



Exercise-induced desaturation in subjects with non-cystic fibrosis bronchiectasis: laboratory-based tests versus field-based exercise tests

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ABSTRACT

Objective: To investigate the validity of field walking tests to identify exercise-induced hypoxemia and to compare cardiorespiratory responses and perceived effort between laboratory-based and field-based exercise tests in subjects with bronchiectasis. **Methods:** This was a cross-sectional study involving 72 non-oxygen-dependent participants (28 men; mean age = 48.3 ± 14.5 years; and mean FEV₁ = 54.1 ± 23.4% of the predicted value). The participants underwent cardiopulmonary exercise testing (CPET) on a treadmill and constant work-rate exercise testing (CWRET) on the same day (1 h apart). In another visit, they underwent incremental shuttle walk testing (ISWT) and endurance shuttle walk testing (ESWT; 1 h apart). Desaturation was defined as a reduction in SpO₂ ≥ 4% from rest to peak exercise. **Results:** CPET results were compared with ISWT results, as were CWRET results with ESWT results. There was no difference in the magnitude of desaturation between CPET and ISWT (−7.7 ± 6.3% vs. −6.6 ± 5.6%; p = 0.10) and between CWRET and ESWT (−6.8 ± 5.8% vs. −7.2 ± 6.3%; p = 0.50). The incremental tests showed an agreement in the magnitude of desaturation in the desaturation and no desaturation groups (42 and 14 participants, respectively; p < 0.01), as did the endurance tests (39 and 16 participants; p < 0.01). The magnitude of desaturation was similar among the participants who did or did not reach at least 85% of the maximum predicted HR. **Conclusions:** Field exercise tests showed good precision to detect desaturation. Field tests might be an alternative to laboratory tests when the clinical question is to investigate exercise-induced desaturation in subjects with bronchiectasis.

Keywords: Bronchiectasis; Oxygen; Hypoxia; Exercise test.

INTRODUCTION

Bronchiectasis is a chronic, progressive and debilitating disease characterized by chronic inflammation, recurrent exacerbations, and progressive loss of pulmonary function.⁽¹⁾ Impaired diffusion capacity and an underlying interstitial lung disease have been reported in bronchiectasis, also contributing to limited pulmonary gas exchange and oxygen desaturation during exertion.^(2,3)

Exercise-induced desaturation is a common finding in chronic respiratory diseases,⁽⁴⁾ and it has previously been demonstrated in patients with bronchiectasis.^(5,6) An official systematic review of the European Respiratory Society and the American Thoracic Society⁽⁷⁾ has highlighted the importance of quantifying oxygen desaturation in patients with chronic pulmonary diseases. This recommendation was based on the relationship between oxygen saturation

and important outcomes, such as severity of the disease, prognosis, and muscle weakness.⁽⁷⁾ In patients with bronchiectasis, poor gas exchange⁽⁸⁾ and hypoxemia⁽⁹⁾ are predictors of mortality. In this context, patients with exertional desaturation should be monitored more regularly than those without, in order to minimize possible negative consequences of repeated episodes of hypoxemia. Cardiopulmonary exercise testing (CPET) with pulmonary gas exchange analysis is the gold standard to assess the causes of exercise limitation,⁽¹⁰⁾ but it is expensive and requires highly trained personnel. Therefore, CPET is not readily available in clinical practice, and it would not be the test of choice for detecting exertional desaturation.

In previous studies, mostly involving patients with COPD, field walking tests were found to be more sensitive in detecting the magnitude of desaturation than were cycle

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ergometer tests.⁽⁷⁾ A similar finding was observed in subjects with bronchiectasis in whom the magnitude of desaturation was found to be higher during an incremental walk test, such as the incremental shuttle walk test (ISWT), than during an incremental cycle ergometer test, such as CPET.⁽⁶⁾ This result is not completely surprising because walking and cycling are completely different activities. However, the degree of exercise-induced desaturation is quite similar between the ISWT and the endurance shuttle walk test (ESWT),⁽¹¹⁾ as well as between the ISWT and the six-minute walk test (6MWT) in subjects with COPD.⁽¹²⁾ Recently, a study has suggested that field walking tests (6MWT, ISWT, and ESWT) can be used interchangeably for the evaluation of the level of exercise-induced desaturation in subjects with non-cystic fibrosis (NCF), because they lead to an equivalent oxygen desaturation.⁽¹³⁾ To date, the magnitude of desaturation in similar modalities of exercise (based on walking) but in different contexts (laboratory or field) has yet to be investigated in subjects with bronchiectasis. Our hypothesis was that incremental tests—CPET on a treadmill or ISWT—and tests at a constant workload—constant work-rate exercise testing (CWRET) on a treadmill or ESWT—would show similar desaturation results. The objective of this study was to investigate the validity of the ISWT and ESWT as reliable tools in order to identify exercise-induced desaturation, comparing cardiorespiratory responses and perceived effort/fatigue between laboratory-based and field-based exercise tests in subjects with NCF bronchiectasis.

