Predictors of Oxygen Desaturation During Submaximal Exercise in 8,000 Patients*

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Study objectives: To determine predictors of oxygen desaturation during submaximal exercise in patients with various lung diseases.

Design and setting: This retrospective case series used pulmonary function laboratory results from all patients referred to a major tertiary-care center.

Patients and measurements: All patients ≥ 35 years old who underwent spirometry, diffusing capacity of the lung for carbon monoxide (DLCO), lung volumes, and pulse oximetry during 3-min submaximal step-test exercise during 1996 were included (4,545 men and 3,472 women). Logistic regression models, correcting for gender, age, and weight, determined the odds ratios (ORs) for oxygen desaturation of ≥ 4% during exercise for each category of lung function abnormality (compared to those with entirely normal lung function).

Results: Approximately 74% of the patients had airways obstruction, while only 5.6% had restriction of lung volumes. One third of those with obstruction had a low DLCO, compared to 56% with restriction, while 2.7% had a low DLCO without obstruction or restriction. The risk of oxygen desaturation during submaximal exercise was very high (OR, 34) in patients with restriction and low DLCO (as in interstitial lung disease) and in patients with obstruction and low DLCO (as in COPD; OR, 18), intermediate (OR, 9) in patients with only a low DLCO, and lowest in those with a normal DLCO (OR, 4 if restricted; OR, 2 if obstructed). A cut point of DLCO < 62% predicted resulted in 75% sensitivity and specificity for exercise desaturation. No untoward cardiac events occurred in any patients during or following the submaximal exercise tests.

Conclusions: The risk of oxygen desaturation during submaximal exercise is very high in patients with a low DLCO. Submaximal exercise tests are safe, even in elderly patients with heart and lung diseases.

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Key words: asthma; chronic bronchitis; emphysema; interstitial lung diseases; oximetry; oxygen desaturation; pulmonary function tests; submaximal exercise

Abbreviations: CI = confidence interval; DLCO = diffusing capacity of the lung for carbon monoxide; LLN = lower limit of the normal range; OR = odds ratio; PFT = pulmonary function test; SpO₂ = pulse oximetric saturation; TLC = total lung capacity

The most common functional impairment in patients with all types of lung diseases is impaired gas exchange. In the early stages of many lung diseases, oxygen saturation is maintained at rest, but when the lung is challenged with increasing demand (exercise), oxygen desaturation may occur. Many previous investigators have studied the predictors of oxygen desaturation during maximal exercise in patients with COPD. However, these studies included only patients with one type of lung disease, so the relative risk of oxygen desaturation for the common categories of lung disease could not be directly compared. Prior studies also did not include relatively healthy persons of the same age range as the patients with lung disease. The purpose of our study was to make such comparisons. Previous studies included only a small number of patients, and their recruiting methods and inclusion and exclusion criteria make it unlikely that their sample is representative of patients seen in a tertiary-care setting.

A maximal exercise test using a treadmill or bicycle ergometer, as used by previous studies, is time-consuming, expensive, risky, and often not easily available. Therefore, we used a simple 3-min submaximal exercise test that is easily and quickly done...
with minimal equipment (a step, a metronome, and a pulse oximeter) in the outpatient setting.

Materials and Methods

The study population included all patients > 35 years old who were referred to the Mayo Clinic pulmonary function laboratory in Rochester, MN, during the calendar year 1996. Those who did not complete all tests (spirometry, static lung volumes, diffusing capacity of the lung for carbon monoxide [DLCO], and pulse oximetry during exercise) were excluded.

Oxygen saturation was estimated at rest and during submaximal exercise using the finger probe of a pulse oximeter (Biox; model 3740; Boulder, CO). The unit was configured to display the average pulse oximetric saturation (SpO2) and pulse rate from the average during the previous 10 s. SpO2 and pulse rate were recorded from the display after 1 min of rest. The patient was then instructed to step up and down for 3 min to the beat of a metronome (set at 60 beats/min). The finger probe was attached to the index finger of the left hand, using a strain relief loop attached with adhesive tape to the forearm. The patient avoided undue motion or fist clenching of the left hand during the exercise, in order to minimize oximeter motion artifact. A 9-inch-high step with a handrail on the right side was used. SpO2 and pulse rate were again recorded immediately before the end of the exercise period.

