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A symptom-limited incremental step test determines maximum physiological responses in patients with chronic obstructive pulmonary disease[☆]

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Summary

Background: Step tests have been used to evaluate exercise tolerance and effort-related hypoxemia in different diseases. A symptom-limited incremental step test (IST) has never been tested in COPD patients.

Aim: To compare maximal physiological responses between an IST and cardiopulmonary exercise testing (CPET), to test the reproducibility of the IST on different days, and to provide a predict equation to estimate VO_2 from the IST in patients with COPD.

Material and methods: At the same day, thirty-four patients (VEF_1 $46 \pm 14\%$ of pred) underwent a CPET on cycle ergometer and the first IST (IST-1) (1 h apart). After 2—5 days, patients repeated the IST (IST-2). Pulmonary gas exchange was measured during all tests.

Results: Peak VO_2 was significantly higher in IST-1 and IST-2 than in CEPT (Mean $\pm$ SD: 1.19 ± 0.39 L, 1.20 ± 0.40 L, 1.07 ± 0.35 L) with no difference for ventilation (VE), heart rate (HR), and perception of effort. ISTs were highly reproducible, with significant intraclass correlation coefficient (CCI [95% confidence interval]) for number of steps ($0.98[0.95—0.99]$), VO_2 ($0.99 [0.98—0.99]$), VE ($0.97[0.93—0.99]$), HR ($0.92[0.81—0.97]$), and SpO_2 ($0.96[0.90—0.98]$). Desaturation was significantly higher for IST-1 and IST-2 compared with cycling (Mean $\pm$ SD:

$-6 \pm 5\%$, $-6 \pm 4\%$, $-3 \pm 3\%$). Number of steps and patient weight explained 81% of the variance in peak VO_2 ($p < 0.001$).

Conclusion: A symptom-limited incremental step test, externally paced, elicits maximal cardiopulmonary and metabolic responses, and is well tolerated and reproducible in patients with COPD.

Introduction

In addition to systemic manifestations, the main consequence arising from chronic obstructive pulmonary disease (COPD) is the exercise intolerance. Cardiopulmonary exercise testing (CPET) remains the gold standard to assess patient's exercise capacity [1], but its use is limited in clinical practice. Hence walk tests have been widely used in subjects with cardiopulmonary diseases for this purpose [2] and as a complement to laboratory-based tests [3] because desaturation occurs during walking but not cycling in a subgroup of patients [4]. In terms of pulmonary function, the patients who presented desaturation on the 6MWT and CPET had greater total lung capacity in comparison with those who presented desaturation only during the 6MWT [4]. The mechanisms involved in this phenomenon are not yet completely understood, and it is speculated that it occurs due to differences in the ventilatory demand and muscle mass used during cycling and walking.

While walk tests such as the 6MWT and shuttle walk test require corridors free from transit, 30 and 10 m in length, respectively, for appropriate execution, the step test is a feasible alternative for evaluating exercise capacity, due to its portability.

The first description of the step test in COPD was in the mid-1980s and it elicited higher ventilation and oxygen uptake (VO_2) in comparison with walking and cycling [5]. The protocol used by Swinburn et al. [5] could be considered a constant workload test as the stepping rate was kept constant (15 steps per minute) throughout the test. The same should be considered for the 6-min stepper test [6], as it is self-paced and limited by time. Therefore, these tests do not allow evaluation of cardiopulmonary responses to the progressive increase in demand.

Recently, our group compared exercise tolerance and physiological responses between two different incremental step test protocols [7]. A longer duration and a higher number of steps were obtained in the symptom-limited incremental step test. However, it is still unknown whether this test determines maximum physiological responses in patients with COPD. Therefore, the objectives of this study were (i) to analyze whether a symptom-limited incremental step test determines maximum physiological responses, and secondarily, (ii) to test the reproducibility of the step test performed on different days, (iii) to compare exercise-induced desaturation between stepping and cycling in patients with COPD, and (iv) to provide a prediction equation for estimating the oxygen uptake (VO_2).

