Supplemental Oxygen and Exercise Performance in Patients with Cystic Fibrosis with Severe Pulmonary Disease

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Patients with cystic fibrosis (CF) and advanced pulmonary disease have pulmonary limitation of exercise, often associated with arterial oxygen desaturation. Improving oxygenation during exercise by providing supplemental oxygen may improve exercise performance in these patients. To test this, we performed graded exercise stress tests in 22 CF patients with severe pulmonary disease (mean PaO₂, 64±2 mm Hg [± SE]; PaCO₂, 46±2 mm Hg; RV/TLC, 57±4 percent; FEV₁, 38±4 percent of predicted; FEF₂₅₋₇₅%, 13±2 percent of predicted; median age, 26 years) and compared them to 21 controls (RV/TLC, 27±4 percent; FEV₁, 112±2 percent of predicted; FEF₂₅₋₇₅%, 80±4 percent of predicted; median age, 29 years). Each subject performed graded exercise stress tests while breathing FlO₂ of 0.21 and FlO₂ of 0.30. Subjects were blinded to the composition of the inspired gas, and the order of testing was randomized. We found that CF subjects exercised longer, had a higher maximal VO₂, higher O₂ pulse, and less arterial oxygen desaturation when receiving supplemental O₂. Control subjects exercised longer when breathing supplemental O₂ but had no significant change in maximal VO₂, O₂ pulse, or SaO₂. Both CF and control subjects had increased end-tidal PCO₂ when exercising while breathing supplemental O₂. We conclude that CF patients with advanced pulmonary disease have increased exercise tolerance and aerobic capacity when exercising while breathing supplemental O₂.

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For editorial comment see page 2

Endurance exercise in normal subjects is limited by the aerobic capacity of exercising muscles and the ability of the cardiovascular system to deliver oxygen to these muscles. The normal respiratory system has sufficient reserve so that it does not contribute to limiting exercise; however, in subjects with severe pulmonary disease such as cystic fibrosis (CF), pulmonary reserve may decrease to the point where limitation of exercise results from the inability of the respiratory system to meet increasing metabolic demands. Severe oxygen desaturation can occur during exercise in patients with chronic obstructive pulmonary disease. Similarly, many CF patients with advanced pulmonary disease develop arterial oxygen desaturation during exercise, which may exacerbate pulmonary hypertension. This has prompted some authors to recommend screening patients with exercise stress tests and restricting physical activity in those patients who develop desaturation; however, exercise has been shown to be beneficial in patients with CF. Exercise promotes deep breathing, coughing, and clearing of secre-

tions. It may also increase ventilatory muscle strength and endurance. Participation in physical activity may improve self-esteem and promote a feeling of well-being.

An alternative solution to restricting exercise would be to prevent exercise-related arterial oxygen desaturation by supplying supplemental O₂, thus enabling patients with CF to derive the benefits of exercise without the risks of hypoxemia; however, little information is available in the literature regarding the effects of supplemental O₂ on exercise in CF patients. Recently, Nixon et al studied the effects of supplemental O₂ on exercise in patients with CF. These investigators demonstrated a decrease in minute ventilation (Ve) and heart rate at maximal exercise but no change in the peak work rate or maximal oxygen consumption (VO₂) achieved. Similarly, Coates et al demonstrated a decrease in Ve but no consistent change in maximal work load achieved when CF patients exercised with supplemental O₂; however, the CF patients studied included subjects with both mild and advanced pulmonary disease. Exercise performance and exercise-related oxygen desaturation in CF correlates with the severity of the decrease in pulmonary function. Thus, the patients studied may not have been those who would benefit most from supplemental O₂.

We hypothesized that breathing supplemental O₂ during exercise would improve exercise tolerance in CF patients with severe pulmonary disease and exercise-related arterial oxygen desaturation. We therefore

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compared exercise performance while breathing FIO₂ of 0.21 and FIO₂ of 0.30 between CF subjects with advanced pulmonary disease and normal healthy controls.

