Aerobic High Intensity One-Legged Interval Cycling Improves Peak Oxygen Uptake in Chronic Obstructive Pulmonary Disease Patients; No Additional Effect from Hyperoxia

Authors

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Key words

- COPD
- endurance
- reduced muscle mass
- 4 × 4 min
- V O 2peak

Abstract

The aim of the present study was to investigate whether hyperoxic aerobic high intensity one-legged interval cycling improves peak oxygen uptake (V O 2peak) compared to normoxic training in patients with severe chronic obstructive pulmonary disease, and to evaluate the acute effect of hyperoxia during one- and two-legged peak exercise testing. Twelve COPD patients were recruited to perform 3 training sessions per week for 8 weeks in hyperoxia (n = 7) or normoxia (n = 5). Each leg was trained 4 × 4 min at 85–95% of the one-legged peak heart rate. One-legged V O 2peak increased in the hyperoxia and normoxia training groups by 24 and 15% (16.1(13.2)–20.0(11.3) and 17.4(15.1)–20.0(6.7) mL·kg⁻¹·min⁻¹) respectively. The corresponding increases in V O 2peak during two-legged testing were 14% in both groups (20.1(11.5)–22.9(10.6) and 18.8(8.5)–21.4(7.3) mL·kg⁻¹·min⁻¹). There were no differences between groups from pre- to post-training. Nor were there any differences between acute hyperoxia and normoxia at the pre- or post-peak exercise test. One-legged aerobic high intensity interval cycling significantly increases V O 2peak in COPD patients. However, breathing supplemental oxygen during training or testing does not appear to improve V O 2peak above the level attained by breathing ambient air.

Introduction

Patients with chronic obstructive pulmonary disease (COPD) have an increased dead space/tidal volume ratio. This induces a ventilatory inefficiency during exercise and is one of the most important causes of decreased exercise tolerance [22]. Interval training at intensities of 85–95% of maximal heart rate has been demonstrated to be superior in increasing V O 2peak in health and disease [14, 32, 36]. Additionally, in COPD patients, high intensity training is demonstrated to be superior to lower intensities when comparing performance after a training intervention [5, 15, 17]. In COPD patients, the reduced oxygen delivery combined with decreased cardiac- and skeletal muscle function constrains the patients from training at these prolonged, lower intensities [17]. Thus, interval training might be a superior training method for COPD patients, allowing them to sustain the high intensity work [1, 2, 34, 39, 40]. Exercise that requires a reduced muscle mass, such as one-legged cycling, places less stress on the respiratory system as ventilation is decreased. This would thereby provide sufficient oxygen rich blood to the working skeletal muscles without competition from respiratory and other skeletal muscle groups [30, 31]. As demonstrated by Harms et al., [13] the increased work of breathing during maximal whole body exercise causes vasoconstriction in locomotor muscles, which compromises perfusion and V O 2. In addition, exercise that requires a reduced muscle mass results in a greater muscle specific power output than during whole body exercise. This is presumably due to greater perfusion and energy supply, accompanied by an increased shear stress, which causes the release of vasodilatory substances in the peripheral vessels of the working muscles [29, 31]. Thus, one-legged cycling allows training at a higher intensity in COPD patients [8], with significantly greater V O 2peak improvements compared with the conventional two-legged cycling [7]. Hyperoxic training in COPD patients might increase oxygen delivery to the exercising skeletal muscles and reduce ventilatory demands by improving the breathing pattern, which has been demonstrated to improve exercise tolerance [11, 12, 20, 24, 37, 38]. Hyperoxic training has also been found to
allow higher training intensities and greater exercise tolerance than normoxic training [10]. Thus, our principal aim was to investigate the effect of hyperoxia during one-legged aerobic high intensity interval training to develop exercise strategies for increasing $\dot{V}O_2^{\text{peak}}$ effectively. We hypothesised that 1) COPD patients performing one-legged aerobic high intensity interval training in hyperoxia will increase the power output and training response to a greater extent than patients training in normoxia and 2) due to a metabolic reserve capacity in the muscles oxygen consumption, acute hyperoxia will increase $\dot{V}O_2^{\text{peak}}$ compared to normoxia at pre- and/or post-test, as more oxygen is available in the vascular bed.