Methods

Subjects

Thirty-four consecutive male subjects with moderate-to-severe COPD [8] were studied. The subjects were clinically stable, their medications had not changed during the study, and they presented resting oxygen saturation higher than 90% in room air. No subjects were receiving medications that could affect exercise responses. Subjects with any musculoskeletal condition that could limit their participation in performing the tests were excluded. Written, informed consent was obtained from all subjects, and the Ethics Committee of the Universidade Nove de Julho approved the study (182476).

Study design

Subjects were tested on two occasions. On the first day, the subjects underwent CPET, and after an hour of rest, they performed the first incremental step test (IST-1). Depending on the availability of the patients, they returned two to five days later to repeat the step test (IST-2). Before carrying out the first step test, a 1-min period of practice was held for familiarization with the step rhythm. All tests were performed at room air. The primary outcomes were VO_2 and number of steps.

Maximal cardiopulmonary exercise testing

The CPET test was carried out on an electromagnetically braked cycle ergometer (Corival; Lode B.V. Medical Technology, Groningen, Netherlands). After 2 min at rest and 2 min more cycling at zero workload, the power was continuously increased in a linear ramp pattern (5–15 W/min). Pulmonary gas exchange and ventilatory variables were recorded breath-by-breath and expressed as 20s-mean. Peak VO_2 was expressed in absolute and predict values [9].

Incremental step test

The subjects stepped up and down on a 20 cm high wooden bench (width 40 cm, depth 60 cm). The stepping rate was dictated by an audio signal played on a compact disc. The initial stepping rate was 10 steps/min with increments of one-step every 30 s up to the limit of tolerance [7,10]. It was allowed to use a handrail if the patient so preferred. In patients who opted for this strategy, the test was repeated in the same way. The criteria for stopping the test were

intolerable symptoms of dyspnea and/or fatigue and the patient's inability to keep the pace for a period of 15 s [7]. The vertical distance was calculated by multiplying the high of the step (0.20) by the number of steps. The performance on IST was compared between patients with lower and higher severity of disease (forced expiratory volume in the first second = FEV_1 ≥50% and <50% of the predicted values, respectively).

Physiologic measures

During all tests, gas exchange parameters were analyzed breath-by-breath (CPX Ultima, Medical Graphics Corporation, St. Paul, MN). ECG tracings and heart rate (HR) were recorded continuously. Maximal voluntary ventilation (MVV) was estimated by $FEV_1 \times 40$ [11]. Pulse oximetric saturation (SpO_2) was measured (Model 7500; Nonin, Plymouth, MN). Change in SpO_2 between rest and exercising ≥4 was considered desaturation [12].

Perception of effort

The subjects were asked to rate dyspnea and leg fatigue at exercise cessation by using the 0–10 Borg's category-ratio scale [13].

Statistical analysis

The results were expressed as mean ± SD. We used one-way repeated measures analysis of variance for comparisons among variables of the two ISTs and the CPET. Intraclass correlation coefficient (ICC) and 95% confidence interval (95% CI) were used to verify the reproducibility between IST-1 and IST-2 for number of steps and peak VO_2, ventilation (VE), HR, and SpO_2. In addition, Bland-Altman analysis was used to compare the two ISTs and the best IST (the test with the greater number of steps climbed) and CPET. Unpaired t-test was used to compare the performance on IST between patients with lower and higher severity of disease. Pearson correlation coefficient was used to correlate the independent variables (age, weight, height, and number of steps) with the dependent variable (VO_2). A multiple linear regression analysis (stepwise) was performed to define a predictive equation for VO_2 from IST considering the same independent variables. The level of statistical significance was set at $p < 0.05$. Statistical tests were performed using the Statistical Package for the Social Sciences version 13.0, 2004 (SPSS, Chicago, IL).

Results

Demographic and lung function data of the subjects are summarized in Table 1.

There were no significant differences in the gas exchange variables and subjective dyspnea and fatigue at rest among IST-1, IST-2, and CPET. At peak exercise, VO_2 (Fig. 1, top panel) and desaturation were significantly higher in both step tests compared with CPET, with no difference for the other variables (Table 2). Desaturation was detected only during the step test in 29% of the subjects. Considering

Table 1 Characteristics of the study group ($n = 34$).

