Sweden.

²Avdelningen för klinisk fysiologi, Akademiska sjukhuset, SE-751 85 Uppsala, Sweden.

³Enheten för sjukgymnastik, Akademiska sjukhuset, SE-751 85 Uppsala, Sweden.

Interval training and continuous training were equally potent in improving peak exercise capacity, functional exercise capacity, dyspnoea, mental health and HRQoL in patients with moderate or severe COPD. At isotime, the physiological response to training differed between the groups, in favour of the interval training.

© 2006 Elsevier Ltd. All rights reserved.

Introduction

Endurance training is one of the cornerstones in pulmonary rehabilitation and improves both exercise capacity and health-related quality of life (HRQoL).¹ Although endurance training in COPD has been extensively studied, there are still questions to be answered regarding training mode, intensity and duration. Most exercise programmes have been based mainly on endurance training with continuous load. High-intensity training has more effect on exercise capacity than low-intensity training² but in patients with severe COPD it can be difficult to sustain high-intensity by the continuous training modality.^{3,4} Dynamic lung hyperinflation (air-trapping) increases progressively during continuous exercise in patients with COPD and contributes importantly to their exercise intolerance.^{5,6}

Interval exercise induces less dynamic hyperinflation than continuous exercise in COPD.^{7,8} This could enable the patients to exercise at a higher intensity and thereby enhance their benefits from physical training. In healthy subjects, interval and continuous training yield similar training effects.⁹ Few, small studies have compared interval training with continuous training in patients with COPD and the results are somewhat inconsistent.^{10–12} Coppoolse et al. compared continuous training with a mixed programme of interval and continuous training and found that peak exercise capacity (W peak) increased only by the mixed training whereas peak oxygen uptake (peak $\dot{V}O_2$) increased only following continuous training.¹⁰ Vogiatzis et al., however, found that both continuous and interval training increased W peak, minute ventilation (\dot{V}_E) and HRQoL, but no significant increase in $\dot{V}O_2$ peak was observed.¹¹ The same group found comparable changes in peripheral muscle adaptations by continuous and interval training.¹² Interval training can be conducted in various ways. Coppoolse et al. used bursts of 1 min at 90% versus 2 min at 45% of baseline W peak, whereas Vogiatzis et al. used 30 s at 100% of baseline W peak versus 30 s rest.^{10–12} The duration of intervals can be of importance, as well as the intensity, and some evidence suggests that long intervals are more efficient than short intervals in healthy, young people.¹³ More studies are needed on the effects of different length and intensities of intervals for patients with COPD.

The primary aim of the present study was to compare the effects on W peak of continuous training with interval training comprising 3-min intervals. Secondary aims were to compare the physiological responses to the two training modes and their effects on functional capacity, dyspnoea, mental health and HRQoL.

Methods

Study subjects

Patients with moderate or severe COPD according to the British Thoracic Society guidelines¹⁴ were consecutively

invited to take part in the study when being referred for training to the Physiotherapy Unit of the Pulmonary Section at the Akademiska Hospital, Uppsala and at the County Hospital in Västerås, Sweden. All were smokers or ex-smokers. The study was approved by the Medical Ethics Committee of Uppsala University and all subjects gave informed consent. Inclusion criteria were COPD with forced expiratory volume in 1 s (FEV_1) <60% of predicted value and FEV_1/VC (vital capacity) <0.7 after bronchodilatation.¹⁴ Exclusion criteria were other diseases that could interfere with exercise such as ischemic coronary disease and musculo-skeletal problems.

Study design

At baseline and after 16 weeks of training, lung function tests, incremental cycle ergometer tests, semi-steady-state cardiopulmonary exercise tests with gas exchange analysis and 12 min walk tests were performed and HRQoL was assessed. Patients were stratified according to disease severity, with $FEV_1 \geq 40\%$ of the predicted value defined as moderate disease, and $FEV_1 < 40\%$ predicted as severe disease, according to the BTS guidelines.¹⁴ After stratification the patients were randomised in blocks of four by the closed envelope method into training with either interval (I-group) or continuous (C-group) load. Training sessions were twice a week for 16 weeks, session duration approximately 90 min. A criterion for fulfilling the training was participation in at least 24 of the 32 sessions.

Testing

Lung function was measured with a Masterlab Trans spirometer, Masterlab Body Plethysmograph and Masterlab Transfer (Erich Jaeger AG, Würzburg, Germany) in accordance with the ATS guidelines.¹⁵ Swedish reference values were used.^{16,17}

A symptom-limited incremental cycle ergometer test (Case 8000 Exercise Testing System, GE Medical Systems, Milwaukee, USA) with continuous ECG-registration was conducted to measure peak work load (W peak). The patients started pedalling at 20 W and the load was increased by 10 W every minute until exhaustion. Oxygen saturation was measured by a pulseoximeter (SpO_2 , Optovent Respons) and heart rate and breathing frequency were registered every minute during exercise. Systolic blood pressure, subjective ratings of perceived exertion (Borg RPE scale) and dyspnoea (Borg CR-10 scale) were recorded every second minute.^{18,19} All variables were measured before and 1, 2, 4 and 10 min after exercise.