**Material and Methods**

**Subjects**

Nineteen COPD patients were assessed for eligibility. All were classified as having seven disease (stage III in accordance with the GOLD-guidelines (Global initiative for chronic obstructive lung disease)) [28]. According to GOLD, COPD stage III is defined by a post bronchodilator forced expiratory volume in one second (FEV$_1$) between 30% and 50% of the predicted value. Four did not meet the inclusion criteria and were therefore excluded. Fifteen were randomly assigned to the hyperoxia training group (HTG) (n=8) or the normoxia training group (NTG) (n=7). One dropped out from the HTG and two from the NTG due to hospitalisation. A flow chart of the participants is displayed in [Fig. 1](#). Patients were recruited from the Department of Pulmonary Medicine at St. Olavs University Hospital Trondheim, Norway. Inclusion criteria were: between 40–70-year-old, FEV$_1$ between 30–50% predicted and a post bronchodilator FEV$_1$/forced vital capacity (FVC) <70%. Exclusion criteria included suffering from diseases other than COPD that would compromise training and testing, and an airway infection within 4 weeks of the study. All patients had a history of cigarette smoking. Subject characteristics are listed in [Table 1](#).

**Spirometry**

Spirometric measurements were performed following recent international recommendations [21]. Measurements of pulmonary function were obtained using spirometer (MasterScreen Pneumo, Jager GmbH & CoKG, Wuerzburg, Germany) while the patients were seated. Spirometric measures were first performed without medication. Then the patient was allowed a 10 min break before a new spirometry test was performed to reveal any bronchial dilation due to the effect of medication and thereby the reversibility of bronchial constriction. The patients were instructed to refrain from using bronchodilatory medication for drug-specific time windows before testing (short lasting $\beta_2$-agonists, Ipratropium bromide, and long time lasting $\beta_2$-agonists for 6, 8, and 24 hours prior to testing, respectively). This was performed to ensure that there was no interference from the medication on the baseline values of the reversibility tests.

**Study design**

All the subjects performed an incremental $\dot{V}O_2^{\text{peak}}$ test in normoxia before and after the 8 weeks of aerobic high intensity one-legged interval cycling. To explore the physiological changes and limitations adopted with the present training intervention and the question of supply/demand limitations, the HTG performed an identical test in hyperoxia (65% oxygen and 35% nitrogen) pre- and post-training in addition to the normoxic test. The order of the normoxic and the hyperoxic test was randomised, but in all cases, the second test was performed after one day of rest. All participants were monitored during each training and testing session, and maintained their prescribed medication during the whole period. All subjects gave written informed consent prior to the study. The project was approved by the ethical committee of the Faculty of Medicine, NTNU, Trondheim, and carried out according to the declaration of Helsinki.

**Maximal graded exercise tests**

All exercise tests were performed using a Monark cycle ergometer (Electronic Ergomedic 839E, Monark Exercise AB, Sweden).

![Fig. 1 Flow chart of the participants from eligibility to analysis.](#)

| Table 1 Anthropometric and spirometric characteristics of the subjects at inclusion. |
|---------------------------------|---------------------------------|---------------------------------|
|                                | Hyperoxia training group (n=8)  | Normoxia training group (n=7)   |
| men/women                       | 2/5                             | 3/2                             |
| age (years)                     | 61 (12)                         | 61 (8)                          |
| height (cm)                     | 168 (16)                        | 171 (0.22)                      |
| body mass (Kg)                  | 73 (23)                         | 71 (45)                         |
| BMI (Kg/m$^2$)                  | 26 (8)                          | 25 (9)                          |
| FEV$_1$ (L)                     | 1.21 (0.94)                     | 1.11 (0.80)                     |
| FEV$_1$ % predicted             | 43 (14)                         | 35 (11)                         |
| FVC (L)                         | 2.40 (1.02)                     | 1.95 (1.56)*                    |
| FVC % predicted                 | 71 (14)                         | 50 (24)*                        |
| FEV$_1$/FVC                     | 50 (17)                         | 55 (18)*                        |
| SpO$_2$ (%)                     | 98 (1)                          | 98 (1)                          |

