Kinetics of Changes in Oxyhemoglobin Saturation during Walking and Cycling

Tests in Chronic Obstructive Pulmonary Disease

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ABSTRACT

BACKGROUND AND OBJECTIVE: The patterns and kinetics of changes in oxyhemoglobin saturation measured with pulse oximetry (ΔSpO_2) in six-minute walking test (6MWT) and cycling test has not been addressed in patients with chronic obstructive pulmonary disease (COPD). **METHODS:** Sixty COPD patients with FEV_1 54±18%pred were evaluated for anthropometrics, oxygen-cost diagram (OCD) score, lung function tests, and the 6MWT and cycling test with SpO_2 measurements. The ΔSpO_2 were compared within individual tests and between both tests. The differences in the variables between desaturators and non-desaturators were compared.

RESULTS: In the 6MWT, four patterns of SpO_2 developed. Desaturation-re-saturation was the most common (46%). $\Delta SpO_2 \geq 3\%$ occurred approximately at 1.2 minutes and the nadir re-saturated at 3.5 min. The ΔSpO_2 between the start and the nadir (ΔSpO_{2SN}) was greater than that between the start and the end (ΔSpO_{2SE}) ($p<0.0001$). The desaturators had less inspiratory muscle strength (IMS), more dyspnea, and shorter distance on the 6MWT, while the re-saturators had greater FEV_1/FVC and less functional residual capacity (all $p<0.05$). In the cycling test, three patterns of SpO_2 developed. Desaturation was the most common (57%). The $\Delta SpO_2 \geq 3\%$ and SpO_{2nadir} occurred at 4.6 min and 6.6 min, respectively, of the 6.8-minute exercise duration. The desaturators had less body mass index, OCD score,

IMS post-exercise, diffusing capacity, SpO_2 and work on walking, and peak exercise performance (all $p<0.05$). In both tests, the ΔSpO_{2SN} during the 6MWT was greater ($p<0.05$) but the ΔSpO_{2SE} was similar ($p=0.79$). The desaturators in both tests had lower OCD scores ($p<0.01$) and poorer peak exercise performance. **CONCLUSIONS:** Measurement of ΔSpO_{2SN} rather than ΔSpO_{2SE} during the 6MWT is recommended because ΔSpO_{2SN} is greater and the SpO_{2nadir} is earlier. In both exercise tests, exertional desaturation can be predicted with the OCD scores and has more capability to predict peak exercise performance than the 6MWT.

Key words: *six-minute walking test, incremental cardio-pulmonary exercise test, desaturation, hypoxemia, chronic obstructive pulmonary disease*

Introduction

Walking may induce hypoxemia or oxyhemoglobin (HbO_2) desaturation (decrease in SpO_2) more profoundly than cycling does in patients with chronic obstructive pulmonary disease (COPD).[1-5] Differences in change (Δ) in PaO_2 or SpO_2 between the two exercise modes are due to utilizing different muscle groups for ventilatory compensations for exercise demand.[1, 3, 6, 7] However, results of previous reports are inconsistent,[8, 9] perhaps due to differences in the definitions of desaturation, modes of exercise, and patient populations.[10]

Patterns and kinetics of SpO_2 during different modes of exercise may also influence the magnitude of ΔSpO_2. There are three types of changes in SpO_2 during the six-minute walk test (6MWT) in different individual studies: desaturated, non-desaturated,[4] and re-saturated during the last few minutes,[4, 9, 11] but are rarely reported in a single study. ΔSpO_2 during 6MWT may be influenced by various stages of COPD[4, 12, 13] and by different protocols in conducting the test, which is self-pacing,[14] conducted with "neutral" verbal encouragement, and with allowed rest.[5, 11] In contrast, ΔSpO_2 during incremental cycling test may be influenced by various stages of COPD[15, 16] but may rarely be influenced by different protocols conducting the test, which is computer-controlled, conducted with verbal encouragement, continuous to symptom-limited exhaustion.

We hypothesized that three types of ΔSpO_2 may occur in one individual study and the nadir of SpO_2 may occur midway during the 6MWT, so merely taking the PaO_2[7] or SpO_2[17] at the start and the end of exercise ($_{SE}$) may be inappropriate.[11] This study aimed to investigate how the patterns and kinetics of ΔSpO_2 in these patients differ in each mode of exercise and between both modes, and how the clinical characteristics differ between patients with and without HbO_2 desaturation.

Methods

Study design

A cohort of COPD patients underwent the 6MWT and symptom-limited cycling test in random order. Changes in their SpO_2 and the other variables during the tests were compared.

Subjects

The diagnosis of COPD was based on the criteria set by the Global Initiative for Chronic Obstructive Lung Disease (GOLD).[18] All of the patients were clinically stable for one month before undergoing the two exercise tests, which were conducted within two weeks. Patients were excluded if they had significant co-morbidities, needed home oxygen therapy, or participated in any physical training program during this study. The Institutional Review Boards of Chang Gung Memorial Hospital and Chung

Shan Medical University Hospital approved this study and all of the participants

provided written informed consent.