A semi-steady-state cardiopulmonary exercise test with breath-by-breath gas exchange analysis (ergospirometry) was performed by all patients recruited at one of the

centres (Uppsala). Measurements of heart rate, SpO₂ and ratings of perceived exertion and dyspnoea were made as described above. The patients wore a mask with a turbine for gas exchange analysis (Oxycon Sigma, Jaeger, Germany) measuring VO₂, VCO₂ (bicarbonate) and V_E. After recording steady-state measurements at rest (approximately 4 min of registration at rest) the patient began pedalling at 20 W. The load was kept constant until the ventilation and oxygen uptake reached a plateau, on average 3–4 min at each level (hence semi-steady-state, as conventional steady-state requires at least 6 min at each level). To keep testing time within reasonable limits (10–15 min) the load was increased by 5, 10, 20 or 30 W depending on the outcome of the first test. This was continued until exhaustion. The test procedure was identical (same steps of load) before and after the training intervention for each patient. The test was performed 30 min after the incremental cycle test (later if needed for all resting parameters to be stable at pre-exercise levels).

Twelve-minute walk tests were performed in a level corridor (34 m) as described by McGavin.²⁰ No encouragement was given and the supervisor did not walk alongside the patient. The patient was asked to cover as much ground as possible in 12 min in his own speed, pausing if necessary. The patient was told the time after 4, 6, 8, 10 and 11 min. Each patient repeated the 12-min walk test on a different day within 1 week at the same time of day, with the same supervisor. This was done both before and after training.

Dyspnoea during activities of daily life was measured by the dyspnoea scale from the Chronic Respiratory Disease Questionnaire (CRDQ).²¹ The patient scores on a 7-graded scale the dyspnoea usually experienced during five self-chosen activities of his life. A higher score indicates less dyspnoea.

Mental health was assessed by the Hospital Anxiety and Depression scale (HAD).²² The score-range in HAD is 0–21, a higher score indicating worse mental health.

General HRQoL was assessed by the Medical Outcomes Survey Short Form 36 questionnaire (SF-36).²³ The SF-36 has eight domains: physical function, role physical, bodily pain, general health, vitality, social function, role emotional and mental health. For each domain the score is from 0 to 100 (most healthy).

Exercise training

Exercise training was performed on an out-patient basis. All sessions started with ergometer cycling. In the I-group the target training intensity was $\geq 80\%$ of the baseline W peak in the “uphill” intervals and 30%–40% of the baseline W peak in the “downhill” intervals. All intervals in the I-group were 3 min, i.e. the high- and low-intensity intervals were equally long. In the C-group the target training intensity was $\geq 65\%$ of baseline W peak. For warming up and cooling down both groups cycled at 30%–40% of baseline W peak for 6 min in the beginning and at the end of each session. Total cycle time was 39 min in both groups, each session to allow for five “uphills” in the I-group, separated by four “downhills” and with warming up before and cooling down afterwards. Consequently, the C-group cycled for 27 min each session at their effective training load. In both groups, exercise load

was kept as high as tolerated at all times, above the target values when possible. All patients scored their dyspnoea and perceived exertion on the Borg scales CR-10 and RPE every 3 min. Target scores for dyspnoea and exertion were ≥ 5 and/or ≥ 15 , respectively, after the “uphill” bursts and at the end of the continuous load. Target intensity, patients’ score and the physiotherapist’s observation of the patient steered the adjustment of exercise load. All patients were taught to use pursed-lip-breathing technique during exercise.

After cycling, the session proceeded once a week with callisthenics and relaxation and once a week with resistance training. The callisthenics were done in the sitting position and consisted of flexibility exercises for thorax, neck and shoulders. The relaxation was ad modum Jacobson.²⁴ The resistance training included exercises for upper and lower limbs as well as the abdominal muscles (10 repetitions, two sets, at about 70% of 1 RM). Callisthenics, relaxation and resistance training were the same in both groups. Patients who desaturated on exercise (SpO₂ < 90%) were given supplemental oxygen during training sessions.

Statistical analysis

The results are expressed as mean and standard deviation (SD) in text and tables but as mean and standard errors of the mean (SEM) in figures. For analysis we used Student’s *t*-test for paired and unpaired observations and ANOVA-repeated measures (one-way for intra-group analysis and two-way for inter-group analysis). For subjective ratings and unevenly distributed data the Wilcoxon’s signed rank test (intra-group) and the Mann-Whitney *U*-test (inter-group) were applied. Calculating with an inter-group difference of training-induced W peak difference of 5 W, 35 patients in each group would yield a power of 80% if $\alpha = 0.05$.

Results

One hundred patients were included, and 60 patients completed the programme (Table 1). The age range was 43–80 years and the range in FEV₁ (% predicted value) was 14%–59%. Ten patients were still smokers (4 in the I-group). The patients who completed the programme had a mean attendance rate of 29 ± 3 of 32 possible sessions (no difference in attendance rate between the two training groups). The 40 patients who did not complete 24 sessions (and were thus excluded) had higher functional residual capacity (5.5 ± 1.2 l versus 4.8 ± 1.3 l; $p < 0.05$), residual volume (4.3 ± 1.2 l versus 3.8 ± 1.1 l; $p < 0.05$) and total lung capacity (7.0 ± 1.3 versus 6.2 ± 1.3 ; $p < 0.01$) than those who completed the programme, indicating a more severe disease in the drop-outs. No other baseline values were different from the patients who completed the programme. The reason for drop-out were exacerbations ($n = 24$), lack of motivation or transport problems ($n = 10$), other diseases ($n = 5$) and family problems ($n = 1$).