FEV$_1$, forced expiratory volume in one second, FVC, forced vital capacity, FEV$_1$/FVC; the percentage of the vital capacity which is expired in the first second of maximal expiration. Data are presented as median (range) for each variable. * Significant difference between groups at inclusion (p<0.05)
The physical test procedure started with a 10 min cycling warm-up period on the ergometer. Throughout the warm-up, work load was set so that the patients could comfortably converse with the exercise physiologist. Following this, the patients had a 3 min rest period during which the test equipment was attached. Then the subjects commenced a graded one-legged maximal exercise test using their dominant leg. Patients sat on the bike, resting their hands in their lap, with the non-working leg placed on the bike between the pedals. The test’s initial work rate was individually determined by the warm up exercise response to prevent the fitter patients from starting at too low an intensity. From the starting work rate, the intensity was increased 5 W each minute until exhaustion. The patients were allowed a 5 min cool down period of unloaded cycling followed by two hours rest, before an identical procedure using both legs was conducted. During the two-legged test, the intensity was increased 10 W each minute until exhaustion. All tests were terminated when the patient reached exhaustion or if the pedal frequency declined under 50 revolutions per minute (RPM). Heart rate, arterial oxygen saturation (SpO₂) and lactate were determined at the end of each test. VO₂, ventilation and respiratory exchange ratio were calculated as mean of the highest VO₂ values during 30 seconds of exercise. They were measured using a computerized breath-by-breath V-max spectra analyzer (SensorMedics 229 California, USA) with a three way breathing valve (Hans Rudolph model 2700 Non Rebreathing Valve) attached to the flow sensor. The hyperoxia testing protocol was identical to the protocol described for testing in normoxia. During the hyperoxia test, a cylinder containing 65 % O₂ and 35 % N₂ was connected to a plastic reservoir balloon (200 liters) and filled with 5 dl of distilled water to humidify the inspired gas. The balloon was connected to a tube and the three way valve, and attached to the flow sensor. The equipment was calibrated immediately before each test. Volume calibration was performed using a 3 L standardised calibration syringe (Hans Rudolph Jäger GmbH, Germany). The calibration was accepted within the range of ± 3 % of 3 L. Gas concentration was calibrated using precision gas mixtures. Gas one consisted of 4 % CO₂ and 16 % O₂, gas two of 24 % O₂ and gas three of 65 % O₂. All three gas mixtures were balanced with nitrogen. Gas one and two were used in calibration prior to the normoxia test, and gas one and three prior to the hyperoxia test. Immediately after the test, patients were asked to give a subjective evaluation of perceived exertion using the Borg rating scale. Volume calibration was performed using a 3 L standardised calibration syringe (Hans Rudolph Jäger GmbH, Germany). The calibration was accepted within the range of ± 3 % of 3 L. Gas concentration was calibrated using precision gas mixtures. Gas one consisted of 4 % CO₂ and 16 % O₂, gas two of 24 % O₂ and gas three of 65 % O₂. All three gas mixtures were balanced with nitrogen. Gas one and two were used in calibration prior to the normoxia test, and gas one and three prior to the hyperoxia test. Immediately after the test, patients were asked to give a subjective evaluation of perceived exertion using the Borg rating scale.