Protocols and measurements

Oxygen-cost diagram (OCD). The OCD was used as a scale for daily activities

assessed by the patients themselves. The patients were asked to indicate a point on an

OCD, a 100-mm long vertical line with everyday activities listed alongside the line,

spaced according to the oxygen requirement associated with the performance of each

task, above which their breathlessness limited them.[19] The distance from zero was

measured and scored.

Pulmonary function testing. Pulmonary function tests to identify COPD were

performed before the exercise tests. The forced vital capacity (FVC), forced expired

volume in one second (FEV_1), forced expired flow rate from 25-75% of vital capacity

(FEF_{25-75}), total lung capacity (TLC), and residual volume (RV) were measured by

pressure-sensitive body plethysmography (6200 Autobox DL, Sensormedics, Yorba

Linda, CA, USA). The best of three technically satisfactory readings was used.[20, 21]

All lung function data were obtained after inhaling 400 μg of fenoterol HCl. The

diffusing capacity for carbon monoxide (D_LCO) was measured using the single-breath

technique. Simple volume calibration was done using a 3-L syringe before each test.

The maximum inspiratory pressure (MIP), indicating inspiratory muscle strength, was measured at RV with a nose clip and a forceful inspiratory maneuver leading to sustained maximal effort for 1-3 sec, and followed by natural release upon fatigue (Micro Medical RPM, Rochester, Kent, UK). Maximum expiratory pressure (MEP), for expiratory muscle strength, was measured at TLC. Both MIP and MEP were performed thrice before and after the cycling test, with a 1-minute recovery period in between. The best result was recorded for analysis.

Six-minute Walking Test. The walking tests were conducted in a temperature-controlled 20-meter corridor. Blood pressure and breathing frequency were measured. The perceived exertion was measured using a modified Borg score[22] at rest, midway through, and at the end of the walk. The 6MWT was conducted with the help of verbal encouragement as per the American Thoracic Society recommendations.[14] The SpO_2 and pulse rate readings were continuously determined by pulse oximetry (Ohmeda or Nellcor) to maximize the signal and minimize motion artifacts. The signals were stable before the recording, and then stored and printed as 4-sec averages. However, the data in this report were for each minute only.

The pulse oximeters were validated by arterial blood gas analysis.[12] Patterns of ΔSpO_2 were identified and classified independently by two investigators. Consensus was reached after discussion if there were any discrepancies. The ΔSpO_2 was reported

as ΔSpO_{2SN} or the ΔSpO_{2SE}. The minimal clinically significant difference (MCSD) of SpO_2 was defined as a decrease $\geq 3\%$ from the start of the exercise.[12]

Each patient performed the 6MWT twice, with >30 min rest in between. The longest distance walked was recorded in meters and then converted to work of walking (D·W) by multiplying the distance in kilometers by the body weight in kilograms.[9]

Maximum cardio-pulmonary exercise testing. After a 2-minute rest from the mounting on the bike, each patient began a 2-minute unloaded cycling followed by a ramp-pattern exercise test to the limit of tolerance using a computer-controlled and electronic-braked cycle ergometer (Medical Graphics or Vmax). Work rate was selected at a slope of 5-20 watts per min according to pre-determined fitness based on a derived protocol formula.[23]

Heart rate, SpO_2, oxygen uptake ($\dot{V}O_2$) (ml/min), CO_2 output ($\dot{V}CO_2$) (ml/min), $\dot{V}_E$, blood pressure, and Borg score were measured. Pulse rate and SpO_2 were measured continuously by pulse oximetry (Ohmeda, or Nonin 7500). Calibrations of the preVent[TM] or mass flow pneumotachograph were performed using a 3-L syringe before each test. The O_2 and CO_2 analyzers were calibrated with standard gases.

Statistical analysis

Data were summarized as mean±standard deviation (SD). Unpaired and paired

t-tests were used to compare the means of variables between the two independent

groups and two dependent groups, respectively. One-way ANOVA was used to

compare the three groups of consistent changes in the variables. All tests were

two-sided and statistical significance was set at $p<0.05$. All statistical analyses were

performed using the SAS version 9 (SAS Institute Inc.) and Microcal Origin v 4.0

(Northampton).

Sample size and power calculations. The changes in ΔSpO_2 between at-start and

nadir (ΔSpO_{2SN}) of the 6MWT were the primary outcomes. We estimated that a

sample size of 21 participants in each group would be required to detect a MCSD in

ΔSpO_2 of 3% with a standard deviation of the change of 4%[9], statistical power of 0.90

and alpha =0.05 using the Power Analysis and Sample Size (NCSS, LLC, Utah,

U.S.A.).

RESULTS

Sixty patients with COPD (59 men), aged 66.7±6.9 years and with a body mass

index (BMI) of 22.4±3.7 kg/m^2 were enrolled (Table 1). Thirty-seven were recruited

from Chang Gung Memorial Hospital and 23 from Chung Shan Medical University

Hospital. Most had stage II or stage III COPD, with elevated static air trapping and

mildly impaired diffusing capacity.

