

Clinical Determinants of the Six-Minute Walk Test (6MWT) in Stable Non-Cystic Fibrosis Bronchiectasis Patients

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Background: The six-minute walk test (6MWT) is a suitable tool for the assessment of functional capacity in patients with chronic pulmonary diseases. This study aimed to assess the clinical determinants of the six-minute walk distance (6MWD), exercise-induced desaturation (EID), and pretest saturation of arterial oxygen (Sat_aO₂) in patients with diffuse non-cystic fibrosis (CF) bronchiectasis.

Materials and Methods: In this cross-sectional study, a total of 57 clinically stable patients with diffuse non-CF bronchiectasis were enrolled. Anthropometric measurements (body mass index [BMI], mid-arm muscle circumference [MAMC], and triceps skinfold thickness [TSF]), spirometric indices (forced expiratory volume in one second [FEV1], forced vital capacity [FVC], and FEV1/FVC ratio), imaging assessment (CT scan), and bacteriological sputum studies were performed, and then, 6MWT was carried out.

Results: The mean 6MWD was measured to be 447.11±94.59 m. The average walked distance in patients with severe, moderate, and mild bronchiectasis was 427.73±92.07, 439.63±102.65, and 485.87±80.47 m, respectively, with no significant difference. The pretest Sat_aO₂ was 88.92±5.59%, 93.75±3.36%, and 94.87±2.88% in the severe, moderate, and mild bronchiectasis groups (P<0.001). A significant inverse correlation was observed between the distance walked and BMI (r=-0.434, P=0.001).

Conclusion: The predictors of 6MWD in stable non-CF bronchiectasis patients were FVC, Sat_aO₂ at rest, BMI, and MAMC. The FEV1, FEV1/FVC, and BMI were independent predictors of Sat_aO₂ at rest. The extension of bronchiectasis was the only predictor of EID during the test.

Key words: Six-minute walk test; Bronchiectasis; Functional capacity

INTRODUCTION

Bronchiectasis is recognized as a chronic pulmonary disease. The occurrence of this disease in one lobe is usually due to bronchial obstruction, while involvement of two or more lobes is attributed to either cystic fibrosis (CF) or non-CF causes. Generally, the CT scan findings of patients with bronchiectasis are diverse (1). The clinical course and treatment of CF bronchiectasis differ from non-CF bronchiectasis, because organs and systems other than

the respiratory tract are involved. According to statistics, the frequency of bronchiectasis is increasing worldwide. A study from the United States showed that bronchiectasis has become more common in the general population (2); therefore, it can be considered as a public health concern. Also, the health consequences of this disease are important for the patients because of both pulmonary and systemic effects. Involvement of the airways, muscular weakness,

continuous inflammation, and cardiac complications can result in the decreased function of these patients (3).

Recent studies have reported a lower level of activity in bronchiectasis patients (4, 5). Different tests are used for the assessment of exercise capacity in patients (6). Although cardiopulmonary exercise testing is the gold standard, it is not available in all settings as it requires advanced equipment; therefore, other tests are used as alternatives. The six-minute walk test (6MWT) is recognized as the most important alternative test. It is a relatively simple and precise tool for the assessment of exercise capacity (7) and widely used in daily practice (8). This test indicates the exercise capacity and prognosis of patients with pulmonary diseases, including bronchiectasis (9), and is used for the follow-up and assessment of treatment response (7).

The initial and most important endpoint in the 6MWT is the walked distance (6MWD) (7). A shorter 6MWD during the test is correlated with higher rates of mortality and hospital admission in bronchiectasis patients (7). Other than distance, an important parameter of this test is decreased arterial oxygen saturation (Sat_aO_2) during activity or exercise-induced desaturation (EID) (7). The Sat_aO_2 slightly increases during activity in healthy individuals, while it reduces in patients with pulmonary diseases. A more advanced stage of the disease is correlated with a lower Sat_aO_2 . Continuous measurement of saturation during the test is important, because the lowest amount of oxygen saturation is not necessarily the final recorded value (10, 11).

The EID represents a reduction in blood oxygen during daily activities. It has been recently shown that EID in patients with pulmonary diseases is correlated not only with daily activity impairments, but also with a poor prognosis (9, 12, 13). Therefore, finding the predictors of EID may help us identify patients who require O_2 therapy during activity. Despite the importance of finding the determinants of 6MWT in bronchiectasis patients, there are limited studies in this area. All previous studies have focused on the determinants of 6MWD and reported

inconsistent results (14-16). Age, sex, spirometry, and CT scan findings seem to have different effects on 6MWD, while their effects on EID have not been investigated. Therefore, this study aimed to assess the determinants of 6MWD, EID, and pretest Sat_aO_2 in patients with diffuse non-CF bronchiectasis.

