Quantitative 15 Steps Exercise Oximetry as a Marker of Disease Severity in Patients with Chronic Obstructive Pulmonary Disease

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Abstract

Background: Hypoxemia is a common complication of chronic obstructive pulmonary disease and a major factor in patients' prognosis and quality of life. The response to exercise has been evaluated by various means but no standardization has been accepted.

Objectives: To suggest a simple outpatient technique for evaluating the response of arterial oxygen saturation to exercise for use as a marker of disease severity.

Patients and methods: Ninety-six patients with various degrees of COPD[1] were divided into three groups: mild (forced expiratory volume in 1 sec >65%), moderate (FEV_1[2] between 50 and 65%), and severe (FEV_1 <50%). Using continuous oximeter recording we measured oxygen saturation during 15 steps of climbing, and quantified oxygen desaturation by measuring the "desaturation area," defined as the area under the curve of oxygen saturation from the beginning of exercise through the lowest desaturarion point and until after recovery to the baseline level of oxygen percent saturation. Desaturation was correlated to spirometry, lung gas volumes, blood gas analysis, and 6 min walking distance.

Results: A good correlation was found between severity of COPD and baseline SaO_2,[3] lowest SaO_2, recovery time, and desaturation area. A negative correlation was found between desaturation area and FEV_1 (r=-0.65), FEV_1/forced vital capacity (r=-0.58), residual volume to total lung capacity (r=0.52), and diffusing lung capacity for carbon monoxide (r=-0.52). In stepwise multiple regression analysis only FEV_1 correlated significantly to desaturation area. A good correlation was noted between 6 min walking distance and desaturation area with the 15 steps technique (r=0.56).

Conclusions: In patients with severe COPD, arterial hypoxemia during exercise can be assessed by simple 15 steps oximetry. This method can serve both as a marker for disease severity and to determine the need for oxygen supplementation.

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Hypoxemia is a common complication of advanced lung disease, causing severe limitation in daily function [1–3]. Hypoxemia can occur at rest, during sleep, or during exercise. It has been shown that in patients with COPD physical activity produces hypoxemia, which is attributed to either a worsening ventilation perfusion mismatch [4,5] or the inability to hyperventilate during exercise [6]. Some investigators have shown that exercise-induced hypoxemia correlates with spirometric values (FEV_1 and FEV_1/FVC[4]) and with diffusion capacity [7–10], but this was not shown by others [11]. Although assessment of exercise hypoxemia has been performed during various activities such as walking [12,13], climbing stairs [14–16] and cycling [7,8,17], no standardization has been accepted worldwide.

We studied exercise oximetry [18] of stepping on and off a step 15 times in an attempt to quantify desaturation in comparison to lung function and 6 min walking in patients with various degrees of COPD.

Patients and Methods

Our study group comprised 96 patients attending the pulmonary clinic who had been diagnosed with obstructive airway diseases according to the American Thoracic Society (ATS) criteria [19]. Many of them had advanced disease and were referred for consultation regarding the possibility of lung volume reduction or lung transplantation. Sixty-six of the patients were men and 30 were women; their ages ranged from 38 to 76 years (mean 62). The patients were divided into three groups according to severity of lung disease: mild (FEV_1>65%), moderate (FEV_1 between 50 and 65%), and severe (FEV_1<50%). All patients underwent spirometry, lung volume measurements, single-breath carbon monoxide diffusion capacity (Medical Graphics, St Paul, MN, USA), and measurement of the

[1] COPD = chronic obstructive pulmonary disease

[2] FEV_1 = forced expiratory volume in 1 sec

[3] SaO_2 = arterial oxygen saturation

[4] FEV_1/FVC = FEV_1/forced vital capacity

distance during 6 min of walking. Ten healthy non-smoking technicians and physicians with normal lung function served as controls.

