6-Minute Walk Testing Is More Sensitive Than Maximal Incremental Cycle Testing for Detecting Oxygen Desaturation in Patients With COPD*  

Magali Poulain, PhD; Fabienne Durand, PhD; Bernard Palomba, PT; François Ceugniet, MD; Jacques Desplan, MD; Alain Varray, PhD; and Christian Préfaut, MD

Study objectives: Some respiratory patients exhibit oxygen desaturation during rehabilitative walking but not during maximal cardiopulmonary exercise testing (CPET). We evaluated exercise-induced desaturation during 6-min walk testing (6MWT) in comparison with CPET in patients with COPD and determined the reproducibility of the phenomenon.

Patients: We tested 80 consecutive patients with COPD (FEV₁, 62.4 ± 2% predicted) and 10 patients with supplementary COPD (FEV₁, 59.1 ± 5% predicted) [mean ± SEM] to determine the reproducibility.

Measurements and results: First, patients with COPD performed cycle CPET (first CPET [CPET-1]). Three days later, they performed two 6MWTs (first 6MWT [6MWT-1] and second 6MWT [6MWT-2]). Pulse oximetric saturation (SpO₂) was recorded every minute in both tests. Three groups emerged: desaturation at 6MWT not observed at CPET (DND) [n = 23], desaturation in both tests (n = 16), and no desaturation in either test (n = 41). Second, to evaluate reproducibility, 10 additional subjects with COPD who exhibited desaturation during two successive 6MWTs but not in CPET performed a second CPET (CPET-2) and a single-bout 6MWT (6MWT-3) in a supplementary trial. When two CPETs were performed, lack of O₂ desaturation was noted in both. O₂ desaturation was confirmed in 6MWT-2 and 6MWT-3 (7.4 ± 1% and 7.4 ± 1.5%, respectively).

Conclusion: Twenty-eight percent of patients with COPD presented DND. The phenomenon was reproducible and not protocol dependent, emphasizing the clinical interest of the 6MWT.

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Key words: COPD; oxygen desaturation; 6-min walking test

Abbreviations: BMI = body mass index; CPET = cardiopulmonary exercise testing; CPET-1 = first cardiopulmonary exercise testing; CPET-2 = second cardiopulmonary exercise testing; DND = desaturation at 6-min walk testing and cardiopulmonary exercise testing; DD = desaturation during both 6-min walk testing and cardiopulmonary exercise testing; HR = heart rate; HRmax = maximal heart rate; NN = no desaturation during either 6-min walk testing or cardiopulmonary exercise testing; RER = respiratory exchange ratio; SaO₂ = arterial oxygen saturation; 6MWT = 6-min walk testing; 6MWT-1 = first 6-min walk testing; 6MWT-2 = second 6-min walk testing; 6MWT-3 = single-bout 6-min walk testing; SpO₂ = pulse oximetric saturation; TLC = total lung capacity; VO₂ = oxygen uptake; VO₂max = maximal oxygen uptake; Wmax = maximal power

Patients with COPD have reduced exercise tolerance. This exercise intolerance and its associated dyspnea are primarily due to airway obstruction but also to a combination of several factors. Peripheral muscular dysfunction has been demonstrated in this population, and although the degree of its impact on exercise capacity and dyspnea has not been established with certainty, rehabilitation programs that include exercise training are able to reduce dyspnea and improve exercise tolerance. In order to pre-

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scribe optimal exercise, however, patients with COPD must first be evaluated, and cardiopulmonary exercise testing (CPET) is most often recommended to assess the level and mechanisms of exercise intolerance and to determine individualized training intensity. The diagnosis of exercise-induced desaturation during this CPET is important not only in terms of pathophysiology but also potentially for therapeutics. Surprisingly, we recently observed that several respiratory patients who did not exhibit O2 desaturation during CPET performed prior to rehabilitation paradoxically showed regular O2 desaturation during the walking component of the rehabilitation program.

O2 desaturation has been studied during different types of exercise testing. PaO2 fell to a lower level during treadmill exercise compared with bicycle exercise in patients with chronic obstructive airway disease. Palange et al9 compared walking and cycling exercise tests in patients with COPD and demonstrated that PaO2 values were lower during walking. This study, however, used a shuttle test, which in fact is a field incremental maximal exercise test and not a pure walking test. Therefore, no data in the literature were found to specifically confirm our clinical observation.