Six-minute walk test

All patients completed the 6MWT but three were excluded due to unstable baseline recording. Overall, the ΔSpO_{2SE} was 3.7±5.1% ($p<0.0001$) (Table 2; Fig. 1) and 70% of patients presented with desaturation, with the MCSD detected at 1.2 min (Fig. 1, lower panel, $p<0.0001$). The desaturation group was further separated into three sub-groups: three out of 57 patients (5%) who desaturated after the 3rd minute; 26 (46%) who desaturated 7.8±5.6% (ΔSpO_{2SN}) ($p<0.0001$) (Table 2; Fig. 2) from the start of walking to the nadir, and then re-saturated at 3.5±1.4 min; and 11 (19%) who desaturated immediately after the start of walking but did not re-saturate. The ΔSpO_{2SE} was less than the ΔSpO_{2SN} ($p<0.0001$).

Forty patients (70%) with desaturation during walking had significantly less inspiratory muscle strength ($p=0.01$), more breathless perception ($p=0.03$), and less walking distance ($p=0.05$) than those without desaturation (Table 3). Patients with desaturation-re-saturation had greater FEV_1/FVC ($p=0.01$) and less air trapping ($p<0.05$) than those with desaturation.

Cycling test

Fifty of the 60 patients completed the symptom-limited cycling test. Thirteen were excluded (10 did not want to perform the test and three had technical difficulties) so SpO_2 analysis was performed in 47 patients (Table 2).

There were two typical patterns of SpO_2 during the cycling test (Fig. 3). Two

patients who presented with irregular patterns of ΔSpO_2 were not shown in Figure 3.

In total, 27 of 47 patients (57%) desaturated during the cycling test. Desaturation was

initially detected in approximately 30% of the loaded exercise (i.e., approximately 2

min of the total 6.8 min exercise duration). The MCSD was detected at 68% of the

loaded exercise (i.e., approximately 4.6 min of the total exercise duration) and the

nadir at 97% (i.e., 6.6 min of the total exercise duration) (Table 2; Fig. 3). Patients

who desaturated had lower BMI and OCD score, poorer lung function, more

tachypnea and perceived breathlessness, and lower work of walking during the

6MWT. They also had poorer cardio-pulmonary function during the peak exercise test

(Table 4).

Comparisons between the two exercise tests

The SpO_2 was significantly different between the two exercise tests at the start of

the loaded exercise ($p<0.0001$) (Table 2). The difference in ΔSpO_{2SN} was significant

($p=0.02$) but not the difference in ΔSpO_{2SE} ($p=0.79$). The timing of MCSD and the

nadir of SpO_2 was much earlier in the 6MWT than in the cycling test (1.2 min and 3.5

min vs. 4.6 min and 6.6 min, respectively) (both $p<0.0001$).

More patients had MCSD during the 6MWT than the cycling test (40 vs. 27) but

the difference was insignificant ($p=NS$). Moreover, 64% (n=30) had consistent ΔSpO_2

in both tests (Table 5). Those with desaturation in both modes of exercise (i.e., DD

type) had poorer OCD score ($p<0.01$) and cardio-pulmonary function at peak exercise ($p=0.04$ to 0.006) (Table 5). Thus, the OCD score might predict exertional desaturation in both sub-maximal and maximum exercise testing.

DISCUSSION

The present study has several important findings. First, in the 6MWT, the ΔSpO_{2SN} was much greater than the ΔSpO_{2SE} (Fig. 1; Table 2). Between the 6MWT and cycling test, the ΔSpO_{2SN} during the 6MWT was greater (Figs. 1 and 3; Table 2). Second, the timing of MCSD (i.e., $\Delta SpO_2 \geq 3\%$) and the nadir of SpO_2 occurred much earlier in the 6MWT than in the cycling test (1.2 and 3.5 min vs. 4.6 and 6.6 min, respectively; both $p<0.0001$). Continuous monitoring and recording of SpO_2 and ΔSpO_{2SN} during the entire 6MWT is more appropriate than merely taking ΔSpO_{2SE}.

Six-minute walk test

The SpO_2 measurement for patients with COPD during the 6MWT has been recommended for routine use because of the high incidence of desaturation[5, 24] and the related severity[25] and mortality.[26] In the ATS guidelines, it is an optional measurement.[14]

In this study, there are four patterns of SpO_2 changes (Figs. 1 and 2). Twenty-six (46%) patients re-saturating during the second half of the 6MWT had better

FEV_1/FVC and smaller FRC than patients without re-saturation (both $p<0.05$; Table 3). These patients may have slowed down on their own volition, or even rested, to compensate for ventilation when the SpO_2 reached nadir. This is supported by a recent study.[11] Nonetheless, walking-induced desaturation remained steady despite taking a rest.[5]

This issue of measuring ΔSpO_{2SN} during the entire 6MWT has not been raised until recently by Fiore et al.[11] However, ΔSpO_{2SN} during the 6MWT is greater and ΔSpO_{2SE} is smaller in this study than in Fiore's study (7.8% vs. 7% and 3.7% vs. 6%, respectively). The proportion of patients with re-saturation is greater in this study than in Fiore's study (26/40 vs. 5/22, $p=0.001$). They did not present the kinetic of SpO_2 changes during the 6MWT.

