A 6MWT index to predict O₂ flow correcting exercise induced SpO₂ desaturation in ILD

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Interstitial lung disease; 6-min walk test; Oxygen therapy; Exercise testing

Summary
Introduction: Ambulatory oxygen (O₂) is prescribed to interstitial lung disease (ILD) patients with mild hypoxemia, breathlessness and dyspnea on exertion. Oxygen titration is generally done with the 6 minute walk test (6MWT) to determine the O₂ flow preventing oxygen saturation by pulse oximetry (SpO₂) from falling below 88%. His study was designed to generate a 6MWT index predicting the O₂ flow allowing completion of the 6MWT without oxygen desaturation.

Methods: Oxygen titration data from a group of 66 ILD patients and 30 controls, were used to generate the algorithm determining an index (O₂-GAP) predicting oxygen flow required to complete a 6MWT without desaturation below 88%. This index was validated in a group of 93 ILD patients.

Results: The O₂-GAP index, as obtained from the derivation population, \( r^2 = 0.97, p < 0.001 \) was shown to correctly predict the oxygen flow required to complete the 6MWT without SpO₂ falling below 88% validated in the validation population \( r^2 = 0.842; p < 0.001 \).
Introduction

The use of long-term oxygen therapy (LTOT) effectively improves disease symptoms and prolongs survival in chronic obstructive pulmonary disease (COPD) patients with severe hypoxemia (resting PaO2 on room air < 55 mmHg) [1–3]. However, oxygen is also administered to individuals with moderate hypoxemia at rest for relief of breathlessness, either as short-burst oxygen therapy or as ambulatory oxygen therapy given during activities of daily living or exercise. Although its efficacy in ameliorating both breathlessness and exercise endurance is supported by a number of studies, there are no data showing that it prolongs survival [4–7].

In patients with interstitial lung diseases (ILDs), a large group of pulmonary disorders classified together because of similar clinical, roentgenographic and physiologic features, gas exchange worsening with exercise is recognized as a central feature in disease pathophysiology [8,9]. The Royal College of Physicians guidelines recommend LTOT in ILD patients with PaO2 below 60 mmHg and also advise to prescribe oxygen to those patients who experience oxygen saturation by pulse oximetry below 90% during a walk test on room air [10]. Oxygen therapy has also been recently recommended by the American Thoracic Society (ATS)/European Respiratory Society (ERS)/Japanese Respiratory Society (JRS)/Latin America Thoracic Association (ALAT) idiopathic pulmonary fibrosis (IPF) guidelines for diagnosis and management, based upon physiological reasons, extrapolation from data in COPD and ethical concern over withholding oxygen therapy [9].

In this regard, ambulatory oxygen therapy has in fact been shown to improve exercise capacity in the 6 minute walk test (6MWT) in IPF patients [11] and a recent retrospective study on ILD patients including a majority of patients with IPF, showed that ambulatory oxygen improves patient performance in the 6MWT and ameliorates breathlessness [12].

A number of exercise tests have been used to evaluate the efficacy of ambulatory and short-burst oxygen supplementation, including the treadmill, cycle ergometry and the 6MWT, with a variety of oxygen supplementation devices [13]. Overall, these studies have shown that the use of ambulatory oxygen reduces exercise induced breathlessness, may speed up recovery from breathlessness and improves exercise capacity [7]. Generally, the amount of supplemental oxygen needed to compensate for exertional hypoxemia is determined by repeating the 6MWT at different oxygen flow rates in order to identify the lowest oxygen flow rate needed to maintain oxygen saturation by pulse oximetry above 88% [5,9,14,15]. Oxygen titration though, a time consuming procedure, is taxing for the dyspneic patient. The aim of this study was to develop and validate a 6MWT index, obtained from a single test performed on room air, capable of predicting the flow of ambulatory oxygen needed to complete the test while maintaining oxygen saturation by pulse oximetry (SpO2) equal or above 88%, without the need of repeated testing using increasing oxygen flow rates.

