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A step test to assess exercise-related oxygen desaturation in interstitial lung disease

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Running title
STEP TEST FOR INTERSTITIAL LUNG DISEASE

ABSTRACT

A 6-min step test (6MST) may constitute a practical alternative for routinely assessing effort tolerance and exercise-related desaturation (ERD) in the primary care of patients with interstitial lung disease (ILD).

Thirty-one patients (19 men) with idiopathic pulmonary fibrosis (N= 25) and chronic hypersensitivity pneumonia were submitted, on different days, to two 6MSTs. Physiological responses were compared with those found on maximal and submaximal (at same $\dot{V}O_2$) cycle ergometer tests. Chronic breathlessness was also determined (Baseline Dyspnea Index, BDI).

Responses to 6MST showed to be highly reproducible: 1.3 ± 2.0 steps/min, ± 5 bpm (HR), ± 50 mL/min ($\dot{V}O_2$), ± 7 L/min ($\dot{V}E$), and ± 2 % (SpO_2). The number of steps climbed in 6 min was correlated to peak $\dot{V}O_2$ and the BDI (R= 0.52 and 0.55, $p<0.01$). There were significant associations among the tests in relation to presence (Δ rest-exercise $SpO_2 \geq 4\%$) and severity ($SpO_2 < 88\%$) of ERD ($p<0.05$); 4 patients, however, presented ERD only in response to 6MST. Resting DL_{CO} and $\Delta P(A\text{-}a)O_2$ were the independent predictors of the number of steps climbed (R^2= 0.40, $p<0.01$).

A single-stage, self-paced 6-min step test provided reliable and reproducible estimates of exercise capacity and ERD in ILD patients.

Introduction

Impaired gas exchange, especially during exertion, is a hallmark of advanced interstitial lung disease (ILD).[1,2] Functional measurements at rest may not be precise in determining the presence and extension of exercise-related oxyhemoglobin desaturation (ERD) in this patient population.[3]

Stepping was first used as a modality of exercise evaluation in the early 40s.[4] In the past decades, step tests have been shown to be clinically useful to estimate exercise tolerance,[5] to evaluate the risk of post-operative complications,[6] and to assess effort-related hypoxemia in different disease states.[7] For this latter purpose, stepping is particularly attractive since it requires a minimum of space and technical expertise, especially if used in association with pulse oximetry.[7] In addition, a higher metabolic demand has been found during step tests as compared to other "field" tests in COPD and cystic fibrosis – but with a similar fall in arterial oxygen saturation (SaO_2).[8-10] No previous study, however, has prospectively investigated the clinical role of a step test in evaluating ERD and exercise tolerance in ILD.

Our aim, therefore, was to determine whether a single-stage, self-paced, 6-min step test (6MST) would provide reliable and reproducible estimates of ERD and exercise capacity in patients with fibrotic ILD. The ultimate goal was to develop an inexpensive and portable test which could be easily used in primary care settings as part of the routine medical evaluation of this patient population.

Material and Methods

Subjects

Forty-five subjects were initially recruited from our ILD outpatients clinic for study participation. Clinical and functional stability was confirmed by the absence of change in medication dosage and FVC values (± 5%) in the preceding 3 months. Inclusion criteria were: (*i*) presence of diffuse interstitial infiltrate on high-resolution computed tomography (HRCT) with evidences of pulmonary fibrosis; (*ii*) FEV_1/FVC > 70% with reduced FVC (below the lower limit of normality) and/or decreased single-breath lung diffusing capacity (Dco), and (*iii*) resting oxygen saturation by pulse oximetry (SpO_2; Ohmeda Biox 3740, Boulder, Colo, USA) at room air ≥ 90%. No patient was receiving long-term oxygen therapy.

Fourteen patients were excluded during the study due to respiratory infections or exacerbation of the underlying disease. The final sample comprised of 31 patients (19 men, aged 34 to 79): 25 with idiopathic pulmonary fibrosis (IPF) and 6 with biopsy-proven chronic hypersensitivity pneumonia (CHP). Fourteen patients with IPF (56%) underwent open lung biopsy and presented with the pattern of usual interstitial pneumonia: diagnosis of IPF in the remaining patients was performed according to the clinical criteria suggested by the ATS/ERS.[11] All subjects signed a written informed consent, which was previously approved by the Institutional Medical Ethics Committee.

Study design

All patients initially rated their level of chronic breathlessness (Baseline Dyspnea Index (BDI)[12] and underwent a ramp-incremental cycle ergometer cardiopulmonary exercise test (CPETmax). After a resting period (1h), patients performed a 6MST with metabolic and ventilatory measurements. On another day (48 hs apart), patients underwent a constant work rate test (CPETsubmax) at same metabolic stress (i.e., at same pulmonary oxygen uptake, $\dot{V}O_2$) of the 6MST. After 1h, the 6MST was repeated.

