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FEATURED CLINICAL TRIAL

Interval versus continuous training in lung transplant candidates: A randomized trial

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KEYWORDS:
chronic obstructive pulmonary disease;
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BACKGROUND: Interval (IT) and continuous training (CT) represent well-established exercise modalities in patients with moderate to severe chronic obstructive pulmonary disease (COPD). However, their effects and feasibility in patients with end-stage COPD remain unclear.

METHODS: Sixty patients (53 ± 6 years, 53% women) being evaluated for lung transplantation where randomly assigned either to IT ($n = 30$, cycling at 100% peak work rate for 30 seconds alternating with 30 seconds of rest) or CT ($n = 30$, cycling at 60% of peak work rate) during a 3-week inpatient rehabilitation program. Both exercise protocols yielded an equivalent amount of total work. Patients had a mean forced expiratory volume at 1 second (FEV_1) of 25% ± 8% of predicted value.

RESULTS: Patients in both groups achieved similar clinically relevant improvements in 6-minute walking distance of 35 ± 29 meters for IT and 36 ± 43 meters for CT, with a between-group difference of 0.3 meters (95% confidence interval, −18.2 to 18.8). Changes in lung function parameters were not significant. Perceived intensity of dyspnea was significantly ($p < 0.05$) lower in IT (Borg 6.2 ± 1.8) compared with CT (Borg 7.1 ± 1.7). Patients required a median of 5 unintended breaks (interquartile range, 2–28) during IT exercise and 29 (interquartile range, 6–68) during CT ($p < 0.001$).

CONCLUSIONS: IT is associated with a lower intensity of dyspnea during exercise and fewer unintended breaks but achieves similar improvements in exercise capacity compared with CT in pre-lung transplant COPD patients.

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Limited exercise capacity is one of the main systemic manifestations of advanced chronic obstructive pulmonary disease (COPD) associated with poor health-related quality of life (HRQL), exacerbations, and increased mortality risk.[1,2] Pulmonary rehabilitation has been demonstrated to improve exercise tolerance, reduce symptoms of dyspnea, and increase HRQL in patients with COPD.[3,4] Therefore, exercise training is regarded as a cornerstone of pulmonary rehabilitation.[5]

Endurance training has been shown to improve exercise capacity on peripheral muscle function in patients with COPD.[6] In addition, there is some evidence that high-intensity endurance training induces greater physiologic benefits than lower-intensity exercise.[7] However, most patients with severe COPD are not able to sustain high-intensity exercise due to serious symptoms of dyspnea and fatigue.[8] Therefore alternative exercise protocols, such as interval training (IT), have gained increasing attention. A recent systematic review of 8 randomized controlled trials including 388 patients with COPD, mostly at Global Initiative for Chronic Obstructive Lung Disease (GOLD) stage II and III, analyzed the effects of IT vs continuous training (CT).[9] The authors concluded that both exercise modalities led to comparable effects in improved exercise capacity and HRQL.

Although there is still a substantial lack of data on endurance training in patients with end-stage lung disease, several groups have proclaimed that IT should be consid-

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ered as an alternative to CT, especially for symptomatic patients with very severe COPD.[9,10] To fill this gap of knowledge, we conducted this prospective randomized controlled trial to assess whether IT is not less effective than CT. Furthermore, we were interested in whether the feasibility of an interval endurance training protocol might be superior to that of continuous endurance training in patients with end-stage COPD listed for lung transplantation (LTx).

Methods and materials

This study was approved by the Bavarian Ethics Committee (identification number 08022) and registered on the Clinical Trials registry (identification number NCT00962078).

Study design

Consecutive patients admitted to a 3-week rehabilitation program (most common setting in Germany for pre-LTx patients to optimize their physical condition) between June 2008 and October 2010 were invited to participate in this randomized controlled parallel group study. Patients were not blinded to intervention, but researchers who performed the 6-minute walking-test (6-MWT), defined as primary outcome parameter, were blinded to the allocation of the patients.

Study population

The study recruited 71 patients. To be included in the study patients had to meet the following inclusion criteria: (1) diagnosis of COPD stage IV in accordance with the GOLD assessment,[11] (2) active listing status for LTx or at least involved in an evaluation process for LTx,[12] and (3) written informed consent. Exclusion criteria were (1) severe exacerbation within the last 4 weeks, (2) clinical signs of right heart failure, or (3) non-compliance with the study protocol.