Spirometry, lung volumes, and DLCO were measured using a system (models 1070 and 1085; Medical Graphics; St Paul, MN) with a body plethysmograph to measure static lung volumes,¹³ according to methods that met or exceeded American Thoracic Society recommendations.¹⁴,¹⁵ Mean reference values (predicted values based on gender, age, and height) and lower limits of the normal range (LLNs) for FEV1, FVC, total lung capacity (TLC), and DLCO were all obtained from the same population-based sample of healthy adult, never-smoking residents from the state of Michigan.¹⁶–¹⁸ We defined (interpreted) common patterns of pulmonary function abnormalities as recommended by the American Thoracic Society:¹⁹ obstruction was defined as FEV1/FVC and FEV1 both below LLN, and restriction and was defined as TLC below the LLN (without obstruction). Subcategories of obstruction and restriction had low DLCO vs DLCO above the LLN. Another category was isolated low DLCO (without obstruction or restriction). The “normal” lung function comparison group included patients without any of the above abnormality patterns. If the patient had anemia, the DLCO was corrected for the most recently measured hemoglobin level.

Analysis

We chose to define oxygen desaturation during exercise as a decrease in SpO2 of ≥ 4% (exercise minus resting), and used this categorical desaturation variable as the dependent (outcome) variable. Multiple logistic regression was used to determine the odds ratio (OR) for the association of oxygen desaturation with each category of lung function abnormality. These models also included the factors known to influence desaturation: age, gender, weight, and height. Log-likelihood ratio tests were used to determine the significance of interaction terms. The final model was determined by stepwise logistic regression, beginning with all main effect variables, then the interaction terms of obstruction and low DLCO, restriction and low DLCO, and gender interactions. Determination of the combined effect of obstruction and low DLCO, and restriction and low DLCO was done by linear combination and verified by manual calculation or the unadjusted OR in each specific subgroup of the population. The fit of these logistic models was determined by the Hosmer-Lemeshow goodness-of-fit test, and logistic regression models were then done using software (Stata Statistical Software, release 6.0; College Station, TX).²⁰

Results

About 16,000 adult patients aged 36 to 95 years underwent testing by 16 technicians during the 1996 calendar year, which included 4,545 men and 3,472 women who completed all four types of lung function tests (n = 8,017). About half of the patients were elderly (> 65 years old). Table 1 presents their mean age, body mass index, and lung function results, stratified by gender. Some patients had improved oxygen saturation during exercise (the normal response of healthy persons), while others experienced oxygen desaturation (Fig 1). DLCO and exercise-induced desaturation were highly correlated (Fig 2).

Three fourths of the patients (n = 5,926) had obstruction, while one third of these patients also had a low DLCO (Table 2). Of the patients categorized with obstruction, 514 also had restriction (a low TLC). Only about 5.6% of the patients had restriction (a low TLC without obstruction, n = 450), while 55.6% of those patients had a low DLCO. Only 3% of the patients had an isolated low DLCO (n = 192). The reference category included 1,449 patients with entirely normal lung function. Overall, 12.6% of the patients experienced oxygen desaturation during the submaximal exercise.

All five categories of pulmonary function test (PFT) result abnormalities were statistically significant independent predictors of an increased risk of oxygen desaturation during exercise (Table 2). Patients with restriction and a low DLCO (often due to an interstitial lung disease) were 34 times as likely as those with normal PFT results to experience oxygen desaturation during submaximal exercise. Those with obstruction and a low DLCO (usually due to COPD) were 18 times more likely have desaturation.

Gender Differences

In the preliminary gender-specific models (controlling for age, weight, and height), the ORs for

Table 1—Lung Function Test Results*  

<table>
<thead>
<tr>
<th>Variables</th>
<th>Women (n = 3,472)</th>
<th>Men (n = 4,545)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>64.6 (12)</td>
<td>66.7 (11)</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.2 (6.7)</td>
<td>28.1 (5.8)</td>
</tr>
<tr>
<td>TLC, L</td>
<td>4.93 (1.05)</td>
<td>6.90 (1.50)</td>
</tr>
<tr>
<td>FVC, L</td>
<td>2.27 (0.63)</td>
<td>3.36 (0.91)</td>
</tr>
<tr>
<td>FEV1, L/min</td>
<td>1.51 (0.55)</td>
<td>2.06 (0.78)</td>
</tr>
<tr>
<td>DLCO, mm CO/min/mm Hg</td>
<td>16.9 (5.54)</td>
<td>21.9 (7.75)</td>
</tr>
</tbody>
</table>