Variables	Mean ± SD	Range
Age (yrs)	67 ± 9	49–83
BMI (kg/m2)	25.8 ± 4.3	18.8–34.5
FVC (L)	3.1 ± 0.7	1.8–4.8
FVC (% predicted)	85 ± 15	57–117
FEV_1(L)	1.3 ± 0.4	0.7–1.3
FEV_1 (% predicted)	46 ± 14	23–77
FEV_1/FVC	42 ± 8	28–60
MVV (L)	52 ± 17	28.4–101.2

BMI; body mass index, FVC; forced vital capacity, FEV_1; forced expiratory volume in 1 s, MVV; maximal voluntary ventilation.

pulmonary function, patients with lower disease severity (FEV_1 ≥50% predicted) showed higher performance at IST than patients with higher severity (FEV_1 <50% predicted) (142 ± 66 steps vs. 84 ± 40 steps, respectively; $p = 0.004$).

The majority of the subjects ($n = 23$) had their best performance on the IST-2; ten patients had their best performance on the IST-1, and one patient had the same performance on both step tests. The step tests were reproducible with ICC analysis for number of steps [0.99
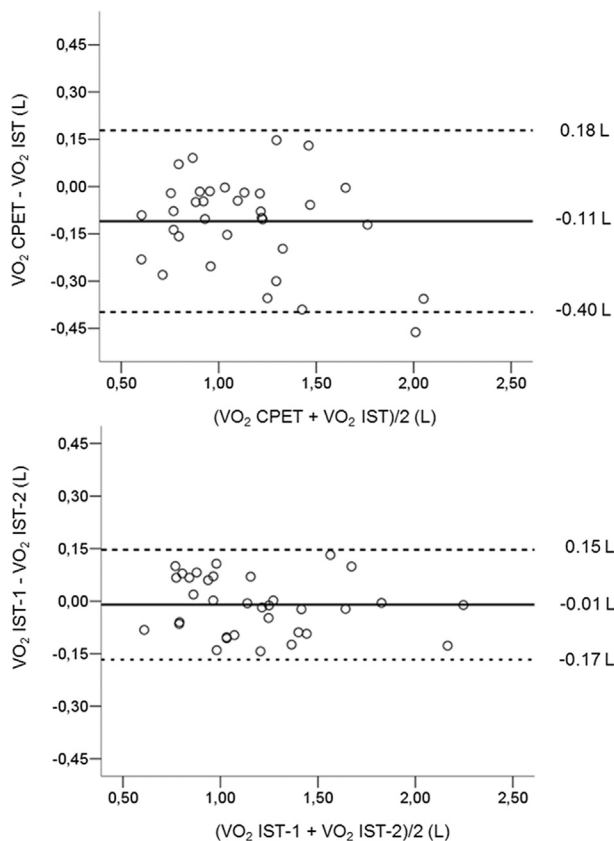

Figure 1 Bland and Altman plots for VO_2 at the peak of CPET and IST (top panel) and for VO_2 at the peak of the two ISTs (bottom panel). The dark line corresponds to the average difference whereas the dotted lines correspond to lower and upper limits of agreement.

Table 2 Data at the peak exercise.

Variables	CPET	IST-1	IST-2
VO_2 (L/min)	1.07 ± 0.35*	1.19 ± 0.39	1.20 ± 0.40
VO_2 (% predicted)	59 ± 17	66 ± 19	67 ± 20
VCO_2 (L/min)	1.11 ± 0.40	1.14 ± 0.42	1.16 ± 0.46
Vt (L)	1.29 ± 0.40	1.24 ± 0.35	1.27 ± 0.35
RR (rpm)	33 ± 8	34 ± 6	33 ± 7
VE (L/min)	41.8 ± 13.6	41.5 ± 13.8	41.9 ± 14.2
VE/VO_2	39.9 ± 8.5*	35.9 ± 7.8	35.4 ± 7.1
VE/VCO_2	38.6 ± 7.0	37.8 ± 9.0	37.7 ± 8.3
VE/MVV	0.82 ± 0.14	0.81 ± 0.13	0.82 ± 0.14
HR (bpm)	144 ± 21	134 ± 21	132 ± 21
% HR predicted	88 ± 13	88 ± 13	86 ± 12
SpO_2 (%)	90 ± 4*	87 ± 5	87 ± 5
ΔSpO_2	-3 ± 3*	-7 ± 5	-7 ± 5
Dyspnea	5.4 ± 2.3	5.4 ± 2.5	5.1 ± 2.2
Fatigue	5.5 ± 2.6	5.2 ± 2.7	5.1 ± 2.7
CPET − % predicted	55 ± 24	—	—
Number of steps (range)	—	107 ± 60 (37−269)	112 ± 63 (32−276)