This study was designed to determine whether exercise-induced desaturation appears in some patients with COPD during walking but not during maximal incremental cycle exercise. In order to evaluate exercise-induced desaturation during walking, we used 6-min walk testing (6MWT), which is well known for its clinical interest, simplicity, and reproducibility. In a population of 80 consecutive patients with COPD, we evaluated the prevalence of exercise-induced desaturation during 6MWT in comparison with maximal cycle CPET. In addition, the reproducibility of the phenomenon was tested.

Materials and Methods

Patients

Eighty consecutive respiratory patients, 44 men and 36 women, admitted to a medical rehabilitation center (Clinique du Souffle “La Solane”: Osseja, France) participated. All these patients presented clinical histories consistent with COPD. The mean age (± SEM) was 60.6 ± 1 years, height was 165 ± 0.009 cm, weight was 74.7 ± 1.6 kg, body mass index (BMI) was 27.3 ± 0.5, and FEV1 was 1.65 ± 0.06 L (62.4 ± 2% predicted; range, 37 to 96%). According to the recent American Thoracic Society criteria, our patients presented moderate (stage IIA) airway obstruction. Fifty-three patients had a history of smoking, 7 patients were currently smoking, and 46 patients had stopped smoking. The patients were in a clinically stable state and had no recent infectious exacerbations. No patients were receiving long-term oxygen therapy. The aim of the study was fully explained to them, and all gave written consent to participate. Study participation began 3.2 ± 0.3 days after admission to the center. Ten supplementary subjects participated in this study in addition to the 80 subjects; their mean age was 66.5 ± 2 years, height was 163 ± 0.02 cm, weight was 79.9 ± 2.3 kg, BMI was 30.3 ± 1.43, and FEV1 was 1.42 ± 0.15 L (59.1 ± 5% predicted).

Lung Function

Lung function measurements were performed using a plethysmograph (V6200 Autobox; SensorMedics; Yorba Linda, CA) to determine total lung capacity (TLC), FVC, and FEV1. The Tiffeneau ratio (FEV1/FVC) was then calculated.

CPET and Cardiopulmonary Parameters

The maximal exercise test was performed on a cycle ergometer (Ergometrics 900; Ergoline; Bitz, Germany) following the individualized protocol usually used in our laboratory. Briefly, we calculated the maximal predicted power output from the predicted maximal oxygen uptake (VO2max) according to the Wasserman equation for theoretical values. We then calculated the estimated VO2max for a given subject by multiplying the predicted VO2max by FEV1 percentage of predicted. Estimated VO2max was then converted to estimated maximal power (Wmax). The 3-min warm-up was conducted at 20% of estimated Wmax, and the load was increased by 8% of estimated Wmax every minute to obtain Wmax output in approximately 10 min. VO2max was assumed to have been reached if three of the four following criteria were met: (1) leveling off of oxygen uptake (VO2) despite increasing load, (2) respiratory exchange ratio (RER) > 1.1, (3) attainment of age-predicted maximal heart rate (HRmax) [210 − 0.65 × age], and (4) inability of the subject to maintain the pedaling frequency despite maximal effort and verbal encouragement. If three criteria were not observed but at least the increase in RER was recorded, we considered that the VO2max was symptom limited.

During exercise testing, gas exchanges were measured continuously using a breath-by-breath automated exercise metabolic system (Vmax series 29C; SensorMedics). The subjects breathed through a mouthpiece with a noseclip in place. Before each test, the volume was calibrated by five inspiratory and expiratory strokes with a 3-L pump at different flow levels, and then the gas analyzers were calibrated with two gas mixtures of known O2 and CO2 concentration. Expired gases were analyzed for O2 with a zirconia solid electrolyte O2 analyzer and for CO2 with an infrared analyzer. VO2, CO2 output, RER, minute ventilation, and its components tidal volume and breathing frequency were averaged during the last 20 s of each load. A 12-lead ECG (Cardiosoft Corina; Marquette Hellige Medical Systems; Freiburg, Germany) was monitored continuously during testing.

