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Research Article

Exercise Performance After Pulmonary Rehabilitation Assessed by Cardiopulmonary Exercise Testing in Patients with Chronic Obstructive Pulmonary Disease: A Single-Centre Pilot Study

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Abstract

Background: Pulmonary rehabilitation improves exercise capacity and health-related quality of life in people with chronic obstructive pulmonary disease (COPD). Cardiopulmonary exercise testing (CPET) can identify individual physiological thresholds that may be used to tailor endurance-training intensity and objectively assess the response to rehabilitation. We evaluated changes in exercise performance and health status after a CPET-guided pulmonary rehabilitation programme.

Methods: This single-centre, open-label, single-arm pilot study included patients with COPD who entered a 12-week rehabilitation programme consisting of three supervised sessions per week. Endurance training on a cycle ergometer was individualized using the anaerobic threshold (AT) and respiratory compensation point (RCP) derived from baseline CPET. CPET, lung function, the COPD Assessment Test (CAT) and the St George's Respiratory Questionnaire (SGRQ) were assessed at baseline and within 30 days after programme completion. This interim analysis includes the nine participants with paired baseline and follow-up data.

Results: Nine participants completed the programme (mean age 68.4 years; five men). Peak oxygen uptake increased from 1000.44 ± 363.73 to 1200.56 ± 263.93 mL/min (mean paired change +200.11 mL/min; 95% CI 36.33 to 363.89; paired t-test $p = 0.0226$; Wilcoxon $p = 0.0391$). Oxygen uptake at AT, work rate at AT and RCP, and oxygen pulse also increased significantly. CAT decreased by 4.78 points (95% CI −6.26 to −3.30; $p < 0.001$), and SGRQ total score decreased by 16.89 points (95% CI −22.65 to −11.12; $p < 0.001$). Eight of nine participants achieved reductions of at least 3 points in CAT and at least 7 points in SGRQ total score. No statistically significant changes were observed in ventilatory efficiency, ventilatory reserve or spirometric indices.

Conclusion: In this small, uncontrolled interim cohort, CPET-guided pulmonary rehabilitation was followed by improvements in peak and submaximal exercise performance and health status, without significant changes in spirometry or ventilatory efficiency. These findings are exploratory and do not establish superiority over standard rehabilitation. Controlled studies are required.

Keywords: *Chronic Obstructive Pulmonary Disease; Pulmonary Rehabilitation; Cardiopulmonary Exercise Testing; Peak Oxygen Uptake; Anaerobic Threshold; Health-Related Quality of Life*

Introduction

Chronic obstructive pulmonary disease (COPD) is a major cause of morbidity and mortality worldwide and is associated with substantial healthcare and societal costs [1]. Dyspnoea and exercise intolerance are among its most disabling manifestations and contribute importantly to impaired health-related quality of life. Exercise limitation in COPD is multifactorial and may reflect ventilatory constraints, dynamic hyperinflation, gas-exchange abnormalities, cardiovascular factors and peripheral skeletal-muscle dysfunction [1,5]. Physical inactivity is also associated with adverse clinical outcomes, including all-cause mortality [14].

Pulmonary rehabilitation is a core component of COPD management and improves exercise capacity, symptoms and health-related quality of life across a broad range of disease severity [2-4]. In routine practice, however, endurance-training intensity may be prescribed using fixed percentages of peak work rate or symptom-limited heart rate, without always accounting for the individual physiological response to exercise.

CPET provides an integrated assessment of the cardiovascular, ventilatory and metabolic responses to exercise. It can identify physiological thresholds, including the anaerobic threshold (AT) and respiratory compensation point (RCP), which may help define individualized training domains and provide objective measures of functional response [6,7]. We therefore evaluated changes in exercise capacity and health status after a pulmonary rehabilitation programme in which cycle-ergometer endurance training was individualized using CPET-derived thresholds.

Aim of the Study

The primary aim was to assess the change in peak oxygen uptake ($\dot{V}O_2$peak) following CPET-guided pulmonary rehabilitation. Secondary aims were to evaluate changes in oxygen uptake at AT, work rate at AT and RCP, oxygen pulse, ventilatory efficiency, ventilatory reserve, lung function, and health status measured using CAT and SGRQ.

Materials and Methods

Study design and setting

This was a single-centre, open-label, single-arm, pre-post interventional pilot study conducted at the Pulmonary Unit of the "C. e G. Mazzoni" Hospital, Ascoli Piceno, Italy. Recruitment began in December 2022. The present manuscript reports an interim analysis of participants who had completed the rehabilitation programme and had available paired assessments.