MATERIALS AND METHODS

Setting and patients

In this cross-sectional study, which was conducted in Qazvin, Iran, a total of 57 patients (≥ 18 years) with diffuse non-CF bronchiectasis (involvement of two or more lobes of the lungs), were enrolled from October 2015 to October 2017. Patients were excluded from the study if they had a history of tuberculosis or any comorbidities. Patients were invited to participate in the study, and written consent forms were collected after the researcher explained the study objectives and methods.

Data collection

On the day of admission, a physician assessed the participants to collect the demographic data.

Anthropometric measurements: The patients' weight and height were measured with precision of 500 g and 1 cm, respectively. The body mass index (BMI) was also calculated based on weight (kg) and height (m^2). A BMI $< 18.5 \text{ kg}/\text{m}^2$ was considered as underweight, while BMI $> 25 \text{ kg}/\text{m}^2$ and BMI $> 30 \text{ kg}/\text{m}^2$ were considered as overweight and obese, respectively (17). The mid-arm muscle circumference (MAMC) was measured at the middle of the arm. Also, the triceps skinfold thickness (TSF) was assessed in the same area by using a standard caliper (Vogel, Germany). The percentiles of MAMC and TSF were calculated for each patient by using standard curves, and all values less than 25% were regarded as malnutrition.

Spirometry: Spirometry was carried out, according to the American Thoracic Society (ATS) guidelines (Jaeger Ltd., Hochberg, Germany) (18). Values and percentages of forced expiratory volume in one second (FEV₁), forced vital capacity (FVC), and FEV₁/FVC ratio were

determined. The severity of disease was defined based on FEV1 (severe: FEV1<50% predicted; moderate: 50%≤FEV1<80% predicted; and mild: FEV1≥80% predicted).

Imaging assessment: High-resolution computed tomography (HRCT) was performed according to the criteria proposed by Naidich et al. (19). The extent of disease was evaluated using a modified scoring system developed by Bhalla et al. (20). All CT scans were acquired and scored by a skilled radiologist.

Bacteriological studies: Morning sputum samples were collected after mouth washing and sent to the laboratory. Smears were studied, as well as cultures in a normal medium. The patients were categorized into three groups, based on the isolated microorganisms from the smears and cultures: *Pseudomonas aeruginosa* infections, non-*Pseudomonas* infections, and no infection. All patients received a 50-mL scaled container and were asked to report the volume of sputum in 24 hours.

6MWT: This test was performed for all patients on the day of admission. It included walking for 30 meters at three-meter intervals, based on the ATS guideline (7). The researcher accompanied the patients during the test and documented the results of tests, including 6MWD, Sat_aO₂ at rest, and changes in Sat_aO₂ during the test.

Statistical analysis

All numerical data are summarized as mean, standard deviation (SD), median, minimum, and maximum.

Categorical data are also expressed as ratio and percentage. For evaluating differences between patients with different severities of the disease, analysis of variance (ANOVA) was performed, along with post-hoc analysis (Tukey's HSD), if applicable. Moreover, correlation and linear regression analyses with backward elimination were performed to determine the predictors of 6MWT results. All analyses were performed in SPSS version 22. P-value less than 0.05 was considered statistically significant in all analyses.

RESULTS

A total of 57 patients (22 males and 35 females) with a definite diagnosis of bronchiectasis were analyzed in this study. The mean age (±SD) of the patients was 44.14±15.8 years (range: 18-72 years). The descriptive data, anthropometric indices, spirometric findings, and 6MWT results are shown in Table 1. Based on the FEV1 values, bronchiectasis patients were categorized into three groups in terms of disease severity: severe (n=26), moderate (n=16), and mild (n=15). Evaluation of data according to this categorization is shown in Figure 1. The mean 6MWD was 427.73±92.07 m in severe bronchiectasis patients and 439.63±102.65 m and 485.87±80.47 m in the moderate and mild groups, respectively; however, the results of ANOVA test showed no significant difference between the groups (P=0.153).