Exercise training

As the pattern of exercise was different, consequently the exercise intensity between the two groups was significantly

Table 1 Baseline characteristics of the 60 subjects that fulfilled the programme.

	I-group, n = 28	C-group, n = 32
Gender (F:M)	25:3	26:6
Age (years)	65 (7)	64 (8)
BMI (kg/m ²)	24.1 (5.0)	23.5 (4.4)
Packyears (pk/day × years)	33 (17)	35 (19)
TLC (liters)	6.0 (1.0)	6.5 (1.5)
TLC (% pred.)	111 (18)	112 (21)
FRC (liters)	4.6 (1.0)	5.0 (1.5)
FRC (% pred.)	142 (33)	145 (41)
RV (liters)	3.7 (0.9)	3.9 (1.2)
RV (% pred.)	184 (52)	188 (63)
VC (liters)	2.3 (0.6)	2.6 (1.0)
VC (% pred.)	70 (16)	69 (22)
FEV ₁ (liters)	0.9 (0.3)	0.8 (0.3)
FEV ₁ (% pred.)	35 (13)	32 (10)
DL _{CO} (% pred.)	55 (18)	46 (16)
Peak Watt (% pred.)	55 (17)	53 (17)

I-group, interval group; C-group, continuous group; F:M, female vs. male gender; % pred., as a percentage of the predicted value; BMI, body mass index; TLC, total lung capacity; FRC, functional residual capacity; RV, residual volume; VC, vital capacity; FEV₁, forced expiratory volume in 1 s; DL_{CO}, diffusion capacity of carbon monoxide. Mean (SD).

different ($p < 0.05$; Fig. 1A). Target exercise intensity was reached at session 5 ± 5 for the I-group ($\geq 80\%$ of W peak) and at session 9 ± 7 for the C-group ($\geq 65\%$ of W peak), but the difference in time to reach target intensity was not significant between the groups ($p = 0.06$). The exercise workload in the high-intensity bursts in the I-group reached 100% of baseline W peak at session 14. Furthermore, during high-intensity intervals at the last sessions, exercise W exceeded baseline W peak ($p < 0.05$) (Fig. 1A). At the last high-intensive interval of cycle training sessions, mean exertion rating was 15.8 ± 1.4 in the I-group and 15.1 ± 2.1 in the C-group ($p = 0.08$). Ratings of dyspnoea at the same time were 5.8 ± 1.4 and 5.2 ± 1.4 , respectively ($p = 0.14$). There was no significant difference between the second and the last week of training in these ratings, indicating adequate progression in exercise load as exercise capacity increased during the study.

Total cycle-workload (the sum of $W \times \text{min}$) per session revealed no significant difference in total workload between the groups, though a tendency towards a higher total work in the C-group was observed ($p = 0.07$). Total workload increased significantly with time ($p < 0.0001$) in both groups (Fig. 1B).

In the resistance training part (the same procedure in both groups) both groups increased the resistance loads successively during the study ($p < 0.001$) both for arm and leg exercises, with no difference between the groups ($p = 0.6$ and 0.3 , respectively).

During exercise, 17 patients (7 in I-group) were given supplemental oxygen via a nasal cannula, just enough to keep the $\text{SpO}_2 \geq 90\%$. Mean oxygen rate was

$1.3 \pm 0.7 \text{ l/min}$, no significant difference between the groups ($p = 0.5$).

Exercise capacity

W peak increased significantly ($p < 0.001$) in both groups after 16 weeks of training by $11 \pm 7 \text{ W}$ in the I-group and by $11 \pm 12 \text{ W}$ in the C-group (Table 2). Peak levels of heart rate, breathing frequency, SpO_2 and subjective ratings of dyspnoea and exertion did not change. VO_2 peak and VCO_2 peak increased in both groups (Table 2) whereas V_E peak increased significantly in the C-group only (Table 2). No difference between the groups was found in any post-exercise peak values or in the change from baseline peak values.

Measurements at *isotime*, i.e. at identical work rates before and after training, showed significantly lower heart rate, perceived exertion and dyspnoea after training in both groups. Significantly lower VO_2 ($-77 \pm 158 \text{ ml/min}$, $p < 0.05$), VCO_2 ($-110 \pm 169 \text{ ml/min}$, $p < 0.05$), V_E ($-3.6 \pm 5.6 \text{ l/min}$, $p < 0.01$) and breathing frequency (-3 ± 3 breaths/min, $p < 0.01$) compared to baseline emerged in the I-group only and these changes from baseline differed significantly between the groups ($p < 0.05$; Table 3, Fig. 2).

Functional exercise capacity, i.e. 12 min walking distance (12 MWD) increased significantly in both groups, with no significant difference between the groups (Table 2).