*Data are presented as mean (SD); BMI = body mass index.
exercise desaturation were similar for men and women in those with airways obstruction (within both categories of normal and low DLCO). However, for patients with an isolated low DLCO, the ORs for men to have desaturation was higher than for women (OR, 10.2 vs 8.5, respectively). The gender-interaction term was statistically significant in the combined model, showing that men in this category were about 1.4 times more likely to experience desaturation than women (95% confidence interval [CI], 1.1 to 1.8). Men with restriction but a normal DLCO (usually a chest-wall abnormality) were about twice as likely as women in this category to have desaturation in gender-specific models, but the gender-interaction term in the combined model was not significant. In addition, women with restriction and a low DLCO (usually due to an interstitial lung disease) were about twice as likely as men in this category to experience desaturation, but the gender-interaction term in the combined model was not significant.

**Predictive Power of DLCO**

The power of DLCO to predict exercise-induced oxygen desaturation was determined by calculating the receiver-operator characteristic. The DLCO was corrected for age, gender, and height by expressing DLCO as a percentage of the predicted value, using the reference equations of Miller et al.\(^\text{16}\) Maximal sensitivity and specificity were determined for all patients (n = 8,017), for those with obstruction (n = 5,926), and for those with restriction (n = 450). The optimal cut points for these three groups were 61.6%, 59.7%, and 54.3% predicted DLCO, respectively. Both sensitivity and specificity for predicting exercise-induced desaturation, using these cut points, were about 75% for each group of patients.

**Discussion**

It is not surprising that patients with interstitial lung disease or COPD are much more likely than persons with normal lung function to experience oxygen desaturation during exercise. Our results are consistent with previous studies that showed that a low DLCO was the strongest predictor of oxygen desaturation (a decrease in PaO\(_2\) or an increase in alveolar-arterial oxygen pressure gradient) during maximal exercise both in patients with COPD\(^9\) and interstitial lung disease.\(^8\)

Patients with normal pulmonary function were unlikely to have oxygen desaturation during submaximal exercise (only 7%). In our 3-min submaximal exercise tests, a low DLCO was a strong predictor of oxygen desaturation, both in those patients with airways obstruction and those with restriction of lung volumes. The ability of all of the preexercise test factors to predict oxygen desaturation during submaximal exercise in any category of abnormal lung function was moderate. The best threshold for predicting oxygen desaturation during exercise without regard to type of lung disease in our study was a DLCO < 62% of predicted, resulting in both a sensitivity and a specificity of about 75%. In a study of patients with interstitial lung diseases, Risk and coworkers\(^8\) found that 74 of 79 patients whose DLCO was < 50% predicted experienced a moderate-to-severe increase in alveolar-arterial oxygen pressure gradient during exercise (> 35 mm Hg), compared to 26 of 94 patients with a DLCO > 70% predicted. However, Kelley and coworkers\(^3\) found that patients with interstitial lung diseases whose DLCO was > 60% of predicted never experienced exercise-induced oxygen desaturation.
Table 2—The Prevalence of Pulmonary Function Abnormalities by Category, and the ORs (Obtained by Logistic Regression) for Predicting Exercise-Induced Oxygen Desaturation*

<table>
<thead>
<tr>
<th>Variables</th>
<th>Desaturated/Total, No.</th>
<th>Desaturated, % of Patients (95% CI)</th>
<th>Odds Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Restriction and low DLco</td>
<td>184/250</td>
<td>73.6 (68–78)</td>
<td>34.1 (24.7–47.1)</td>
</tr>
<tr>
<td>Obstruction and low DLco</td>
<td>107/1,965</td>
<td>5.4 (4.5–6.5)</td>
<td>17.7 (13.8–22.7)</td>
</tr>
<tr>
<td>Only low DLco, men</td>
<td>40/107</td>
<td>37.4 (28–47)</td>
<td>10.2 (8.2–12.6)</td>
</tr>
<tr>
<td>Only low DLco, women</td>
<td>28/85</td>
<td>32.9 (23–44)</td>
<td>8.5 (7.1–10.2)</td>
</tr>
<tr>
<td>Restriction (normal DLco)</td>
<td>43/200</td>
<td>21.5 (16–28)</td>
<td>4.0 (3.0–5.3)</td>
</tr>
<tr>
<td>Obstruction (normal DLco)</td>
<td>506/3,961</td>
<td>12.8 (12–14)</td>
<td>2.1 (1.7–2.5)</td>
</tr>
<tr>
<td>Normal lung function</td>
<td>100/1,449</td>
<td>6.9 (5.7–8.3)</td>
<td>1.00</td>
</tr>
<tr>
<td>Totals</td>
<td>1,008/8,017</td>
<td>12.6</td>
<td></td>
</tr>
</tbody>
</table>