Measurements

Pulmonary function tests

Spirometric tests without bronchodilators were performed on the CPF-System (Medical Graphics Corp.-MGC, St Paul, MN, USA). Static lung volumes were determined by breath-by-breath open-circuit nitrogen wash-out (PF-DX System, MGC, USA). Carbon monoxide diffusing capacity (DL_{CO}) was measured by the modified Krogh technique (PF-DX System, MGC, USA). Absolute values were compared with theoretical values for the adult Brazilian population.[13-15] Arterial blood samples were obtained from radial artery puncture in standard anaerobic conditions (ABL 330; Radiometer, Copenhagen, Denmark).

Cardiopulmonary exercise testing (CPET)

The exercise tests were performed at room air. They were carried out on an electromagnetically-braked cycle ergometer (CPE 2000, MGC, USA). The following data were obtained breath-by-breath (MGC-CPX System. MGC, USA) and were expressed as 15-s average: pulmonary O_2 uptake and CO_2 production ($\dot{V}O_2$ and $\dot{V}CO_2$, mL/min), minute ventilation ($\dot{V}_E$, L/min), tidal volume (V_T, L), respiratory rate (RR, breaths/min), and ventilatory equivalents for O_2 and CO_2 ($\dot{V}_E/\dot{V}O_2$, $\dot{V}_E/\dot{V}CO_2$, L/L). Electrocardiographic tracings and heart rate (HR, beats/min) were recorded continuously: oxygen pulse ($\dot{V}O_2$/HR, mL/min/beat) was calculated. Subjects were asked to rate "shortness of breath" and "leg effort" and at exercise cessation by using the 0-10 Borg's category-ratio scale.

A Δ(rest-exercise) SpO_2 > 4% was considered as indicative of ERD.[7] Supplemental oxygen was not administered unless SpO_2 < 80% and there was intense distress or breathlessness and/or a clinical indication was present as judged by the accompanying laboratory physician. In case of need of supplemental O_2, the subject was excluded as we needed accurate $\dot{V}O_2$ measurements in the present study.

Incremental exercise test (CPETmax). During the CPETmax the work rate was continuously increased in a linear "ramp" pattern (5 to 15 W/min) and was individually selected in such a way the ramp duration was > 8 and < 12 min. Peak $\dot{V}O_2$ values were compared with those predicted by Neder *et al.*.[16]

Constant work-rate exercise test (CPETsubmax). The CPETsubmax was performed at a previously selected WR to achieve a similar $\dot{V}O_2$ of the 6MST. Considering that the metabolic cost of stationary cycle ergometry at a given pedalling rate depends on the external power output and the body mass actually displaced (i.e. that of the legs), leg masses (LM) were estimated from body weight using the following gender-specific equations [17]:

LM men (kg)= 0.231 x weight (kg) + 6.78

LM women (kg)= 0.334 x weight (kg) – 0.41

The worload needed to generate a given $\dot{V}O_2$ was then estimated as [17]:

WR= $\dot{V}O_2$ (ml/min) – (16.8 x LM) + 75] - 10.6.

6-min step test (6MST)

The 6MST was performed on a 20 cm-high, single-step device with no handles. The general principles of the test were based on the current ATS/ACCP recommendations for the 6-min walking test (6 MWT).[18] Patients were instructed to walk up and to down the platform as fast as possible during a 6-minute period: they were also told that they could slow down if necessary and even make stops for resting if they wish. Standardized encouragement was given each minute ("You are doing well, keep going") using an even tone of voice: patients were also told every minute for how long they still have to climb the step. Patients established their own cadence. The number of steps per minute (i..e, the rate of stepping) was recorded. The same computer-based system described on the *Cardiopulmonary Exercise Testing* section was used to record metabolic and ventilatory variables: SpO_2 values (%) were obtained as described above.

Data analysis

Data are presented as mean ± standard deviations (SD) or median (ranges) for variables with parametric and non-parametric distributions, respectively. One-way ANOVA (with post-hoc Bonferroni) or Friedman´s test were used to evaluate differences among the tests. Pearson's product-moment coefficients assessed linear association. Agreement between 6 MST replicates or between test modalities were evaluated by the Bland-Altman procedure. Chi-square (Fisher exact) test was used to evaluate the association between categorical data. Backward stepwise multiple regression analysis was used to determine the resting predictors of the number of steps climbed in the 6MST. The probability of a type I error was set at 5% ($p<0.05$).

Results

Sample characteristics

On average, patients presented with mild-to-moderate restrictive dysfunction with low DL_{CO} values which were typically proportional to the level of lung volume reduction (Table 1). As expected, peak aerobic capacity was reduced as compared to the predicted values (peak $\dot{V}O_2$= 69.9 ± 14.9% predicted), with 25/31 patients presenting with peak $\dot{V}O_2$ values below the lower limit of normality.