VO_2; oxygen uptake, VCO_2; pulmonary carbon dioxide production, Vt; tidal volume, RR; respiratory rate, VE; ventilation, VE/VO_2; ventilatory equivalent for O_2, VE/VCO_2; ventilatory equivalent for CO_2, VE/MVV; ventilation to maximum voluntary ventilation, HR; heart rate, SpO_2; pulse oximetric saturation, CPET; cardiopulmonary exercise testing.
*$p < 0.0001$ CPET vs. StT-1 and StT-2.

(0.97−0.99)], VO_2 [0.99 (0.98−0.995)], VE [0.97 (0.94−0.98)], HR [0.93 (0.85−0.96)], and SpO_2 [0.97 (0.94−0.99)] and by the quite low bias from the Bland−Altman analysis for VO_2 (Fig. 1, bottom panel) and other variables (Table 3). For number of steps, the mean bias was also quite low, but with a wide lower and upper limit of agreement (Fig. 2).

There were significant correlations between the VO_2 in the best IST and age ($r = -0.38$, $p = 0.026$), weight ($r = 0.51$, $p = 0.002$), height ($r = 0.39$, $p = 0.022$), and number of steps ($r = 0.79$, $p < 0.0001$). Among the parameters correlated with peak VO_2 in the univariate analysis, number of steps and patient weight remained independent predictors after stepwise multiple regression analysis ($R^2 = 0.81$, $p < 0.001$). The data from the multiple linear regression analysis are shown in Table 4.

Discussion

In the present study, we have shown that a symptom-limited incremental step test determines maximum

cardiopulmonary and metabolic responses, is reproducible, and leads to more profound hypoxemia. In addition, number of steps and patient weight explained 81% of the variation of the peak VO_2.

As with conventional exercise testing protocols performed on treadmill and cycle ergometer, step tests can be classified either incremental or constant workload. Protocols with progressively increasing rates of work are more suitable when the clinical objectives are to quantify maximal exercise capacity and evaluate the profile of changes in the metabolic, cardiovascular, and ventilatory variables. While there is a significant body of literature comparing the physiologic responses between CPET and walk tests, a symptom-limited incremental step test has never been validated in patients with COPD. However why
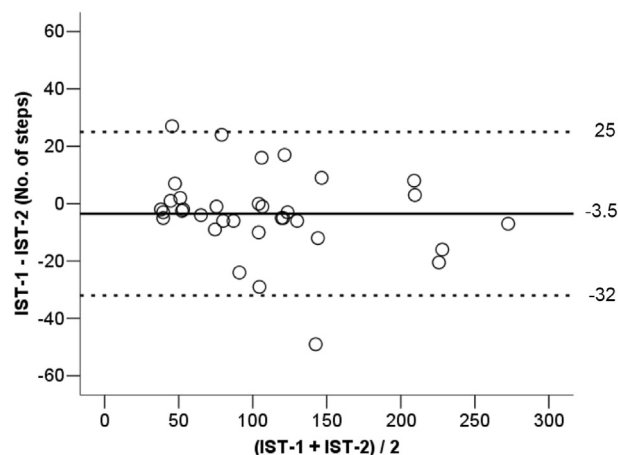
Table 3 Results from Bland−Altman analysis.

Variables	CPET − IST[a]	IST-1 − IST-2
	Mean difference ± 95% CI	Mean difference ± 95% CI
HR (bpm)	1.3 (−18 to 20)	2.4 (−19 to 24)
VE (L)	0.3 (−11. to 12)	0.10 (−9.5 to 5.1)
SpO_2 (%)	3.6 (−2.4 to 9.6)	−0.03 (−3 to 3)

[a] The best IST. CPET: cardiopulmonary exercise testing. IST: incremental step test, HR: heart rate, VE: ventilation, SpO_2: pulse oximetric saturation.