METHODS

This was a cross-sectional study involving patients with NCF bronchiectasis. The inclusion criteria were being ≥ 18 years of age, not depending on oxygen, being a nonsmoker, presenting with no other chronic lung or cardiovascular diseases, and being in a stable clinical condition (absence of changes in spirometry, dyspnea, cough, general condition, medications and doses, as well as in viscosity and color of secretions in the four weeks preceding entry into the study).⁽¹⁴⁾ Patients who were unable to perform or understand how to perform the proposed tests were excluded, as were those who had decided to withdraw from the study. Bronchiectasis was diagnosed in accordance with followed the British Thoracic Society guideline for NCF bronchiectasis⁽¹⁴⁾ and was confirmed by HRCT.

The study was conducted in two visits. At the first visit, spirometry was performed, BMI was calculated, and the perception of dyspnea was assessed by the modified Medical Research Council (mMRC) scale.⁽¹⁵⁾ In addition, the participants were randomized to perform either CPET and CWRET or ISWT and ESWT. A bronchodilator (albuterol, 400 μg) was administered 15 minutes prior to the tests. At the second visit, seven days later, spirometry was performed again to evaluate clinical stability, and the participants performed the second set of tests. Desaturation was considered

present if there was a reduction in $\text{SpO}_2 \geq 4\%$ from rest to peak exercise.⁽⁴⁾

Spirometry was performed using Ultima CPX (MGC Diagnostics Corporation, Saint Paul, MN, USA). Acceptability and reproducibility criteria adopted for the technical procedures were those recommended by the Brazilian guidelines for lung function testing.⁽¹⁶⁾ We collected data on FVC, FEV_1 , and FEV_1/FVC ratio expressed in absolute values and as a percentage of the predicted value for the Brazilian population.⁽¹⁷⁾

The CPET was conducted on a treadmill (Millennium Classic; Inbramed/Inbrasport, Porto Alegre, RS, Brazil), using the protocol recommended by Balke and Ware,⁽¹⁸⁾ including constant speed estimated on the basis of the physical fitness of the participant (pulmonary function and baseline dyspnea assessed by the mMRC scale). Increments of one percent in the inclination were imposed every minute. Considering the period of workload increment, the test should last 8–12 min. Measurements of HR (Polar Precision Performance; Polar Electro Inc., Bethpage, NY, USA) and SpO_2 (finger pulse oximeter model 9500; Nonin, Plymouth, MN, USA) were continuous during the test. Blood pressure (BP) was measured every 2 min of exercise. The Borg scale was used to rate the perception of dyspnea and leg fatigue⁽¹⁹⁾ at rest and immediately after the end of the exercise.

The ISWT was performed in accordance with the original description⁽²⁰⁾ in a 10-m hallway. The test was stopped if the participant could not follow the rhythm delivered by the sound. The test was also stopped if the participant showed chest pain, intolerable dyspnea, leg cramps, staggering, diaphoresis, or a pale/ashen appearance.⁽⁷⁾ Measurements of HR and SpO_2 were continuous during the test (using the same devices described for CPET) and recorded every minute. The BP and the Borg scale scores for the perception of dyspnea and leg fatigue⁽¹⁹⁾ were obtained at rest and immediately after the end of the exercise. The ISWT was performed twice (30 min apart).⁽⁷⁾ The best walk distance was expressed in absolute value and as a percentage of the predicted value.⁽²⁰⁾

The CWRET was performed one hour after the CPET using the same maximum speed as that used for CPET and a maximum inclination of 75%. Electrocardiogram tracing, HR, and SpO_2 were continuously measured during the test. The BP was measured every 2 min of exercise. The Borg scale measured the perception of dyspnea and leg fatigue⁽¹⁹⁾ at rest and immediately after the end of the exercise.