Material and methods

Design of the study

The study was designed to generate an algorithm to predict the flow of supplemental oxygen [in liters per minute (l/min) to be administered through a nasal cannula] required to maintain oxygen saturation by pulse oximetry equal or above 88% during the 6MWT in ILD patients, as monitored by pulse oximetry. To this end, a group of 66 individuals with ILD and from 30 subjects without cardiopulmonary disease, were evaluated at the pulmonary function testing laboratory (PFT lab) of the Respiratory Diseases Unit of the Tor Vergata University Hospital, Rome. The algorithm hitherto derived was prospectively validated in a group of 93 ILD-affected individuals.

The oxygen supplementation estimated by the algorithm was defined as "O2-GAP index" so that when the 6MWT is carried out on room air, the "O2-GAP index" indicated the flow of supplemental oxygen required to maintain oxygen saturation by pulse oximetry equal to or above 88%. When the 6MWT was performed by patients already on supplemental oxygen, the "O2-GAP index" indicated the extra flow of oxygen required to complete the test.

The study was approved by the Independent Ethics Committee of the Tor Vergata University Hospital (Rome, IT) and was conducted in accordance with the Declaration of Helsinki (number: 156/12).

Derivation population

A population of 96 subjects was evaluated between October 1, 2008 and December 31, 2009. It was comprised of 66 ILD-affected individuals, referred for dyspnea on exertion, and 30 non ILD-affected subjects as the control group, with pulmonary function tests within normal range and no apparent clinico-radiological signs of cardiopulmonary disease, who were referred for perceived breathlessness that resulted imputable to deconditioning, metabolic causes (obesity) or anxiety. The ILD patient group was comprised of 30 individuals with IPF, nine with non specific interstitial pneumonia (NSIP), nine with sarcoidosis, four with cryptogenic organizing pneumonia (COP), three with hypersensitivity pneumonitis (HP), one with berylliosis, two with undifferentiated connective tissue disease, one with rheumatoid arthritis (RA), one with histiocytosis-X (HX), one with lymphangioleiomyomatosis (LAM), one with neurofibromatosis, and two with scleroderma. All subjects underwent pulmonary function testing and the 6MWT. Individuals whose oxygen saturation by pulse oximetry fell below 88% during the test underwent oxygen titration, as described in the 6MWT Section. The demographic, biological, pulmonary function and echocardiographic characteristics of the derivation population are shown in Table 1.
Table 1 Subjects’ characteristics of the derivation population.

<table>
<thead>
<tr>
<th></th>
<th>Control group (n = 30)</th>
<th>ILD (n = 66)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, n (%)</td>
<td>19 (63)</td>
<td>36 (55)</td>
</tr>
<tr>
<td>Age, yrs (a)</td>
<td>67 ± 12</td>
<td>69 ± 10</td>
</tr>
<tr>
<td>Height, cm (b)</td>
<td>165 ± 11</td>
<td>162 ± 9</td>
</tr>
<tr>
<td>Weight, kg (b)</td>
<td>80 ± 17</td>
<td>76 ± 13</td>
</tr>
<tr>
<td>Body mass index, kg/m² (a)</td>
<td>29 ± 5</td>
<td>29 ± 5</td>
</tr>
<tr>
<td>FEV₁, %PR (a)</td>
<td>100 ± 15</td>
<td>81 ± 23**</td>
</tr>
<tr>
<td>FVC, %PR (a)</td>
<td>98 ± 22</td>
<td>81 ± 24**</td>
</tr>
<tr>
<td>FEV₁/FVC, % (a)</td>
<td>79 ± 7</td>
<td>77 ± 19</td>
</tr>
<tr>
<td>TLC, %PR (a)</td>
<td>98 ± 15</td>
<td>75 ± 19**</td>
</tr>
<tr>
<td>RV, %PR (a)</td>
<td>101 ± 28</td>
<td>75 ± 22**</td>
</tr>
<tr>
<td>DLCO, %PR (a)</td>
<td>79 ± 16</td>
<td>48 ± 22**</td>
</tr>
<tr>
<td>6MWT-distance, %PR (a)</td>
<td>89 ± 28</td>
<td>72 ± 27**</td>
</tr>
<tr>
<td>SpO₂ at rest, % (a)</td>
<td>97 ± 2</td>
<td>95 ± 2**</td>
</tr>
<tr>
<td>6MWT SpO₂ nadir, % (a)</td>
<td>95 ± 2</td>
<td>85 ± 6**</td>
</tr>
<tr>
<td>PAPs, mmHg (a,b)</td>
<td>N/A</td>
<td>39 ± 12</td>
</tr>
</tbody>
</table>

BMI: body mass index; FEV₁: forced expiratory volume in 1 s; FVC: forced vital capacity; TLC: total lung capacity; RV: residual volume; DLCO: diffusing lung capacity for carbon monoxide; 6MWT: six minute walk test; PAPs: systolic pulmonary artery pressure; N/A: not available.