Figure 2 Bland−Altman plot for number of steps.

Table 4 Predictor variables for VO_2 (mL) at IST obtained from multiple linear regression analysis.

	Unstandardized coefficients (B)	95% confidence interval for B	Standardized coefficients	p-value	Part correlation
Constant	−221.576	−552 to −109		0.181	
No. of steps	4.833	3.8−5.9	0.745	<0.001	0.74
Weight	12.019	7.6−16.4	0.437	<0.001	0.44

VO_2 pred (L): $-221.576 + (4.833 \times$ No. of steps$) + (12.019 \times$ patient weight$)$.

to purpose one more exercise testing if the literature is replete of field tests for use in patients with cardiopulmonary diseases? Walking tests are the most commonly used for assessing of functional capacity, but they not necessarily reflect the patient's ability to perform another type of exercise. It is possible that some patients do not complain of walking limitations but have limitations with stair climbing, as the latter is a more strenuous activity [14]. The main issues with the stair climbing test are that there is no standardization regarding how to perform it or how the results should be expressed. More importantly, the number of stairs per flight and the height of the stairs are not the same in all rehabilitation centers, which compromise the external validity of the test [15].

Maximum performance and portability are the main advantages of IST over walking tests and stair-climbing tests, which facilitate the evaluation of exercise capacity in any environment. Thus, IST can serve as either laboratory-based testing when pulmonary gas exchange is available, or a field-based test when conducted outside of this context. Thus, when a gas analysis system is available during the IST, the main outcome might be VO_2, and when the IST is performed as a field test, the number of steps would be the main outcome. Others advantages are the possibility of performing the test using an electrocardiogram, as well as measuring symptoms (dyspnea and fatigue) throughout the test.

Given its incremental feature, it was expected that our protocol would induce a similar cardiopulmonary response at peak exercise as the CPET. We also anticipated higher oxygen consumption during stepping, due to the greater muscle mass involved in this activity, which is also more overloaded by the constant vertical displacement of the body. A previous study demonstrated a higher VO_2 peak (25%) during stepping than during cycling in patients with COPD [5]. In our study, this difference was smaller (12%), probably due to differences between the step-test protocols. The protocol described by Swinburn et al. [5] was performed on a 25 cm platform with a fixed rate of 15 steps/minute, and patients were able to complete, on average, less than 5 min of test, although its duration had been fixed at 10 min. The range of the number of steps climbed was lower than with our protocol (14−126 vs. 32−276, respectively). The fact that the patients discontinued the test early leads us to infer that the protocol used by Swinburn et al. [5] determined an intense to very intense effort. Thus, we speculate that the higher difference in peak VO_2 between cycling and stepping in the Swinburn study (25%) compared to ours (12%) occurred because of the slow component of oxygen uptake kinetics

in the former study. During constant workload exercise in a heavy to very heavy intensity, the primary component of VO_2 kinetics is supplemented by an additional slow component, which causes an excess of VO_2 and a delay in the steady state [16], justifying that no patient reached the steady state for VO_2 and VE, despite the stepping rate being kept constant throughout the protocol used by Swinburn et al. [5]

As observed previously in walking tests [17], the majority of patients achieved the best performance in the second IST, which is also confirmed by the negative mean difference in the Bland−Altman analysis (Table 3), demonstrating that there is a learning effect. Beyond the high ICC, the limits of agreement for oxygen uptake (from −0.17 mL to 0.15 mL) and saturation (from −3% to 3%) at peak exercise are small enough for us to be confident in high degree of reliability for cardiopulmonary responses during both incremental step tests. The limits of agreement were wider for number of steps (Table 4); for that reason, a practice test is required. The Chester Step Test (CST) presented even smaller limits of agreement (−20 to 18) for number of steps [18]. Compared with our protocol, the CST has a substantial increase in work rate (five steps every 2 min), and changes in work intensity have been related to the magnitude of the perception of symptoms [19,20]. Therefore, ample changes in work intensity precipitates the perceived exertion at the moment the test stage changes, leading patients to discontinue the test at a similar stage as that achieved in the previous test [18], contributing to its high reproducibility. On the other hand, despite being reproducible, the CST had a very short duration in patients with COPD, which is not suitable for assessing physiological responses during exercise.