Fifteen patients exceeded the anaerobic threshold ($\text{VCO}_2 > \text{VO}_2$ during ergospirometry) before training

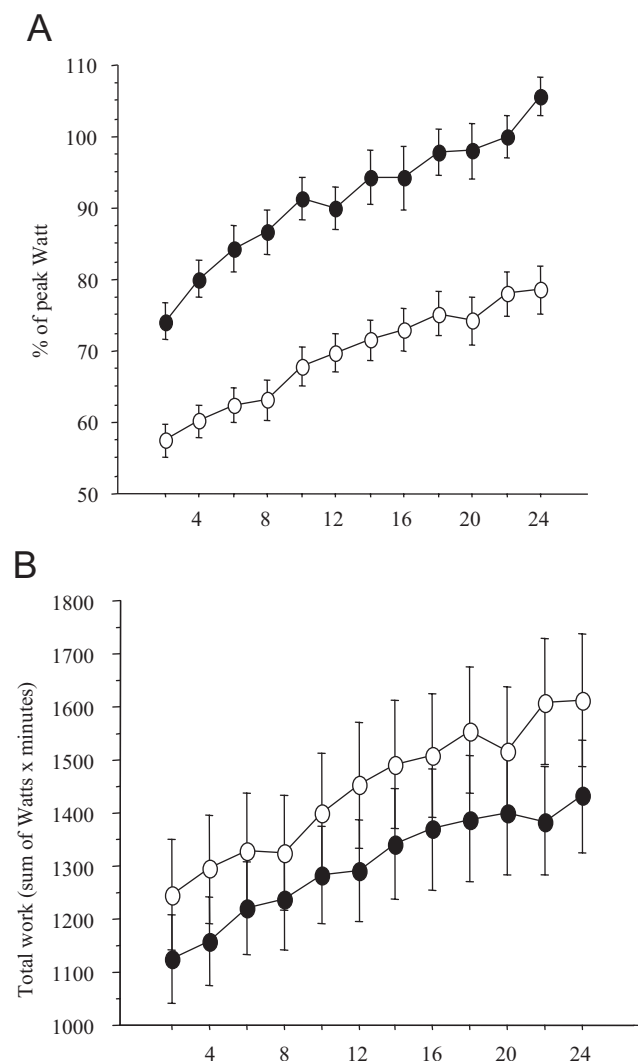


Figure 1 The development in exercise load during time. Every second session is shown. Filled circles: I-group, $n = 28$; open circles: C-group, $n = 32$. Mean and SEM. (A) The exercise-load expressed as percent of peak Watt at baseline during the high-load bursts in the I-group and during continuous load in the C-group at the different sessions throughout the study. (B) The total amount of work in each of the groups at training sessions 2–24.

(7 in the I-group) and 16 patients after training (8 in the I-group). Nine of these were the same both before and after training. No difference in the effect of training was seen in the patients who exceeded the anaerobic threshold compared to the others, nor in the patients with supplemental oxygen compared to the others.

Dyspnoea, mental health and HRQoL

Dyspnoea during daily activities decreased significantly after training in both groups (Table 4). Mental health (anxiety and depression) was also significantly improved by training in both groups. The domains “vitality” and “mental health” from SF-36 significantly improved in both groups, whereas “social function” and “general health” improved signifi-

cantly in the I-group only (Table 4). There was, however, no significant difference between the groups in the change from baseline in any of the questionnaires. Lung function did not change during the study.

Discussion

In the present study it was demonstrated that 3-min interval training is an efficient training mode for COPD patients. This is clinically relevant, as 3-min intervals are easily conducted in group training sessions for patients with COPD. Interval and continuous training equally improved W peak, on average 11 W. The improvement was similar to previous studies^{25,26} and larger than 5.5 W which was the weighted mean difference of the 15 studies included in the meta-analysis by Lacasse et al.¹ The improvement in W peak was consistent with the findings of Vogiatzis et al.¹¹ but differed from the results of Coppoolse et al., as W peak increased only in the I-group in their study.¹⁰ In both our groups, peak values of VO_2 and VCO_2 increased significantly, whereas V_E peak increased in the C-group only. This is not in agreement with the findings of Vogiatzis et al., who found no increase in peak values of VO_2 or VCO_2 in either group, but increased V_E peak in both groups.¹¹

At isotime, VO_2 , VCO_2 and V_E were significantly more decreased in the I-group, indicating that the interval training resulted in a larger reduction in oxygen cost and ventilation at sub-maximal exercise than the continuous training. No decrease in VO_2 , VCO_2 or V_E was found in the C-group at isotime. This is in line with the findings of Coppoolse et al.,¹⁰ who found that only interval training decreased the VO_2/W ratio, but differs from Vogiatzis et al., who found that VO_2 , VCO_2 and V_E decreased significantly in both groups at isotime (no difference between the groups), as well as breathing frequency.¹¹ Isotime breathing frequency was only decreased in our I-group and we consider this to be the most likely explanation for the decreased V_E at isotime. Decreased ventilatory demand and oxygen consumption at isotime is an indicator of more increased sub-maximal work capacity by endurance testing,²⁷ but as no endurance tests were done in the present study, it is not clear whether the difference between the groups at isotime would have affected endurance time. Markedly decreased dyspnoea, perceived exertion and heart rate were found in both groups at isotime, in agreement with Vogiatzis.¹¹ As shown above, our study confirms several findings from the quoted studies, but there are some prominent inconsistencies as well.^{10–12} We can only speculate about the reasons for these inconsistencies. Firstly, the length and intensity of the intervals differed between our study and the studies quoted above^{10–12} which might affect the results, as changes in peak oxygen uptake and ventilatory demand during exercise are larger after training with intervals lasting 3–5 min than after short-interval training in healthy people.^{13,28} Secondly, in our study, training sessions included resistance training once a week, which might have enhanced the response to training.^{29,30} Thirdly, 85% of our patients were women whereas in the other studies 83%–100% of the patients were men.^{10–12} Recent studies indicate that the skeletal muscles adapt to COPD differently in men and women.^{31,32} As both interval and

Table 2 Results (peak values) from incremental cycle testing, 12 min walking tests and semi-steady-state tests with ergospirometry.