**Materials and Methods**

**Subjects**

Twenty-two patients with severe CF and 21 normal age-matched controls were studied. Patients with CF were recruited from the Pulmonary Division of Childrens Hospital, Los Angeles. All patients had pulmonary symptoms, signs, and radiologic changes characteristic of CF. The diagnosis of CF was confirmed by pilocarpine iontophoretic sweat chloride determinations during childhood, which showed sweat chloride concentrations greater than 60 mEq/L. For the purpose of this study, patients were defined as having severe pulmonary disease when their resting PaO₂ was less than 70 mm Hg, when PaCO₂ was greater than 45 mm Hg, or when they had required multiple hospital admissions for pulmonary exacerbations within the preceding year. All patients received standard therapy with pancreatic enzymes and vitamins. Most patients received bronchodilators, and some patients were receiving antibiotics at the time of study. Patients were studied when clinically stable, either as outpatients or at the end of a two-week to three-week hospital admission for a pulmonary exacerbation.

Control subjects were healthy adults recruited from members of the hospital staff. No control subjects smoked, had cardiopulmonary disease, or received any medications.

Informed consent was obtained from each subject. The study was approved by the Institutional Review Board of Childrens Hospital, Los Angeles.

**Pulmonary Function Tests**

All subjects underwent pulmonary function testing in the pulmonary function laboratory of Childrens Hospital, Los Angeles, located at sea level (mean atmospheric pressure, 751 mm Hg). All measurements for each subject were performed on the same day. The vital capacity and its subdivisions were measured from a slow exhalation with a wedge spirometer (Medisecne model 3000). The FVC, FEV₁, FEF25-75%, and maximal expiratory flow-volume curves were obtained from forced expiration into the wedge spirometer. Functional residual capacity and airway resistance were measured with a body pressure plethysmograph (Sensormedics 2800 Autobox) by the methods of Dubois et al. Specific airway conductance was calculated from the simultaneously determined airway resistance and thoracic gas volume. Individual test results were analyzed and considered abnormal if they were greater than ±2 SD from available reference values.

Resting arterial blood gas levels were obtained from CF subjects only. Samples were analyzed by a blood gas analyzer (Ciba-Corning model 178).

**Exercise Testing**

Each subject performed two graded exercise stress tests on a treadmill. One test was performed with FIO₂ of 0.21 and the other with FIO₂ of 0.30. The order of testing was FIO₂ of 0.21 first in 12 CF subjects and ten controls, and FIO₂ of 0.30 first in the remaining ten CF subjects and 11 controls. The exercise equipment was calibrated separately for the two tests, and subjects rested for at least 1 h between tests. Subjects were blinded to the composition of the gas mixture being administered.

Subjects inhaled and exhaled through a mouthpiece from which inspired and expired gas concentrations were continuously analyzed with a rapid-response zirconium O₂ analyzer and infrared CO₂ analyzer by a computerized breath-by-breath system (Sensormedics 4400). Inhaled and exhaled tidal volumes were measured with a turbine digital volume transducer (Sensormedics 4400). From these, the following gas exchange parameters were measured on a breath-by-breath basis: VE; V̇O₂; carbon dioxide production (V̇CO₂); respiratory exchange ratio (R = V̇CO₂/V̇O₂); and ventilatory equivalents for oxygen (VeO₂/VO₂) and carbon dioxide (VeCO₂/VO₂). The O₂ pulse (volume of O₂ added to the pulmonary blood per heart beat) was calculated by dividing the VO₂ by the heart rate. The anaerobic threshold (AT) was determined by gas exchange criteria; specifically, the point at which ventilation increased nonlinearly with respect to VO₂, the respiratory exchange ratio increased, end-tidal O₂ tension increased, the VE/VO₂ ratio began to increase while the VE/VO₂ ratio remained constant or was falling, and VO₂ increased nonlinearly relative to VO₂. The point at which the majority of these parameters agreed was taken as the anaerobic threshold. Heart rate was continuously monitored by electrocardiogram, transcutaneous arterial O₂ and CO₂ tension (tcPO₂ and tcPCO₂) by transcutaneous electrode (Transend cutaneous gas system; Sensormedics), and SaO₂ by pulse oximeter (Nellcor Inc.).