The use of the step tests to evaluate oxygen desaturation has been described previously in patients with lung diseases [12,21,22]. However, to the best of our knowledge, this is the first time desaturation is compared between a step test and the CPET in patients with COPD. Patients desaturate to a greater extent during IST. This finding is in line with previous investigations that have shown that desaturation is greater during walking field tests compared to cycling [23,24]. Unlike the studies comparing cycling and walking, the difference in the magnitude of desaturation between stepping and cycling in the present study cannot be attributed to dissimilarity in ventilatory responses, because VE/VCO_2 was similar among the tests. We speculate that the main component involved in greater desaturation during stepping is the increased work that results from the displacement of the body weight against gravity, which leads to lower mixed venous oxygen saturation

compared to cycling. It is still unclear whether desaturation levels in the walking tests and the incremental step test are similar. Although a previous study showed a similar drop in arterial oxygen pressure between walking (2.6 mmHg) and stair climbing (2.4 mmHg) [14], another one [25] found lower SpO_2 levels in the 1-min stair step test than in the 6MWT (90.2 ± 6.6 vs. 91.8 ± 5.9, respectively; $p = 0.015$). It is interesting to point out that the former study selected only patients with COPD in the severe and very severe classifications (GOLD criteria), while the latter included patients with different lung diseases.

The present study also demonstrated that number of steps and patient weight are determinants of aerobic capacity assessed by the step test in patients with COPD. These two variables entered in an equation used to estimate the work performed during stair climbing (work = step height in meters $\times$ step/minute $\times$ weight in kg $\times$ 0.1635) [26], and number of steps is also a predict variable to estimate VO_2 during stepping up and down on a single platform [27]. Our study is the first to establish an equation to predict VO_2 from a step test in patients with COPD. A prospective application of this equation to test its accuracy in predicting VO_2 should be tested in further studies.

Some limitations occurred in our study. The tests order was not randomized. However, the similar physiological responses at the peak of both ISTs demonstrate that the CPET did not influence the first IST performed after CPET.

We did not test different step heights, but we believe that this factor would only be important in extremes of height (i.e., much taller and shorter individuals). The higher values of peak VO_2 obtained in the step test compared to cycling demonstrates that this aspect was not relevant to the patients evaluated in our study. Although stepping performance (number of steps) was about 60% less in patients with worse FEV_1, we were unable to determine whether the results of this test differed according to varying degrees of COPD severity. In addition, it is not yet clear whether the desaturation observed in the step test correlates with that observed during daily living activities.

Although the IST elicited maximum physiological responses, this does not imply that it can replace the CPET, as the CPET has reference values established for both maximum exercise and dynamic responses, as well as the criteria for determining cardiovascular, ventilatory, and peripheral limitations. However, the IST can be a complementary evaluation of exercise-induced hypoxemia. In addition, the IST can be used to determine the intensity (number of steps) of stepping training, which has been used as part of aerobic training for patients with COPD [28–32]. Moreover, in the context of rehabilitation, the number of steps performed on IST could be used to quantify the responsiveness of interventions to improve exercise tolerance.

In conclusion, a symptom-limited incremental step test does elicit maximum cardiopulmonary and metabolic responses and is reproducible in patients with COPD.

Authorship

Dr Simone Dal Corso contributed to the conception and design of the study, acquisition of data, analysis and interpretation of data, and preparation of the article.

MSc Anderson Alves de Camargo contributed to the data collection, analysis, and interpretation.

Dr Meyer Izibicki contributed to the data collection, analysis, and interpretation.

Dr Carla Malaguti contributed to data interpretation and preparation of the article.

Dr Luiz Eduardo Nery contributed to the conception and design of the study, analysis and interpretation of data, and preparation of the article.

Conflicts of interest

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