*Desaturation is defined as patients within each row of PFT-abnormality category who experienced oxygen desaturation (≥ 4% fall in \( \text{SpO}_2 \)) during submaximal exercise.

In a study of 48 patients with moderate-to-severe COPD, Owens and coworkers found that a cut point of > 55% predicted DLco had 82% specificity and 100% specificity for excluding exercise-induced desaturation. Therefore, if a patient’s DLco is below approximately 70% of predicted (using modern DLco techniques and reference equations) and knowledge of oxygen desaturation during submaximal exercise (of the type and duration often encountered by the patient) would affect their therapy, then a submaximal exercise test (6-min walk or shuttle walking test with pulse oximetry) or a maximal exercise test should be done.

Safety

There were no worrisome complications (side effects) of these 3-min step tests, despite half of the patients being elderly, with a relatively high prevalence of cardiovascular disease. No patients have had syncope or cardiovascular collapse related to > 100,000 such tests done at this location during the 1980s and 1990s. Although physicians and equipment for cardiopulmonary resuscitation are available in the pulmonary function laboratory, they have not been needed to treat complications from this submaximal exercise test. Our rationale for not performing ECG monitoring during this test is that all of the patients who perform this test ambulate to the testing area, often using the stairs, without ECG monitoring. If we were to perform ECG monitoring, we would be obliged to train the technicians to recognize and respond to changes in the ECG during the test, and the testing time would be more than doubled, due to the need to place and remove the monitoring electrodes.

Type of Lung Disease

The pulmonary function abnormality categories are strongly associated with types of lung disease.

The obstruction category with low DLco is usually associated with COPD (specifically emphysema) due to cigarette smoking. Obstruction with a normal DLco may be due to asthma or chronic bronchitis. Restriction with a low DLco (and without obstruction) is often associated with an interstitial type of lung disease. Restriction with a normal DLco is usually due to one of many types of extrapulmonary disorders that limit the depth of inhalation. An isolated low DLco (without obstruction or restriction, and after correcting for anemia) is often associated with a pulmonary vascular disease, or an early interstitial lung disease (which has not yet lowered the TLC to below the LLN for that patient).

Study Limitations

A limitation of our classification scheme is that the PFT abnormality classification groups include more than one type of lung disease. Many of the patients were undergoing diagnostic workups when their PFTs were ordered; they were merely asked if they knew their diagnosis at the time of testing, and we did not use this information. Also, we did not ask permission to later take data from their medical charts, so we lack an International Classification of Diseases-type of discharge diagnosis. Although the sample is very large and all patients tested during a 12-month period were included, this group of patients may not be representative of patients seen by physicians seen in other settings and geographic areas. As demonstrated by their 7% rate of exercise-induced desaturation, our reference group includes a few patients with diseases that cause oxygen desaturation during exercise, such as cardiovascular diseases or circulatory shunts. Therefore, they are not the ideal reference group. However, some of the falls in \( \text{SpO}_2 \) during exercise in this group were probably due to both measurement errors and the choice of a 4% cut point used to define desaturation.

Many first-generation and second-generation
pulse oximeters are known to be relatively sensitive to motion artifact during exercise, often leading to underestimation of \( \text{SpO}_2 \) during exercise.\(^{21–23}\) The technicians in our study noted the \( \text{SpO}_2 \) display at the end of the exercise period and recorded the value that seemed stable for about 5 s. It is unlikely that they were biased by knowledge of the patients’ working diagnosis or spirometry results when they estimated the end-of-exercise \( \text{SpO}_2 \), so the ORs that we report were probably not altered by inaccuracy of the pulse oximeters.

References

20. Stata statistical software, release 6.0. College Station, TX: STATA Corporation, 1999