All participants provided informed consent for the clinical assessments and use of anonymized data.

Participants

Eligible participants had COPD with post-bronchodilator $FEV_1/FVC < 0.70$, $FEV_1 \geq 30\%$ predicted, CAT score ≥10 and fewer than two exacerbations in the previous year without hospitalization, corresponding to the inclusion criteria applied at the time of recruitment under the GOLD 2022 framework. Patients unable to perform activities of daily living and those with chronic respiratory failure receiving long-term oxygen therapy were excluded.

Assessments and rehabilitation programme

At baseline, participants underwent a pulmonary assessment, completion of CAT and SGRQ, spirometry and measurement of static lung volumes (total lung capacity by nitrogen washout), and symptom-limited incremental CPET. Inhaled treatment was reviewed and optimized according to the clinical recommendations in use at the time. A physiatric assessment was used to define the rehabilitation plan, taking the baseline CPET findings into account.

The programme consisted of three supervised sessions per week for 12 weeks (36 planned sessions). Each session included group respiratory physiotherapy and approximately 20 minutes of cycle-ergometer endurance training. The cycle-ergometer work rate was individualized according to the training domain delimited by AT and RCP. Participants were also advised to perform home-based exercises. The 12-week duration reflected the centre's established protocol; the study was not designed to compare programme duration or to determine whether extending rehabilitation beyond 6-8 weeks provides additional benefit.

Within 30 days after programme completion, participants underwent repeat pulmonary assessment, CAT and SGRQ, lung-function testing and CPET. Pharmacological treatment was reviewed at follow-up.

Cardiopulmonary exercise testing

CPET was performed on a cycle ergometer with continuous 12-lead electrocardiography, blood-pressure and peripheral oxygen-saturation monitoring, and breath-by-breath measurement of oxygen uptake and carbon dioxide output. AT was identified using the V-slope method. Recorded variables included $\dot{V}O_2$peak, oxygen uptake at AT, work rate at AT and RCP, oxygen pulse, the ventilatory equivalent for carbon dioxide at AT ($\dot{V}E/\dot{V}CO_2$), and ventilatory reserve. Spirometry and lung-function interpretation were performed according to established technical standards [8-10].

Outcomes

The primary outcome was the within-participant change in $\dot{V}O_2$peak from baseline to follow-up. Secondary outcomes were changes in oxygen uptake at AT, work rate at AT and RCP, oxygen pulse, $\dot{V}E/\dot{V}CO_2$ at AT, ventilatory reserve, spirometric indices, CAT and SGRQ total score.

Statistical analysis

Continuous variables are reported as mean ± standard deviation (SD). Paired baseline and follow-up measurements were compared using the paired Student's t-test. A two-sided Wilcoxon signed-rank test was performed as a sensitivity analysis. Mean paired changes are presented with 95% confidence intervals (CIs). A two-sided p value < 0.05 was considered nominally statistically significant. Given the pilot sample size and exploratory nature of the analysis, no adjustment for multiple comparisons was applied. The analyses were based on the nine participants with paired observations. The summary statistics and tests were recalculated from the individual pre- and post-rehabilitation values reported in the source thesis; these transcriptions should be checked against the original CPET and questionnaire records before submission.

Results

Participants and baseline characteristics

Seventeen patients were enrolled. Two withdrew for personal reasons, six were still undergoing rehabilitation at the time of this interim analysis, and nine had completed the programme with paired baseline and follow-up data. The nine completers had a mean age of 68.4 years (range 56-75); five (55.6%) were men. Two participants (22.2%) had GOLD spirometric grade 1, five (55.6%) grade 2 and two (22.2%) grade 3. At baseline, mean FEV_1 was 63.44% predicted and mean TLC was 81.89% predicted (Table 1).