6MWT

6MWT was performed twice (first 6MWT [6MWT-1] and second 6MWT [6MWT-2]) with at least 15 min between tests to allow heart rate (HR) to return to its initial rest value. Subjects were asked to walk at their own maximal pace along a perimeter of 31.5 m. They were asked to cover as much ground as possible while maintaining a steady pace without running during the allotted time. No encouragement was given, and subjects were informed each minute of the time remaining. The patients were allowed to stop, but they could start again, if possible, within the allocated 6 min. Distance covered in 6 min, oxygen saturation, and HR, which was measured by a Sport Tester (Polar; Kempele, Finland) every minute, were recorded. The dyspnea score measured on a visual analog scale before and at the end of the test was...
also recorded to determine if scores had returned to initial values by the beginning of 6MWT-2. 6MWT-2 values were always better than those of 6MWT-1; 6MWT-2 values are reported.

### O₂ Desaturation and Blood Gas Analysis

Pulse oximetric saturation (SpO₂) was measured during both tests using pulse oximetry (Nonin 8500 M; Nonin Medical; Minneapolis, MN). Desaturation was defined as a fall ≥ 4% of the resting SpO₂ value during at least the last 3 min of the cycling or walking tests.† To estimate blood gas levels during the cycle test, arterialized blood was collected at the ear lobe at rest, and maximal exercise and samples were immediately analyzed for PaO₂, PaCO₂, and pH (BGE; Instrumentation Laboratory; Milan, Italy).

### Protocol

#### O₂ Desaturation Comparison

On the first day of the study, subjects underwent lung plethysmography and resting ECG and performed their first CPET (CPET-1) on a cycle ergometer. SpO₂ was recorded throughout exercise, and arterialized blood gas levels were recorded at rest and maximal load. One to three 6MWT-2 values were always recorded to determine if scores had returned to initial values. 6MWT-2 values were always better than those of 6MWT-1; 6MWT-2 values are reported.

#### Reproducibility of the Phenomenon

To evaluate the reproducibility of the phenomenon, a supplementary trial was held. Ten subjects who were not part of the original study group of 80 members, but who exhibited arterial desaturation during two successive 6MWT but not during CPET, performed a second CPET (CPET-2) and a single-bout 6MWT (6MWT-3). CPET-2 and 6MWT-3 were performed in the same protocol conditions as in the first stage (9 ± 1 days and 6 ± 1 days, respectively, after the first test). SpO₂ and HR were recorded continuously during both tests, while arterialized blood gases were drawn at rest and during the last 20 s of cycling exercise.

### Statistics

The results are expressed as mean ± SEM. We used a one-way analysis of variance to compare anthropometric, plethysmographic, and gasometric data. A stepwise multiple regression analysis was used to evaluate independent variables explaining the variance of desaturation in 6MWT.

Variation coefficients were calculated to compare the two CPETs and 6MWT-2 and 6MWT-3. One-way repeated-measure analyses of variance were used to compare kinetic values of SpO₂ between the two CPETs and the two 6MWTs. Statistical analysis was performed using a statistical software package (SigmaStat 2.03; Jandel Scientific; Erkrath, Germany); p < 0.05 was considered significant.

### Results

#### O₂ Desaturation Comparison

No between-group difference was noted for resting levels of SpO₂ (Table 1). 6MWT was performed 2.5 ± 0.5 days after the CPET. The fall in SpO₂ measured between rest and the last stage of exercise is reported in Figure 1. These data allowed us to determine three different groups.

The first group showed desaturation at 6MWT that was not observed at CPET (DND). The DND group comprised 23 subjects (28.75% of the total population). The desaturation in SpO₂ (fall of 7 ± 0.4%) as previously defined persisted 5.08 ± 0.1 min during 6MWT. The second group showed desaturation during both 6MWT and CPET (DD). The DD group comprised 16 subjects (20% of the total population). The desaturation in SpO₂ (fall of 6.66 ± 0.76%) persisted 5 ± 0.1 min during 6MWT and 4.3 ± 0.3 min during CPET.