Reproducibility of the step tests

All patients were able to successfully complete the step tests without complications: supplemental O_2 was not needed in any patient. Two patients, however, showed very low levels of SpO_2 (slightly below 80%, Figure 1): supplemental O_2 was not administered as these patients did not refer intense dyspnoea and the ECG tracing was within the normality (see *Methods*). There were no significant between-test differences on the total number of steps climbed and the rate of climbing (steps/min): mean bias ± 95% confidence interval of the differences were 1.1 ± 1.5 steps and 1.3 ± 2.0 steps/min, respectively. Similarly, HR, $\dot{V}O_2$, SpO_2, and $\dot{V}E$ did not differ between the tests more than ± 5 bpm, ± 50 mL, ± 1.5 %, and 7 L/min, respectively ($p>0.05$).

Exercise-related desaturation (ERD)

There were no significant differences among the tests in relation to presence and severity of ERD (Table 2). As shown in Figure 1, mean bias ± 95% confidence interval of the SpO_2 differences (%) between 6MST versus CPETmax and CPETsubmax were -1.8 ± 4.0 % and -0.3 ± 3.2 %, respectively. Twenty-five patients had significant ERD (ΔSpO_2 > 4%) during the CPETmax: 24 of them also presented ERD in response to the 6MST ($p<0.05$). Similarly, 25/26 patients who presented with ERD during the CPETsubmax showed significant desaturation in response to stepping ($p<0.05$, Table 3). Interestingly, however, 4 patients had ERD in response to 6MST but not in the CPETmax: 3 of them also did not desaturate in the CPETsubmax. Similarly, although there was a significant between-test association in relation to ERD severity, some patients desaturated below 88% only in response to the 6MST (Table 3). There was a significant correlation between ΔSpO_2 with $\dot{V}O_2$ achieved in the 6MST (R = 0.78, $p<0.01$).

Physiological responses to stepping and cycling

Stepping was associated with a near-maximum metabolic stress as compared to CPETmax (Table 2): as shown in Figure 2, mean bias ± 95% confidence interval of the between-test peak $\dot{V}O_2$ differences was only -60 ± 115 mL/min. Importantly, the total number of steps climbed was significantly related to both peak $\dot{V}O_2$ in the CPETmax and BDI (R= 0.52 and 0.55, respectively - $p<0.05$).

No significant differences on the physiological adjustments were found between 6MST and CPETsubmax tests (at same $\dot{V}O_2$) (Table 2). However, there was a trend for higher R and $\dot{V}E/\dot{V}O_2$ values during cycling as compared to stepping, i.e., $\dot{V}CO_2$ values tended to be higher at same metabolic demand during CPETsubmax than stepping (Table 2).

Determinants of performance in the 6MST

We also analysed the physiological determinants of the exercise capacity in the 6MST (number of steps climbed). In similarity with other tests of functional capacity in ILD patients [19], D_{LCO} (% predicted) and $\Delta P(A\text{-}a)O_2$ (mmHg) were found to account for 40% (R^2= 0.40) of the variability in this outcome after a multiple regression analysis:

Number of steps in the 6MST= (0.59 x D_{LCO}) – [0,88 x $P(A\text{-}a)O_2$, mmHg] + 90.8.

Discussion

The present study showed that a self-paced, single-stage, 6-min step test (6MST) can provide reproducible and reliable estimates of the presence and severity of pulmonary gas exchange impairment in patients with stable, mild-to-moderate fibrotic ILD. In addition, the total number of steps climbed (and the rate of climbing) was related to peak aerobic capacity and breathlessness on daily life. Therefore, the 6 MST is a portable and inexpensive alternative to assess the current level of functional impairment and disability in the primary care of this patient population.

Stepping as an ergometric modality

This seems to constitute the first published study to prospectively validate a step test in patients with fibrotic ILD. We found that between-day reproducibility of the 6MST was very high (Table 2). This was true not only for the physiological variables but also for the total "work" performed – as estimated by the number of steps climbed – and the rate of climbing. In this context, it could be speculated that due to the repetitive nature of the exercise movements, the patients tend to adopt a relatively constant rate of climbing throughout the test. Intra-individual variability of a number of physiological variables (HR, $\dot{V}O_2$, SpO_2 and $\dot{V}E$) were also quite low and they compare well to those described in response to more traditional exercise tests in these patients.[19] An important aspect was the use of a single 20 cm step: lower steps may provide insufficient metabolic stress (i.e., the subjects would need to climb up faster, increasing the risk of falls)[4-5] and higher steps would prove too difficult to climb for older subjects with knee and hip problems.