Table 1. The anthropometric, spirometry and 6MWT characteristics of the patients

	Test / index	Mean (SD)	Median	Minimum	Maximum
Anthropometric indices	BMI (kg/m ²)	25.02 (6.48)	25.08	13.49	40.37
	MAMC (cm)	15.35 (8.47)	15.23	.40	34.00
	TSF (mm)	5.29 (4.19)	4.00	0.50	17.50
Spirometry	FEV1 (%)	57.49 (23.32)	53.90	22.30	131.60
	FVC (%)	69.73 (20.04)	67.00	35.00	128.50
	FEV1/FVC	66.77 (12.11)	66.77	42.51	89.95
6MWT measures	6MWD (m)	447.11 (94.59)	455.50	162.00	636.00
	6MWD (%)	73.46 (12.96)	76.00	33.00	99.00
	Sat _a O ₂ at rest (%)	91.79 (5.17)	93.00	74.00	99.00
	Sat _a O ₂ after 6MWT (%)	88.41 (9.99)	91.00	37.00	98.00
	EID (%)	3.32 (7.65)	2.00	-3.00	13.00

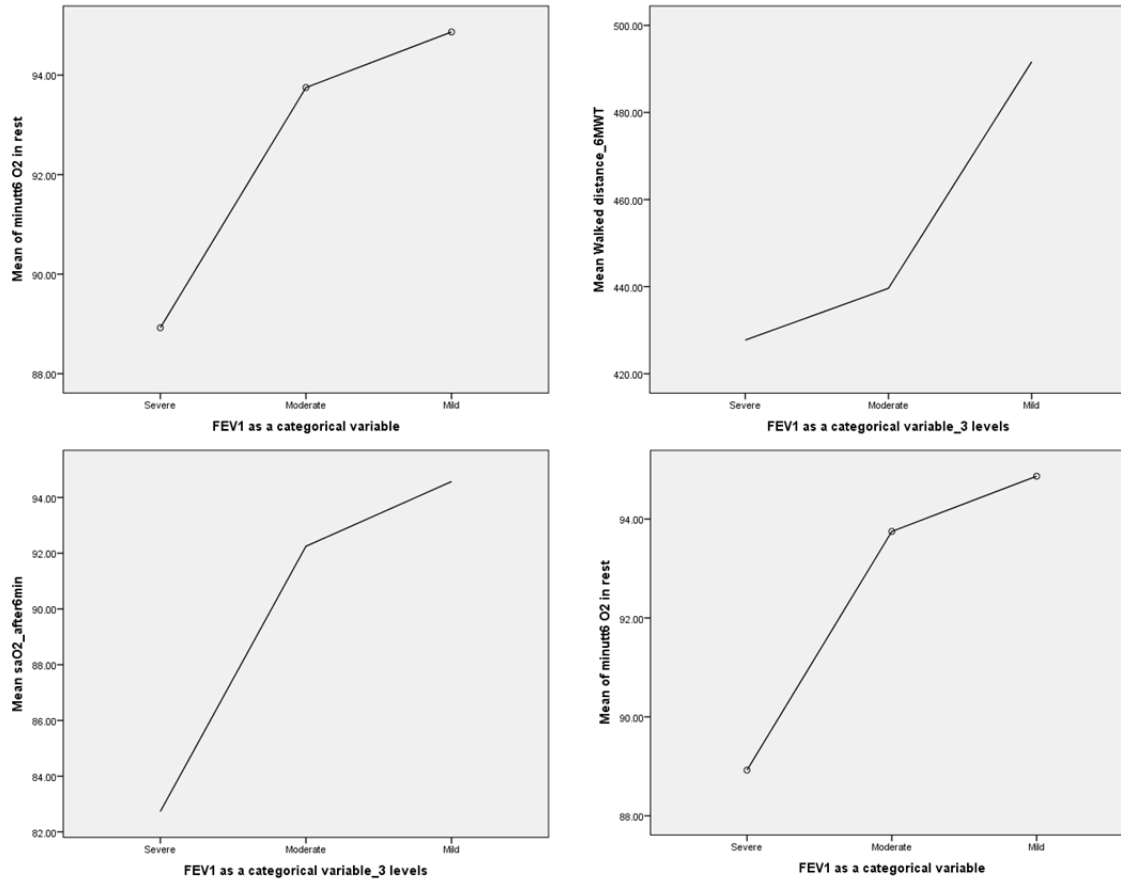


Figure 1. 6MWT variables in mild, moderate and severe disease

The 6MWD percentile was $73.55 \pm 14.56\%$, $72.77 \pm 13.79\%$, and $75.73 \pm 10.98\%$ in the severe, moderate, and mild bronchiectasis groups, respectively; the difference between the groups was not significant ($P=0.817$). The Sat_aO_2 at rest was also examined in the groups. The Sat_aO_2 was $88.92 \pm 5.59\%$ in the severe bronchiectasis group and $93.75 \pm 3.36\%$ and $94.87 \pm 2.88\%$ in the moderate and mild groups, respectively; there was a significant difference between the groups ($P < 0.001$). The results of post-hoc analysis (Tukey's HSD test) showed a significant difference between the severe bronchiectasis group and both moderate and mild groups ($P=0.003$ and $P < 0.001$, respectively); nevertheless, the moderate and mild groups were not significantly different ($P=0.765$).

Regarding the FEV1/FVC ratio, the patients were categorized into two groups of obstructive disease ($< 70\%$)

and non-obstructive disease ($\geq 70\%$). The 6MWD was significantly different between these two groups. The patients with an obstructive disease had an average 6MWD of 431.95 ± 95.61 m, while the non-obstructive group had a mean 6MWD of 490.64 ± 75.17 m ($P=0.041$). Also, the mean 6MWD percentile in the obstructive and non-obstructive groups was $73.34 \pm 14.11\%$ and $75.64 \pm 10.70\%$, respectively, without any significant difference ($P=0.579$). Moreover, analysis of Sat_aO_2 at rest did not indicate any significant differences between the groups ($P=0.104$).

The 6MWD showed a significant inverse correlation with BMI ($r=-0.434$, $P=0.001$) and sputum volume ($r=-0.315$, $P=0.023$). Conversely, the correlation between the 6MWD percentile ($r=0.531$, $P < 0.001$) and Sat_aO_2 at rest was found to be positive ($r=0.291$, $P=0.028$). A linear regression analysis was performed to find significant factors in