Compressed air and a mixture of 30 percent O₂ with the balance N₂ were connected via a T-piece to a reservoir (Douglas bag; Collins), which was connected via oxygen tubing to the subject's mouthpiece. Gases were not humidified. The flow of gas to the reservoir was controlled by a one-way valve, so that subjects were unaware of which gas mixture they were receiving. Subjects breathed the gas mixture until SaO₂ and transcutaneous PaO₂ and PaCO₂ values were stable for at least 15 minutes prior to exercise. In all exercise studies, data were initially measured for 3 min at rest. Treadmill speed was then increased each minute until a speed of 7 km/h was reached, following which the grade was increased each minute until the subject could no longer exercise. Recovery data were collected for 3 min. The same protocol for increase in work load was used for all subjects and was designed in an attempt to have subjects reach near-maximal VO₂ in approximately 8 to 12 min.

All results are expressed as the mean ± SEM unless otherwise specified. Parameters were compared between groups by means of the independent t-test. Comparison of paired data on FIO₂ of 0.30 vs FIO₂ of 0.21 was performed by the paired t-test. The sex of the CF subjects vs controls was compared by χ² analysis.

**Results**

Twenty-two CF patients and 21 normal age-matched controls were studied. Clinical characteristics and pulmonary function values are shown in Table 1. The median age of the CF subjects was 26 years (range, 14 to 46 years), and the median age of controls was 29 years (range, 19 to 37 years) (NS). Seventeen (77 percent) of the CF subjects and 11 (52 percent) of the controls were male subjects (NS). The pulmonary function tests and arterial blood gas levels of the CF subjects showed severe pulmonary disease. Control subjects had normal pulmonary function.

All subjects exercised until exhaustion. In only one case was the exercise stress test terminated by the physician. In that instance, the CF subject was noted to become deeply cyanotic and develop an unsteady gait, and the test was terminated despite the subject indicating that he could continue.

Both CF subjects and controls exercised significantly longer while breathing FIO₂ of 0.30 than when breathing FIO₂ of 0.21 (Table 2). Heart rate at maximal exercise was not significantly different while breathing FIO₂ of 0.30 than FIO₂ of 0.21 in either CF subjects or controls. Heart rates in CF patients at maximal
Table 1—Characteristics of Population Studied*

<table>
<thead>
<tr>
<th></th>
<th>Cystic Fibrosis</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of subjects</td>
<td>22</td>
<td>21</td>
</tr>
<tr>
<td>Male subjects (percent)</td>
<td>17 (77)</td>
<td>11 (52)</td>
</tr>
<tr>
<td>Median age, yr (range)</td>
<td>26 (14-46)</td>
<td>29 (19-37)</td>
</tr>
<tr>
<td>Height, cm</td>
<td>170±2</td>
<td>166±3</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>55±2</td>
<td>64±4</td>
</tr>
<tr>
<td>TLC, percent of predicted</td>
<td>104±4</td>
<td>104±2</td>
</tr>
<tr>
<td>RV/TLC, percent</td>
<td>57±4</td>
<td>27±4</td>
</tr>
<tr>
<td>FEV1, percent of predicted</td>
<td>38±4</td>
<td>112±21</td>
</tr>
<tr>
<td>FEF25-75%, percent of predicted</td>
<td>13±2</td>
<td>80±41</td>
</tr>
<tr>
<td>FEV1/FVC, percent</td>
<td>54±2</td>
<td>85±11</td>
</tr>
<tr>
<td>Resting SaO2, percent</td>
<td>91±1</td>
<td>98±9</td>
</tr>
<tr>
<td>PaO2, mm Hg</td>
<td>64±2</td>
<td>NA</td>
</tr>
<tr>
<td>PaCO2, mm Hg</td>
<td>46±2</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Age expressed as median value. All other data are means ± SEM. NA, not applicable.

*p<0.05.