The acute response to hyperoxic testing
One legged cycling testing
At pre-test, there were no significant differences in VO₂peak or work load when comparing hyperoxia and normoxia in one-legged peak exercise testing. SpO₂ was significantly higher in hyper-
oxia compared to normoxia by 5%. The post test results also showed no significant differences in one-legged VO₂peak or work load when comparing hyperoxia and normoxia. Post test SpO₂ remained significantly higher (by 5%) in hyperoxia compared to normoxia. One-legged cycling in hyperoxia gave significant increases from pre- to post-training in VO₂peak (ml·kg⁻¹·min⁻¹) by 22%, work load by 38% and ventilation by 24%. Data are presented in Table 3.

Two-legged cycling testing
There was no significant difference between the pre-test two-legged VO₂peak values for hyperoxia and normoxia. However, hyperoxia resulted in a significantly higher work load (by 10%), respiratory exchange ratio (by 15%), SpO₂ (by 4%), and a significantly lower ventilation (by 14%) when compared to normoxia. At post test, there was no significant difference in two-legged VO₂peak between hyperoxia and normoxia. Work load, SpO₂ and heart rate were significantly higher in hyperoxia by 20, 6 and 6% respectively, whereas ventilation was 6% lower. Two-legged cycle training in hyperoxia resulted in significant increases in VO₂peak and work load from pre- to post-training by 18 and 36% respectively. Data are presented in Table 3.

Training SpO₂
The median SpO₂ during training was 99% in the HTG and 93% in the NTG. This was significantly different (p < 0.05).

Discussion
The major finding of the present study is that 8 weeks of aerobic high intensity one-legged interval cycling produced large increases in VO₂peak which were not different between groups breathing ambient air or supplemental oxygen. One-legged VO₂peak increased by 24 and 15% in the HTG and NTG, respectively, whereas two-legged VO₂peak increased by 14% in both groups.

Training response, testing in normoxia
One-legged training effect
It was hypothesised that an improved SpO₂ during training in the HTG would result in improved oxygen delivery and therefore improved aerobic energy turnover in the peripheral muscles. This in turn would result in an increased training work load and improved VO₂peak compared to the NTG [10]. Reduced pulmonary function decreases SpO₂ [23]. Thus, the discrepancy in SpO₂ can be attributed to the differences in pulmonary functions between


Table 2 Peak one- and two-legged cycling in normoxia pre- and post-training.

<table>
<thead>
<tr>
<th>VO₂peak</th>
<th>One leg cycling</th>
<th>Two legs cycling</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pre HTG</td>
<td>post HTG</td>
</tr>
<tr>
<td>L·min⁻¹</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.30 (0.68)</td>
<td>1.46 (0.58)*</td>
</tr>
<tr>
<td>ml·kg⁻¹·min⁻¹</td>
<td>16.1 (13.2)</td>
<td>20.0 (11.3)*</td>
</tr>
<tr>
<td>ml·kg⁻¹·min⁻¹</td>
<td>67.7 (48.9)</td>
<td>82.2 (41.2)*</td>
</tr>
<tr>
<td>W (watt)</td>
<td>65 (40)</td>
<td>85 (40)</td>
</tr>
<tr>
<td>VE (L·min⁻¹)</td>
<td>37.7 (20.5)</td>
<td>44.7 (17.6)*</td>
</tr>
<tr>
<td>R</td>
<td>1.05 (0.14)</td>
<td>1.05 (0.11)</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>94 (6)</td>
<td>93 (9)</td>
</tr>
<tr>
<td>HR (beats·min⁻¹)</td>
<td>156 (48)</td>
<td>163 (47)</td>
</tr>
<tr>
<td>La (mmol·L⁻¹)</td>
<td>5.00 (4.22)</td>
<td>5.36 (4.63)</td>
</tr>
<tr>
<td>Borg scale</td>
<td>16 (3)</td>
<td>17 (5)</td>
</tr>
</tbody>
</table>

VO₂peak: peak oxygen uptake, W; work load, VE; ventilation, R; respiratory exchange ratio, SpO₂; arterial oxygen saturation, HR; heart rate, La; lactate. Data are presented as median (range) for each variable. * Significant difference from pre-to post-training within groups (p < 0.05). # Significant difference from groups at inclusion (p < 0.05). " Significant difference between groups at inclusion (p < 0.05).