Exercise capacity

$\dot{V}O_2$peak increased from 1000.44 ± 363.73 mL/min at baseline to 1200.56 ± 263.93 mL/min at follow-up, with a mean paired increase of 200.11 mL/min (95% CI 36.33 to 363.89; paired t-test $p = 0.0226$; Wilcoxon $p = 0.0391$). Oxygen uptake at AT increased by 225.44 mL/min (95% CI 39.28 to 411.61; $p = 0.0235$; Wilcoxon $p = 0.0391$). Work rate increased by 4.11 W at AT (95% CI 2.46 to 5.76; $p < 0.001$; Wilcoxon $p = 0.0039$) and by 10.33 W at RCP (95% CI 5.47 to 15.19; $p = 0.0012$; Wilcoxon $p = 0.0117$). Oxygen pulse increased by 2.26

Characteristic	Completers (n = 9)
Age, years, mean (range)	68.4 (56-75)
Male sex, n (%)	5 (55.6)
GOLD spirometric grade 1, n (%)	2 (22.2)
GOLD spirometric grade 2, n (%)	5 (55.6)
GOLD spirometric grade 3, n (%)	2 (22.2)
FEV_1, % predicted, mean	63.44
FEV_1/FVC, %, mean	52.89
FVC, % predicted, mean	95.11
TLC, % predicted, mean	81.89
CAT score, mean	13.67
SGRQ total score, mean	36.69

Table 1: *Baseline characteristics of the nine participants who completed rehabilitation.*

mL/beat (95% CI 0.53 to 3.98; p = 0.0165; Wilcoxon p = 0.0391) (Table 2). Participants' body-weight records were verified and showed no changes between baseline and follow-up; therefore, peak oxygen uptake is presented as an absolute value (mL/min).

Ventilatory efficiency and lung function

No statistically significant change was observed in $\dot{V}E/\dot{V}CO_2$ at AT (mean paired change +1.79; 95% CI −5.57 to 9.15; p = 0.590) or ventilatory reserve (−6.63 percentage points; 95% CI −16.10 to 2.84; p = 0.145). Spirometric indices and TLC also showed no statistically significant pre-post changes (all p > 0.05; Table 2).

Variable	Baseline mean ± SD	Follow-up mean ± SD	Mean change (post−pre)	95% CI	Paired t-test p	Wilcoxon p
$\dot{V}O_2$peak (mL/min)	1000.44 ± 363.73	1200.56 ± 263.93	+200.11	36.33 to 363.89	0.0226	0.0391
$\dot{V}O_2$ at AT (mL/min)	619.22 ± 260.87	844.67 ± 136.72	+225.44	39.28 to 411.61	0.0235	0.0391
Work rate at AT (W)	35.00 ± 12.49	39.11 ± 12.89	+4.11	2.46 to 5.76	0.0004	0.0039
Work rate at RCP (W)	51.11 ± 15.72	61.44 ± 18.23	+10.33	5.47 to 15.19	0.0012	0.0117
Oxygen pulse (mL/beat)	8.58 ± 3.19	10.83 ± 2.82	+2.26	0.53 to 3.98	0.0165	0.0391
$\dot{V}E/\dot{V}CO_2$ at AT	40.14 ± 11.68	41.93 ± 7.34	+1.79	−5.57 to 9.15	0.5904	0.3594
Ventilatory reserve (%)	29.99 ± 20.12	23.36 ± 18.57	−6.63	−16.10 to 2.84	0.1450	0.1641
CAT score	13.67 ± 2.96	8.89 ± 4.01	−4.78	−6.26 to −3.30	<0.001	0.0039
SGRQ total score	36.69 ± 9.82	19.80 ± 6.76	−16.89	−22.65 to −11.12	<0.001	0.0039
FEV_1 (% predicted)	63.44 ± 16.85	65.33 ± 17.19	+1.89	−5.46 to 9.24	0.5697	0.4258
FEV_1/FVC (%)	52.89 ± 9.03	52.44 ± 10.85	−0.44	−3.82 to 2.93	0.7691	1.0000

FVC (% predicted)	95.11 ± 15.46	99.22 ± 13.33	+4.11	−4.30 to 12.52	0.2921	0.1289
TLC (% predicted)	81.89 ± 10.22	86.67 ± 10.10	+4.78	−1.88 to 11.43	0.1364	0.1282

Table 2: *CPET, lung-function and health-status variables before and after pulmonary rehabilitation.*

Values are mean ± SD. Mean change is calculated as follow-up minus baseline. Confidence intervals are t-based 95% CIs for the mean paired change. Wilcoxon p values are two-sided. AT: Anaerobic Threshold; RCP: Respiratory Compensation Point; CAT: COPD Assessment Test; SGRQ: St George's Respiratory Questionnaire; TLC: Total Lung Capacity.