**p<0.001.

Exercise while breathing both FIO2 of 0.21 and FIO2 of 0.30 were significantly lower than controls, who achieved near-maximal heart rates during exercise while breathing both FIO2 of 0.21 and FIO2 of 0.30 (p<0.001 for FIO2 of 0.21 and p<0.002 for FIO2 of 0.30). The respiratory exchange ratio was 1.2 or more in both CF subjects and controls exercising while breathing FIO2 of 0.21 and FIO2 of 0.30.

All CF subjects showed arterial oxygen desaturation when exercising while breathing FIO2 of 0.21, with a mean drop in SaO2 of 12±2 percent (range, 2 to −32 percent). In contrast, SaO2 fell by only 5±1 percent (range, +1 to −13 percent) during exercise on the arbitrarily chosen FIO2 of 0.30 (p<0.001). The SaO2 values did not change significantly in controls during exercise while breathing FIO2 of 0.21 vs FIO2 of 0.30.

Maximal VO2 in CF subjects was significantly greater while breathing FIO2 of 0.30 than FIO2 of 0.21. Despite the longer duration of exercise and the higher VO2 achieved while breathing FIO2 of 0.30, there was no difference in the increase in heart rate, VE, or respiratory exchange ratio at maximal exercise. In contrast to the CF subjects, control subjects showed no consistent alteration in maximal VO2 when exercising while breathing FIO2 of 0.30 vs FIO2 of 0.21.

Maximal O2 pulse was significantly higher while breathing FIO2 of 0.30 than FIO2 of 0.21 in CF subjects, although it was still lower than the controls (p<0.02). Controls showed no change in O2 pulse when breathing FIO2 of 0.30.

The level of VO2 at which the anaerobic threshold occurred did not differ during exercise while breathing FIO2 of 0.30 or FIO2 of 0.21 in either the CF or control groups. The SaO2 at the time that the anaerobic threshold was reached was significantly higher during exercise while breathing FIO2 of 0.30 than when breathing FIO2 of 0.21 in both CF subjects (p<0.001) and controls (p<0.05).

The VE and breathing reserve (the difference between MVV and VE at maximal exercise, expressed as a percentage of MVV) at maximal exercise in CF subjects did not differ significantly when breathing FIO2 of 0.30, as compared to FIO2 of 0.21. The VE/ FVC ratio at maximal exercise did not differ significantly in CF subjects when breathing FIO2 of 0.30, as compared to FIO2 of 0.21. The VE/VO2 ratio at maximal exercise fell in the CF subjects exercising while breathing FIO2 of 0.30, as compared to FIO2 of 0.21. In control subjects, the VE and VE/FVC ratio fell and breathing reserve increased at maximal exercise when breathing FIO2 of 0.30, but VE/VO2 did not change significantly.

The VCO2 at maximal exercise in CF subjects was significantly higher while breathing FIO2 of 0.30 than when breathing FIO2 of 0.21. The VE/VCO2 ratio fell in the CF subjects exercising while breathing FIO2 of

Table 2—Results of Exercise

<table>
<thead>
<tr>
<th></th>
<th>Cystic Fibrosis</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of exercise, min</td>
<td>7.9±0.4</td>
<td>9.3±0.7</td>
</tr>
<tr>
<td>∆SaO2, percent</td>
<td>12±2</td>
<td>3±1</td>
</tr>
<tr>
<td>Maximal heart rate, beats per min</td>
<td>167±4</td>
<td>184±3</td>
</tr>
<tr>
<td>Respiratory exchange ratio</td>
<td>1.2±0</td>
<td>1.4±0</td>
</tr>
<tr>
<td>Maximal VO2, ml/kg/min</td>
<td>25±2</td>
<td>35±2</td>
</tr>
<tr>
<td>Oxygen pulse, ml per beat</td>
<td>5±1</td>
<td>13±1</td>
</tr>
<tr>
<td>AT, ml/kg/min VO2</td>
<td>17±1</td>
<td>23±2</td>
</tr>
<tr>
<td>VE, L/min</td>
<td>50±5</td>
<td>88±6</td>
</tr>
<tr>
<td>Maximal VE/FVC, percent</td>
<td>47±3</td>
<td>51±2</td>
</tr>
<tr>
<td>Breathing reserve, L/min</td>
<td>23±5</td>
<td>39±3</td>
</tr>
<tr>
<td>Maximal VE/VO2</td>
<td>38±1</td>
<td>41±2</td>
</tr>
<tr>
<td>Maximal VCO2, ml/kg/min</td>
<td>28±2</td>
<td>46±3</td>
</tr>
<tr>
<td>VE/VCO2</td>
<td>32±1</td>
<td>30±1</td>
</tr>
<tr>
<td>∆PvO2, mm Hg</td>
<td>10±1</td>
<td>5±1</td>
</tr>
<tr>
<td>∆PvCO2, mm Hg</td>
<td>6±1</td>
<td>2±1</td>
</tr>
</tbody>
</table>