The time to desaturation in the 6MWT predicts 24-hour SpO_2 changes in COPD patients with a PaO_2 between 60 and 70 mm Hg.[27] Exertional desaturation after the first minute of the 6MWT forecasts a 74% probability of desaturation in daily activities, while exertional desaturation after 3.5 minutes of the 6MWT negatively predicts (100%) desaturation in whole-day events.[27] However, most previous studies report ΔSpO_{2SE}[4, 8, 17, 28] or ΔPaO_{2SE},[7] but no differences in ΔSpO_{2SE} or ΔPaO_{2SE} between the two modes of exercise have been reported in previous studies[7, 8] and in the present one. A previous study measured SpO_2 on the 3rd minute, but the nadir

might not occur exactly on the 3rd minute, thereby missing the point.[4]

Those with desaturation had marginally lower OCD score and diffusing capacity and significantly weaker inspiratory muscle strength, and more dyspnea, shorter distance walked, and relative tachycardia during the walking test (all *p=0.07 to <0.05;* Table 3). One previous study reported that the mean SpO_2 during the 6MWT was modestly related to lung function (D_{LCO}, FEV_1/FVC, and peak flow rate, r=0.48-0.55) but not related to perceived breathlessness and the distance walked.[29] Another study reported that the resting SpO_2 was significantly related to FEV_1 and the distance walked[5] and to FEV_1 plus $FEF_{25-75\%}$[30]. The sensitivity and specificity of exertional desaturation were 75% when D_{LCO} threshold was set at $60\%_{pred}$.[31] $D_{LCO} > 80\%_{pred}$ plus resting SpO_2 has been used to exclude the evolution of exertional desaturation[32]. The disagreement in the variables of lung function, dyspnea score, and the walking performance in relation to SpO_2 between the study and the previous reports might be due to the different definition of SpO_2 and COPD populations.[10]

Cycling Test

Non-desaturation may be due to increased ventilation and improved $\dot{V}/\dot{Q}$ matching. The mechanisms of SpO_2 desaturation are related to hypoventilation secondary to airway obstruction,[4, 12, 33] decreased mixed venous PO_2, deterioration of $\dot{V}/\dot{Q}$ matching and diffusing capacity, and increased shunting,[10, 33] but not necessarily

to increased pulmonary vascular resistance.[34]

In this study, BMI, OCD score, lung function (including peak flow rate and D_LCO), perceived breathlessness, HbO_2 saturation, and work of walking during the 6MWT, and cardio-pulmonary function at peak exercise are worse in those with desaturation (Table 4). This is partly consistent with previous reports, as exertional desaturation is predicted by $FEV_1 <35\%_{pred}$ plus $D_LCO <35\%_{pred}$[15] and is excluded by $D_LCO >55\%_{pred}$[15] or $FEV_1/FVC >0.5$ plus $D_LCO >20$ ml/min/mm Hg[16]. After the cycling test, the inspiratory muscles are weaker in patients with desaturation (Table 4), indicating that HbO_2 saturation may influence the recovery of inspiratory muscles after exercise. This might be concomitantly due to intercostal muscle blood flow limitation during intense exercise as shown using near infra-red spectroscopy.[35] Exertional desaturation during a maximum exercise test may be significantly related to poorer anthropometrics and lung function at rest, and impacts on the exercise capability of daily activities and on sub-maximal and maximum exercises.

6MWT versus Cycling Test

At the start of the 6MWT, SpO_2 was significantly lower ($p<0.0001$; Table 2), which is consistent with another report.[2] It is possible that there is relatively more hyperventilation triggered by unloaded pedaling during the cycling test than that triggered by standing ready for the walking test. Unfortunately, ventilation during the

walking test was not measured for comparison.

The work load in the cycling test increased more slowly than in the walking test. An incremental cycling test ideally lasts for 10 min, hence 85% of the maximum exercise intensity takes 8.5 minutes. In contrast, the intensity of walking is approximately 85% of the maximum exercise intensity for patients with COPD.[9] The timing of reaching asymptote of heart rate change during the 6MWT reportedly develops by the 3rd minute, as in constant work-rate exercise.[8] In turn, the exercise intensity of the early phase of 6MWT is much heavier than that of the cycling test. Consequently, the 6MWT causes earlier HbO_2 desaturation, if ever, than the cycling test (MCSD and nadir time, 1.2 and 3.5 min vs. 4.6 and 6.6 min, respectively) (Table 2; Figs. 1 and 3).

The re-saturation that occurs in the 6MWT does not happen in the cycling test. The cycling test is considered an external pacing exercise mode wherein the load is increased regularly and smoothly by a computer, while the walking test is an internal pacing exercise mode controlled by the patients themselves. The notion is compatible with a previous report that re-saturation develops after rest.[11]

Poulain et al. reported three sub-groups of COPD patients based on significant HbO_2 desaturation in both the 6MWT and the cycling test (DD), in neither test (NN) and in the 6MWT alone (DND).[4] The present study has more DD patients and fewer

NN patients ($p<0.001$), and four unique NDD-types (i.e., desaturation in the cycling

test alone). The patients here may have more severe airway obstruction than those in

Poulain's study.[4]

Poulain et al. also reported that the severity of FEV_1/FVC was related to the

agreement in occurrence of HbO_2 desaturation between the 6MWT and cycling test.[4]

The DD sub-group had the lowest FEV_1/FVC while the NN sub-group had the highest.

