Baseline Oxygen Saturation Predicts Exercise Desaturation Below Prescription Threshold in Patients With Chronic Obstructive Pulmonary Disease

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Background: Recent studies of exercise-induced hypoxemia in patients with chronic obstructive pulmonary disease (COPD) have shown that oxygen supplementation during exertion increases exercise tolerance and alleviates dyspnea. Although measurements of forced expiratory volume in 1 second and diffusion capacity for carbon monoxide (DLCO) are known to predict exercise-induced desaturation in patients with COPD, baseline oxygen saturation has never been studied as a predictor of exercise-induced desaturation.

Methods: A retrospective analysis was performed of 100 consecutive patients with forced expiratory volume in 1 second–forced vital capacity ratio of 70% or less who underwent exercise testing for desaturation. Any desaturation to 88% or less with exercise was considered significant. Nineteen patients with total lung capacity of 80% or less were excluded to avoid evaluating those with combined obstructive and restrictive defects; 81 patients remained available for study.

Results: Nineteen (51%) of 37 patients with resting saturation of 95% or less desaturated with exercise as opposed to 7 (16%) of 44 with resting saturation of 96% or greater (P = .001). The sensitivity and the negative predictive value of baseline saturation of 95% or less as a screening test for exercise desaturation were 73% and 84%, respectively. If all patients with DLCO of 36% or less were excluded, 40 patients were left for study. Eight (40%) of 20 patients with baseline saturation of 95% or less compared with 0 of 20 with resting saturation of 96% or greater desaturated with exercise (P = .006). In this subset, the sensitivity and the negative predictive value of baseline saturation of 95% or less as a screening test for exercise desaturation both improved to 100%.

Conclusions: In patients with COPD, baseline saturation of 95% or less is a good screening test for exercise desaturation, especially in patients with DLCO greater than 36%. This readily available office screening procedure merits further study in larger prospective patient cohorts.

Arch Intern Med. 2001;161:732-736

LONG-TERM oxygen supplementation is valuable therapy in the outpatient treatment of patients with hypoxemic chronic obstructive pulmonary disease (COPD). Secondary effects of persistent hypoxemia, including pulmonary hypertension and erythrocytosis, might be reversed with long-term oxygen administration. In certain populations, oxygen supplementation enhances neuropsychiatric performance and results in improved exercise tolerance. The Nocturnal Oxygen Therapy Trial and the British Medical Research Council Trial of the early 1980s established that the use of supplemental oxygen in patients with chronically hypoxic COPD reduced mortality at 1 year. Earlier studies have suggested early mortality in patients with COPD who are normoxic at rest but experience exercise desaturation. Oxygen supplementation with exertion can increase peak exercise level, decrease minute ventilation, improve exercise tolerance, decrease dyspnea, and prevent transitory increases in pulmonary arterial pressure and pulmonary vascular resistance at submaximal workloads. Previous studies have determined that baseline forced expiratory volume in 1 second (FEV₁) or diffusion capacity for carbon monoxide (DLCO) can serve as screening tests to predict which COPD patients will desaturate with exercise. These studies require a trained technician and testing in an approved pulmonary function laboratory. Baseline oxygen saturation measured by standard pulse oximetry (SpO₂) could represent a simple and readily available office screening procedure for exercise desaturation in patients with COPD. Therefore, a retrospective review of 100 consecutive patients...
PATIENTS AND METHODS

PATIENT SELECTION

A review of the database of the pulmonary function laboratory at Wake Forest University Baptist Medical Center, Winston-Salem, NC, was performed retrospectively from December 1, 1997, to October 31, 1999. Patients who had undergone exercise testing for desaturation and had spirometry with FEV₁/FVC of 70% or less were considered eligible for inclusion in this study. If lung volume measurements had also been performed, patients were excluded if total lung capacity (TLC) was 80% or less to avoid evaluating those with combined obstructive and restrictive defects. If the TLC maneuver was not done, the single-breath alveolar volume taken during DLCO measurement was used as a surrogate value for TLC. Spirometry, helium dilution lung volume, and DLCO measurements were all performed using the Collins DSPLUS system (WE Collins, Braintree, Mass). Diffusion capacity for carbon monoxide, TLC, and residual volume measurements were recorded if they had been performed, but they were not required for enrollment. The number of days between exercise testing and spirometry, lung volumes, or DLCO measurements were recorded and are presented as mean ± SEM. The predicted normal values for spirometry and lung volumes are taken from Crapo et al.; predicted values for DLCO are taken from Miller et al. Patient demographics and pulmonary function measurements are presented as mean ± SD.