The ESWT was performed as recommended,⁽²¹⁾ being performed one hour after the ISWT and using the same interruption criteria as in the ISWT. The ESWT speed was 85% of the peak oxygen uptake during the ISWT, as determined by the following regression equation: oxygen uptake = $4.19 + (0.025 \times \text{ISWT distance})$.^(20,21) The HR and SpO_2 were continuously measured during the test. The BP and the Borg scales for the perception

of dyspnea and leg fatigue⁽¹⁹⁾ were obtained at rest and immediately after the end of the exercise.

The present study was conducted in accordance with the principles of the Declaration of Helsinki, and the Research Ethics Committees of the *Nove de Julho* University (Reference no. 451538) and the São Paulo State University (Reference no. 0921/11) approved the study. All participants gave written informed consent.

Statistical analysis

We used the Shapiro-Wilk test to determine whether the data had normal or non-normal distribution. Data with parametric distribution were expressed as means and standard deviations, and those with nonparametric distribution (Borg and mMRC scale scores) were expressed as medians and interquartile ranges.

The baseline characteristics between the groups of the participants who did and did not desaturate were compared by the unpaired Student's t-test. Comparisons between CPET and ISWT, as well as between CWRET and ESWT were analyzed by the paired Student's t test for parametric data and by the Wilcoxon test for nonparametric data. The agreement regarding the level of desaturation between CPET and ISWT, as well as between CWRET and ESWT, were analyzed by the chi-square test and Cohen's kappa coefficient (< 0.00, no agreement; 0.00-0.20, slight agreement; 0.21-0.40, fair agreement; 0.41-0.60, moderate agreement; 0.61-0.80, substantial agreement; and 0.81-1.00, perfect agreement).⁽²²⁾ Accuracy, sensibility, specificity, and predictive values (and their respective 95% CIs) were also calculated. The unpaired Student's t-test was used in order to compare SpO₂ between the groups of participants who reached ≥ 85% and < 85% of the maximum predicted HR in the incremental and endurance tests. Statistical significance was set at $p < 0.05$. All statistical analyses were performed using the SPSS Statistics software package, version 20.0 (IBM Corporation, Armonk, NY, USA). The post hoc power of the sample was calculated taking into account the chi-square test, because the basis of the present study was to investigate whether there was an association between desaturation (yes or no) and exercise tests (ISWT vs. CPET and ESWT vs. CWRET). The program G*Power, version 3.1 (Heinrich Heine University, Düsseldorf, Germany)⁽²³⁾ was used for this analysis.

RESULTS

A convenience sample of 92 individuals was recruited; 17 declined to participate. Therefore, 75 were included in the study. Of those, 3 were excluded (2 did not perform all tests, and 1 did not perform the tests correctly). A total of 72 individuals were therefore studied, 28 of whom were male. Most of the participants were normal-weight women with a restrictive and/or obstructive pattern on spirometry (Table 1). With regard to baseline characteristics, only pulmonary function test results differed between those who did or did not present with desaturation (Table 1).

A similar behavior in SpO₂ was observed, minute by minute, during the incremental and constant workload tests (Figure 1). Most subjects presented with desaturation in all tests (CPET: 74%; ISWT: 65%; CWRET: 64%; and ESWT: 68%). There was no difference in the levels of desaturation between the incremental and constant work-rate walk tests (Table 2). The agreement analysis between CPET and ISWT demonstrated that, of the 72 study participants, 42 presented with desaturation in both tests, and 14 presented with no desaturation in either tests (chi-square test = 17.287; $p < 0.01$). Comparing CWRET and ESWT, in the sample as a whole, 45 participants presented with desaturation in both tests, and 15 presented with no desaturation in either tests (chi-square test = 16.394; $p < 0.01$). Retrospective power analysis for both chi-square tests was 0.99. Table 3 summarizes the agreement analysis.

Distance, total exercise time, HR, systolic BP, and perception of dyspnea and leg fatigue were greater in CPET than in ISWT. Similarly, HR, systolic BP, and perception of dyspnea were greater in CWRET than in ESWT (Table 2). Regardless of the test, desaturation was similar among the participants who reached at least 85% of the maximum predicted HR or not (Table 2).

DISCUSSION

Field-based exercise tests with similar profiles to those of laboratory-based exercise tests induce similar oxygen desaturation in subjects with bronchiectasis. Cardiorespiratory responses and perception of effort were higher in laboratory-based tests than in field-based tests. Field tests are accurate for the detection of desaturation, demanding less effort from participants than do laboratory-based tests.