Randomization procedure

Allocation concealment was administered by a third party within the clinic who was not involved in patient recruitment. The decision to accept or reject a participant into the study was made without knowledge of the next assignment in the sequence. As a randomization scheme, 2 permuted blocks of equal length with a ratio of 1:1 were used.

Intervention

Patients followed a multidisciplinary 3-week inpatient rehabilitation program that included exercise units on 5 to 6 days/week. Apart from the type of endurance training, the rehabilitation program was identical for both groups and consisted of medical care, breathing therapy, education (eg, disease management or nutritional counseling), and psychologic support (eg, coping strategies). Strength training consisted of 3 × 20 repetitions (resistance was consistently adjusted to the maximum tolerated load) of 4 to 6 exercises selected from leg press, knee extension, hip abduction/adduction, pull back, pull-down, and arm dips.

Patients were assigned to moderate intense CT ($n = 35$) or high-intensity IT ($n = 36$). The target work rate for patients in the CT group was 60% of peak work rate (PWR). This intensity is commonly used for endurance training in COPD.[5,10] IT consisted of 30-second bouts of cycling at 100% of PWR alternating with 30 seconds of rest (0% of PWR), an exercise scheme that has been successfully applied in several COPD studies.[13–15] The total amount of exercise time per session increased from 10 to 30 minutes in CT and from 12 to 36 minutes in IT, yielding an isocaloric total work in both groups (for exercise progression see e-Figure 1, available on the JHLTonline.org Web site).

During the second and third week, exercise training was split into 2 sessions per day (eg, 2 × 10 minutes, 2 × 11 minutes, etc).[16] This approach was chosen to adjust the amount of exercise training to the capabilities of severely disabled pre-LTx patients. If work rate was considered too low (modified Borg ratings < 3 for perceived exertion), patients completed another incremental cycle test to adjust exercise intensity. Patients who needed to rest during the endurance training due to exhaustion were allowed to do so but were encouraged to continue cycling as soon as possible. Ninety percent of the patients used supplemental oxygen as prescribed.

Outcomes and measurements

The primary outcome parameter of the study was the change in 6-minute walking distance (6-MWD), which was performed in accordance with the guidelines from the American Thoracic Society (ATS).[17] The best result out of 2 tests on Days 1 and 2 was used as the baseline value to exclude learning effects.[18]

A symptom-limited incremental cycle ergometer test (Cardiomed Bike, Proxomed Medical, Alzenau, Germany) was conducted to determine PWR. Patients started pedaling at 10 W, with an increase of 10 W every minute until exhaustion.[19]

Lung function was measured with a Master Screen Body Plethysmograph (Jaeger, Wuerzburg, Germany) in accordance with ATS guidelines.[20]

Patients were monitored during exercise training by a SenTec Digital Monitoring System (SMB-SW:06.21.01/MPB-SW: 04.04.05, SenTec AG, Therwil, Switzerland). In addition to oxygen saturation, this device was used to determine transcutaneously measured pressure of arterial carbon dioxide ($TcPco_2$). Compared with the snapshot view of traditional capillary blood gas analysis, the advantage of this technique is the continuous recording of $TcPco_2$. Measuring and controlling $TcPco_2$ in patients with end-stage COPD enhances safety and reveals information about the respiratory system during exercise in these patients.

To evaluate the feasibility of the exercise protocols, patients were asked to rate the intensity of perceived dyspnea and leg fatigue during exercise on a modified Borg scale (0 to 10). We also recorded the number and duration of unintended breaks when patients had to interrupt endurance training due to exhaustion. General HRQL was assessed by the validated German version of the Medical Outcomes Survey Short-Form 36 (SF-36) questionnaire.[21]

All measurements were performed on Days 1 and 21 of the rehabilitation program.