EXERCISE FOR DESATURATION

Baseline SpO₂ was documented using a handheld pulse oximeter (model N-20; Nellcor Inc, Hayward, Calif) with a finger clip. All exercise testing consisted of a 6-minute walk test at a moderate pace on a flat surface performed under the supervision of a respiratory therapist while the pulse oximeter was worn by the patient. Estimated walking distance for men was calculated using the following formula: \[7.57 \times \text{height (cm)} - [5.02 \times \text{age}] - [1.76 \times \text{weight (kg)}] - 309 \text{ m.} \]

Population data were analyzed using the t test. Statistical analysis of experimental data was performed using χ² or Fisher exact testing. Discriminating cutoff values for baseline SpO₂ and DLCO were estimated by visual inspection of the data and subsequently confirmed by statistical analysis. Comparisons were made between incidence of exercise desaturation in all patients with baseline SpO₂ of 96% or greater and 95% or less. The sensitivity and the negative predictive value of baseline SpO₂ of 95% or less as a clinical screening test for exercise desaturation were calculated by standard methods. If DLCO measurements were also available, subgroup analysis was performed on patients with DLCO greater than 36%. The sensitivity and the negative predictive value of baseline SpO₂ of 95% or less as a screening test for exercise desaturation in patients with DLCO greater than 36% were also calculated. Any \( P \leq .05 \) was considered statistically significant.

RESULTS

One hundred patients with FEV₁/FVC of 70% or less who had undergone exercise testing were considered eligible for study. Ninety-two (92%) of these patients had lung volumes previously recorded (92 patients with TLC or single-breath alveolar volume 89 and residual volume). Nineteen patients with TLC of 80% or less were excluded, leaving 81 patients available for analysis. Four of these 19 patients were excluded because of single-breath alveolar volume of 80% or less. Of the remaining 81 patients, DLCO measurements were documented for 70 (86%). The study population consisted of 42 men and 39 women with a mean age of 64.2 ± 11.0 years (range, 42-84 years). The Table lists patient demographics and pulmonary function data for the entire study population and for the 2 groups with baseline SpO₂ of 96% or greater and 95% or less. Patients with resting SpO₂ of 95% or less had more severe obstructive lung disease, as documented by lower mean FEV₁/FVC (\( P = .04 \)), with a trend toward lower mean percentage of predicted FEV₁ and FVC (\( P = .13 \) and \( P = .32 \), respectively). There were no significant differences in TLC or resting DLCO. The group with baseline SpO₂ of 95% or less also exhibited lower exercise tolerance, with a mean walking distance of 297.9 ± 148.8 m compared with 374.2 ± 131.2 m in the group with baseline SpO₂ of 96% or greater (\( P = .02 \)). All pulmonary function testing was performed within a mean of 1 year of the exercise test. Twenty-six (32%) of 81 patients desaturated to 88% or less with walking. All 26 patients desaturated 4% or more from baseline values. Nineteen (51%) of 37 patients with resting saturations of 95% or less as opposed to 7 (16%) of 44 with resting saturations of 96% or greater desaturated with exercise (\( P = .001 \) (Figure 1). The sensitivity and the negative predictive value of a resting saturation of 95% or less as a screening test for exercise desaturation were 73% and 84%, respectively. Receiver operating characteristic curve analysis was used to confirm that the best combination of sensitivity and specificity occurred at a baseline SpO₂ cutoff value of 95% (Figure 2).