The rationale for using a 6-minute test was based on the well-validated 6 MWT: it could be speculated, however, that a shorter test would improve patients´ compliance and test safety. As mentioned, the rate of stepping was remarkably constant in all patients (Table 2), suggesting that a 2- to 3-min test would also provide a reasonable estimate of exercise capacity.[7] Nevertheless, it is possible that peak $\dot{V}O_2$ would be underestimated in these patients, especially considering ILD patients may present with very slow $\dot{V}O_2$ kinetics during exercise.[24] In addition, the nadir of SpO_2 could not be reached in a test shorter than 6 min test as ERD was significantly related to $\dot{V}O_2$ at exercise cessation – which has been found to increase progressively during the test (data not shown). Future studies, therefore, are needed to evaluate whether shorter step tests,[7] even using different number of steps, are also clinically useful in this patient population.

Clinical Implications

Abnormal gas exchange (hypoxemia and increased A-a gradient) plays a central role in limiting maximal exercise capacity in patients with ILD. In addition, ERD has been associated to healthy-related quality of life [20], pulmonary hypertension [21], and survival.[22] More recently, ERD during field tests – such as the 6 MWT and the shuttle walk test - has been shown to be significantly related to survival in idiopathic interstitial pneumonia.[23-25]

Routine assessment of ERD by such exercise field tests in primary care settings, however, has been hampered for the need of large spaces (at least a 100-ft hallway for the 6MWT), specific equipment (an audio tape for the shuttle walking test) and additional personnel (e.g. physiotherapists). Moreover, the quantification of ERD during 6MWT may be unreliable in some ILD patients [25] and the test may require an examiner to walk with the patient to increase its safety. In contrast, the 6MST requires a portable single-stage step which can be made available in any medical attending room; in addition, test monitoring is simpler and the number of steps climbed can be easily counted. This test, therefore, may allow that exercise capacity and ERD be obtained during routine consultations to the physician with major advantages in terms of reducing costs and increasing the frequency of functional evaluations of ILD patients.

Contrasting stepping versus cycling in ILD

As submaximal cycling is frequently used to assess ERD, we also compared the ventilatory and cardiovascular responses at same metabolic stress in both exercise modalities. However, the muscle mass involved on upright exercise is clearly larger than that recruited during stationary cycling: assuming a linear relationship between muscle mass and cardiac output, it is likely that patients needed to increase O_2 extraction during cycling to maintain the same $\dot{V}$

O_2 of the 6MST. Moreover, the work rate per unit of muscle mass is likely to be higher during cycling as compared to upright exercise[26]; as a consequence, the lactate production/clearance ratio is also higher at a given submaximal $\dot{V}O_2$ in this exercise modality. In fact, we did find a trend to higher $\dot{V}CO_2$ and R during cycling as compared to 6MST which is consistent with an earlier lactate threshold during cycling – as found previously in patients with COPD.[27-29]

In this context, Palange and co-workers found that ERD was more prominent in walking than cycling [27] and Poulain et al. demonstrated that the 6MWT was more sensitive than cycling to induce ERD in patients with COPD [30]. Interestingly, this was also the case for some of our patients, especially when the 6MST was compared to CPETmax (Table 2). As commented above, upright exercise is likely to be associated with lower mixed venous partial pressure for oxygen (SvO_2) and higher cardiac output than cycling– two known factors to conspire against the homeostasis of intra-pulmonary gas exchange in ILD patients. In addition, upright exercise may have a higher impact on pulmonary gas exchange inefficiency (i.e., higher V_D/V_T) due to differences in body posture, lung volumes, and/or central hemodynamics [27].

Study limitations

We did not compare stepping to treadmill or walking tests: it is therefore conceivable that patients´ maximal potential for ERD has not been reached in the present study. We used pulse oximetry to follow exercise oxygenation levels:

although this is a clinically-valid alternative, it should be recognised that signal reliability and stability decreases markedly with readings under 80% [31]. In the present study, however, only 2 patients showed such very low levels of SpO_2 (Figure 1): future studies involving more severe patients should assess whether pulse oximetry would remain reliable during stepping exercise. It also remains to be determined whether the test is an acceptable strategy of exercise evaluation in more severe patients. In fact, we did not include patients under long-term oxygen therapy since they would likely need supplemental O_2 during exercise and $\dot{V}O_2$ was a relevant study outcome. Additionally, further studies should be performed to investigate whether the test would be sensitive to interventions in different fibrotic ILD – such as to supplemental oxygen.

Conclusions

A single-stage, self-paced 6-min step test was able to provide reliable and reproducible estimates of exercise capacity and oxyhemoglobyn desaturation in patients with stable, mild to moderate ILD. The test may prove to constitute an inexpensive and portable alternative for the routine functional evaluation of this patient population in the primary care.