6MWD. Using a backward elimination method, the remaining factors in the model were BMI, Sat_aO₂ at rest, MAMC, and FVC (Table 2), which were considered for the accurate prediction of 6MWD.

Moreover, a linear regression analysis was performed to find possible significant predictors of Sat_aO₂ at rest. Based on the backward method, the remaining predictors with significant effects on Sat_aO₂ included BMI, FEV1, and FEV1/FVC ratio (Table 3). These factors were considered for an accurate prediction of Sat_aO₂ at rest in patients. Finally, a logistic regression analysis was conducted to determine effective factors in EID. According to the backward Wald stepwise elimination, the extent of bronchiectasis in CT scan was the only effective factor in reducing Sat_aO₂ (95% CI: 0.293-0.963, P=0.0371).

Table 2. Factors remained in the model: predictors for the 6MWD

	Standardized Coefficients	p-value	95% Confidence Interval for β	
			Lower Bound	Upper Bound
Constant	$\alpha = -161.132$	0.497	-638.731	316.467
FVC	$\beta = 0.253$	0.073	-0.174	3.716
Sat_aO₂ at rest	$\beta = 0.337$	0.018*	1.147	11.529
BMI	$\beta = -0.414$	0.004*	-10.346	-2.199
MAMC	$\beta = 0.370$	0.009*	1.228	8.027

*statistically significant

Table 3. Factors remained in the model: predictors for the Sat_aO₂ at rest

	Standardized Coefficients	p-value	95% Confidence Interval for β	
			Lower Bound	Upper Bound
(Constant)	$\alpha = 17.345$	0.021*	2.745	31.945
FEV1	$\beta = 0.375$	0.002*	0.050	0.210
FEV1/FVC	$\beta = -0.221$	0.054	-0.210	0.002
BMI	$\beta = 0.146$	0.060	-0.005	0.239

*: statistically significant.

DISCUSSION

A total of 57 patients (22 males and 35 females) with a definite diagnosis of bronchiectasis were analyzed in this study. The mean age (\pm SD) of the patients was 44.14 \pm 15.8 years (range: 18-72 years). The descriptive data,

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CONCLUSION

Based on the present results, FEV1, FEV1/FVC, and BMI were independent predictors of Sat_aO_2 at rest in bronchiectasis patients. Also, FVC, Sat_aO_2 at rest, BMI, and MAMC were related to 6MWD. The extent of pulmonary involvement in CT scans was the only predictor of EID during the test. However, age and sex were not significantly associated with the 6MWT results.

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Conflict of Interest: None to declare

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