Statistical analysis

We determined that a sample size of 30 patients in each group would show the non-inferiority of IT, assuming non-inferiority at the margin of the minimal clinically important difference (MCID)

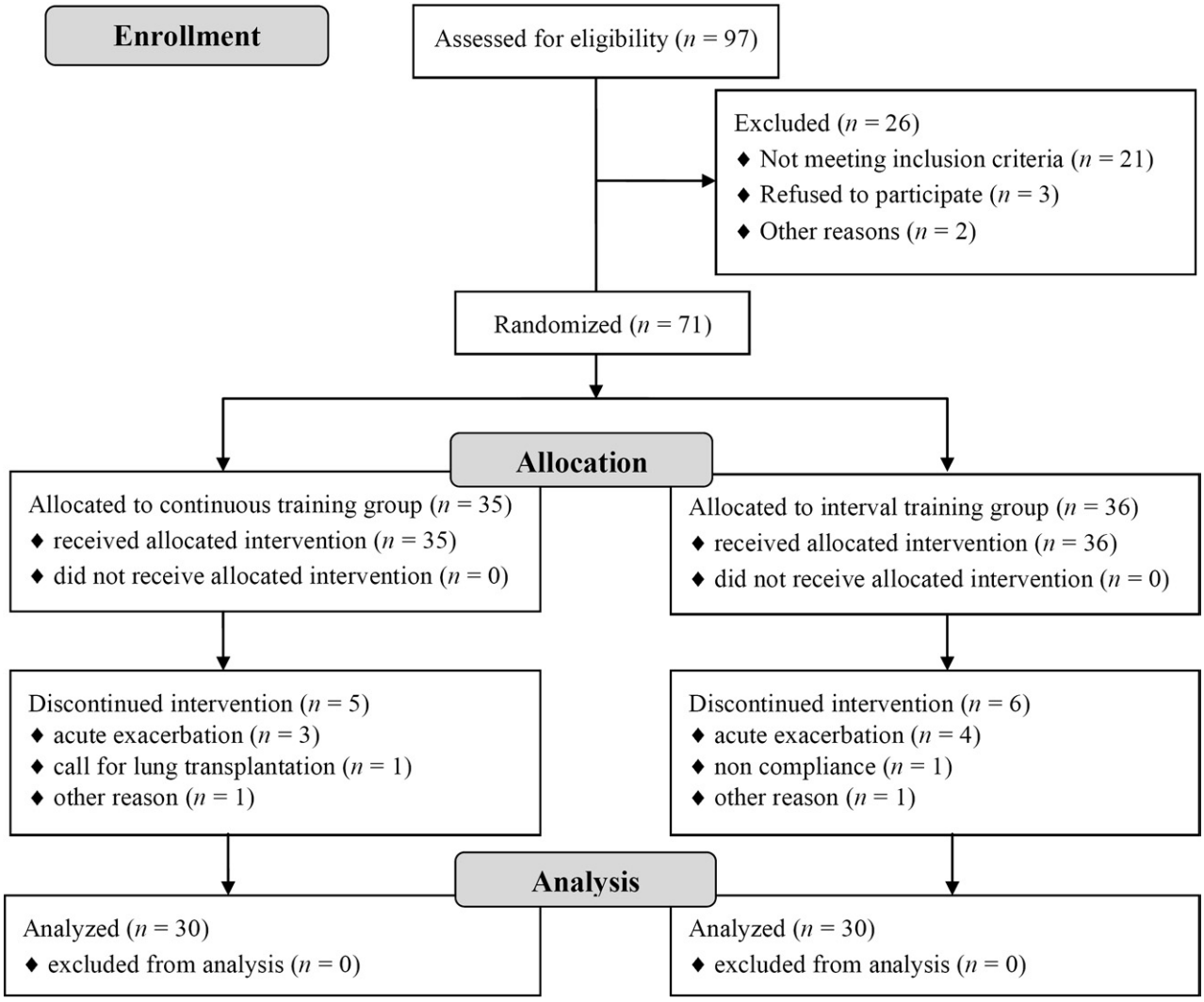

Figure 1 Study flow diagram.

of 26 meters[22] in the 6-MWD between groups yielding a power of 80% at a two-sided $\alpha = 0.05$.