References

1. Hansen JE, Wasserman K. Pathophysiology of activity limitation in patients with interstitial lung disease. *Chest* 1996; 109:1566-1576.
2. Harris-Eze AO, Sridhar G, Clemens RE, Zintel TA, Gallagher CG, Marciniuk DD. Role of hypoxemia and pulmonary mechanics in exercise limitation in interstitial lung disease. *Am J Respir Crit Care Med* 1996; 154:994-1001.
3. Chetta A, Marangio E, Olivieri D. Pulmonary function testing in interstitial lung diseases. *Respiration* 2004; 71:209-213.
4. American College of Sports Medicine. Guidelines for exercise testing and prescrition. 4th. ed., 1997. Lea & Febiger, Philadelphia.
5. Shapiro A, Shapiro Y, Magazanik A. A simple test to predict aerobic capacity. *J Sports Med Phys Fitness* 1976; 16: 209-214.
6. Bolliger CT, Perruchoud AP. Functional evaluation of the lung resection candidate. *Eur Respir J* 1998;11:198-212.
7. Hadeli KO, Siegel EM, Sherrill DL, Beck KC, Enright PL. Predictors of oxygen desaturation during submaximal exercise in 8,000 patients. *Chest* 2001; 120(1):88-92.
8. Swinburn CR, Wakefield JM, Jones PW. Performance, ventilation, and oxygen consumption in three different types of exercise test in patients with chronic obstructive lung diseases. *Thorax* 1985; 40:581-586.
9. Casas A, Vilaro J, Rabinovich R, Mayer A, Barbera JA, Rodriguez-Roisin R, Roca J. Encouraged 6-min walking test indicates maximum sustainable exercise in COPD patients. *Chest* 2005; 128:55-61.
10. Balfour-Lynn IM, Prasad SA, Laverty A, Whitehead BF, Dinwiddie R. A step in the right direction: assessing exercise tolerance in cystic fibrosis. *Pediatr Pulmonol* 1998; 25:278-284.

11. American Thoracic Society/European Respiratory Society International Multidisciplinary Consensus Classification of the Idiopathic Interstitial Pneumonias. *Am J Respir Crit Care Med* 2002; 165:277-304.
12. Mahler, DA, Wells, CK. Evaluation of clinical methods for rating dyspnea. *Chest* 1988; 93,580-586.
13. Pereira CBSP, Simões JG, Pereira FWJ. Valores de referência para a espirometria em uma amostra da população brasileira adulta. *J Pneumol* 1992; 18:10- 22.
14. Neder JA, Andreoni S, Castelo-Filho A, Nery LE. Reference values for lung function tests. I. Static volumes. *Braz J Med Biol Res* 1999; 32:703 - 717.
15. Neder JA, Andreoni S, Peres C, Nery LE. Reference values for lung function tests. III. Carbon monoxide diffusing capacity (transfer factor). *Braz J Med Biol Res* 1999; 32: 729- 737.
16. Neder JA, Nery LE, Castelo A, Andreoni S, Lerario MC, Sachs A, Silva AC, Whipp BJ. Prediction of metabolic and cardiopulmonary responses to maximum cycle ergometry: a randomized study. *Eur Respir J* 1999; 14:1304-1313.
17. Neder JA, Nery LE, Andreoni S, Sachs A, Whipp BJ. Oxygen cost for cycling as related to leg mass in males and females, aged 20 to 80. *Int J Sports Med* 2000; 21:263-269.
18. American Thoracic Society. ATS Statement: guidelines for the six minute walk test. *Am J Respir Crit Care Med* 2002; 166:11-17.
19. Marciniuk DD, Gallagher CG. Clinical exercise testing in interstitial lung disease. *Clin Chest Med* 1994;15:287-303.
20. Nishiyama O, Taniguchi H, Kondoli Y, Nishiyama O, Taniguchi H, Kondoh Y, Kimura T, Ogawa T, Watanabe F, Nishimura K. Health-related quality of life in patients with idiopathic pulmonary fibrosis.What is the main contributing factor? *Respir Med* 2005; 99:408-414.

21. Hawrylkiewicz I, Izdebska-Makosa Z, Grebska E, Zielinski J. Pulmonary haemodinamics at rest and on exercise in patients with idiopathic pulmonary fibrosis. *Bull Eur Physiopathol Respir* 1982; 18:403-10.
22. King TE, Tooze JA, Schwarz MI, Brown KR, Cherniack RM. Predicting survival in idiopathic pulmonary fibrosis: scoring system and survival model. *Am J Respir Crit Care Med* 2001; 164: 1171-1181.
23. Lama VN, Flaherty KR, Toews GB, Colby TV, Travis WD, Long Q, Murray S, Kazerooni EA, Gross BH, Lynch JP 3rd, Martinez FJ. Prognostic value of desaturation during a 6-minute walk test in idiopathic interstitial pneumonia. *Am J Respir Crit Care Med* 2003; 168:1084-1090.
24. Moloney ED, Clayton N, Mukherjee DK, . Gallagher CG, Egan JJ. The shuttle walk exercise test in idiopathic pulmonary fibrosis. *Respir Med* 2003; 97:682-687.
25. Eaton T, Young P, Milne D, Wells AU. Six-minute walk, maximal exercise tests: reproducibility in fibrotic interstitial pneumonia. *Am J Respir Crit Care Med* 2005; 171:1150-1157.
26. Richardson S, Hardman AE. Endurance fitness and blood lactate concentration during stepping exercise in untrained subjects. *Br J Sports Med* 1989; 23:190-193.
27. Palange P, Forte S, Onorati P, Manfredi F, Serra P, Carlone S. Ventilatory and metabolic adaptations to walking and cycling in patients with COPD. *J Appl Physiol* 2000; 8:1715-1720.
28. . Christensen CC, Ryg MS, Edvardsen A, Skjonsberg OH. Effect of exercise mode on oxygen uptake and blood gases in COPD patients. *Respir Med* 2004; 98:656-660.
29. Troosters T, Vilaro J, Rabinovich R, Casas A, Barbera JA, Rodriguez-Roisin R, Roca J. Physiological responses to the 6-min walk test in patients with chronic obstructive pulmonary disease. *Eur Respir J* 2002; 20:564-569.