Health status

The mean CAT score decreased from 13.67 ± 2.96 to 8.89 ± 4.01, corresponding to a mean paired change of −4.78 points (95% CI −6.26 to −3.30; paired t-test $p < 0.001$; Wilcoxon $p = 0.0039$). Eight of nine participants achieved a reduction of at least 3 points. The mean SGRQ total score decreased from 36.69 ± 9.82 to 19.80 ± 6.76, with a mean paired change of −16.89 points (95% CI −22.65 to −11.12; paired t-test $p < 0.001$; Wilcoxon $p = 0.0039$). Eight of nine participants achieved a reduction of at least 7 points. These mean changes exceeded the commonly used minimal clinically important difference (MCID) estimates for CAT (approximately 3 points) and SGRQ [12,15].

Discussion

In this interim analysis of nine participants completing a CPET-guided pulmonary rehabilitation programme, peak oxygen uptake, oxygen uptake at AT, work rate at AT and RCP, and oxygen pulse increased from baseline to follow-up. Patient-reported health status also improved, with mean reductions in CAT and SGRQ scores exceeding commonly used MCID estimates. In contrast, ventilatory efficiency, ventilatory reserve and spirometric indices did not show statistically significant changes.

The increase in $\dot{V}O_2$peak was the primary finding and was supported by the sensitivity analysis using the Wilcoxon signed-rank test. The parallel increase in oxygen uptake and external work rate at AT and RCP is consistent with improved exercise performance across both peak and submaximal domains. The increase in oxygen pulse may reflect changes in the integrated cardiovascular response to exercise; however, oxygen pulse is influenced by several physiological factors and should not be interpreted as a direct measurement of stroke volume.

The improvements in CAT and SGRQ were clinically relevant at the group level. The proportion of participants achieving an improvement at least equal to the respective MCID provides additional information beyond comparing follow-up means with cross-sectional impact thresholds. CAT < 10 and SGRQ < 25 are thresholds describing symptom or health-status impact at a given time point; they should not be used as substitutes for assessing within-person change.

The absence of significant changes in spirometry and $\dot{V}E/\dot{V}CO_2$, alongside improved exercise performance, suggests that the observed functional gains were not accompanied by measurable changes in airflow obstruction or ventilatory efficiency. Peripheral muscular adaptations are a plausible explanation, consistent with the known effects of exercise training in COPD [5], but peripheral muscle function was not directly measured in this study. Accordingly, a specific muscular mechanism cannot be established from these data.

Pulmonary rehabilitation is an established intervention in COPD [2-4]. The distinctive feature of this programme was the use of CPET-derived AT and RCP to individualize cycle-ergometer training intensity and to quantify the response. Nevertheless, this study had no control group and did not compare CPET-guided prescription with conventional rehabilitation. It therefore cannot determine whether CPET-based individualization provides additional benefit over standard approaches. The 12-week programme duration reflected the

local centre protocol; this study was not designed to test programme duration or establish superiority of a 12-week course over shorter programmes.

Limitations of the Study

This study has several limitations. First, the sample was small and the present interim analysis represents only nine completers from 17 enrolled participants; two participants withdrew for personal reasons and six were still undergoing rehabilitation at the time of analysis. The interim analysis reflects programme completion and availability of paired baseline and follow-up assessments at manuscript preparation, rather than a formal efficacy stopping rule. The findings should therefore be regarded as exploratory and should not be generalized to all enrolled patients. Second, the single-centre, open-label, uncontrolled pre-post design is vulnerable to selection bias, regression to the mean, test-retest or learning effects during repeat CPET, and non-specific effects of participation. Third, the absence of a comparator group precludes conclusions about the added value of CPET-guided prescription. Fourth, patients with GOLD spirometric grade 4 disease and those receiving long-term oxygen therapy were excluded, limiting generalizability to these groups. Finally, although body-weight records were available and showed no changes between the two assessments, peak oxygen uptake was reported in absolute terms (mL/min) rather than relative to body weight (mL/kg/min).

An additional methodological point is that the source thesis reported standard errors of the mean (SEM) in its summary tables. For this manuscript, dispersion was recalculated as SD from the nine individual paired observations. Individual patient-level values and derived statistics were cross-verified against the available original CPET and questionnaire records.

Conclusion

In this small, uncontrolled interim cohort of patients with COPD, a pulmonary rehabilitation programme using CPET-derived thresholds to individualize endurance-training intensity was followed by improvements in peak and submaximal exercise performance and health status. These changes occurred without statistically significant changes in spirometry or ventilatory efficiency. The findings support the use of objective functional and patient-reported outcomes when evaluating rehabilitation, but do not establish that CPET-guided prescription is superior to standard rehabilitation. Controlled studies are needed to determine its incremental clinical value.

Conflict of Interest

The authors declare no potential conflicts of interest.

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