Fifteen steps exercise protocol

A finger oximeter (8500, Nonin Medical, Plymouth, MN, USA) with continuous online recording of pulse rate and oxygen saturation was connected to each patient. The data were sampled every 2 sec and the mean value was recorded every 10 sec. A step measuring 25x50 cm by 20 cm height was used at the clinic, and patients were asked to climb up and down the step 15 times as fast as they could (without any fixed pacing). Each test was repeated twice and the mean values were taken. When oximeter readings were not optimal, as detected by a yellow or red signal, the data were discarded. The timing of the exercise was recorded (exercise time), as was the time from start to lowest saturation (desaturation time) and the time from lowest saturation to recovery to baseline level (recovery time). The total test time was defined as the time from the start of the exercise to complete recovery (summation of desaturation and recovery times). Baseline oxygen saturation, lowest saturation, and the highest pulse were recorded. The desaturation area was defined as the area below 98% saturation during the complete maneuver [Figure 1] and was calculated using the triangular area between baseline saturation and 98%. {(Baseline SaO_2–lowest SaO_2) x 0.5 test time + (98%–baseline SaO_2) x test time}.

Statistical analysis

Linear regression and stepwise multiple regression analysis were made between baseline SaO_2, lowest saturation, as well as desaturation area and FEV_1, FEV_1/FVC, RV/TLC[5], TLC and DLCO[6] (% or % of predicted values). Linear correlation was analyzed between the desaturation area and 6 min walking distance, and comparison between groups was made using ANOVA. The level of significance was set at $P \leq 0.05$.

Results

All patients performed the study without difficulty. Table 1 presents the three groups of patients according to the severity of their disease. There was no significant difference between the groups with regard to age and sex. Table 2 summarizes the desaturation data for all groups. Exercise time was slower in patients with the more severe disorder. Baseline oxygen saturation was 97.1±1.2 in the control group and 96.1±1.3, 94.5±2 and 91.2±3.9 in groups 1,2 and 3, respectively. These differences between the groups were significant, as were differences in lowest saturation. The SaO_2 difference between baseline and the lowest SaO_2 was significantly larger in the more severe group — 6.7% in group 3 as compared to 3.5% and 2.3% in groups 2 and 1, respectively.

Desaturation time was longer in the more severe group and occurred later, after the end of the effort. Similarly,

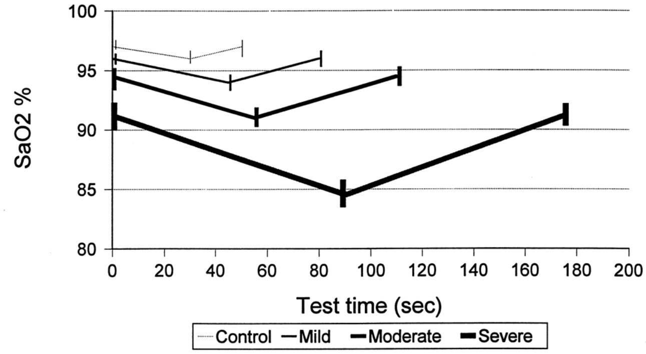

Figure 1. Desaturation curves for controls and patients with chronic obstructive pulmonary disease

Table 1. Patients' demographic and lung function data

	Severe disease (n=62)	Moderate disease (n=14)	Mild disease (n=20)
Age (yr)	61±10	62±14	54±15
Female/Male	12/50	8/6	10/10
FVC (%)	52±15	78±14	97±13
FEV_1 (%)	30±10	57±4	83±15
FEV_1/FVC (%)	46±10	61±10	72±8
FEF_{25-75} (%)	12±5	27±8	48±20
PEFR (%)	41±16	72±31	89±17
TLC (%)	117±22	109±20	110±11
RV/TLC (%)	68±9	50±12	44±10
DLCO (%)	60±20	98±31	108±26
DL/VA (%)	80±26	102±31	115±23
PaO_2 mmHg	61.2±10.9	68.8±9.6	74.5±9.6
$PaCO_2$ mmHg	44.2±6.6	36.8±3.2	35.7±2.6

All presented data are predicted normal (mean ± SD).
DL/VA = corrected diffusion capacity for alveolar volume.