Data are presented in mean and standard deviation or mean and 95% confidence interval (CI) unless otherwise stated. Within-group differences were analyzed using paired *t*-tests. Between-group comparisons of changes in outcome parameters were assessed with unpaired *t*-tests. For subjective ratings and unevenly distributed data the Wilcoxon signed rank test (intra-group) and the Mann-Whitney *U*-test (inter-group) were applied. The level of significance was set at $p < 0.05$. All data analysis was performed using PASW Statistics 18.0 software (SPSS Inc, Chicago, IL).

Results

Baseline characteristics

Sixty of 71 patients completed the study (for drop-out reasons see Figure 1) and were considered for the final per-protocol analysis. Owing to the advanced stage of the disease, patients showed an extreme limitation of respiratory capacities (baseline values see Table 1). Mean forced expiratory volume at 1 second (FEV_1) was 25% ± 8% of predicted value on admission. Furthermore a low Tiffeneau Index (FEV_1/inspiratory vital capacity) of 35% ± 8% predicted, as well as a low diffusion capacity if lung for carbon monoxide (DLCO) of 26% ± 10% predicted, reflect the degree of physical limitation in these patients. At discharge, none of the lung function parameters were significantly different from baseline values (Table 2).

Effects on exercise performance and HRQL

Pulmonary rehabilitation was effective in both groups, as assessed by a significant increase in 6-MWD of 35 ± 28 meters in the IT group and 36 ± 42 meters in the CT group (Figure 2). Exercise capacity during the incremental cycle test (Figure 2) also significantly increased in both groups without any group difference (IT, 12 ± 8 W; CT, 9 ± 10 W). Although all sum scores of the SF-36 improved, only the physical health summary score in the CT group (4.3 ± 6.9 points) and the mental health summary score (9.7 ± 13.0 points) in the IT group

Table 1 Baseline Characteristics in Patients Receiving Interval and Continuous Training

	Patients randomized to rehabilitation		Patients completing rehabilitation	
Characteristics[a]	Interval (n = 35)	Continuous (n = 36)	Interval (n = 30)	Continuous (n = 30)
Age, years	52 ± 6	55 ± 7	52 ± 6	55 ± 6
Female sex	18 (51)	20 (56)	15 (50)	17 (57)
Long-term oxygen therapy	32 (89)	33 (92)	27 (90)	27 (90)
Body mass index, kg/m^2	24 ± 4	24 ± 3	24 ± 4	24 ± 3
Patient status				
Evaluation for LTx	17 (49)	19 (53)	14 (47)	16 (53)
On the active list for LTx	18 (51)	17 (47)	16 (53)	14 (47)
6-MWD, meters	286 ± 105	308 ± 96	290 ± 109	313 ± 98
6-MWD, % predicted [b]	39 ± 14	44 ± 13	40 ± 14	45 ± 13
Peak work rate, W	43 ± 20	45 ± 24	44 ± 22	46 ± 24
FEV_1, liters	0.7 ± 0.2	0.8 ± 0.2	0.7 ± 0.2	0.8 ± 0.3
FEV_1, % predicted [c]	24 ± 8	27 ± 7	23 ± 8	27 ± 7
FEV_1/IVC, % [c]	36 ± 9	38 ± 11	34 ± 7	36 ± 10
D_{LCO}, % predicted [c]	26 ± 11	28 ± 11	24 ± 10	28 ± 11
Pa_{O_2}, mm Hg [d]	54 ± 6	55 ± 7	54 ± 7	55 ± 8
Pa_{CO_2}, mm Hg [d]	44 ± 7	43 ± 9	44 ± 8	43 ± 9
Short-Form 36 SS				
Physical health, points	26 ± 8	25 ± 7	26 ± 7	24 ± 7
Mental health, points	40 ± 15	48 ± 15	39 ± 16	48 ± 16

6-MWD, 6-minute walking-distance; D_{LCO}, diffusion capacity of the lung for carbon monoxide; FEV_1, forced expiratory volume in 1 second; IVC, inspiratory vital capacity; LTx, lung transplantation; Pa_{CO_2}, partial pressure of arterial carbon dioxide; Pa_{O_2}, partial pressure of arterial oxygen; SS, summary score.

[a]Continuous data are presented as mean ± standard deviation and categoric data as number (%).