The third group showed no desaturation during either 6MWT or CPET (NN). The NN group comprised 41 subjects (51.25% of the total population). In CPET, there was no significant difference between the falls in SpO₂ and the falls in capillary arterial oxygen saturation (SaO₂) [DND, 2.78 ± 0.3% vs 2.5 ± 0.5%; DD, 6.6 ± 0.76% vs 6.4 ± 1.5%; and NN, 2.02 ± 0.4% vs 1.7 ± 0.3%, respectively, for SpO₂ and capillary SaO₂].

There was no significant between-group difference for age, weight, height, BMI, and FEV₁. Significant difference was noted in NN vs DD for FEV₁/FVC, and for TLC in NN vs DD and in DND vs DD (p < 0.05; Table 1).

Table 2 shows no between-group difference in symptom-limited Vo₂ (expressed in liters per minute) and symptom-limited VO₂ (expressed in

Table 1—Anthropometric, Plethysmographic, and Gasometric Characteristics at Rest in 80 Patients With COPD*

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>DND (n = 23)</th>
<th>DD (n = 16)</th>
<th>NN (n = 41)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, yr</td>
<td>62 ± 2</td>
<td>56 ± 2</td>
<td>61 ± 1</td>
<td>NS</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>74.3 ± 2.8</td>
<td>76.3 ± 4.2</td>
<td>74.2 ± 2.3</td>
<td>NS</td>
</tr>
<tr>
<td>Height, cm</td>
<td>165 ± 0.01</td>
<td>168 ± 0.01</td>
<td>163 ± 0.01</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>27.2 ± 0.98</td>
<td>26.8 ± 1.22</td>
<td>27.6 ± 0.7</td>
<td>NS</td>
</tr>
<tr>
<td>FEV₁, % predicted</td>
<td>59.5 ± 3.4</td>
<td>58.9 ± 6.4</td>
<td>64.8 ± 3.2</td>
<td>NS</td>
</tr>
<tr>
<td>Range</td>
<td>39–81</td>
<td>29–57</td>
<td>37–86</td>
<td></td>
</tr>
<tr>
<td>FEV₁/FVC, %</td>
<td>54 ± 2.7</td>
<td>48.09 ± 4.6</td>
<td>60.5 ± 1.8</td>
<td>&lt; 0.05†</td>
</tr>
<tr>
<td>TLC, % predicted</td>
<td>98.2 ± 5</td>
<td>112.6 ± 4.8</td>
<td>97.3 ± 3</td>
<td>&lt; 0.05†</td>
</tr>
<tr>
<td>SpO₂ at rest before 6MWT, %</td>
<td>94.6 ± 0.4</td>
<td>95 ± 0.7</td>
<td>95.2 ± 0.2</td>
<td>NS</td>
</tr>
<tr>
<td>SpO₂ at rest before CPET, %</td>
<td>93.6 ± 0.3</td>
<td>95.3 ± 0.4</td>
<td>95.2 ± 0.2</td>
<td>NS</td>
</tr>
</tbody>
</table>

*Values are presented as the mean ± SEM. NS = not statistically significant.
†Difference between DD and NN.
‡Difference between DND and DD.
Reproducibility of the Phenomenon

There were no significant differences between the 10 supplementary subjects and the DND group for age, weight, height, or FEV₁. In the supplementary trial, no significant difference was noted for any variable between either CPET or 6MWT. These results were confirmed using the variation coefficient (Table 3). Figure 2 shows the kinetics of Sp₂O₂ at three times: at rest, at the middle of exercise, and at the end of exercise for the two exercise tests and the repetitions of both. The lack of O₂ desaturation was therefore confirmed in CPET-2, and 6MWT-3 confirmed the O₂ desaturation for walking exercise.

Discussion

This study essentially shows the following: (1) 28% of patients with COPD present DND, and (2) this phenomenon is reproducible.