Table 2. 15 Steps exercise desaturation data

	Control (0) (n=10)	*P* 0–1*	Mild (Group 1) (n=20)	*P* 1–2**	Moderate (Group 2) (n=14)	*P* 2–3***	Severe (Group 3) (n=62)
Exercise time (sec)	31±8	0.02	40±10	NS	46±10	0.03	53±11
Baseline SaO_2 (%)	97.1±1.2	NS	96.1±1.3	0.005	94.5±2	0.01	91.2±3.9
SaO_2 lowest (%)	96.3±1.6	0.02	93.8±1.9	0.01	91.0±2.6	0.001	84.5±5.5
SaO_2 difference (%)	0.8 ±1.3	0.05	2.3±1.7	0.05	3.5±1.6	0.004	6.7±3.4
Desaturation time (sec)	28±28	NS	46±30	NS	52±18	0.001	88±29
Recovery time (sec)	20±23	NS	33±27	0.02	58±26	0.015	89±43
Total test time (sec)	48±49	NS	79±45	0.04	110±34	0.001	177±59
Desaturation area (sec%)	93±130	0.04	267±222	0.03	584±355	0.0007	1,926±1,399

*Control vs. group 1; **Group 1 vs. group 2; ***Group 2 vs. group 3.

[5] RV/TLC = residual volume to lung capacity
[6] DLCO = diffusing lung capacity for carbon monoxide

recovery to baseline took longer in the most severe group. The most significant differences were noted in desaturation areas between groups. Figure 1 depicts the different desaturation curves and desaturation area for the control and COPD groups.

When correlating 15 steps desaturation and spirometry, we found a good linear correlation between baseline SaO_2, lowest SaO_2, total test time, and desaturation area to FEV_1, FVC, FEV_1/FVC and RV/TLC ratio. TLC did not correlate well with desaturation, and DLCO correlated to lowest SaO_2 and desaturation area. Desaturation area correlated strongly with FEV_1 (r=-0.65), FVC (r=-0.60) and DLCO (r=-0.52). No correlation was observed with TLC.

When performing multiple regression analysis, only FEV_1 remained as a significant independent factor on saturation area (multiple R=0.613, R^2=0.376). Desaturation area could be calculated as Desaturation Area= 2,977–34.2 x FEV_1.

Despite the good correlation, it can be seen that in group 3 (FEV_1<50%) only half of the patients desaturated strongly (desaturation area>1,500 sec%. Conversely, in groups 1 and 2 (FEV_1>50%) none of the patients had significant desaturation (desaturation area>1,500 sec%). Similarly, when DLCO was higher than 60% predicted, significant desaturation was rare; however, at lower levels of DLCO, desaturation was variable.

Desaturation and 6 min walking distance

Figure 2 shows a correlation between 6 min walking distance and desaturation area in 51 patients (r=0.57). A correlation was also noted between 6 min and test time (r=-0.7), but *not* with basal saturation (r=0.33) or with lowest desaturation (r=0.2).

Discussion

Hypoxemia, which worsens with exercise, occurs commonly in COPD [7,8]. It has a major effect on patients' quality of life, and has prognostic implications following pulmonary surgery [19,20] and probably on long-term survival as well. It was recently shown that daily activities cause significant hypoxemia, and in some cases desaturation was far worse than estimated by rest SaO_2 or as expected from sleep hypoxemia [21].