30. Poulain M, Durand F, Palomba B, Ceugniet F, Desplan J,Varray A, Préfaut C. 6-Minute Walk Testing is more sensitive than maximal incremental cycle testing for detecting oxygen desaturation in patients with COPD *Chest* 2003;123:1401-1407.
31. Hannhart B, Michalski H, Delorne N, Chapparo G, Polu JM. Reliability of six pulse oximeters in chronic obstructive pulmonary disease. *Chest* 1991;99:842-846

Table 1 – Resting patient characteristics.

Variables	Values
Demographic and anthropometric	
Male/female	19 / 12
Age, yrs	58 ± 11
Body mass index, kg/m^2	26.2 ± 2.9
Clinical and smoking histories	
Dyspnea	
Duration, mo	36 (4-120)
Baseline Dyspnea Index	9 (6-12)
Smoking	
Ex-smokers, no (%)	14 (45.2)
Pack-years	21.2 ± 10.7
Pulmonary function	
Spirometry	
FVC, L	2.5 ± 0.7
FVC, % pred	77.3 ± 18.1
FEV_1, L	2.1 ± 0.6
FEV_1, % pred	77.6 ± 19.0
FEV_1/FVC	82.0 ± 6.6
Static lung volumes	
TLC, L	4.1 ± 1.1
TLC, % pred	71.8 ± 15.8
Lung diffusing capacity	
DL_{CO}, mL/min/mmHg	14.8 ± 5.8
DL_{CO}, % pred	49.8 ± 17.6
DL_{CO}/VA, % pred	84.0 ± 20.5
Gas exchange	
PaO_2, mmHg	78.2 ± 9.7
$\Delta P(A\text{-}a)O_2$, mmHg	10 (1-36.5)
SaO_2, %	95 ± 2
SpO_2, %	94 ± 3

Definition of abbreviations: FVC: forced vital capacity, FEV_1: forced expiratory volume in one second, TLC: total lung capacity, DL_{CO}: carbon monoxide diffusing capacity, VA: alveolar ventilation, PaO_2: arterial pressure of oxygen; $\Delta P(A\text{-}a)O_2$ = alveolar-arterial gradient for oxygen; SaO_2: arterial oxyhemoglobin saturation; SpO_2: oxyhemoglobin saturation by pulse oximetry.
Continuous data are presented as mean ± SD or median (range).

Table 2 – Physiological and perceptual responses to 6-min step test (6 MST) and submaximal and maximal cardiopulmonary exercise (CPET) tests.

	6MST	CPET	
Variables		**CPETsubmax**	**CPETmax**
Metabolic			
$\dot{V}O_2$, L/min	0.98 ± 0.22	0.99 ± 0.21	1.09 ± 0.30*
$\dot{V}O_2$, % maximal	90.6 ± 10.0	91.3 ± 9.5	___
$\dot{V}CO_2$, L/min	0.93 ± 0.23	1.07 ± 0.27	1.27 ± 0.30*
RQ	0.95 ± 0.06	1.06 ± 0.09	1.15 ± 0.10*
Ventilatory			
$\dot{V}E$, L/min	44.1 ± 10.2	50.0 ± 14.2	60.7 ± 14.5*
$\dot{V}E/\dot{V}O_2$, L/L	45.7 ±11.0	51.3 ± 14.1 †	56.9 ± 14.4 †
$\dot{V}E/\dot{V}CO_2$, L/L	48.6 ± 11.7	47.6 ± 12.3	49.3 ± 12.1
RR, breaths/min	35 ± 8	37 ± 10	44 ± 11*
V_T, L	1.28 ± 0.33	1.37 ± 0.36	1.43 ± 0.39
$\dot{V}E$ /MVV	0.46 ± 0.17	0.52 ± 0.20	0.62 ± 0.21*
Gas exchange			
Δ SpO_2, %	8 (1-16)	8 (2-16)	6 (0-16)
Δ $SpO_2/\dot{V}O_2$, %/L	8.2 (0.7-21.6)	7.3 (1.4-21.0)	5.2 (0-20.3)‡
Δ $SpO_2 \geq 4\%$	28 (90.3)	26 (83.9)	25 (80.6)
$SpO_2 < 88\%$	14 (45.2)	13 (41.9)	12 (38.7)
Cardiovascular			
$\dot{V}O_2$/HR, mL/min/beat	7.4 ± 1.8	7.4 ± 1.7	7.4 ± 1.7
HR, bpm	135 ± 14	137 ± 15	150 ± 14*
HR, % pred	84.4 ± 8.4	85.2 ± 9.2	93.9 ± 9.1*
Symptoms			
Dyspnea score	4 (0-10)	4.5 (0-10)	7 (0-10)*
Leg effort score	4.5 (0-10)	5 (0-10)	7 (4-10)*