Supplemental O2 and Exercise in CF Patients (Marcus et al)
0.30, as compared to FIO₂ of 0.21. Controls showed no change in either VCO₂ or \( \dot{V}E/\dot{V}CO₂ \) with FIO₂ of 0.21 vs FIO₂ of 0.30.

The PETCO₂ rose in all subjects at maximal exercise as compared to rest; however, in both CF subjects and controls, there was a greater increase in PETCO₂ during exercise while breathing FIO₂ of 0.30 than during exercise when breathing FIO₂ of 0.21. The increase in PETCO₂ during exercise while breathing FIO₂ of 0.30 was greater in the CF subjects than the controls (\( p<0.001 \)). The change in PETCO₂ from rest to maximal exercise ranged from \(-2\) to \(+17\) mm Hg (mean, \(+10.0\pm1.1\) mm Hg) in CF subjects breathing FIO₂ of 0.21 and from \(+2\) to \(+30\) mm Hg (mean, \(+16.2\pm2.2\) mm Hg) in CF subjects breathing FIO₂ of 0.30. In control subjects, PETCO₂ changes ranged from \(-2\) to \(+15\) mm Hg (mean, \(+5.1\pm1.2\) mm Hg) while breathing FIO₂ of 0.21 and from \(+1\) to \(+19\) mm Hg (mean, \(+8.1\pm1.1\) mm Hg) while breathing FIO₂ of 0.30.

No subject demonstrated arrhythmias or ST-segment changes on the ECG during exercise. When asked at the conclusion of testing, the majority of both CF and control subjects could not distinguish which test was with supplemental oxygen. The order in which testing was performed did not affect results in either CF or control subjects.

**DISCUSSION**

By design, we studied a group of CF patients with advanced pulmonary disease. The CF subjects had hypoxemia at rest, CO₂ retention, severe hyperinflation, and severe airway obstruction, indicating severe pulmonary disease.

This study confirmed that CF patients with severe pulmonary disease have decreased exercise tolerance. Exercise was abnormally limited by pulmonary mechanisms, as shown by decreased breathing reserve, CO₂ retention, and marked arterial oxygen desaturation at maximal exercise. Pulmonary limitation of exercise in the CF subjects exercising with FIO₂ of 0.21 was associated with arterial oxygen desaturation and therefore decreased O₂ delivery to and processing by the tissues. This was demonstrated by the low VO₂ and O₂ pulse at maximal exercise while breathing FIO₂ of 0.21, compared to the controls. The CF patients achieved a respiratory exchange ratio of 1.2 at maximal exercise while breathing FIO₂ of 0.21; however, maximal heart rates were not attained. Thus, these patients were limited in exercise by pulmonary mechanisms prior to cardiovascular limitation of exercise. The decreased breathing reserve with FIO₂ of 0.21 in CF patients, as compared to controls (\( p<0.02 \)), also suggests pulmonary limitation of exercise. This confirms the findings of other investigators.\(^{2-5,21}\) Additional factors, such as malnutrition with resultant loss of muscle mass, may have contributed to exercise limitation. In contrast to the CF subjects, controls achieved nearly maximal heart rates during exercise while breathing both FIO₂ of 0.21 and FIO₂ of 0.30, indicating that they exercised at or near their physiologic maximum.

