

# Factors Associated with Exertional Desaturation in Patients with Chronic Obstructive Pulmonary Disease

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**Abstract:** The six minute walk test (6MWT) has a prognostic role in patients with chronic obstructive pulmonary disease (COPD). The aim of this study was to determine the factors associated with desaturation during the 6MWT in patients with COPD. This study utilized data from the prospective KOREA COPD Subgroup Study (KOCOSS) cohort. The results of the 6MWT performed at enrollment were analyzed in this study. A total of 1789 participants performed the 6MWT. Among them, 185 (10.3%) experienced desaturation during 6MWT. Old age, ex-smoker, low forced expiratory volume in one second (%), and high COPD assessment test score were significantly associated with exertional desaturation.

**Keywords:** COPD, desaturation, six minute walk test

## Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive disease characterized by dyspnea, cough, and sputum. Although the burden of COPD varies from country to country, overall the burden is high globally.<sup>1</sup> The six minute walk test (6MWT) has a prognostic role in patients with COPD. The 6MWT can provide valuable information, especially regarding exercise capacity. In addition to lung function, the 6MWT result is an important component of the body mass index, airflow obstruction, dyspnea, and exercise performance (BODE) index.<sup>2</sup> Moreover, patients who experienced desaturation during the 6MWT had a worse prognosis.<sup>3</sup> Thus, it is clinically important to identify patients with desaturation using the 6MWT. However, the 6MWT is not readily available in routine clinical practice. It requires trained personnel. Moreover, patients may have difficulty cooperating with the test. Additionally, there is a risk of adverse events during the test. Thus, it is desirable that the physician predicts patients who are likely to experience desaturation during 6MWT and selectively perform the test. Decreased exercise capacity in COPD is highly complex, involving a wide range of contributing factors.<sup>4</sup> Reduced exercise



capacity is usually associated with a decline in lung function. However, in addition to significant airflow limitations, the degree of emphysema, depressed mood, and perception of dyspnea symptoms were also related to a decreased exercise capacity.<sup>5</sup> Moreover, little has been known regarding the factors associated with exertional desaturation. The aim of this study was to determine the factors associated with desaturation during the 6MWT in patients with COPD.

## Methods

### Study Population

This study utilized data from the prospective COPD cohort. The KOREA COPD Subgroup Study (KOCOSS) is a nationwide, multicenter, prospective cohort study involving patients with COPD recruited from 58 tertiary referral hospitals in South Korea. This cohort has been used for numerous studies since 2012. Patients with post bronchodilator forced expiratory volume in one second (FEV<sub>1</sub>)/force vital capacity (FVC) < 0.7 and a history of ≥ 10 pack years smoking were defined as COPD. All hospitals involved in the study obtained approval from their respective institutional review board committees, and informed consent was obtained from all patients. The study was performed in accordance with the Declaration of Helsinki.

### Six Minute Walk Test

The results of the 6MWT performed at enrollment were analyzed in this study. The 6MWT was performed according to the American Thoracic Society guideline.<sup>6</sup> Oxygen saturation was measured before and immediately after the test. Desaturation was defined as a ≥ 4% reduction between pre and post and post-test oxygen saturation < 90%.<sup>7</sup>

### Statistical Analysis

Differences between groups were assessed using the chi-square or Fisher's exact test for categorical variables and Student's *t*-test or Wilcoxon Rank-Sum Test for continuous variables. Binary logistic regression was performed to find factors associated with exertional desaturation. *P* values less than 0.05 were considered significant. All statistical analyses were performed with R software (version 4.4.0; R Foundation for Statistical Computing, Vienna, Austria).