Table 3 One and two-legged peak exercise in hyperoxia pre and post in the HTG.

<table>
<thead>
<tr>
<th>VO₂peak</th>
<th>One leg cycling</th>
<th>Peak exercise</th>
<th>Two legs cycling</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre training</td>
<td>Post training</td>
<td>Pre training</td>
</tr>
<tr>
<td>L·min⁻¹</td>
<td>1.17 (0.81)</td>
<td>1.38 (0.48)*</td>
<td>1.44 (0.76)</td>
</tr>
<tr>
<td>ml·kg⁻¹·min⁻¹</td>
<td>15.7 (15.2)</td>
<td>19.1 (11.0)*</td>
<td>18.4 (15.2)</td>
</tr>
<tr>
<td>ml·kg⁻¹·min⁻¹</td>
<td>65.3 (57.0)</td>
<td>77.0 (37.0)*</td>
<td>79.2 (55.8)</td>
</tr>
<tr>
<td>W (watt)</td>
<td>65 (40)</td>
<td>90 (40)*</td>
<td>110 (90)*</td>
</tr>
<tr>
<td>VE (L·min⁻¹)</td>
<td>33.3 (13.1)</td>
<td>41.2 (9.7)*</td>
<td>37.0 (10.9)*</td>
</tr>
<tr>
<td>R</td>
<td>1.12 (0.40)</td>
<td>1.22 (0.49)</td>
<td>1.23 (0.41)*</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>99 (1)*</td>
<td>99 (3)*</td>
<td>99 (1)*</td>
</tr>
<tr>
<td>HR (beats·min⁻¹)</td>
<td>156 (48)</td>
<td>163 (47)</td>
<td>168 (53)</td>
</tr>
<tr>
<td>La (mmol·L⁻¹)</td>
<td>4.81 (6.51)</td>
<td>5.27 (3.30)</td>
<td>6.15 (4.10)</td>
</tr>
<tr>
<td>Borg scale</td>
<td>15 (5)</td>
<td>17 (4)</td>
<td>16 (5)</td>
</tr>
</tbody>
</table>

VO₂peak: peak oxygen uptake, W; work load, VE; ventilation, R; respiratory exchange ratio, SpO₂; arterial oxygen saturation, HR; heart rate, La; lactate. Data are presented as median (range) for each variable. * Significant difference from pre-to post-test in hyperoxia (p < 0.05). # Significant difference from hyperoxia and normoxia at pre- and post-test (p < 0.05).
the two groups. However, even though SpO$_2$ was significantly different between the two groups during training (by 99 and 93% in the HTG and NTG, respectively), the present study failed to demonstrate a higher VO$_{2peak}$ and work load in the HTG compared to the NTG after the training intervention. A possible explanation might be that when performing one-legged cycling, the working muscles were sufficiently saturated with oxygen even when breathing ambient air due to the redistribution of blood from the respiratory to the working muscles [31] and therefore the additional oxygen was redundant. Indeed, Pedersen et al. [27] demonstrated that in healthy subjects, both the diffusive and the convective oxygen transport to the muscle cell appears to be sufficient in small muscle group exercise in hyperoxia and normoxia. Furthermore, in previous studies, muscle biopsies have revealed that high intensity training increases the levels of aerobic enzymes and the capillary density of leg muscles following such training [6,17–19]. The great increases in VO$_{2peak}$ and work load in one- and two-legged cycling from pre- to post-training in the two treatment groups, indicate that such a training effect occurred in the present study. However, the supplemental oxygen does not appear to have added to this adaptive response.