Although several protocols have been suggested to assess exercise hyopxemia, no method has been accepted as the gold standard. The most common methods used are stair-climbing: 1 to 2 flights [19], 5 flights (125 stairs) [16], 36 stairs climbed (maximal) [20], distance walking (6,10, and 12 min) [12]; and bicycle ergometry with different protocols [7,8,17] . Moreover, the degree of hypoxemia is assessed differently: the lowest arterial oxygen pressure or Sao_2 achieved, mean PaO_2[7] or SaO_2 during exercise, and maximal drop of PaO_2 or SaO_2 from baseline. Despite the variable assessment methods mentioned above, what is accepted worldwide as one of the best methods to assess

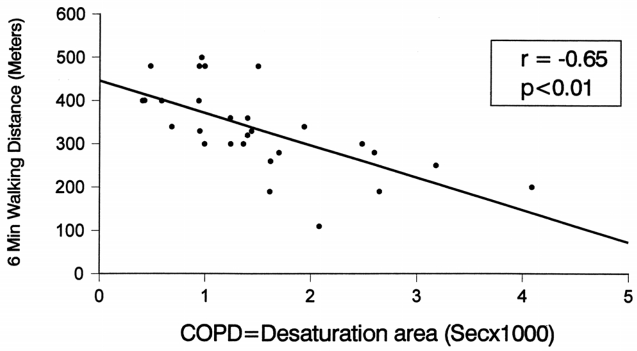

Figure 2. Linear correlation between 6 min walking distance to desaturation area

cardiopulmonary reserve incremental is progressive exercise testing with expired gas analysis. However, due to the high cost, complicated equipment and the need for trained staff, this method is not widely practiced.

In our study we tried to develop a simple model to quantify hypoxemia, using a mild fixed effort. The concept of *desaturation area* takes into account the baseline saturation as well as the severity of desaturation and recovery to baseline. We found a good correlation between 15 steps oximetry desaturation to FEV_1, FVC, FEV_1/FVC, RV/TLC and DLCO. Owens et al. [8] used progressive incremental cycle ergometry and found a good correlation between DLCO and FEV_1 to desaturation measured by oximetry. Conversely, Ries et al. [11], using a similar protocol with a 3 min interval arterial stick, observed a poor correlation with FEV_1 and DLCO. They found that desaturation was rare in patients with mild obstructive changes, and could not be predicted from the spirometric data in the group whose condition was more severe. Our data support their findings in that none of our patients with FEV_1 above 50% had significant hypoxemia (desaturation area >1,500 sec%); while in those with FEV_1 below 50%, desaturation was more common but unpredictable. Similarly, normal or low DLCO could not predict desaturation although a general correlation was found. We believe, therefore, that in order to assess the severity of COPD in patients with FEV_1 <50%, 15 steps exercise oximetry should be used routinely as an aid in decision making with regard to therapy, oxygen supplementation, and prognosis.

When comparing the 6 min walking distance to 15 steps oximetry, we and others [20] observed a good correlation. This was also shown in studies that attempted to assess the risk of lung resection. Both stair-climbing (more than 44 stairs) and 6 min walking (more than 1,000 feet) were predictive of a low complication rate [21]. It seems that these two simple methods are complementary — 6 min walking to assess ventilatory reserve, and 15 steps oximetry to assess the gas exchange reserve.

Our study has several clinical implications. Firstly, in severe COPD, steps oximetry can be used to assess the severity of lung disease and the need for oxygen supple-

[7] PaO_2 = arterial oxygen pressure

mentation, even when rest saturation is above 90% [22]. Secondly, this test can be used to evaluate the patient's ability to undergo surgical stress such as in lung resection [23] or other major surgery. Thirdly, with therapeutic intervention, either medical or surgical (i.e., volume reduction surgery), oximetry may be easily assessed in the outpatient clinic. Lastly, steps oximetry may be used as an additional means of evaluating pulmonary disability in patients with COPD.

In conclusion, 15 steps oximetry can serve as a simple outpatient test for assessing the severity of COPD. The quantitation of the test is useful not only to measure severity but to determine whether supplemental oxygen is required.

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An empty man is full of himself.

Anonymous

A human being should be able to change a diaper, plan an invasion, butcher a hog, conn a ship, design a building, write a sonnet, balance accounts, build a wall, set a bone, comfort the dying, give orders, cooperate, act alone, solve equations, analyze a new problem, pitch manure, program a computer, cook a tasty meal, fight efficiently, and die gallantly. Specialization is for insects.

Robert A. Heinlein, "The Notebook of Lazarus Long"