This relationship is not seen in the present study. Body height and OCD scores are

significantly related across the DD, DND-NDD, and NN sub-groups (Table 5).

Patients in the DD sub-group have significantly less active daily lives, suggesting that

the OCD score can predict exertional HbO_2 desaturation in both exercise modes;

diffusing capacity plays only a marginally significant role. The discrepancies between

the study and Poulain's study are perhaps due to the various speeds and volitional

rests in the 6MWT (Tables 3-5).

Study Limitations

There are concerns regarding the accuracy of measuring SpO_2 by pulse

oximetry.[36, 37] The pulse oximeters used in the study were validated by arterial blood

gas analysis.[12] The pattern of heart rate readings remained constantly exponential

when there was SpO_2 re-saturation. Extraction of arterial blood during the field walk

test is technically difficult in the prompt collection of arterial blood at the end of the

walking test. This problem may cause the inconsistency in the previous reports.[1, 3, 7] In a previous study, blood that was immediately sampled within 15 sec after the end of walking showed insignificant difference in PaO_2 between the 6MWT and cycling test.[7] However, two other reports demonstrated significant differences in PaO_2.[1, 3] Sampling blood within 15 seconds is technically demanding and inappropriate as it was shown in this study that SpO_2 re-saturated significantly within 16 ± 14.1 sec during the recovery phase of the cycling test. Although arterial blood sampling during the treadmill walking test is feasible, the test is an external pacing modality unlike the field walking test. Earlobe blood sampling is an alternative and is less invasive,[4] but it has questionable accuracy.[38] Pursed lips breathing[39] could not be evaluated on the 6MWT as the study was not designed for this. Lastly, the 6MWT performance was not significantly different across the DD, DND-NDD, and NN sub-groups (Table 5) but was different between the non-desaturation and desaturation sub-groups (Table 3), suggesting a grouping effect. The DND and NDD (n=4) sub-groups were combined because of their small sample sizes.

CONCLUSIONS

Monitoring of SpO_2 and recording of the $\Delta SpO_{2Start-Nadir}$ during the entire six-minute walk test is recommended because $\Delta SpO_{2Start-Nadir}$ is greater than

$\Delta SpO_{2Start\text{-}End}$ and the timing of SpO_{2nadir} during the 6MWT occurs earlier compared to

the cycling test. Oxygen-cost diagram scores can predict the agreement in occurrence

of SpO_2 changes in both tests. Exertional desaturation in both tests can predict a

poorer peak exercise performance than a walking performance.

Acknowledgments

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LEGEND

Figure 1. *Upper panel*: SpO_2 (%) as a function of exercise duration (min) during the

six-minute walk test in 57 patients with COPD after excluding three patients due

to technical difficulties in pulse oximetry. Solid square: group mean; bars:

standard errors. *Lower panel*: Patients with (n=40) and those without

desaturation (n=17). Solid circle: group mean of patients without desaturation;

solid triangle: group mean of patients with desaturation; bars: standard errors;

arrows: minimal clinically significant desaturation (i.e., ≥3%); dotted line: all

$p < 0.0001$, comparisons of the mean SpO_2 of each minute with the zero time

point; dashed line: all $p < 0.001$ to < 0.01, comparisons of the mean SpO_2 of each

minute with the 1st minute; dotted-dashed line: both $p < 0.05$, comparisons of the

mean SpO_2 of the 5th and 6th min with the 3rd min; short dotted line: both $p < 0.01$

to < 0.05, comparisons of the mean SpO_2 of the 5th and 6th min with the 4th min.

Figure 2. SpO_2 (%) as a function of exercise duration (min) during the six-minute

walk test in 40 COPD patients with SpO_2 desaturation. The patients were divided

into three subgroups based on the patterns of SpO_2 changes. *Upper panel*: Solid

square: the group mean of SpO_2 desaturation after the 3rd minute of exercise; bars:

standard errors; dashed line: all $p < 0.05$, comparisons of the mean SpO_2 with the

3rd minute. *Middle panel*: Solid square: the group mean of SpO_2 desaturation

from the start of exercise and re-saturation to the SpO_2 nadir at 3.5 ± 1.4 min

(open circle); dashed line: $p<0.0001$, comparisons of the SpO_2 of the 5th and 6th

min with the 3rd min; dotted line: $p<0.001$, comparisons of the SpO_2 of the 5th

and 6th min with the 4th min; dotted-dashed line: $p<0.01$, comparisons of the

SpO_2 of the 6th min with the 5th min. *Lower panel*: Solid square: the group mean

of SpO_2 desaturation from the start of exercise, without re-saturation; dashed line:

$p=0.08$, comparison of the SpO_2 of the 6th min with the 5th min.

Figure 3. SpO_2 (%) as a function of exercise duration (min) during the cycling test in

47 COPD patients, excluding two with irregular SpO_2 patterns. The 45 patients

were separated into two sub-groups based on the patterns of SpO_2 changes. Solid

square: the group mean of SpO_2 with desaturation (solid line) and without

desaturation (dashed line), and their standard errors (positive and negative bars

respectively). *$p<0.05$; +$p<0.001$, and **$p<0.0001$ as compared with the zero time

point. Arrow indicates where the minimal clinically significant desaturation (i.e.,

$\geq3\%$) occurred.