[b]Reference values from Troosters et al.[23]

[c]Reference values from Matthys et al.[24]

[d]Measured by capillary blood gas analysis at rest without supplement oxygen.

increased significantly. For intention-to-treat analyses, see Table 2.

Feasibility to exercise protocols

The number of exercise sessions and total work performed was equivalent in both groups (Table 3). Only 2 patients in the CT group and 1 patient in the IT group were referred to another incremental cycle test within the second week to adjust exercise intensity because their perceived exertion was regarded as too low (Borg < 3). Oxygen supplementation during exercise mostly yielded oxygen saturation ≥ 88% (Table 3). Because the results for $TcPco_2$ during exercise were equivalent on Days 1 and 21, values of Day 1 measurement are provided as an example (Figure 3). Measurement of $TcPco_2$ during exercise showed a slight increase from baseline 42 ± 8 to 47 ± 12 mm Hg in the IT group and from 42 ± 7 to 46 ± 9 mm Hg in the CT group. At 5 to 10 minutes after completing the exercise session, all patients reached at least their baseline level of $TcPco_2$ or even slightly below that (IT, 41 ± 8 mm Hg; CT, 41 ± 7 mm Hg).

Although exercise duration increased in both groups, ratings of perceived exertion in both groups decreased by a similar amount. The mean overall rating for dyspnea on the Borg scale was significantly ($p < 0.05$) lower in the IT group (6.2 ± 1.8) compared to the CT group (7.1 ± 1.7; Figure 4). Ratings for leg fatigue were slightly but not significantly higher in CT (5.6 ± 2.1) than in IT (4.9 ± 1.9; e-Figure 2, available on the JHLTonline.org Web site). Overall, unintended breaks during exercise were significantly ($p < 0.01$) less frequent in the IT group (n = 12), with a median number of 5 breaks (interquartile range [IQR], 2–28) and of shorter duration (median, 5 minutes; IQR, 2–25 minutes) than in CT-group (n = 22), with a median number of 29 breaks (IQR, 6–68) lasting for a median of 43 minutes (IQR, 7–65 minutes).

No serious adverse events, as defined by the study protocol, were observed.

Discussion

Former trials investigating different endurance training protocols mostly included patients with COPD at GOLD stages II to III with FEV_1 values between 33% and 55% predicted.[14,25–29] Our study extended these findings to the GOLD stage IV by revealing that exercise training is also effective in very disabled COPD patients before LTx.

IT and CT can both induce comparable effects in exercise capacity. These findings are in line with results of previous studies. Puhan et al[26] randomized 98 less ventila-

Table 2 Comparison of Treatment Effects of Interval and Continuous Training

	Per protocol analysis				
	Mean changes from baseline				
Outcome[a]	Interval (n = 30)	Continuous (n = 30)	Difference (95% CI)	p-values	Difference in ITT (95% CI)
Primary					
6-MWD, m	35.4 ± 28.9[b]	35.7 ± 42.2[b]	0.3 (−18.2 to 18.8)	0.89	1.1 (−15.6 to 17.8)
6-MWD, % pred[c]	14.1 ± 12.7[b]	15.5 ± 25.1[b]	1.4 (−8.9 to 11.7)	0.78	1.5 (−7.5 to 10.5)
Secondary					
PWR, W	12.0 ± 8.5[b]	9.3 ± 10.1[b]	−2.7 (−7.5 to 2.2)	0.38	−2.0 (−6.5 to 2.5)
FEV_1, liters	0.0 ± 0.1	−0.0 ± 0.1	0.0 (−0.1 to 0.0)	0.055	0.1 (−0.1 to 0.0)
FEV_1, % pred[d]	0.9 ± 2.9	−0.7 ± 3.8	−1.6 (−3.3 to 0.1)	0.064	−1.4 (−2.8 to 0.1)
FEV_1/IVC, %[d]	± 0.1	−0.0 ± 0.1	−0.0 (−0.1 to 0.0)	0.061	−0.0 (−0.0 to 0.0)
D_{LCO}, % pred[d]	0.2 ± 5.3	−2.6 ± 4.4	−2.8 (−6.2 to 0.6)	0.096	−2.4 (−5.2 to 0.4)
Pa_{O_2}, mm Hg	1.7 ± 5.7	−1.7 ± 6.1	−3.4 (−6.4 to −0.3)	0.60	−2.9 (1.3 to −5.4)
Pa_{CO_2}, mm Hg	−0.6 ± 4.6	−0.6 ± 7.5	−0.0 (−3.2 to 3.1)	0.85	−0.0 (−2.7 to 2.7)
Short-Form 36 SS					
Physical health	2.3 ± 9.5	4.3 ± 6.9[b]	2.0 (−3.0 to 7.0)	0.43	1.5 (−2.5 to 5.6)
Mental health	9.7 ± 13.0[b]	2.9 ± 10.9	−6.8 (−14.1 to 0.5)	0.066	−5.5 (−11.5 to 0.4)