Definition of abbreviations: $\dot{V}O_2$: oxygen uptake, $\dot{V}CO_2$: carbon dioxide output, RQ: respiratory quotient, $\dot{V}E$: ventilation; RR: respiratory rate, V_T: tidal volume, MVV: maximal voluntary ventilation, ΔSpO_2: resting SpO_2 – lowest SpO_2, $\dot{V}O_2$/HR: oxygen pulse.

$p<0.05$: * CPETmax > 6 MST and CPETsubmax; † CPETmax and submax > 6 MST; ‡ CPET max < 6 MST and CPETsubmax.

Continuous data are presented as mean ± SD, median (range) or number of subjects (proportions).

Table 3 – Association between exercise-related oxygen desaturation in response to 6-min step test (6 MST) and submaximal and maximal cardiopulmonary exercise (CPET) tests.

	6MST	
	Yes	**No**
Δ $SpO_2 \geq 4\%$		
CPETmax		
Yes	24*	1
No	4	2*
CPETsubmax		
Yes	25*	1
No	3	2*
$SpO_2 < 88\%$		
CPETmax		
Yes	10*	2
No	4	15*
CPETsubmax		
Yes	12*	1
No	2	16*

Definition of abbreviation: SpO_2= oxihemoglobyn saturation by pulse oximetry; ΔSpO_2: resting SpO_2 – lowest exercise SpO_2.

*p<0.05 (chi-square test).

FIGURE LEGENDS

Figure 1. A Bland-Altman plot of the between-test differences on the nadir of oxyhemoglobyn saturation by pulse oximetry (SpO_2) in patients with interstitial lung disease. Note that the 95% confidence interval of the 6-min step test–submaximal cardiopulmonary exercise test differences (6MST-CPETsubmax) were lower than those found for 6MST-maximal cardiopulmonary exercise test (CPETmax).