Table 1. Demographic data and lung function of patients with COPD (n=60)

Variable	Mean±SD	% pred
Age, year	66.7±6.9	-
Sex, M:F	59:1	-
Height, cm	164.3±6.4	-
Weight, kg	60.9±12.2	-
Body mass index, kg/m^2	22.4±3.7	-
Cigarette, p·y	39.4±14.9	-
Hypertension, n	22	-
Diabetes mellitus, n	4	
Heart disease, n	1	-
Oxygen-cost diagram, mm	70±15	-
FVC, L	2.7±0.7	89±23
FEV_1, L	1.3±0.5	54±18
Stage I/II/III/IV, n	4/30/21/5	-
FEV_1/FVC, %	48±13	-
TLC, L	5.8±1.3	117±27
RV/TLC, %	51±11	-
D_LCO, ml/mm Hg/min	15.6±5.8	77±26

Abbreviations: FVC, forced vital capacity; FEV_1, forced expired volume in one second; TLC, total lung capacity; RV, residual volume; D_LCO, diffusing capacity for carbon monoxide

Table 2. Comparison of oxyhemoglobin saturation (S_PO_2) and exercise duration
between two types of exercise test (n=60)

	6MWT*	Cycling¶	*p* value
S_PO_2, %			
Start	95.2±2	96.5±1.8	<0.0001
Nadir	87.2 ±6.7[§]	91.3±3[§]	0.003
End	91.4±5.6[†,‡]	92.4±3.4[†]	0.18
ΔSpO_2 SN	7.8±5.6[8]	4.9±3.1	0.02
ΔSpO_2 SE	3.7±5.1	3.8±3.4	0.79
Nadir time[†], min	3.5±1.4	6.6±2.5	<0.0001
Exercise duration, min	6	6.8±2.4	0.02

*6MWT: six-minute walk test, 3 patients encountered technical difficulties

¶Ten patients not willing to perform the cycling test and 3 with technical difficulties
were excluded from analysis.

Note: ΔSpO_2 SE, difference between the start and the end; ΔSpO_2 SN, difference
between the start and the nadir; [†]Nadir time from the start; paired t-tests performed
between two modes of exercise test in 47 subjects. [§,†]Comparisons between the start
and the nadir or the,end separately, and [‡]comparison between the nadir and the end,
were all *p*<0.0001; [8] comparison between ΔSpO_2 SE and ΔSpO_2 SN was *p*<0.0001.

Table 3. Comparison of differences between the no-desaturation and desaturation groups during the 6MWT, and between the desaturation-resaturation and desaturation-throughout groups

Group	No desaturation (n=17)	Desaturation (n=40)		*p* value
OCD score, mm	75±14	67±15		0.07
D_{CO}%pred, %	87±24	73±27		0.07
MIP, cm H_2O	80±9	66±19		0.01
6MWT				
Borg, end	2±1.4	3.2±2.4		0.03
HR, 4th min	109±17	124±34		0.06
HR, 5th min	110±17	124±30		0.06
Distance, m	442±79	387±118		0.05
Sub-groups		Desat-resaturation (n=26)	Desaturation (n=14*)	*p* value
FEV_1/FVC		0.52±0.25	0.4±0.13	0.01
TLC, L		5.5±4.2	6.1±1.1	0.07
FRC, L		3.8±4.8	4.5±1.2	<0.05

Abbreviations: OCD, oxygen-cost diagram; D_{CO}, diffusing capacity for carbon monoxide; MIP, maximum inspiratory pressure; 6MWT, six-minute walk test; HR, heart rate; TLC, total lung capacity; FRC, functional residual capacity

*The 14 patients, included 11 patients with desaturation from the start of walking throughout the test, plus 3 patients with desaturation from the 3rd minute of walking till the end.

Table 4. Differences in demographics, lung function, 6MWT, and peak exercise between patients with and those without desaturation during the cycling test (mean±SD)

|	No desaturation (n=18)	Desaturation (n=27)	p value
Body mass index, kg/m^2	23.8±3.7	21.7±3.3	0.05
Oxygen-cost diagram score, mm	80±11	65±14	0.0002
Peak flow rate, L/s	4.1±1.3	2.9±1.5	0.006
Peak flow rate% pred	57%±18%	41%±22%	0.008
D_LCO% pred	84%±21%	68%±23%	0.02
Post MIP, cm H_2O	84.9±14.7	66.9±22.3	0.02
6MWT			
Breathing frequency$_{@6min}$, b/min	23.5±3.6	28.0±6.3	0.004
Borg$_{@3min}$	2.1±1.4	3.4±2.5	0.03
$SpO_{2@1min}$, %	94.7±1.7	92.3±3.0	0.01
$SpO_{2@3min}$, %	92.6±3.8	88.6±6.7	0.01
$SpO_{2@6min}$, %	93.9±2.8	89.7±5.6	0.002
ΔSpO_{2SE}, %	1.8±3.0	5.1±5.5	0.01
Distance·Weight, kg·km	28.6±4.7	23.0±9.7	0.02
Cycling test			
$\dot{V}O_{2peak}$, L/min	1.3±0.3	1±0.4	0.01
$\dot{V}CO_{2peak}$, L/min	1.3±0.3	1±0.5	0.03
O_2 pulse$_{peak}$, ml/min/beat	9.6±2.5	7.1±2.1	0.01
$\Delta\dot{V}O_2/\Delta WR$	8.1±1.1	6.6±2.2	0.01
Systolic BP$_{peak}$, mm Hg	200.7±30.7	222.3±36.7	0.04
$\dot{V}_{Epeak}$, L/min	43.6±10	36.4±13.1	0.04
Tidal volume$_{peak}$, L	1.4±0.2	1.1±0.4	0.001
Inspiratory duty cycle$_{peak}$	0.44±0.04	0.41±0.05	0.03