	I-group		C-group	
	Baseline	16 weeks	Baseline	16 weeks
<i>Incremental cycle test</i>	<i>n</i> = 28		<i>n</i> = 32	
Watt	61 (20)	72 (22)***	64 (22)	75 (27)***
Heart rate (beats/min)	131 (2)	132 (20)	134 (17)	133 (19)
Breathing frqv. (breaths/min)	31 (4)	30 (6)	30 (7)	30 (8)
Dyspnoea (Borg CR-10)	7.9 (2.0)	7.2 (1.4)*	7.9 (1.6)	7.2 (1.6)
Exertion (Borg RPE)	17.3 (1.5)	17.0 (1.2)	17.3 (1.3)	16.7 (1.3)
<i>Walking test</i>	<i>n</i> = 28		<i>n</i> = 32	
12MWD (m)	834 (185)	909 (203)***	870 (165)	964 (155)***
<i>Ergospirometry</i>	<i>n</i> = 25		<i>n</i> = 28	
VO ₂ peak (ml/min)	988 (286)	1041 (299)*	973 (292)	1119 (297)***
VCO ₂ peak (ml/min)	944 (326)	999 (363)*	942 (346)	1091 (349)**
V _E peak (l/min)	34.9 (10.8)	36.0 (11.3)	34.8 (10.1)	38.4 (9.3)*

I-group, interval-group; C-group, continuous-group; Watt, exercise capacity on incremental cycle test; breathing frqv., breathing frequency; dyspnoea, dyspnoea score on the Borg CR-10 scale; exertion, score on the Borg-RPE-scale; 12MWD, 12 min walking distance; VO₂ peak, oxygen uptake; VCO₂, carbon dioxide in exhaled air; V_E, minute ventilation. Difference from baseline within group: Mean (SD).

**p* < 0.05,

***p* < 0.01,

****p* < 0.001.

Table 3 Effect of training on the responses to exercise at identical work rate and duration (isotime) in the incremental cycle test and the semi-steady-state test.

	I-group		C-group	
	Baseline	16 weeks	Baseline	16 weeks
<i>Incremental cycle test</i>	<i>n</i> = 28		<i>n</i> = 32	
Watt ^a	60 (21)		63 (24)	
Heart rate (beats/min)	130 (20)	125 (18)*	134 (15)	127 (16)***
Breathing frqv. (breaths/min)	31 (4)	28 (6)**	30 (7)	28 (7)
Dyspnoea (Borg CR-10)	7.9 (2.0)	5.4 (1.4)***	7.8 (1.7)	5.3 (2.0)***
Exertion (Borg RPE)	17.3 (1.4)	14.9 (1.7)***	17.1 (1.3)	14.4 (2.3)***
<i>Ergospirometry</i>	<i>n</i> = 25		<i>n</i> = 28	
Watt ^b	45 (20)		49 (24)	
VO ₂ (ml/min)	987 (288)	912 (279)*,†	985 (283)	1011 (258)
VCO ₂ (ml/min)	943 (328)	834 (313)*,†	925 (346)	937 (349)
V _E (l/min)	34.9 (10.9)	31.2 (9.9)**	34.4 (10.2)	34.0 (7.9)

I-group, interval-group; C-group, continuous group; breathing frqv., breathing frequency; dyspnoea, dyspnoea score on the Borg CR-10 scale; exertion, score on the Borg-RPE-scale; VO₂, oxygen uptake; VCO₂, carbon dioxide in exhaled air; V_E, minute ventilation. Mean (SD).

**p* < 0.05,

***p* < 0.01,

****p* < 0.001 within group,

†*p* < 0.05 between groups.

^aIsotime load in the incremental test.

^bIsotime load in the semi-steady-state test.

continuous training induce changes in peripheral muscle,¹² the different gender distribution between the studies might make a difference.

Functional exercise capacity (12 MWD) increased similarly in both groups. In most studies on physical training for COPD patients the 6 min walk test has been used and therefore our