(a) Mean ± SD (T test, **p < 0.01).
(b) Data refer to 20 patients.

Validation population

To validate the algorithm determining the O₂-GAP index, a population of 93 ILD-affected individuals undergoing exercise testing with the 6MWT was prospectively evaluated. They were 37 individuals with IPF, 20 with NSIP, 15 with sarcoidosis, five with COP, four with HP, two with berylliosis, two with undifferentiated connective tissue disease, three with RA, two with scleroderma, one with chronic eosinophilic pneumonia, one with BX, and one with amiodarone induced fibrosis. The demographic, biological, pulmonary function and echocardiographic characteristics of the validation population are shown in Table 2.

All subjects performed the 6MWT on room air using a portable device with pulse oximeter capability (Spirodoc, MIR, Rome, Italy) carrying the O₂-GAP determining algorithm in its electronic memory (International Patent – PCT/ IT2010/000361) [16]. In those individuals whose oxygen saturation by pulse oximetry would fall below 88% during the test, the 6MWT was repeated to validate the O₂-GAP index obtained at the end of the test on room air, by determining the flow of supplemental oxygen needed to complete the test without oxygen desaturation.

Pulmonary function testing

Complete pulmonary function testing (PFT), including forced vital capacity (FVC) and diffusing lung capacity (DLCO), determined with the single breath technique, was carried out according to the ATS guidelines [17] on a Master Screen Body PFT (Jaeger, Würzburg, Germany) using European Coal and Steel Community reference spirometric values [18]. All subjects had PFTs within a week of the 6MWT. In addition, a subpopulation of study subjects underwent echocardiographic estimate of systolic pulmonary artery pressure.

Six minute walk test

The 6MWT was performed in a 30 m, straight indoor hallway in accordance with the ATS guidelines [19]. All patients included in the derivation and the validation populations were tested under standardized conditions by trained operators. Heart rate and oxygen saturation were measured at rest (baseline), every minute during the test and at the end of the test until recovery. A Nellcor N-20PATM Handheld Pulse Oximeter (Nellcor BS; Nellcor, Hayward, CA) was used in the derivation population and a Spirodoc (MIR, Rome, Italy) in the validation population. The algorithm was loaded onto the latter pulse oximetry device (Spirodoc, MIR, Rome, Italy, patent pending) for use with the validation population.

Supplemental oxygen was administered through a nasal cannula, using commercially available integrated E-cylinder, valve and regulator device (Rivoira, Milan, Italy) carried by the patient as per guideline recommendations [19]. Oxygen titration was carried out according to Leach RM et al. [5], with sequential 6MWTs performed with two liter increments from room air to six liters per minute (l/min), until a SpO₂ ≥88% was obtained. Twenty minutes of rest were allowed between tests. The lowest flow rate required...
to complete a 6MWT with a SpO₂ ≥88% was recorded as the appropriate oxygen supplementation. The distance walked during the 6MWT (6MWT-distance) was expressed both as absolute value in meters and as % predicted value (% pr), using the Enright and Sherill equations [20].

**O₂-GAP index predicting algorithm**

To generate the algorithm all the individual outcome variables of the 211 6MWT (with and without oxygen supplementation) performed by the subjects in the derivation population were analyzed. Specifically the outcomes analyzed included the SpO₂ (mmHg) before and through the test, the duration of the test (minutes), the recovery time (seconds) necessary to reach the resting SpO₂ after the end of the 6MWT and the predicted distance (%), compared to normality as indicated by the Enright and Sherill equation [20].