**One-legged training effect on two-legged performance**

After one-legged cycling training, both groups increased VO$_{2peak}$ and work load in two-legged cycling from pre- to post-training. This is in line with Dolmage and Goldstein who showed large increases in whole body VO$_{2peak}$ after one-legged training. The increase in whole body VO$_{2peak}$ was even greater after one-legged compared to two-legged training [7]. Klausen et al. [16] demonstrated that in six young healthy subjects, leg blood flow and leg oxygen uptake were reduced during two-legged exercise compared to one-legged. Therefore, leg vascular conductance is elevated during one-legged exercise, which could account for the greater adaptive response after one-legged vs. two-legged training. The present study revealed no significant differences in VO$_{2peak}$ or work load between the two treatment groups from pre- to post-training. This is in line with other studies demonstrating no further improvements in the training effect from hyperoxic training compared to normoxia [12,33,41]. In contrast, Emtner et al. [10] found that their COPD patients could exercise at a higher intensity during hyperoxic training, and that they improved exercise capacity significantly more than the normoxia training group. However, none of their patients significantly improved VO$_{2peak}$ pre- to post-training.

**Acute response, testing in hyperoxia**

Testing in hyperoxia was performed to acutely increase SpO$_2$ and thus intracellular oxygen pressure [20]. This should increase VO$_{2peak}$ provided a muscle reserve capacity was present in the muscles during normoxic conditions. This could be expected, particularly post training as the muscular endurance capacity would be improved. Even though hyperoxia is suggested to be a vasoconstrictor in peripheral vascular beds [38], it has been demonstrated that a higher oxygen content in the arterial blood in hyperoxia counteracts the vasoconstrictor effect of oxygen [9] on the microvasculature. This might improve exercise tolerance through improvements in the delivery of oxygen to tissues [26].

**One-legged acute response**

Testing in hyperoxia did not reveal any additional effect in one-legged VO$_{2peak}$ compared to testing in normoxia pre- or post-training. SpO$_2$ was significantly higher by 5% during one-legged testing in hyperoxia compared to normoxia at both pre- and post-test. The present findings demonstrate that even with an elevated SpO$_2$ level in hyperoxia, the working muscles were acutely limited in their ability to increase VO$_{2peak}$ compared to normoxia. This might be due to an inability of the skeletal muscles to utilise the increased oxygen content in the periphery. This is in accordance with Pedersen et al. [27] who found no difference in VO$_{2peak}$ in hyperoxia compared to normoxia despite a higher plasma-to-muscle cell oxygen gradient. This implies that a peripheral limitation exists in the muscle’s ability to utilise the available oxygen. Additionally, the increased SpO$_2$ in hyperoxia compared to normoxia might not be enough to induce an acute effect on oxygen delivery to the peripheral muscles.