6-MWD, 6-minute walking-distance; CI, confidence interval; D_{LCO}, diffusion capacity of the lung for carbon monoxide; FEV_1, forced expiratory volume in 1 second; ITT, intention to treat; IVC, inspiratory vital capacity; Pa_{CO_2}, partial pressure of arterial carbon dioxide; Pa_{O_2}, partial pressure arterial oxygen; PWR, peak work rate; SS, summary score.

[a]Continuous data are data are presented as mean ± standard deviation.

[b]Significant ($p < 0.05$) within-group change.

[c]Reference values from Troosters et al.[23]

[d]Reference values from Matthys et al.[24]

tory limited patients with COPD (FEV_1, 34% ± 9% predicted) to IT or CT during an inpatient rehabilitation of also 3 weeks in duration. Within this setting comparable to our study, both groups demonstrated physiologic benefits, with no differences between groups increasing in exercise capacity or HRQL. Vogiatzis et al[14] investigated 36 COPD patients (FEV_1, 45% ± 4% predicted) randomly assigned to IT or CT. The authors concluded that IT elicits substantial training effects that were similar in magnitude to those produced by CT at 50% exercise intensity but doubled exercise time. Although patients in this study took part in a considerably longer lasting exercise program than in our

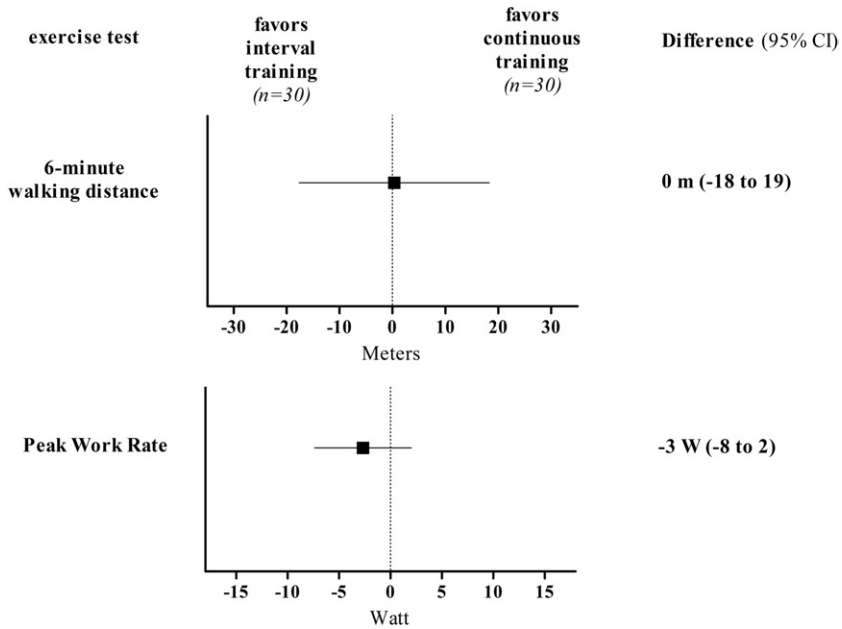

Figure 2 Boxes with 95% confidence interval (CI) represent the point estimate for the difference of 6-minute walking distance and peak workload assessed by the incremental cycle test from Day 1 to 21 during in-patient rehabilitation in the interval or continuous training group.