Abbreviations: Post MIP, maximum inspiratory pressure measured after the cycling exercise; 6MWT, six-minute walk test; Δ, difference; $\dot{V}O_2$, oxygen uptake; $\dot{V}CO_2$, CO_2 output; O_2 pulse, $\dot{V}O_2$/heart rate; $\Delta\dot{V}O_2/\Delta WR$, slope of change in $\dot{V}O_2$ and change in work rate; $\dot{V}_E$, minute ventilation; Inspiratory duty cycle, inspiratory time/breathing cycle time

Table 5. Comparisons of demographic data, lung-function, and exercise response among the four types of agreements in SpO_2 changes between two exercise tests

Variables	Type			p value
	DD (n=23, 49%)	DND-NDD[*] (n=17, 36%)	NN (n=7, 15%)	
Age, yr	64.8±4.6	66.7±7.2	64.3±7.5	NS
Height, cm	166.1±5.7	161.4±6.2	168.6±5	<0.05
BMI, kg/m^2	22.4±4.2	22.2±3.3	23.1±1.9	NS
OCD score, mm	66±14	74±14	84±6	<0.01
FVC, L	2.7±0.7	2.4±0.5	2.8±0.7	NS
FEV_1, L	1.2±0.5	1.2±0.4	1.4±0.3	NS
FEV_1/FVC, %	47±15	50±12	50±11	NS
TLC, L	6.3±0.9	5.7±1.3	6.5±1	NS
RV/TLC, %	54±9	54±13	56±10	NS
D_LCO, ml/mm Hg/min	15.6±5.6	14.7±4.7	19.9±6.2	0.09
6MWT				
Distance, meter	400±111	395±97	474±73	NS
Distance·weight, km·kg	25±10	24.4±5	29.6±7.2	NS
Borg @ 6 min	4.7±2	3.6±2.2	5.8±2.4	NS
Cycling test				
$\dot{V}O_{2peak}$, L/min	0.97±0.35	1.12±0.36	1.38±0.36	0.04
$\dot{V}CO_{2peak}$, L/min	1.04±0.45	1.18±0.45	1.42±0.37	0.06
O_2P_{peak}, ml/beat	7±1.9	8.3±2.7	10±2.8	0.03
V_{Tpeak}, L	1.1±0.38	1.31±0.29	1.53±0.22	<0.01