Furthermore, we have shown that the administration of supplemental O₂ during exercise in CF patients with advanced pulmonary disease enables them to exercise for a longer period of time, without a concomitant increase in heart rate or \( \dot{V}E \). While breathing supplemental O₂, CF subjects had an increased maximal VO₂. While breathing supplemental O₂, CF subjects also had a decreased \( \dot{V}E/\dot{V}O₂ \) ratio at maximal exercise, indicating increased pulmonary efficiency when breathing FIO₂ of 0.30. In addition, supplemental O₂ ameliorated arterial oxygen desaturation during exercise and increased O₂ pulse. In the controls, supplemental O₂ resulted in a longer duration of exercise, a lower \( \dot{V}E \), and an increased breathing reserve, but no other changes.

Subjects with CF exercised longer while breathing supplemental O₂ than when breathing FIO₂ of 0.21. This difference is unlikely to be due to differences in effort alone. The mean respiratory exchange ratio was 1.2 for both studies, indicating anaerobic metabolism of substrate at maximal exercise. Heart rate at maximal exercise was the same for both studies. These facts suggest that motivation and effort were equivalent on both levels of FIO₂. As exercise limitation in subjects with severe pulmonary disease results from pulmonary limitation, improving oxygenation resulted in improved efficiency and improved exercise performance in these patients. Thus, CF subjects in our study had a significant improvement in maximal VO₂ while breathing supplemental O₂ and hence had a better aerobic capacity. Control subjects also exercised longer with supplemental O₂ than with FIO₂ of 0.21; however, controls did not have a higher maximal VO₂ while breathing supplemental O₂. Possible explanations include the effects of hyperoxia on pulmonary ventilation, vascular smooth muscle, and cellular metabolism.\(^{20}\) It is difficult to compare the results of this study to other studies in the literature, due to the different protocols and higher FIO₂ used in other studies.\(^{20}\)

Maximal O₂ pulse was significantly higher while breathing supplemental O₂ than when breathing FIO₂ of 0.21 in CF subjects, although it was still lower than the controls. This probably reflected the improvement in blood oxygenation but may also have been partly due to increased myocardial contractility. Controls showed no change in O₂ pulse.

The administration of supplemental O₂ to CF subjects resulted in hypoventilation relative to the metabolic load. This resulted in a decreased \( \dot{V}E/\dot{V}O₂ \) and \( \dot{V}E/\dot{V}CO₂ \) at maximal exercise while breathing supplemental O₂ as compared to FIO₂ of 0.21. The \( \dot{V}E \) at
maximal exercise in CF subjects breathing supplemental O₂ did not increase, possibly because mechanical limitation to sustained high levels of V̇E had been reached. This is supported by the fact that the CF subjects attained high V̇̇E/FVC ratios at maximal exercise while breathing either supplemental O₂ or room air. In normal subjects the V̇̇E/FVC ratio at maximal exercise reaches 45 to 58 percent.³¹ Because supplemental O₂ uncoupled tissue O₂ delivery from ventilation, maximal V̇̇O₂ was increased despite the absence of an increase in ventilation. The increased FÌO₂ may also have decreased the ventilation required for given work loads, allowing the subject to achieve a higher work load with the same maximum ventilation. In addition, the administration of supplemental O₂ may have suppressed the carotid chemoreceptor drive, resulting in a decreased V̇E for a given work load.²⁰