Table 3 Description of Endurance Training Programs

Characteristic[a]	Interval training (n = 30)	Continuous training (n = 30)	Difference (95% CI)	p-value
Exercise sessions, No.	14.9 ± 1.9	14.7 ± 1.5	−0.2 (−1.1 to 0.6)	0.60
Supplemental O_2 during exercise, liters/min	3.7 ± 1.9	3.4 ± 1.0	−0.3 (−1.1 to 0.5)	0.47
Average work rate for exercise sessions				
High-intensity interval, W	43.6 ± 22.0			
High-intensity interval, % of PWR	99.3 ± 6.6			
Resting interval, W	0.0 ± 0.0			
Constant intensity, W		29.3 ± 17.5		
Constant intensity, % of PWR		61.5 ± 14.9		
Parameters during first exercise session				
Lowest Spo_2, %	91.6 ± 4.6	92.9 ± 3.0	1.3 (−0.7 to 3.3)	0.20
Peak $TcPco_2$, mm Hg	46.7 ± 11.5	45.9 ± 8.7	−0.9 (−6.2 to 4.5)	0.75
Overall dyspnea during exercise[b]	6.2 ± 1.6	7.2 ± 1.4	1.0 (0.2 to 1.8)	0.012
Overall leg fatigue during exercise[b]	4.9 ± 1.9	5.6 ± 2.1	0.6 (−0.4 to 1.7)	0.22
Average work, kJ				
During first exercise week	20.0 ± 10.6	21.1 ± 13.9	1.1 (−5.3 to 7.5)	0.73
During second exercise week	31.0 ± 16.0	33.1 ± 22.6	2.1 (−8.0 to 12.3)	0.68
During third exercise week	38.3 ± 19.2	42.6 ± 29.1	4.4 (−8.6 to 17.4)	0.50
Overall total work	87.9 ± 43.0	95.4 ± 64.9	7.5 (−21.0 to 36.0)	0.60
Patients with unintended breaks, No.	12	22		
Total unintended breaks, No.	5 (2–28)	29 (6–68)		0.021[c]
Total duration of unintended breaks, min	5 (2–25)	43 (7–65)		0.005[c]

CI, confidence interval; PWR, peak work rate, Spo_2, oxygen saturation by pulse oximetry; $TcPco_2$, transcutaneous pressure of carbon dioxide.
[a]Continuous data are presented as mean ± standard deviation or median (interquartile range).
[b]Assessed by the modified Borg scale, range 0–10 points.
[c]Mann-Whitney U-test.

trial (12 vs 3 weeks), improvements of PWR were similar (IT, 14 ± 7 W; CT, 13 ± 6 W) to ours (IT, 12 ± 8 W; CT, 9 ± 10 W). A reason for this comparable improvement could be that Vogiatzis et al did not provide additional resistance training for their patients as we did in our trial. A further study from the same group demonstrated that IT and CT provided similar improvements in cross-sectional areas of type I and IIa muscle fibers as well as in aerobic enzyme activities.[29]

In the present study, improvements in 6-MWD were consistent with one of the generally used levels of MCID for patients with COPD of 35 meters.[30] This increase in 6-MWD becomes even more relevant when referring to the recently published MCID of 26 meters specifically recommended for patients with severe COPD.[22] Exercise capacity during the incremental cycle test also increased significantly and was clinically relevant above the suggested MCID of 4 W.[22]

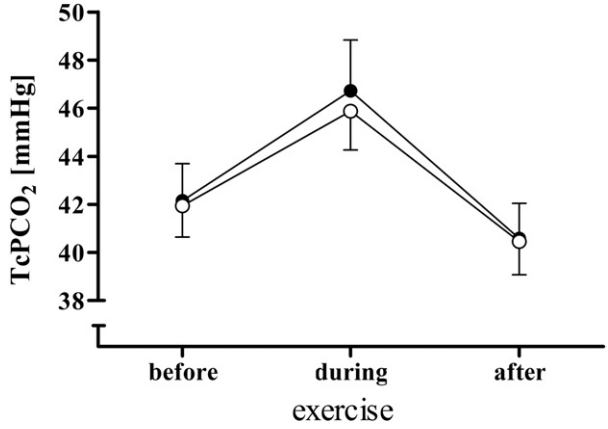

Figure 3 Changes of transcutaneous pressure of arterial carbon dioxide ($TcPco_2$). Resting values before and 10 minutes after exercise, peak values during 10 to 12 minutes of cycling (mean ± standard error of the mean) in the continuous (white circles, n = 30) and interval (black circles, n = 30) training groups on Day 1 of inpatient rehabilitation.