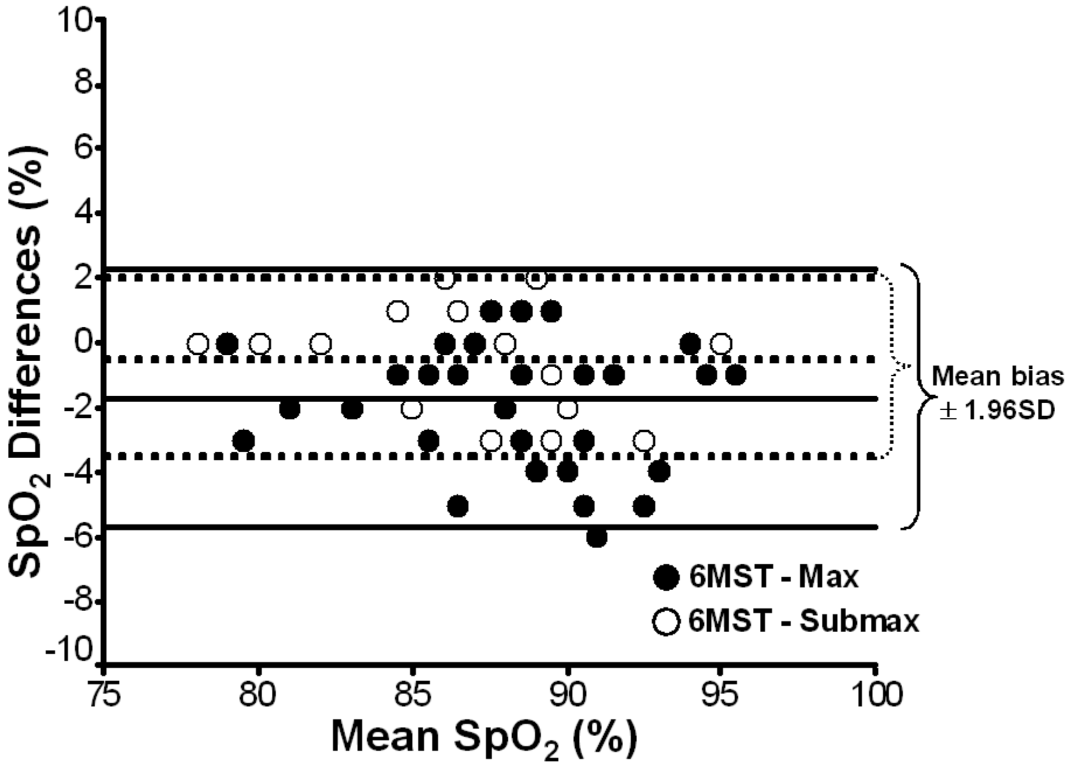
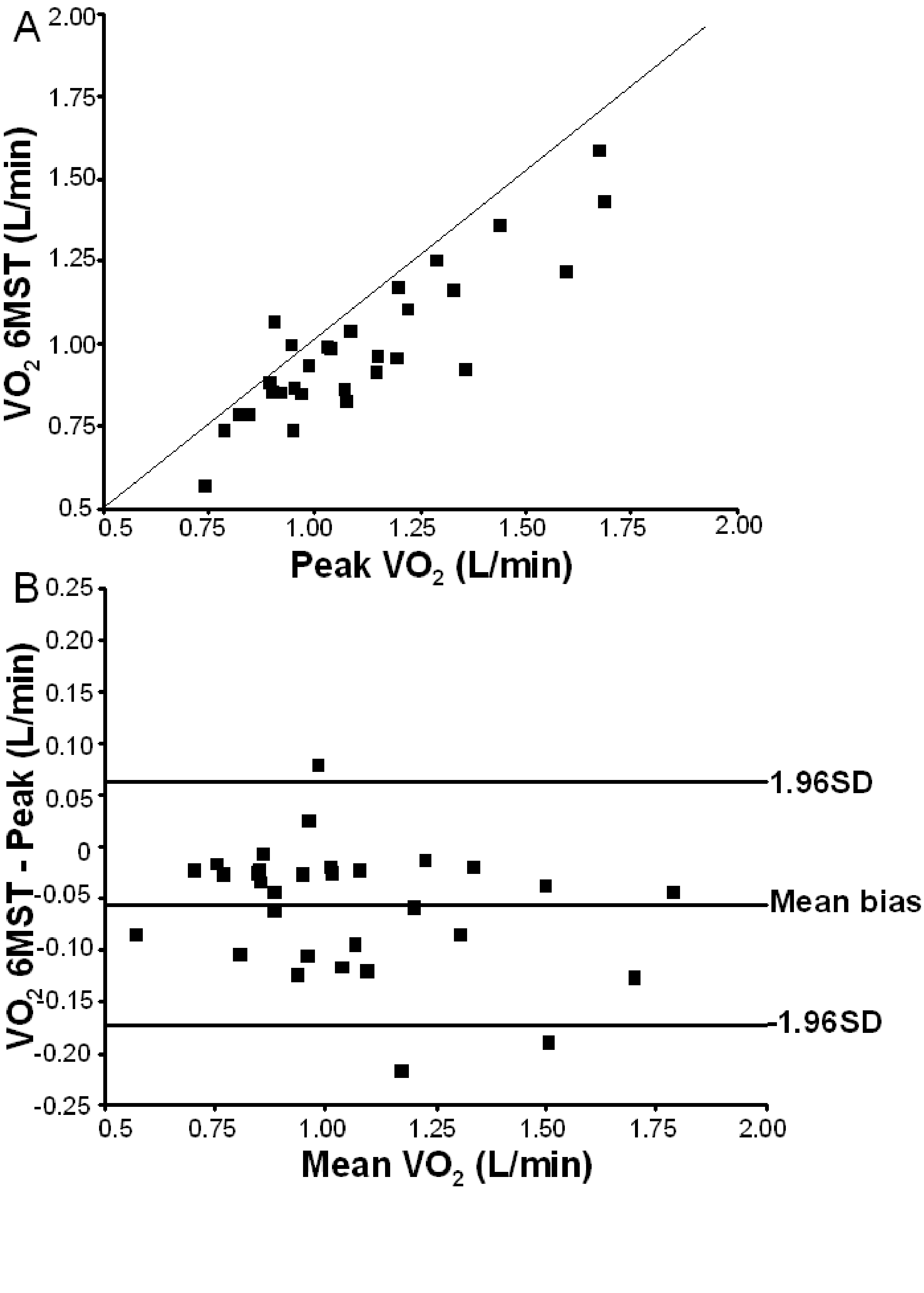


Figure 2. The 6 MST was related to a near-maximum metabolic stress as compared to CPETmax:: $\dot{V}O_2$ values were close to the line of identity (*panel A*) and a Bland-Altman analysis revealed a narrow 95% confidence interval for the between-test differences (*panel B*).


A
VO2 6MST (L/min)
Peak VO2 (L/min)
B
VO2 6MST - Peak (L/min)
1.96SD
Mean bias
-1.96SD
Mean VO2 (L/min)