Abbreviation: DD, $\Delta S_PO_2 \geq 3\%$ occurred in both the walk test and in the cycling test; DND-NDD, $\Delta S_PO_2 \geq 3\%$ in either the 6MWT or the cycling test; NN, $\Delta S_PO_2 \geq 3\%$ occurred in neither test; BMI, body mass index; OCD, oxygen-cost diagram; RV, residual volume; O_2P, oxygen pulse $= \dot{V}O_2$/heart rate
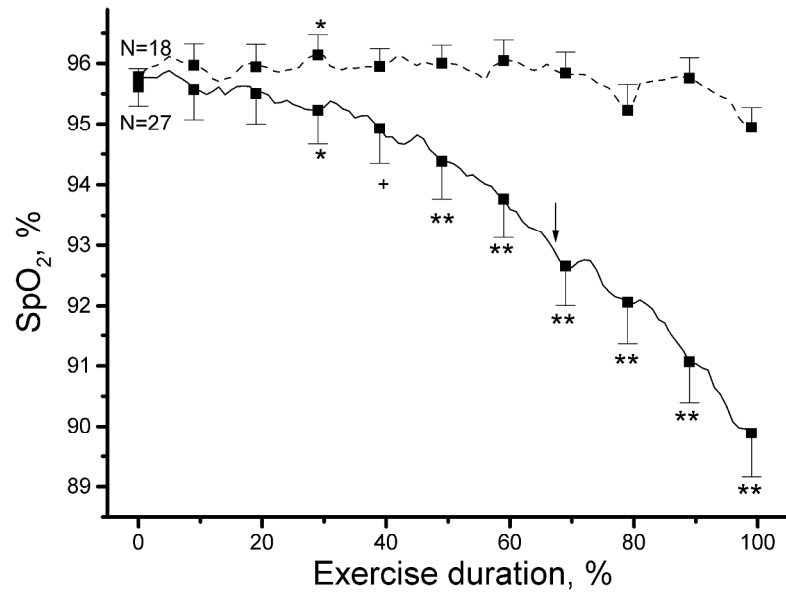
[*]The DND and NDD was combined as a sub-group because there were only four patients in the NDD subgroup.
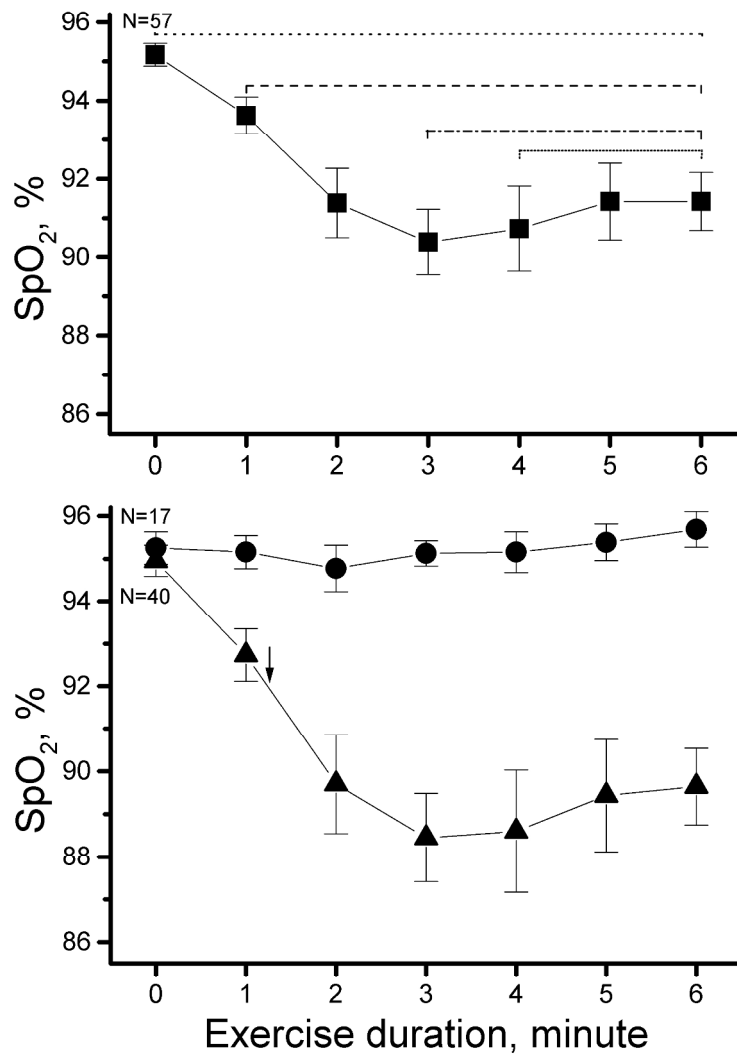
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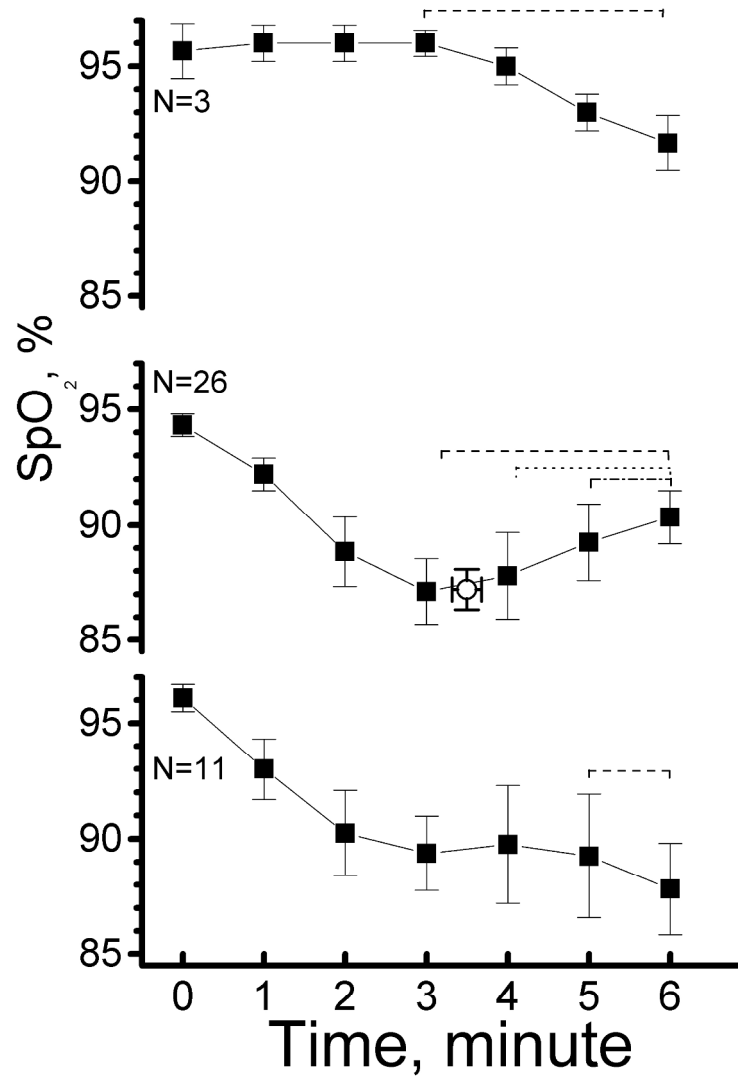
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