Oxygen desaturation cannot commonly be predicted from data obtained at rest. Therefore, exercise testing is important to determine patients who may present with desaturation during exertion.⁽²⁴⁾ Because CPET is not readily available in clinical practice, field walking tests can be an alternative for the assessment of exercise-induced desaturation, because they have low costs and are easy to perform.⁽⁷⁾

Exercise-induced desaturation has previously been demonstrated in individuals with bronchiectasis.⁽⁶⁾ In that population, the level of desaturation is higher during ISWT than during CPET performed on a cycle ergometer.⁽⁶⁾ In addition, 21% of patients who showed desaturation during ISWT showed no desaturation during CPET.⁽⁶⁾ Similar results have been observed in subjects with COPD.^(12,25,26) This finding might have occurred because the incremental CPET was performed on a cycle ergometer. However, an incremental walk test on a treadmill also led to a significantly lower PaO₂ than did an incremental cycle ergometer test in subjects with COPD.⁽²⁷⁾ Therefore, tests performed on a cycle ergometer may underestimate the real desaturation during exercise, making walk tests more sensitive for detecting desaturation.⁽⁷⁾

Table 1. Characteristics of the sample as a whole and of those who did and did not desaturate.^a

Variable	Total sample (N = 72)	Group		p
		No desaturation (n = 14)	Desaturation (n = 58)	
Age, years	48 ± 15	51 ± 16	48 ± 14	0.48
Male sex	28 (38.9)	3 (21.4)	25 (43.1)	0.11
Weight, kg	64.4 ± 14.4	64.2 ± 17.0	64.5 ± 13.8	0.96
Height, m	1.6 ± 0.1	1.6 ± 0.1	1.6 ± 0.1	0.53
BMI, kg/m ²	25.3 ± 5.5	25.5 ± 6.4	25.3 ± 5.3	0.89
mMRC score	2.0 [1.0-2.0]	2.0 [0.8-2.0]	2.0 [1.0-2.0]	0.55
FVC, L	2.3 ± 0.8	2.6 ± 0.8	2.3 ± 0.8	0.22
FVC, % predicted	68.7 ± 20.0	82.2 ± 22.5	65.5 ± 18.2	0.02
FEV ₁ , L	1.5 ± 0.6	1.9 ± 0.6	1.4 ± 0.6	0.01
FEV ₁ , % predicted	54.1 ± 23.4	74.1 ± 27.7	49.3 ± 19.6	< 0.01
FEV ₁ /FVC	0.6 ± 0.1	0.7 ± 0.1	0.6 ± 0.1	0.01

mMRC: modified Medical Research Council dyspnea scale. ^aValues expressed as mean ± SD, n (%), or median [IQR].

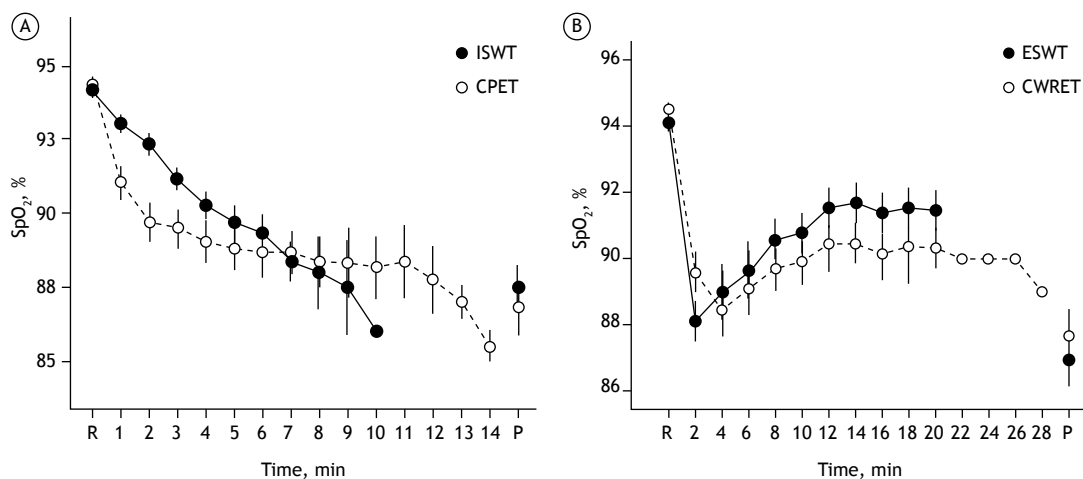


Figure 1. In A, comparison between the incremental shuttle walk test (ISWT) and cardiopulmonary exercise testing (CPET) regarding the variation of SpO₂ during the tests. In B, comparison between the endurance shuttle walk test (ESWT) and constant work-rate exercise testing (CWRET) regarding the variation of SpO₂ during the tests. The error bar (P) corresponds to the standard error.