**Two-legged acute response**

No effect was found on VO$_{2peak}$ during two-legged testing in hyperoxia compared to normoxia, at pre- or post-test even though SpO$_2$ was significantly higher in hyperoxia on both occasions by 4 and 6%, respectively. An interesting finding is that the two-legged work load was 9 and 20% higher when testing in hyperoxia compared to normoxia at pre- and post-test, respectively. Simon et al. [35] demonstrated that despite an increased work load, peak oxygen uptake reached a plateau in some COPD patients. This indicates that the blood flow to the peripheral muscles and the oxygen extraction in the tissue were limited. The present findings might also be explained by reduced ventilation in hyperoxia allowing the patients to sustain exercise for a longer period of time without suffering from dyspnoea. Our findings are in accordance with those of Somfay et al. [38], who demonstrated that end-exercise ventilation was lower in COPD patients when 40% oxygen was respired. This might be due to oxygen’s ability to improve exercise tolerance by a carotid body inhibition that directly reduces ventilation and thereby ventilatory muscle fatigue [38]. Even though VO$_{2peak}$ increased to the same extent in hyperoxia and normoxia in the present study, the greater improvement in work load in acute hyperoxia indicates that the patients could perform a greater external work in hyperoxia. Several studies have reported increased exercise performance when testing in hyperoxia compared to normoxia [10,11,31,33,38]. Different test methods were used to establish improvements in performance, such as time to exhaustion and walking distance. The studies conclude that exercise performance is enhanced in hyperoxia, demonstrated either by an increased work load, walking distance, prolonged time to exhaustion or decreased ventilation. These training responses may be attributable to changes in the anaerobic component or work economy, and therefore might not be directly attributed to an increase in VO$_{2peak}$. The previous investigations did not measure VO$_{2peak}$ which reveals the exact rate of oxygen uptake and utilisation in the muscles during severe exercise [3]. An increased work load in acute hyperoxia compared to normoxia without any further increase in VO$_{2peak}$ confirms that a linear relationship between peak work load and VO$_{2peak}$ is not present in our study. However, the present study is in accordance with other studies demonstrating increased external work in acute hyperoxia. The superior work capacities in the present study, as well as in the other studies cannot, however, be attributed to an increased VO$_{2peak}$. Even though SpO$_2$ was significantly increased

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in hyperoxia during peak exercise testing in the HTG, no effect on \( V_{O2\text{peak}} \) compared to testing in normoxia could be demonstrated. This is contrary to the hypothesis of the present study. The results indicate that the patients were \( V_{O2\text{peak}} \) limited by the muscles ability to utilise the supplemental oxygen and thus demonstrated no peripheral muscle reserve capacity at pre- or post-test.

The results from the present study add information to the discussion of the best clinical guidelines for COPD patients and exercise. A limitation in the current study is the lack of arterial and venous oxygen pressure (\( PO_2 \)) measurements during exercise. Measures of arterial \( PO_2 \) and blood flow might have provided additional insight to the oxygen dynamics of the working skeletal muscles during small muscle mass exercise in hyperoxia and normoxia. Another limitation of the present study is different training protocols between the two groups as the pulmonary functions and \( SpO_2 \) values were significantly different. The measurement of \( PO_2 \) would have been a better method in assessing the effects of lung disease on pulmonary gas exchange than \( SpO_2 \). This is because \( SpO_2 \) would still remain above 93 %, despite a fall in arterial \( PO_2 \) to 70 mm Hg, as the \( O_2 \) dissociation curve at this point is insensitive to changes in \( PO_2 \). However, as the increase in \( V_{O2\text{peak}} \) and work load did not differ from pre- to post-training between the two groups, the heterogeneity in pulmonary function and \( SpO_2 \) does not seem to be important when it comes to one-legged training effects in the present study. The finding that hyperoxia did not increase the training effect above the level attained in normoxia is supported by the acute responses of hyperoxia during peak exercise testing in the HTG. It was demonstrated that despite a significantly higher \( SpO_2 \) in hyperoxia during peak one-legged cycling pre- and post-training, no difference in \( V_{O2\text{peak}} \) or work load was found. Thus the training intensity and thereby training effect did not increase in hyperoxia, contradicting our hypotheses. As the training was one-legged cycling, the central limitations to exercise were minimised and the muscular oxygen content might have been well preserved, even in normoxia, resulting in no hyperoxic effect. The field of rehabilitation using hyperoxic training in COPD patients needs to be further investigated with the study of muscle biopsies and the evaluation of histological and biochemistry markers.

In conclusion, the results from the present study demonstrate that 8 weeks of aerobic high intensity interval cycling alternating between legs significantly enhanced \( V_{O2\text{peak}} \) and work load in both one- and two-legged testing. There was no additional benefit of training in hyperoxia compared to normoxia. Neither did acute hyperoxia at pre- or post-tests induce any beneficial effects on \( V_{O2\text{peak}} \) compared to normoxia despite significantly higher work loads, indicating oxygen demand limitation to \( V_{O2\text{peak}} \).

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