O₂ Desaturation Definition

We defined O₂ desaturation as a fall in Sp₂O₂ of 4% below resting value that persists for at least the last 3 min of the exercise test. The fall of 4% was validated in a study of exercise-induced hypoxemia in athletes. This 4% fall was defined as a fall of 2% to account for the right shift of the variability between either CPET or 6MWT. These results were confirmed using the variation coefficient (Table 3). Figure 2 shows the kinetics of Sp₂O₂ at three times: at rest, at the middle of exercise, and at the end of exercise for the two exercise tests and the repetitions of both. The lack of O₂ desaturation was therefore confirmed in CPET-2, and 6MWT-3 confirmed the O₂ desaturation for walking exercise.

Table 2—CPET-1 and 6MWT-2 Parameters in 80 Patients With COPD*

<table>
<thead>
<tr>
<th>Parameters</th>
<th>CPET-1 (n = 80)</th>
<th>6MWT-2 (n = 80)</th>
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<tbody>
<tr>
<td></td>
<td>Rest (n = 23)</td>
<td>End (n = 23)</td>
</tr>
<tr>
<td></td>
<td></td>
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<tr>
<td>V̇O₂ L/min</td>
<td>0.26 ± 0.01</td>
<td>1.06 ± 0.06</td>
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<tr>
<td></td>
<td>59 ± 2</td>
<td>52 ± 4</td>
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<tr>
<td>% predicted</td>
<td></td>
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<td></td>
<td>0.24 ± 0.01</td>
<td>1.23 ± 0.07</td>
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<td></td>
<td>13.8 ± 0.69</td>
<td>48.5 ± 2.3</td>
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<td></td>
<td>0.94 ± 0.02</td>
<td>1.16 ± 0.01†</td>
</tr>
<tr>
<td></td>
<td>81 ± 5</td>
<td>76 ± 6</td>
</tr>
<tr>
<td>Wmax, L/min (n = 23)</td>
<td>132 ± 2</td>
<td>135 ± 3</td>
</tr>
<tr>
<td>HRmax, beats/min</td>
<td>110 ± 1</td>
<td>115 ± 3</td>
</tr>
<tr>
<td></td>
<td>93.6 ± 0.43</td>
<td>91.04 ± 0.61†</td>
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<td></td>
<td>67.47 ± 1.52</td>
<td>63.77 ± 1.51†</td>
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<tr>
<td></td>
<td>93.6 ± 0.39</td>
<td>90.90 ± 0.47†</td>
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<td></td>
<td>508 ± 15</td>
<td>469 ± 19</td>
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<td></td>
<td>119 ± 3</td>
<td>119 ± 4</td>
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<tr>
<td></td>
<td>91 ± 2†</td>
<td>88 ± 2</td>
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<tr>
<td>HR at 6MWT-2/HR at symptom-limited</td>
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*Values are presented as the mean ± SEM. VCO₂ = carbon dioxide output; V̇R = minute ventilation.

1p < 0.01, difference between DND and DD.
2p < 0.01, difference between DND and NN.
3p < 0.01, difference between DD and NN.
Evidence of the Phenomenon and Reproducibility

Our study highlights three types of SpO2 response to exercise. Exercise-specific responses have already been suggested by Palange et al8 who showed different O2 desaturation values during walking and cycling exercise. Although these studies suggested the existence of a specific DND population, this is the first time to our knowledge that desaturation is reported during a walking test vs a maximal cycle test. A relatively large number of subjects showed this phenomenon, and it was thus important to determine its reproducibility. No significant difference was noted between the variables of CPET and 6MWT-2 and 6MWT-3, and this finding was strengthened by the low variation coefficient. These results confirm a study by Covey et al15 who showed the reliability of two symptom-limited exercise tests performed approximately 2 weeks apart and a study by Guyatt et al10 who showed the reproducibility of 6MWT. The fact that we found the same results in 6MWT-2, the reference test, and 6MWT-3, which was a single-bout exercise, excluded a potential effect of exercise repetition on O2 desaturation and indicated that the phenomenon was not protocol dependent. In all, 28% of our total COPD population showed DND, and the reproducibility of this phenomenon was confirmed in 10 other patients. 6MWT therefore seems to have more clinical interest than expected. It is currently a valid tool to measure the functional status of patients, reflect their capacity to undertake day-to-day activities, and assess the effectiveness of therapies such as pulmonary rehabilitation. Our results suggest that 6MWT may also have the potential to become a diagnostic test as well, either to measure dynamic hyperinflation as demonstrated by Marin et al16 or to unmask exercise-induced desaturation as shown in this work. 6MWT does not negate the need for CPET to assess the level and mechanisms of exercise intolerance, to detect cardiac failure, and to determine individual training intensity. 6MWT and CPET are complementary tests, but our study suggests that limiting 6MWT use only to investigating exercise tolerance may need to be reconsidered.