In the present study, walk tests showed comparable levels of desaturation, even when using different approaches (incremental or endurance exercise tests). One previous study has demonstrated that the level of desaturation in subjects with bronchiectasis was similar during the 6MWT, ISWT, and ESWT (-6.8 ± 6.6 ; -6.1 ± 6.0 ; and -7.0 ± 5.4 , respectively) and suggested that field walking tests can be used interchangeably for the evaluation of the level of exercise-induced desaturation in those subjects.⁽¹³⁾ The same was found in patients with COPD when ISWT was compared with ESWT⁽¹¹⁾ and 6MWT.⁽²⁶⁾

Incremental and endurance exercise tests induced more intense cardiovascular and ventilatory responses, as well as a higher perception of dyspnea, when performed on a treadmill rather than in a corridor/hallway. This is because there are important differences in the gait mechanics between these two forms of walking.⁽²⁸⁻³¹⁾ Treadmill walking requires greater effort and higher energy expenditure to maintain lateral

balance control.^(29,31,32) Furthermore, most patients are not familiar with that activity.⁽³³⁾ However, in our study, participants were allowed to support themselves using their hands on the treadmill. When subjects walk on a treadmill with hand support, there is a considerable reduction in the demand of walking and their responses change significantly. When hand support is allowed, body balance control increases, and energy consumption and the demand to maintain balance control decreases.^(29,31,32) Because hand support was allowed in the present study, exercise time increased, and, consequently, more intense cardiopulmonary responses and higher perception of dyspnea were found in the tests performed on a treadmill.

Subjects that presented with desaturation had worse lung function parameters. This is not a surprising result because exertional desaturation has been associated with lower FEV₁ and worse prognosis.⁽³³⁾ We observed that the magnitude of desaturation was similar in the groups of participants who did and did not reach

Table 2. Performance and cardiorespiratory responses, as well as perception of dyspnea and leg fatigue, during the walk tests (N = 72).^a

Variable	CPET	ISWT	p	CWRET	ESWT	p
SpO ₂	86.8 ± 7.0	87.5 ± 6.0	0.23	86.8 ± 6.9	86.9 ± 7.2	0.17
ΔSpO ₂	-7.7 ± 6.3	-6.6 ± 5.6	0.10	-6.8 ± 5.8	-7.2 ± 6.3	0.50
Distance, m	690.14 ± 265,8	455.4 ± 123.3	< 0.01	797.7 ± 490.4	756.4 ± 559.6	0.57
Speed, km/h	4.7 ± 1.0	5.3 ± 0.8	< 0.01	4.7 ± 1.0	5.1 ± 0.7	< 0.01
Slope, %	10.4 ± 4.0	N/A	N/A	7.9 ± 3.0	N/A	N/A
Distance, % of predicted	N/A	57.0 ± 15.2	N/A	N/A	N/A	N/A
Time, min	8.5 ± 2.5	7.11 ± 1.28	< 0.01	9.9 ± 5.8	8.9 ± 6.5	0.29
HR, bpm	148.9 ± 19.3	135.1 ± 20.4	< 0.01	144.7 ± 19.8	135.7 ± 20.3	< 0.01
HR, % of predicted	87.0 ± 9.0	78.9 ± 11.4	< 0.01	84.5 ± 9.9	79.3 ± 11.8	< 0.01
HR ≥ 85% of predicted	44 (61.1)	23 (31.9)	< 0.01	30 (41.7)	26 (36.1)	< 0.01
SpO ₂ (HR ≥ 85% of predicted)	87.3 ± 5.8	86.8 ± 5.9	0.77	87.9 ± 5.5	85.6 ± 7.4	0.19
ΔSpO ₂ (HR ≥ 85% of predicted)	-7.1 ± 5.0	-7.6 ± 5.8	0.74	-6.5 ± 4.8	-8.3 ± 6.1	0.23
HR < 85% of predicted	28 (38.9)	49 (60.1)	< 0.01	42 (58.3)	46 (63.9)	< 0.01
SpO ₂ (HR < 85% of predicted)	86.1 ± 8.4	87.9 ± 6.1	0.33	87.5 ± 7.1	87.7 ± 7.0	0.91
ΔSpO ₂ (HR < 85% of predicted)	-8.6 ± 8.0	-6.2 ± 5.5	0.17	-7.0 ± 6.4	-6.6 ± 6.4	0.73
SBP, mmHg	154.8 ± 17.7	136.3 ± 20.2	< 0.01	153.1 ± 16.3	138.1 ± 17.8	< 0.01
DBP, mmHg	79.9 ± 10.5	77.3 ± 9.5	0.48	79.4 ± 11.5	77.0 ± 10.2	0.05
Borg scale, dyspnea	5 [4-8]	4 [3-7]	< 0.01	5 [4-7]	4 [2-6]	< 0.01
Borg scale, leg fatigue	5 [3-7]	3 [2-6]	< 0.01	4 [2-7]	4 [2-6]	0.30