No patients with DLCO greater than 36% predicted and baseline saturation of 96% or greater desaturated with walking. If all patients with DLCO of 36% predicted or less were excluded, 40 patients remained for
subgroup analysis. Eight (20%) of these 40 patients desaturated to 88% or less with walking. Eight (40%) of 20 patients with resting saturation of 95% or less compared with 0 of 20 patients with resting saturation of 96% or greater desaturated with exercise ($P = .006$) (Figure 3).

The sensitivity and the negative predictive value of baseline saturation of 95% or less as a screening test for exercise desaturation in patients with DLCO greater than 36% both improved to 100%.

**COMMENT**

Chronic obstructive pulmonary disease is a worldwide health issue, affecting up to 15 million people in the United States in 1995, and is responsible for as many as 18.6 deaths per 100,000 persons.\(^2\)\(^2\)\(^3\) Over the past 3 decades, the role of long-term oxygen therapy in the outpatient setting also has become widely applied for resting hypoxemia and exercise desaturation.\(^\text{8}\)\(^\text{,12}\)\(^\text{,15}\) However, no screening test has emerged as a completely reliable predictor of which patients with COPD will desaturate during exercise and subsequently require oxygen supplementation.

Pulse oximetry is a simple, readily available office procedure that provides an accurate measure of arterial saturation at rest. However, use of pulse oximetry during exercise has been challenged as a poor measure of true arterial desaturation.\(^\text{2}\)\(^4\) Although transcutaneous oximetry might poorly correlate with co-oximetry or direct measurement of arterial oxygen tension during exercise, oximetry trends noted during exercise have been proven reliable and are used for prescription of oxygen therapy.\(^\text{2}\)\(^1\)\(^\text{,25}\) Earlier studies evaluating other physiologic variables as predictors of exercise desaturation used a decrease in $\text{SpO}_{2}$ of 2% to 4% or greater from baseline as significant.\(^\text{16}\)\(^\text{,17}\) Although such levels of desaturation might

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**Patient Demographics and Pulmonary Function Data**

<table>
<thead>
<tr>
<th>Sex, M/F</th>
<th>Total (N = 81)</th>
<th>≤96% (n = 44)</th>
<th>≤95% (n = 37)</th>
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<tr>
<td></td>
<td></td>
<td>21/23</td>
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<td>Age, y</td>
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<td>FEV₁, L</td>
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<td>FVC, L</td>
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<td>2.64 ± 0.89</td>
<td>2.44 ± 0.89</td>
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<td>FEV₁/FVC</td>
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<td>52.0 ± 13.0</td>
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<tr>
<td>TLC, % predicted</td>
<td>102.0 ± 13.7</td>
<td>102.0 ± 11.9</td>
<td>102.0 ± 15.8</td>
<td>&gt;.99</td>
</tr>
<tr>
<td>RV, % predicted</td>
<td>160.6 ± 49.3</td>
<td>152.2 ± 41.2</td>
<td>170.5 ± 56.6</td>
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<tr>
<td>DLCO, % predicted</td>
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<tr>
<td>FEV₁/FVC</td>
<td>49.4 ± 13.3</td>
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<td>43.4 ± 21.1</td>
<td>.92</td>
</tr>
</tbody>
</table>

* Data are given as mean ± SD or mean ± SEM for time intervals, except age. $\text{SpO}_{2}$ indicates oxygen saturation by pulse oximetry; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity; TLC, total lung capacity; RV, residual volume; and DLCO, diffusion capacity for carbon monoxide.
be physiologically significant and represent a poor prognostic sign, only desaturations to SpO2 of 88% or less are of interest clinically. It is this lower value that allows the physician to prescribe oxygen therapy as part of outpatient management of the patient with COPD.\textsuperscript{10,11,21}

Our retrospective cohort of 81 patients included those with documented obstructive disease. Among these patients, we found that oxygen desaturation to 88% or less with exercise tended not to occur when the patient’s baseline SpO2 was 96% or higher. This cutoff value provided sensitivity of 73% and negative predictive value of 84%. If previous DLCO measurements are known at the time of baseline SpO2 recording, patients with DLCO greater than 36% and SpO2 of 96% or greater should not require subsequent exercise testing because of the excellent sensitivity of this combination of screening variables (100%). This new screening test would allow the physician to determine which patients might need exercise testing by performing a simple office oximetry, with better sensitivity and negative predictive value than formal pulmonary function tests. When available, previous DLCO measurements will add to the sensitivity of a baseline screening oxygen saturation.