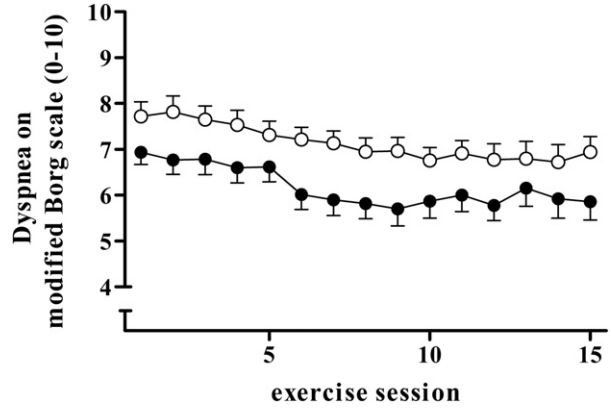

Figure 4 Ratings of perceived dyspnea (mean ± standard error of the mean) are shown for patients during continuous (white circles, n = 30) or interval (black circles, n = 30) training on a cycle ergometer during a 3-week inpatient rehabilitation program (5 exercise sessions/week).

Common concerns about exercise training in patients with end-stage COPD refer to global respiratory insufficiency causing a considerable increase in partial pressure of CO_2. Our data did not confirm this adverse effect. During exercise training $TcPCO_2$ increased merely to mild hypercapnia. More importantly, $TcPCO_2$ rapidly returned to baseline levels or even below within 10 minutes after participants finished their exercise sessions (Figure 3). We did not observe persistently elevated $TcPCO_2$ levels after exercise training in any of our patients. Monitoring $TcPCO_2$ enhances safety during exercise, particularly in individuals with hypercapnia.

Although we did not find differences between IT and CT in improving exercise capacity, another issue may be considered more favorable for IT. Though the assessment of feasibility of the given exercise protocols in LTx candidates was not the major aim of this study, we would like to discuss our findings cautiously. Patients undergoing IT perceived significantly lower intensities of dyspnea and leg fatigue during cycling than patients performing CT. This difference could already be observed at the baseline of the study and was maintained over the study period for each single exercise session. Owing to higher levels of dyspnea during exercise, patients in the CT group needed significantly more unintended breaks during endurance training. The number of breaks in the CT group also increased continuously over time, whereas patients in the IT group were able to keep a similar frequency of breaks during inpatient rehabilitation (e-Figure 3, available on the JHLTonline.org Web site). Both could have contributed to the larger increase in the SF-36 mental health score in the IT group. So far only one previous trial[26] has also found a better adherence to IT than CT protocols with regard to the number of unintended breaks, although this difference was not as remarkable as the one observed in our study. Because most patients with end-stage COPD are often frustrated from the burden of physical limitations in daily life, it is important to provide an exercise protocol that these patients can manage. This could encourage these them to adhere to exercise training also in the longer term.

This randomized controlled trial has some limitations. Firstly, a common problem often found in trials comparing IT and CT is the small absolute difference in exercise intensity due to a low PWR. However, even small differences in exercise intensity may reflect meaningful changes in patients with very severe COPD. Secondly, for some patients in the CT group endurance training also had an interval character due to the high number of unintended breaks. Thirdly, the total number 60 patients enrolled in this study can still be regarded as a small sample size. Finally, patients were not enrolled in a follow-up investigation because our study focused on the short-term effects of different endurance training protocols in LTx candidates during supervised rehabilitation and not on long-term maintenance of exercise programs.

In conclusion, our findings support the evidence of former trials[25-27,29,31,32] suggesting that there are no differences between the effects of IT and CT on improving exercise capacity or HRQL. This trial demonstrated similar effects in COPD patients before LTx. Furthermore, we found that IT is associated with a lower intensity of dyspnea during exercise and fewer unintended breaks. Further studies are needed to ascertain durability of these training effects and its effects on outcomes after LTx.

Disclosure statement

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Supplementary data

Supplementary data are available in the online version of this article at JHLTonline.org.

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