**Statistical analysis**

Statistical analysis was carried out employing STATA 11 software (TX USA 2010), SPSS software and GraphPad Prism software. Group comparisons were made using Student’s t-test or one-way analysis of variance (ANOVA) as appropriate. A P value of less than 0.05 was considered statistically significant. Univariate correlations were examined using Pearson’s product moment-correlation.

**Results**

**Derivation of the algorithm determining the O₂-GAP index**

The demographic, biological and pulmonary function characteristics of the derivation population are shown in Table 1. ILD-affected individuals and control subjects were not significantly different with regard to demographic and biological characteristics.

In contrast, they had significantly different reduced forced vital capacity (FVC), diffusing lung capacity for carbon monoxide (DLCO) and distance walked in the 6MWT (Table 1).

The O₂-GAP index was determined by the following algorithm (protected by the International Patent — PCT/IT2010/000361) [16]:

\[
\text{Algorithm core} = \left[ \frac{\text{AUCgap}/\text{MT}}{\sqrt{\text{PPD} + \sqrt{\text{RT}}}} \right]^2 + \sqrt{\text{RT}}
\]

\[
\text{O₂-GAP index} = \frac{\text{Algorithm core} - 8.35}{4.56}
\]

AUCgap is the difference between the area under the curve delimited by the function \( f(x) = 100 \) and the area under the curve of SpO₂ of the patient during the test. The area is delimited by T0 and T6 (expressed in minutes); when the test was interrupted earlier than 6 min, T would be equal to T minutes walked. MT (minutes of test) is the time of the test (expressed in minutes). BaseSpO₂gap is the difference between 100 and the SpO₂ at rest. RT (recovery time) is the recovery time (in seconds) needed for SpO₂ to return to its initial value. PPD (percent predicted distance) is the MWT distance expressed in percent according to the Enright and Sherill equation [20].

A number of variables was significantly different between individuals requiring no oxygen and those requiring supplemental oxygen to complete the 6MWT, but as shown in Table 3 none of them though was able to discriminate among tests clustered according to the magnitude of oxygen flow needed, as determined by oxygen titration.

By computational analysis of the 6MWT variables recorded from the subjects included in the derivation population we obtained a composite dependent variable \( f(x) \) called “algorithm core”. The control group, including subjects without pulmonary disease and without spirometric abnormalities, was analyzed in order to identify a “zero-point” for the algorithm model. As showed in Fig. 1, the algorithm core is significantly correlated with the oxygen supplementation \( (r^2 = 0.97, p < 0.001) \) and allows to discriminate tests clustered according to oxygen flow needed to complete the walk test. The geometric solution of the equation “algorithm core = \( 4.56 X + 8.35 \)” predicts the magnitude of supplemental oxygen flow required by each subject to complete the 6MWT without oxygen desaturation. This figure is hereafter defined as O₂-GAP index.

By applying the equation to the 6MWT performed by the same subjects with the amount of supplemental oxygen corresponding to that predicted by the O₂-GAP index determined on the first test on room air, we were able to show that the O₂-GAP index re-calculated on ambulatory oxygen was zeroed out, or significantly reduced in comparison with the first O₂-GAP index \( (p < 0.05; \text{Fig. 2}) \).

**Validation of the algorithm determining the O₂-GAP index**

Of the 93 ILD-affected subjects included in the validation population, 45 completed the 6MWT on room air while maintaining oxygen saturation by pulse oximetry equal to or above 88%, while 48 desaturated during the test and required oxygen supplementation to complete the 6MWT (Table 2, Fig. 3). Demographic and biological characteristics of the individuals who did desaturate during the test were not different from those who did not. Physiological parameters, FVC, DLCO and the 6MWT-distance were significantly worse in those who did desaturate while systolic pulmonary artery pressure at echocardiography was not (Table 2).

There was a statistically significant correlation between the observed magnitude of the supplemental flow of oxygen required for patients desaturating on room air to complete the 6MWT while maintaining oxygen saturation by pulse oximetry equal to or above 88% and the predicted O₂-GAP index value \( (r = 0.918; r^2 = 0.842; p < 0.001) \) (Fig. 4). On average, the supplemental flow of oxygen predicted by the O₂-GAP index was in excess of the flow determined by oxygen titration in the same subjects by 0.7 l/min. On the other hand, the O₂-GAP index was below the flow of oxygen determined by titration in only three subjects (Fig. 4).
Consistent with the improvement of oxygen saturation, the supplemental flow of oxygen was also adequate to improve exercise capacity in patients desaturating on room air. Their average 6MWT-distance rose from 226 ± 161 m on room air to 405 ± 96 m on supplemental oxygen (p < 0.0001).