Owens et al\textsuperscript{17} first looked at various aspects of pulmonary function testing to determine whether certain variables reliably predict the development of desaturation with exercise on a cycle ergometer in patients with COPD. These data revealed that only DLCO and FEV\textsubscript{1} were reliable predictors of exercise desaturation, with a sensitivity of 68% for a DLCO less than 53% predicted and a sensitivity of 46% for an FEV\textsubscript{1} less than 53% predicted. In our cohort, a baseline SpO2 of 95% or less had a sensitivity of 73% as a predictor of exercise desaturation, higher than for either variable in the study by Owens et al.\textsuperscript{17} Desaturation of 4% or more with exercise was considered significant in the study by Owens et al\textsuperscript{17}; therefore, the published sensitivity values might have been higher if only desaturations to 88% or less were considered important. Although there was no difference in mean baseline SpO2 between the group of patients who desaturated and those who did not, a specific SpO2 cutoff value was not evaluated as a predictor for arterial desaturation with exercise in this previous cohort.

Kelley et al\textsuperscript{16} studied DLCO as a predictor of oxygen desaturation during treadmill exercise in patients with COPD as well as idiopathic pulmonary fibrosis and other restrictive disorders. This study observed that a DLCO of less than 50% predicted is highly suggestive of exercise desaturation, with a sensitivity of 89%. Desaturation was more closely associated with reduced DLCO than with reduced resting oxygen saturation.\textsuperscript{16} However, these authors considered desaturation of 2% or higher from initial baseline SpO2 as significant. Using this cutoff value for exercise desaturation, a baseline SpO2 of 95% or less was not a good screening value for a decrease in arterial desaturation with exercise. Reevaluation of these data, considering only desaturation values of 4% or greater as significant, reveals that 9 (12%) of 78 patients with baseline SpO2 of 96% or greater as opposed to 16 (64%) of 25 with baseline SpO2 of 95% or less desaturated with exercise (\(P = .001\)). The sensitivity and the negative predictive value of a baseline SpO2 of 95% or less as a screening test for exercise desaturation in this reevaluation are then 64% and 89%, respectively, comparable to the sensitivity values for DLCO and FEV\textsubscript{1} from the study by Owens et al.\textsuperscript{17} The sensitivity value of 89% for DLCO derived by Kelley et al\textsuperscript{16} might be overestimated as the inclusion of patients with restrictive pulmonary diseases in the study group favored an increase in the sensitivity of DLCO as a screening test because many patients with some restrictive disorders exhibit low resting DLCO and severe exercise desaturation despite high SpO2 at rest. Data from the trial by Kelley et al\textsuperscript{16} did not allow post hoc subgroup analysis of patients with COPD alone.

In conclusion, our retrospective data suggest that routine baseline SpO2 measurement may be a good screening test for the likelihood of exercise desaturation in patients with COPD. All patients in our study had documented obstructive disease alone, with FEV\textsubscript{1}/FVC of 70% or less and TLC greater than 80%. When only desaturation to 88% or less is considered significant, baseline SpO2 of 96% or greater provides similar screening sensitivity as previously studied measures of pulmonary function such as DLCO and FEV\textsubscript{1}. Baseline SpO2 of 96% or greater may provide sufficient sensitivity to forgo exercise testing in patients with COPD, especially in those who have previously documented DLCO greater than 36%. These results merit further study in a larger prospective patient cohort.

Accepted for publication September 21, 2000.


We thank David Bowton, MD, for his suggestions on statistical analysis and the employees of the pulmonary function laboratory at Wake Forest University Baptist Medical Center for their assistance in acquisition of patient data.
REFERENCES