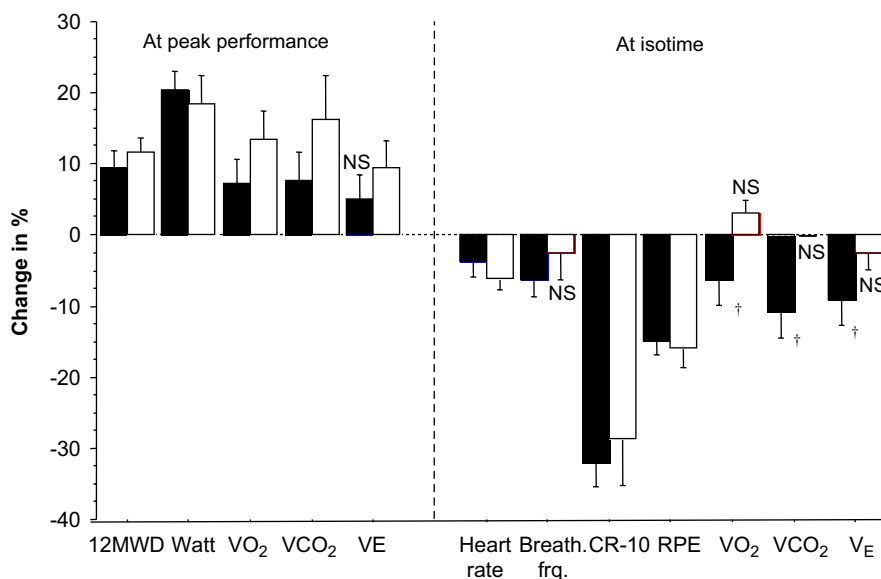


Figure 2 The change from baseline at peak performance and at isotime after training, expressed as percent (mean and SEM). Black bars: interval-group, white bars: continuous-group. All shown bars indicate a significant change within group, except those labelled "NS". †, $p < 0.05$ between the groups; 12MWD, 12 min walking distance; Watt, exercise capacity; VO_2 , oxygen uptake; VCO_2 , carbon dioxide in exhaled air; V_E , minute ventilation; CR-10, dyspnoea; RPE, perceived exertion.

Table 4 Health-related quality of life at baseline and after 16 weeks of training.

	I-group, $n = 28$		C-group, $n = 32$	
	Baseline	16 weeks	Baseline	16 weeks
Dyspnoea (CRDQ)	16.5 (4.1)	19.2 (5.2)*	14.8 (3.0)	18.5 (4.9)**
Anxiety (HAD)	7.2 (4.5)	5.2 (4.3)**	6.9 (3.5)	4.8 (3.9)*
Depression (HAD)	5.8 (3.6)	4.3 (3.6)*	5.4 (3.2)	4.0 (3.0)**
SF-36				
Physical function	37.0 (14.2)	41.1 (22.4)	41.7 (19.6)	38.3 (19.5)
Role physical	32.6 (35.7)	35.4 (39.6)	35.6 (41.9)	33.7 (40.0)
Bodily pain	68.9 (16.5)	79.2 (22.9)	69.6 (23.9)	75.7 (23.9)
General health	33.4 (16.5)	41.2 (20.2)**	39.5 (17.2)	46.3 (21.9)
Vitality	46.7 (23.8)	54.8 (24.7)*	44.8 (21.4)	56.9 (21.2)**
Social function	66.0 (26.1)	75.0 (23.6)*	70.7 (23.4)	73 (24.4)
Role emotional	48.4 (44.7)	61.3 (40.5)	53.8 (45.3)	64.0 (45.1)
Mental health	65.1 (25.0)	75.8 (17.3)*	69.1 (19.5)	75.7 (16.9)**

I-group, interval-group; C-group, continuous group; CRDQ, Chronic Respiratory Disease Questionnaire dyspnoea scale (0–35); HAD, Hospital Anxiety and Depression Scale (0–21); SF-36, Short Form 36 (0–100).

Mean (SD).

* $p < 0.05$,

** $p < 0.01$ within group.

results could not be directly compared with these studies. In a meta-analysis, the mean weighted difference before and after training was 49 m in the 6 min walk test.¹ In our study, 12MWD increased by 75 and 94 m, respectively, in the two groups and we consider this increase to be close to the increase in the 6 min test quoted above.

At baseline, most of the scores indicated poor mental and physical health status and HRQoL. Compared to the results from the Swedish Health Survey II,³³ the SF-36 scores in both groups were very low. In both groups dyspnoea, anxiety,

depression and HRQoL improved after training. The improvement in dyspnoea was above the clinically significant difference for this domain.^{34,35} The distinct decrease in anxiety and depression after training was interesting, as those symptoms are common problems in COPD, and anxiety in combination with low HRQoL is an important factor for rehospitalisation in COPD.^{36,37} As training improved anxiety and HRQoL in both groups, training after hospitalisation may decrease the risk of readmissions. This is supported by Man et al. who recently showed that early rehabilitation after

hospitalisation is safe and effective.³⁸ The main changes in SF-36 scores were similar in both groups, with improvements mainly in the more psychological domains. The absence of improvement in the physical domains of the scale was not in line with increased physical performance. It has previously been found that HRQoL correlates poorly to physical performance.^{35,39}

The difference in training intensity between the groups was fairly constant throughout the study, with a similar increase ratio in both groups. The successive increase in workload during the study is an example of the usefulness of the Borg scales for dosing exercise. We did not initially choose the workload in order to obtain the same total workload in both groups, as we wanted to investigate the effects of the two different training modalities when both groups were exercising as hard as possible. However, total workload was not significantly different between the groups throughout the study.