The CF and control subjects both demonstrated increased PETCO₂ during exercise while breathing FÌO₂ of 0.30 and FÌO₂ of 0.21, although this increase was more marked when breathing FÌO₂ of 0.30 for both groups. The PETCO₂ values during exercise increase relative to PCO₂ levels.²⁹ Thus, the PETCO₂ at maximal exercise may not reflect arterial values. In the controls, there was no significant difference in the change in the transcutaneous P₇CO₂ values during exercise while breathing FÌO₂ of 0.30, as compared to FÌO₂ of 0.21, suggesting that the controls may not have retained CO₂ during exercise; however, CF subjects had a significant increase in both PETCO₂ and P₇CO₂ during exercise while breathing FÌO₂ of 0.30 and FÌO₂ of 0.21, with the increase being more pronounced when breathing FÌO₂ of 0.30. This is similar to the findings of other investigators, who have shown that subjects with CF may have elevated PETCO₂ during exercise,²³ and that the increase in PETCO₂ is more marked when subjects exercise while breathing supplemental O₂.²⁰,²¹ In addition, Vyas et al²² demonstrated an increase in PCO₂, using indwelling arterial catheters, in patients with chronic airway obstruction during exercise while breathing supplemental O₂. A possible explanation for the CO₂ retention is that the patients had relative hypoventilation while breathing supplemental O₂, due to mechanical limitation. Another possibility is that the increased S₇O₂ in the CF subjects resulted in decreased buffering of hemoglobin and a resultant increase in F₇CO₂. The clinical relevance of this increase in F₇CO₂ is uncertain.

Previous studies in adults with chronic obstructive pulmonary disease have shown that supplemental O₂ results in increased exercise endurance,⁶,³⁵,³⁶ decreased V̇E,⁷,³²,³³ and increased maximal V̇̇O₂.²⁸ Previous studies of the effects of supplemental O₂ on exercise in CF patients have shown a decrease in V̇E and heart rate and an increase in PETCO₂ during exercise while breathing supplemental O₂.²⁰,²¹ This is consistent with our results; however, previous studies have not shown changes in the peak work rate or maximal V̇̇O₂ achieved. The difference between our study and the previous studies is that the other studied groups consisted of patients with a spectrum of severity, who generally had milder pulmonary disease than our group. It is not known whether the patients studied by Coates et al²¹ developed desaturation during exercise. As exercise performance and exercise-related oxygen desaturation in CF correlate with the severity of the decrease in pulmonary function,²,³,⁹,¹ⁱ,¹⁰,²² patients with milder pulmonary disease may not be the group that would benefit most from supplemental O₂. The CF subjects in our group all had advanced pulmonary disease (mean FEF₂₅-₇₅%, 13 percent of predicted) with marked arterial oxygen desaturation during exercise, and therefore less O₂ delivery to the tissues. This may not be true for patients with milder disease. Furthermore, the administration of an FÌO₂ of 1.0 in the study by Coates et al.²¹ as compared to the FÌO₂ of 0.30 used in our study, may have resulted in more chemoreceptor suppression and hypoventilation. Cropp et al²⁴ studied eight CF subjects during exercise with FÌO₂ of 0.21 and FÌO₂ of 0.50 and found that the administration of supplemental O₂ prevented arterial oxygen desaturation and increased the duration of exercise at 80 percent of peak work capacity. These investigators²⁴ showed that patients with the highest degree of desaturation benefited most from supplemental O₂.

Supplemental O₂ may also improve exercise tolerance by preventing hypoxic bronchoconstriction.²⁰ In addition, it may act by relieving hypoxic pulmonary artery constriction and reversing pulmonary vascular constriction.²⁰ Our study did not address these mechanisms. Submaximal exercise may be a better reflection of the activities of daily living than maximal exercise. Our study did not examine the effects of supplemental O₂ on submaximal exercise.

A regular exercise regimen is beneficial for patients with CF. Exercise may help in clearing secretions,¹⁴,¹⁸ increasing ventilatory muscle strength and endurance,¹⁶,¹⁸ and improving self-esteem.¹⁹ We have demonstrated that even CF patients with advanced pulmonary disease may exercise safely with supplemental O₂. In CF patients with advanced pulmonary disease, pulmonary limitation may be severe enough to restrict the normal activities of daily living. The provision of supplemental O₂ may increase their endurance sufficiently to enable them to carry out the activities of daily living, thus improving their quality of life.

In conclusion, we have shown that supplemental O₂ can increase exercise tolerance and aerobic capacity and can decrease exercise-related arterial oxygen desaturation. We speculate that by administering supplemental O₂ to patients with CF and advanced
pulmonary disease and thereby increasing their exercise tolerance, their quality of life can be improved.

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