## Results

A total of 1789 participants performed the 6MWT. Among them, 185 (10.3%) experienced desaturation during the 6MWT. Baseline characteristics of the patients were shown in Table 1. The desaturation group was significantly older compared to the no desaturation group (*P* = 0.010). The desaturation group had a lower body mass index (BMI) (22.1 vs 23.1, *P* < 0.001). Current smokers were significantly less frequent in the desaturation group (15.7% vs 31.0%, *P* < 0.001). The desaturation group had a significantly lower saturation of partial pressure oxygen before and after the test. However, the total walking distance did not differ significantly between two groups. All measured lung function parameters,

**Table 1** Comparison Between Patients with Desaturation and No Desaturation

Variables	Desaturation (n = 185)	No Desaturation (n = 1604)	P value
Male	183 (98.9%)	1564 (97.5%)	0.309
Age	70.0 (7.7)	68.5 (7.5)	0.010
BMI	22.1 (3.4)	23.1 (3.3)	<0.001
Smoking status			
Current	29 (15.7%)	496 (31.0%)	<0.001
Ex	156 (84.3%)	1106 (69.0%)	
Pack years	47.9 (27.8)	43.9 (23.3)	0.192

(Continued)

Table 1 (Continued).

Variables	Desaturation (n = 185)	No Desaturation (n = 1604)	P value
Exacerbation in the previous year			
Moderate	35 (22.9%)	227 (17.9%)	0.162
Severe	25 (16.3%)	94 (7.4%)	<0.001
Moderate to severe	44 (28.8%)	248 (19.5%)	0.010
6MWT			
SpO <sub>2</sub> (%) before test	94.4 (2.9)	96.4 (2.2)	<0.001
SpO <sub>2</sub> (%) after test	82.6 (11.5)	95.2 (2.6)	<0.001
Total distance (m)	382 (131)	391 (113)	0.986
Comorbidity			
MI	6 (3.2%)	71 (4.4%)	0.573
CHF	4 (2.2%)	51 (3.2%)	0.651
DM	33 (17.8%)	284 (17.7%)	1.000
GERD	13 (7.0%)	125 (7.8%)	0.827
Dyslipidemia	21 (11.4%)	195 (12.2%)	0.826
History of tuberculosis	56 (30.3%)	365 (22.8%)	0.031
mMRC	1.80 (1.01)	1.29 (0.89)	<0.001
CAT	18.2 (8.1)	14.0 (7.7)	<0.001
SGRQ-C	42.8 (22.8)	29.8 (20.4)	<0.001
BDI	8.40 (9.30)	6.46 (7.87)	0.011
BAI	5.43 (8.24)	4.22 (6.53)	0.124
PFT			
FEV <sub>1</sub> (L)	1.37 (0.55)	1.76 (0.56)	<0.001
FEV <sub>1</sub> (%)	47.4 (18.4)	59.5 (17.0)	<0.001
FVC (L)	3.21 (0.80)	3.45 (0.74)	<0.001
FVC (%)	77.9 (17.6)	82.7 (15.2)	<0.001
FEV <sub>1</sub> /FVC (%)	42.6 (12.0)	51.0 (11.3)	<0.001
DL <sub>CO</sub> (%)	46.9 (17.3)	65.7 (19.8)	<0.001
WBC (/mm <sup>3</sup> )	7550 (2360)	7280 (2280)	0.120
Eosinophil (/mm <sup>3</sup> )	250 (285)	236 (273)	0.361

**Notes:** Data are expressed as mean (standard deviation) or number (%). PFT results were post bronchodilator ones.

**Abbreviations** BMI, body mass index; 6MWT, six minute walking test; SpO<sub>2</sub>, saturation of partial pressure oxygen; MI, myocardial infarction; CHF, congestive heart failure; DM, diabetes mellitus; GERD, gastroesophageal reflux disease; mMRC, modified Medical Research Council; CAT, COPD assessment test; SGRQ-C, St. George's Respiratory Questionnaire-COPD; BDI, Beck Depression Inventory; BAI, Beck Anxiety Inventory; PFT, pulmonary function test; FEV<sub>1</sub>, forced expiratory volume in one second; FVC, forced vital capacity; DL<sub>CO</sub>, diffusion capacity of the lung for carbon monoxide; WBC, white blood cell.