Hypotheses for the Phenomenon

Several hypotheses can be advanced to explain the DND: (1) the walking distance covered; (2) walking distance in relation to severity of obstruction; (3) the greater muscle mass involved in walking than in cycling; (4) the type of exercise, rectangular or triangular; or (5) the difference in ventilatory demand and/or breathing pattern reported between walking and cycling. No significant between-group difference was noted in the walking distance in 6MWT. Our three groups covered approximately the same distance, whereas only the DD group and the DND group showed O2 desaturation during the walk. In the DD group, the distance covered in association with the HR at the end of the test explained 50% of the variability in the O2 desaturation. The DND group showed a trend toward greater walking distance of approximately 40 m, although distance did not explain the variability in O2 desaturation for this group, which confirms the report of Mak et al17 that O2 desaturation during walking is not correlated with distance.

It has been reported that FEV1 impairment and perceived breathlessness are correlated with walking distance in patients with COPD.17 The patients of the DND and DD groups, who showed a tendency toward more greatly impaired FEV1 than the NN group and the same maximal dyspnea, covered the same distance as the NN group, which suggests that FEV1 was not the main factor to explain the distance covered. Our results confirmed those of Troosters et al18 who reported that FEV1 is not implicated in 6MWT use only to investigating exercise tolerance may need to be reconsidered.
the equation prediction of walking distance. DD patients presented a lower FEV₁/FVC ratio and greater TLC than DND patients, however, which suggests that the desaturation in DD patients in all tests could be explained by the specific pathophysiology, ie, emphysema.

During exercise testing, the muscle mass involved in running with a treadmill protocol is greater than in cycling with a cycle ergometer protocol. The greater muscle mass involved in running could increase muscular O₂ extraction, thereby inducing a substantial decrease in venous pressure of O₂. We do not, however, know whether the muscle mass used during high-intensity walking is greater than during cycling in patients with COPD.

In any case, the patients were at approximately 91% of their HRmax from the second minute of 6MWT, which indicates that this test is rectangular. The cycle test is triangular, and the patients maintained the same HR until 2 min before the end of testing. Therefore, even though the intensity was maximal during the cycle test, a higher submaximal intensity was maintained for a longer period during 6MWT, which may indicate higher VO₂ demand and thus lower venous pressure of O₂.

Ventilatory demand may differ with different types of activity, and breathing pattern may thus differ as well. Triathletes exhibiting exercise-induced desaturation were noted to have a different ventilatory pattern in running compared with cycling. During a shuttle test in patients with COPD, Palange et al showed an increase in physiologic dead space/tidal volume ratio, which is consistent with the observations in triathletes. The type of activity (ie, walking vs cycling) may affect the occurrence of desaturation.

Celli et al and Delgado et al further showed that the arm muscles are active during walking exercise in some patients with COPD and this might be a source of reflex impulses to the respiratory centers, leading to dysynchronous breathing and thereby impairing gas exchange. In this study, however, we did not measure breathing pattern or ventilatory demand during the walking test, and further studies are needed. Another point that should be mentioned is that cycling was an unfamiliar form of exercise for our patients. Several studies have reported a higher ventilatory demand in patients with COPD during cycling exercise as compared with walking. The association of this hyperventilation and the possible favorable breathing pattern during cycling could explain the lack of O₂ desaturation observed during the cycle test.

**CONCLUSION**

In conclusion, this study clearly showed that 28% of patients with COPD presented DND. This phenomenon was reproducible and not protocol dependent, suggesting a broader range of clinical applications for 6MWT. The mechanisms of this phenomenon remain unknown, but our data suggest they are multifactorial.
Because desaturation during walking exercise could lead to the prescription of O₂ de-ambulation, further investigation is needed to better understand our findings and possibly to improve the rehabilitation programs of patients with COPD.

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