CPET: cardiopulmonary exercise testing; ISWT: incremental shuttle walk test; CWRET: constant work-rate exercise testing; ESWT: endurance shuttle walk test; ΔSpO₂: SpO₂ at rest minus SpO₂ at the peak of exercise; SBP: systolic blood pressure; DBP: diastolic blood pressure. ^aValues expressed as mean ± SD, n (%), or median [IQR].

Table 3. Accuracy, sensitivity, specificity, predictive values, and agreement between laboratory-based and field-based exercise tests.^a

Variable	ISWT vs. CPET	ESWT vs. CWRET
Accuracy	77.8 (66.4-86.7)	83.3 (72.7-91.1)
Sensitivity	79.3 (66.0-89.0)	84.9 (72.4-93.3)
Specificity	73.7 (48.8-90.9)	79.0 (54.4-94.0)
PPV	89.4 (76.9-96.5)	84.9 (72.4-93.3)
NPV	56.0 (34.9-75.6)	65.2 (42.7-83.6)
Kappa	0.481 (0.265-0.649)	0.475 (0.234-0.678)

ISWT: incremental shuttle walk test; CPET: cardiopulmonary exercise testing; ESWT: endurance shuttle walk test; CWRET: constant work-rate exercise testing; PPV: positive predictive value; and NPV: negative predictive value. ^aValue (95% CI).

the maximum predicted HR (≥ 85% and < 85%, respectively) in the incremental and constant load walk tests. These findings suggest that the highest cardiac load occurred due to a better performance on the tests rather to a tachycardic response to hypoxemia. When healthy individuals who showed desaturation at the end of the ISWT were compared with those who showed no desaturation at the end of the test, no difference was found in cardiac stress between the groups (88.3 ± 9.3% vs. 87.6 ± 9.6% of maximum predicted HR).⁽³⁴⁾

The present study has some limitations. Although we used a convenience sample, a post hoc power analysis indicated that our sample was sufficient to show associations between the tests being compared in relation to our main objective. Pulmonary function analysis was performed only by spirometry. We know that the evaluation of DLCO would increase sensitivity for detecting gas exchange abnormalities. However, the study was not aimed at investigating the determinants

of exercise-induced desaturation. Although SpO₂ was recorded every minute, a more accurate comparison of the tests regarding the time to achieve desaturation was not possible in our study.

In conclusion, the magnitude of desaturation was similar between incremental walk tests (CPET and ISWT) and constant workload walk tests (CWRET and ESWT), demonstrating that field walking tests showed good precision to detect desaturation. Cardiorespiratory responses, perceived effort, and perception of fatigue were greater in laboratory-based than in field-based exercise tests. In this context, field walking tests might be an alternative to laboratory-based tests when the objective is to investigate exercise-induced desaturation in subjects with bronchiectasis.

AUTHOR CONTRIBUTIONS

CHYO: conception and design of the study; data acquisition, analysis, and interpretation; drafting of

the manuscript; and final approval of the version to be published. AJ: data analysis and interpretation; critical revision of the manuscript for important intellectual content; drafting of the manuscript; and final approval of the version to be published. AAC: conception and design of the study; data analysis; critical revision of the manuscript for important intellectual content; and final approval of the version to be published. MIZF: data analysis; critical revision of the manuscript for important intellectual content; and final approval of the version to be published. RAA and SZR: data analysis

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