**Table 2** Factors Associated with Desaturation

	Odds Ratio (95% CI)	P value
Age	1.04 (1.01–1.07)	0.009
BMI	0.94 (0.89–1.00)	0.053
Ex-smoker	2.10 (1.28–3.59)	0.004
History of tuberculosis	1.34 (0.88–2.01)	0.160
FEV <sub>1</sub> (%)	0.97 (0.96–0.98)	<0.001
CAT score	1.04 (1.02–1.07)	<0.001
Exacerbation in the previous year	1.09 (0.70–1.66)	0.703

**Abbreviations:** CI, confidence interval; BMI, body mass index; FEV<sub>1</sub>, forced expiratory volume in one second; CAT, COPD assessment test.

including FEV<sub>1</sub>, FVC, FEV<sub>1</sub>/FVC, and diffusion capacity of the lung for carbon monoxide were significantly lower in the desaturation group. The desaturation group reported worse dyspnea scores on the modified Medical Research Council and a poorer quality of life on the COPD assessment test (CAT) score and St. George's Respiratory Questionnaire-COPD. The percentage of patients with a previous history of exacerbation in the last year was significantly higher in the desaturation group (28.8% vs 19.5%,  $P < 0.001$ ).

For multivariable analysis, age, BMI, smoking status, history of tuberculosis, FEV<sub>1</sub> (%), CAT score, and exacerbation in the previous year were used. Table 2 showed the results of logistic regression analysis. Among the variables, age, smoking status, FEV<sub>1</sub> (%), and CAT score were significantly associated with exertional desaturation.

## Discussion

The results of the KOCOSS cohort study showed that the 6MWT was associated with variable factors. To the best of our knowledge, this is the first study that identified factors associated with exertional desaturation during the 6MWT. It is ideal to perform the 6MWT in every COPD patient. However, due to limited resources, it is necessary to select patients with a high probability of desaturation. Thus, our results can provide valuable information regarding potential candidates for the 6MWT in real clinical practice.

The clinical importance of desaturation during the 6MWT has been reported in a few studies. Takigawa et al showed that oxygen desaturation was an independent risk factor of death.<sup>8</sup> Casanova et al also found that oxygen desaturation predicted mortality (relative risk, 2.63).<sup>9</sup> Waatevik et al showed that patients with desaturation had a 50% increased risk for experiencing later exacerbation.<sup>3</sup> Kim et al suggested that exertional desaturation may be a predictor of rapid decline in lung function.<sup>10</sup>

In this study, we found that approximately 10% of COPD patients experienced desaturation during the 6MWT. These patients are at high risk of desaturation during pulmonary rehabilitation or exercise. Thus, it is reasonable to provide supplemental oxygen to these patients during pulmonary rehabilitation or exercise. Since the COVID-19 pandemic, home-based pulmonary rehabilitation has been implemented in many institutions. Additionally, regular physical activity and exercise are recommended for all COPD patients. However, in these patients, exertional desaturation may be underdiagnosed since the 6MWT is not routinely performed in clinical practice. Thus, our study results can guide the indication for 6MWT and identify potential exertional desaturators in routine clinical practice.

## Conclusion

In conclusion, several factors differed significantly between desaturation and no desaturation groups. Old age, ex-smoker, low FEV<sub>1</sub> (%), and a high CAT score were independently associated with desaturation. Physicians may predominantly perform the 6MWT in patients with these risk factors.

## Abbreviations

6MWT, Six minute walk test; BAI, Beck Anxiety Inventory; BDI, Beck Depression Inventory; BMI, body mass index; BODE, body mass index, airflow obstruction, dyspnea, exercise performance; COPD, chronic obstructive pulmonary disease; CAT, COPD assessment test; CI, confidence interval; CHF, congestive heart failure; DL<sub>CO</sub>, diffusion capacity of the lung for carbon monoxide; DM, diabetes mellitus; FEV<sub>1</sub>, forced expiratory volume in one second; FVC, force vital capacity; GERD, gastroesophageal reflux disease; KOCOSS, The KOREA COPD Subgroup Study; MI, myocardial infarction; mMRC, modified Medical Research Council; PFT, pulmonary function test; SGRQ-C, St. George's Respiratory Questionnaire-COPD; SpO<sub>2</sub>, saturation of partial pressure oxygen; WBC, white blood cell.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

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