Our results show, in line with Vogiatzis,¹¹ that two training sessions per week are beneficial to patients with COPD although others have found this to be insufficient.⁴⁰ We noticed a much larger training effect in the current study than in a previous investigation of training twice a week for 8 weeks,⁴¹ indicating that the total number of training sessions might be as important as the number per week. In the present study the training intensity was still increasing after 24 sessions, implying that the subjects might have improved even further with more prolonged training. The optimal training duration is still not known for these patients and possibly the limited training time offered might contribute to somewhat poor long-term results after training in follow-up studies.^{41–43}

In Sweden, women have caught up with men in the prevalence of and mortality in COPD.⁴⁴ The majority of women in our study reflects the gender distribution referred to pulmonary rehabilitation at our clinics during the time of the study. We can only speculate that this might indicate that women were either more often offered referral to pulmonary rehabilitation by their physicians or were more likely to accept such an offer than the men.

As expected, the drop-out ratio was high in the current study which is in agreement with some other intervention studies of patients with severe COPD.^{45,46} This may have affected the power, as less than 35 patients in each group completed the study. The drop-outs suffered from more severe disease than those who completed and the main reason for drop-out was exacerbations, which occur more frequently in severely ill patients.

We conclude that 3-min interval training and continuous training were equally potent in increasing W peak in patients with moderate to severe COPD. This was true for functional exercise capacity, dyspnoea, mental health and HRQoL as well. Differences in physiological response to training at isotime emerged between the groups, in favour of the interval training.

Acknowledgements

Special thanks to Monica Fredriksson, physiotherapist, and Ulrike Spetz-Nyström, research nurse, for their valuable help. This paper was supported by grants from The Swedish

Heart-Lung Foundation, The County Council of Uppsala and various funds at Uppsala University.

References

1. Lacasse Y, Brosseau L, Milne S, Martin S, Wong E, Guyatt GH, et al. Pulmonary rehabilitation for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2002(3);CD003793.
2. Casaburi R, Patessio A, Ioli F, Zanaboni S, Donner CF, Wasserman K. Reductions in exercise lactic acidosis and ventilation as a result of exercise training in patients with obstructive lung disease. *Am Rev Respir Dis* 1991;143(1):9–18.
3. Punzal PA, Ries AL, Kaplan RM, Prewitt LM. Maximum intensity exercise training in patients with chronic obstructive pulmonary disease. *Chest* 1991;100(3):618–23.
4. Maltais F, LeBlanc P, Jobin J, Berube C, Bruneau J, Carrier L, et al. Intensity of training and physiologic adaptation in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 1997;155(2):555–61.
5. O'Donnell DE, Revill SM, Webb KA. Dynamic hyperinflation and exercise intolerance in chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2001;164(5):770–7.
6. O'Donnell DE, Bertley JC, Chau LK, Webb KA. Qualitative aspects of exertional breathlessness in chronic airflow limitation: pathophysiological mechanisms. *Am J Respir Crit Care Med* 1997;155(1):109–15.
7. Vogiatzis I, Nanas S, Kastanakis E, Georgiadou O, Papazahou O, Roussos C. Dynamic hyperinflation and tolerance to interval exercise in patients with advanced COPD. *Eur Respir J* 2004;24(3):385–90.
8. Sabapathy S, Kingsley RA, Schneider DA, Adams L, Morris NR. Continuous and intermittent exercise responses in individuals with chronic obstructive pulmonary disease. *Thorax* 2004;59(12):1026–31.
9. American college of sports medicine position stand. The recommended quantity and quality of exercise for developing and maintaining cardiorespiratory and muscular fitness, and flexibility in healthy adults. *Med Sci Sports Exercise* 1998;30(6):975–91.
10. Coppoolse R, Schols AM, Baarends EM, Mostert R, Akkermans MA, Janssen PP, et al. Interval versus continuous training in patients with severe COPD: a randomized clinical trial. *Eur Respir J* 1999;14(2):258–63.
11. Vogiatzis I, Nanas S, Roussos C. Interval training as an alternative modality to continuous exercise in patients with COPD. *Eur Respir J* 2002;20(1):12–9.
12. Vogiatzis I, Terzis G, Nanas S, Stratakos G, Simoes DC, Georgiadou O, et al. Skeletal muscle adaptations to interval training in patients with advanced COPD. *Chest* 2005;128(6):3838–45.
13. Franch J, Madsen K, Djurhuus MS, Pedersen PK. Improved running economy following intensified training correlates with reduced ventilatory demands. *Med Sci Sports Exercise* 1998;30(8):1250–6.
14. BTS guidelines for the management of chronic obstructive pulmonary disease. The COPD guidelines group of the standards of care committee of the BTS. *Thorax* 1997;52(Suppl 5):S1–28.
15. Standardization of spirometry—1987 update. Official statement of American thoracic society. *Respir Care* 1987;32(11):1039–60.
16. Hedenstrom H, Malmberg P, Agarwal K. Reference values for lung function tests in females. Regression equations with smoking variables. *Bull Eur Physiopathol Respir* 1985;21(6):551–7.
17. Hedenstrom H, Malmberg P, Fridriksson HV. Reference values for lung function tests in men: regression equations with smoking variables. *Ups J Med Sci* 1986;91(3):299–310.