In addition, the amount of supplemental flow of oxygen also improved upon these patients breathlessness at rest (Borg score on room air, 1 ± 1.7, on ambulatory oxygen 0.6 ± 1.2, p < 0.05), but not on dyspnea on exercise.

Discussion

Typically, the ILD-affected patients present with impaired gas exchange. This may be caused by multiple abnormalities, including ventilation/perfusion mismatch, O2 diffusion limitation, low mixed venous pO2, right-to-left intracardiac shunt or pulmonary hypertension [21]. In these patients, gas exchange deteriorates during exercise leading to markedly decreased oxygen saturation by pulse oximetry and O2 arterial blood pressure [22]. Although both long-term and ambulatory oxygen therapy have been recommended for IPF patients with mild hypoxemia [9], there is no firm agreement on how to gauge the need for oxygen supplementation. The cardiopulmonary exercise test (CPET) is not as sensitive as the 6MWT for detecting oxygen desaturation in patients with respiratory disease [23,24]. In addition, the 6MWT is a simple and efficient low cost tool with which to evaluate the performance of individuals during sub-maximal exercise. It can be safely applied to patients with heart and/or advanced lung disease and it has been shown to be highly reproducible in patients with pulmonary fibrosis [25]. Although the 6MWT is the most commonly used test to prescribe oxygen therapy, most guidelines do not give clear indications on how to dose supplemental oxygen for ambulatory oxygen therapy. Consequently, recommendations for oxygen prescription vary in different countries [26].

This study has some limitations. Firstly, patients were not familiarized with the 6MWT and the possibility that oxygen titration itself improved the patient performance due to a learning effect cannot be ruled out. On the other hand, the increased work of carrying the oxygen cylinder in the repeat tests could have a negative effect on the test. Secondly, the study population included ILD patients with different interstitial diseases. Although all patients had reduced lung volumes without marked flow obstruction, patients with different interstitial disorders may have varying degrees of parenchymal and vascular derangement differently affecting gas exchange. Thirdly, the formula was computed on data obtained using a continuous oxygen flow nasal cannula (CFNC) device, and the results cannot be extended as such to pulse dose devices.

Even with these limitations, this study shows that the O2-GAP composite index can predict the flow (l/min) of supplemental ambulatory oxygen required to complete a 6MWT without desaturation, while the individual variables of the algorithm core, such as the 6MWT-distance, the 6MWT SpO2 nadir and the distance walked, when used independently do not correlate with the dose of ambulatory oxygen to be supplemented. It also shows that the O2-GAP index allows to "titrate" ambulatory oxygen dose with a single 6MWT. The algorithm core of the O2-GAP index was designed with the primary goal of identifying a dose of oxygen sufficient to prevent dyspnea, oxygen desaturation and breathlessness on exercise. Hence, the O2-GAP index slightly overestimated the oxygen flow required to maintain oxygen saturation by pulse oximetry during the 6MWT in the majority of patients while underestimating it in three patients only. As ILD patients, and the IPF affected in particular, tend not to develop

Table 3

<table>
<thead>
<tr>
<th>One-way ANOVA and Bonferroni’s post test</th>
<th>P values</th>
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<tbody>
<tr>
<td></td>
<td>SpO2 at rest</td>
</tr>
<tr>
<td>0 l/min vs 2 l/min</td>
<td>***</td>
</tr>
<tr>
<td>0 l/min vs 4 l/min</td>
<td>***</td>
</tr>
<tr>
<td>0 l/min vs 6 l/min</td>
<td>***</td>
</tr>
<tr>
<td>2 l/min vs 4 l/min</td>
<td>ns</td>
</tr>
<tr>
<td>2 l/min vs 6 l/min</td>
<td>ns</td>
</tr>
<tr>
<td>4 l/min vs 6 l/min</td>
<td>ns</td>
</tr>
</tbody>
</table>

*p < 0.05, **p < 0.01, ***p < 0.001, ns: p > 0.05.