18. Borg GA. Psychophysical bases of perceived exertion. *Med Sci Sports Exercise* 1982;14(5):377–81.
19. Borg G. Perceived exertion as an indicator of somatic stress. *Scand J Rehabil Med* 1970;2(2):92–8.
20. McGavin CR, Gupta SP, McHardy GJ. Twelve-minute walking test for assessing disability in chronic bronchitis. *Br Med J* 1976;1(6013):822–3.
21. Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW. A measure of quality of life for clinical trials in chronic lung disease. *Thorax* 1987;42(10):773–8.
22. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;67(6):361–70.
23. Brazier JE, Harper R, Jones NM, O’Cathain A, Thomas KJ, Usherwood T, et al. Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *Br Med J* 1992;305(6846):160–4.
24. Jacobson E. *Progressive relaxation*, 2nd ed. Chicago: University of Chicago Press; 1938.
25. Emtner M, Porszasz J, Burns M, Somfay A, Casaburi R. Benefits of supplemental oxygen in exercise training in nonhypoxemic chronic obstructive pulmonary disease patients. *Am J Respir Crit Care Med* 2003;168(9):1034–42.
26. Troosters T, Gosselink R, Decramer M. Short- and long-term effects of outpatient rehabilitation in patients with chronic obstructive pulmonary disease: a randomized trial. *Am J Med* 2000;109(3):207–12.
27. Porszasz J, Emtner M, Goto S, Somfay A, Whipp BJ, Casaburi R. Exercise training decreases ventilatory requirements and exercise-induced hyperinflation at submaximal intensities in patients with COPD. *Chest* 2005;128(4):2025–34.
28. Seiler S, Sjursen JE. Effect of work duration on physiological and rating scale of perceived exertion responses during self-paced interval training. *Scand J Med Sci Sports* 2004;14(5):318–25.
29. Ortega F, Toral J, Cejudo P, Villagomez R, Sanchez H, Castillo J, et al. Comparison of effects of strength and endurance training in patients with chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2002;166(5):669–74.
30. Spruit MA, Gosselink R, Troosters T, De Paepe K, Decramer M. Resistance versus endurance training in patients with COPD and peripheral muscle weakness. *Eur Respir J* 2002;19(6):1072–8.
31. Yquel RJ, Tessonneau F, Poirier M, Moinard J, Pillet O, Manier G. Peak anaerobic power in patients with COPD: gender related differences. *Eur J Appl Physiol* 2006;97(3):307–15.
32. Janaudis-Ferreira T, Wadell K, Sundelin G, Lindstrom B. Thigh muscle strength and endurance in patients with COPD compared with healthy controls. *Respir Med* 2006;100(8):1451–7.
33. Persson LO, Karlsson J, Bengtsson C, Steen B, Sullivan M. The Swedish SF-36 health survey II. Evaluation of clinical validity: results from population studies of elderly and women in Gothenburg. *J Clin Epidemiol* 1998;51(11):1095–103.
34. Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clin Trials* 1989;10(4):407–15.
35. Wijkstra PJ, Van Altena R, Kraan J, Otten V, Postma DS, Koeter GH. Quality of life in patients with chronic obstructive pulmonary disease improves after rehabilitation at home. *Eur Respir J* 1994;7(2):269–73.
36. Gudmundsson G, Gislason T, Janson C, Lindberg E, Hallin R, Ulrik CS, et al. Risk factors for rehospitalisation in COPD: role of health status, anxiety and depression. *Eur Respir J* 2005;26(3):414–9.
37. Dahlen I, Janson C. Anxiety and depression are related to the outcome of emergency treatment in patients with obstructive pulmonary disease. *Chest* 2002;122(5):1633–7.
38. Man WD, Polkey MI, Donaldson N, Gray BJ, Moxham J. Community pulmonary rehabilitation after hospitalisation for acute exacerbations of chronic obstructive pulmonary disease: randomised controlled study. *Br Med J* 2004;329(7476):1209.
39. Engstrom CP, Persson LO, Larsson S, Sullivan M. Health-related quality of life in COPD: why both disease-specific and generic measures should be used. *Eur Respir J* 2001;18(1):69–76.
40. Ringbaek TJ, Broendum E, Hemmingsen L, Lybeck K, Nielsen D, Andersen C, et al. Rehabilitation of patients with chronic obstructive pulmonary disease. Exercise twice a week is not sufficient!. *Respir Med* 2000;94(2):150–4.
41. Arnardottir RH, Sorensen S, Ringqvist I, Larsson K. Two different training programmes for patients with COPD: a randomised study with 1-year follow-up. *Respir Med* 2006;100(1):130–9.
42. Bestall JC, Paul EA, Garrod R, Garnham R, Jones RW, Wedzicha AJ. Longitudinal trends in exercise capacity and health status after pulmonary rehabilitation in patients with COPD. *Respir Med* 2003;97(2):173–80.
43. Brooks D, Krip B, Mangovski-Alzamora S, Goldstein RS. The effect of postrehabilitation programmes among individuals with chronic obstructive pulmonary disease. *Eur Respir J* 2002;20(1):20–9.
44. <www.sos.se/epc/epceng.htm#epid>.
45. Bendstrup KE, Ingemann Jensen J, Holm S, Bengtsson B. Out-patient rehabilitation improves activities of daily living, quality of life and exercise tolerance in chronic obstructive pulmonary disease. *Eur Respir J* 1997;10(12):2801–6.
46. Finnerty JP, Keeping I, Bullough I, Jones J. The effectiveness of outpatient pulmonary rehabilitation in chronic lung disease: a randomized controlled trial. *Chest* 2001;119(6):1705–10.