Figure 1

O2-GAP algorithm core distribution by Whiskers box (10–90 percentile) of n = 211 6MWTs performed by the study population; f(X) represents the dependent variable of the algorithm that predicts the O2-GAP index.
hypercarbia until terminally ill, the data strongly suggest that the O2-GAP index could be safely and reliably used in clinical management of these patients.

Oxygen titration is both time consuming and expensive and may not be carried out routinely in the follow up of ILD patients. A survey carried out by Wijkstra et al. in 2001 showed that oxygen at rest, during sleep and during exercise was variably prescribed by pulmonologists [26] without standardized titration, as recommended by the Royal College of Physicians in the UK. In this context, a standardized measure, such as the O2-GAP, might be of considerable help with simplifying oxygen prescription and might provide a reference against which to compare individual protocols [11,15,26]. Not only does it allow to reliably determine ambulatory oxygen dose within a single 6MWT, but it also allows re-assessing oxygen dosage in patients already on supplemental oxygen as the algorithm recalculates the O2-GAP with a 6MWT on supplemental oxygen to determine the "extra" oxygen required. In this regard, it is worth noticing that, different from 6MWT parameters such as oxygen saturation or distance walked, the O2-GAP index is not affected by the oxygen supplementation, as it may measure oxygen requirement in addition to the O2 flow already administered, thus allowing the comparison of 6MWTs performed over time, at different oxygen flow rates.

A number of studies has compared CFNC and DOD devices for oxygen supplementation, suggesting that they perform similarly, at lead for oxygen supplementation [27,28]. Our study evaluated the validity of the O2-GAP index using continuous oxygen flow by standard nasal cannula. Further studies are needed to assess the applicability and clinical utility of the measure of the O2-GAP index to using currently available oxygen conserving devices.

To the best of our knowledge, the O2-GAP index is the first index capable of estimating the dose of oxygen supplementation in patients with ILD, upon the performance of a single 6MWT. In the context of the lack of standardization of oxygen prescription to dyspneic ILD patients, the availability of an algorithm that can be uploaded on the electronic memory of portable pulse oximetry devices, might considerably simplify oxygen titration and facilitate the use of the 6MWT for oxygen prescription.

Contribution of authors
Josuel Ora designed the project and wrote the paper. Luigino Calzetta designed and implemented the mathematical model. Gabriella Pezzuto, Paola Rogliani and Ermanno Puxeddu designed the project and provided critical revision of the article. Lucia Senis, Alessia Mari and Silvia Portalone performed clinical studies. Gregorino Paone conducted the statistical analyses. Cesare Saltini conceived and supervised the project, and wrote the paper. Josuel Ora and Cesare Saltini are guarantors of the paper.

Conflict of interest and funding disclosure
Josuel Ora does not have any conflict of interest to report. Luigino Calzetta has received grants from M.I.R. Medical International Research S.r.L. in the past 5 years; LC is an inventor on the patent application "Saltini C, Boschetti PS,
Calzetta L; Portable device for monitoring and reporting of medical information for the evidence-based management of patients with chronic respiratory disease. Italy. 2010. International Patent – PCT/IT2010/000361” filed by M.I.R. in Rome (It) and may receive royalties from the sale of devices using the algorithm described in the paper. Gabriella Pezzuto does not have any conflict of interest to report. Lucia Senis does not have any conflict of interest to report. Gregorino Paone does not have any conflict of interest to report. Alessia Mari does not have any conflict of interest to report. Silvia Portalone does not have any conflict of interest to report. Paola Rogliani does not have any conflict of interest to report. Ermanno Puxeddu does not have any conflict of interest to report. Cesare Saltini is an inventor on the patent application “Saltini C, Boschetti PS, Calzetta L; Portable device for monitoring and reporting of medical information for the evidence-based management of patients with chronic respiratory disease. Italy. 2010. International Patent – PCT/IT2010/000361” filed by M.I.R. Rome (It) and may receive royalties from the sale of devices using the algorithm described in the paper.

References


Domiciliary oxygen therapy services: clinical guidelines and

Nasilowski J, Przybylowski T, Zielinski J, Chazan R. Comparing


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