

Peak power estimated from 6-minute walk distance in Asian patients with idiopathic pulmonary fibrosis and chronic obstructive pulmonary disease

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Author's contributions

Ryo Kozu is responsible for the design of this study, collection of the data, the analysis and interpretation of the data and preparation of the manuscript.

Sue Jenkins provided intellectual input to the design of this study, the analysis and interpretation of the data and to preparation of the manuscript.

Hideaki Senjyu contributed to the design of this study, provided intellectual input to the interpretation of the data and contributed to the preparation of the manuscript.

Hiroshi Mukae contributed to the analysis and interpretation of the data and preparation of the manuscript.

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Summary at a glance

This study investigated whether 6MWD provides a good estimate of the peak power (P_{peak}) achieved during a cycle ergometry test in Asian subjects with IPF and COPD. The strong relationship between 6MWD and P_{peak} may allow individualized prescription of cycle-based training when a measurement of P_{peak} is unavailable.

ABSTRACT

Background and objective: Pulmonary rehabilitation guidelines recommend cycle ergometry training at an intensity that exceeds 60% of peak power (P_{peak}) with the aim of achieving a physiologic response. However, many clinicians do not have access to an incremental cycle ergometry test (ICET) to allow prescription of training intensity. No studies have investigated whether the 6-minute walk test (6MWT) can be used to estimate the P_{peak} achieved during an ICET in subjects with IPF or in Asian subjects with COPD.

Methods: 90 Japanese subjects (IPF $n=45$, COPD $n=45$) undertook a 6MWT and a symptom-limited ICET in random order. Anthropometry, quadriceps strength and lung function were measured.

Results: Exercise tests were prematurely terminated in 10 subjects with IPF due to profound oxygen desaturation ($\text{SpO}_2 < 80\%$). The ICET elicited higher peak heart rates, dyspnea and leg fatigue in both subject cohorts (all $P < 0.01$). The magnitude of oxygen desaturation was greater during the 6MWT ($P < 0.01$). 6MWD was strongly associated with P_{peak} ($r=0.80$, $P < 0.01$) in both subject cohorts. In subjects with IPF, the predictive equation that accounted for the greatest proportion of variance in P_{peak} included 6MWD and FVC %pred ($R^2 = 0.70$). In the COPD subjects, 6MWD alone accounted for 64% of the variance in P_{peak} and the inclusion of other variables did not increase R^2 .

Conclusions: P_{peak} can be estimated from the 6MWT in Japanese subjects with IPF and COPD. This may allow individualized prescription of the intensity for cycle-based training based on the 6MWT.

INTRODUCTION

Exertional dyspnea and exercise intolerance are cardinal symptoms of IPF. The responsible mechanisms include mechanical restriction to breathing, impairments in gas exchange, and circulatory and cardiovascular limitations.¹⁻³ Peripheral muscle impairment, as a consequence of physical inactivity and treatment with oral corticosteroids, may also have a significant role in limiting exercise capacity.⁴ These abnormalities indicate a role for pulmonary rehabilitation in this patient cohort.⁵

In patients with IPF, recent studies provide evidence that supervised exercise training, as part of a pulmonary rehabilitation program (PRP), is associated with a reduction in dyspnea and improvements in functional exercise capacity and quality of life.⁶⁻⁸

Current guidelines for exercise training in patients with chronic lung disease include a recommendation for lower limb endurance training.^{9,10} Optimally, this type of exercise should be prescribed at an intensity that exceeds 60% of peak power (P_{peak}) with the aim of achieving the greatest physiologic response.¹⁰ In PRPs, this training most often takes the form of walking and cycle-based exercise.^{9,10}

In clinical practice, field walking tests such as the 6-minute walk test (6MWT), are commonly used by health professionals who provide PRPs to assess functional exercise capacity, prescribe the intensity for walking training and as an outcome measure.^{10,11} In randomised controlled trials showing a benefit from pulmonary rehabilitation in subjects with IPF, walking training has been prescribed at an intensity equivalent to 80% of the walking speed achieved on the baseline 6MWT.^{6,12}

Prescription of the intensity for cycle-based exercise training relies on a measurement of P_{peak} achieved during a symptom limited incremental cycle ergometry test (ICET). However, resources for PRPs are often constrained and

exercise testing is generally limited to one type of exercise test of which field walking tests (i.e. 6MWT and incremental shuttle walk test) are most commonly used.^{10,13-15} The ability to estimate P_{peak} from the results of a field walking test would enable prescription of the initial training intensity without the requirement of an ICET thereby reducing the burden on the patient and the healthcare system.¹⁰ To date, there are no published studies that have examined the relationship between P_{peak} and 6MWD or compared responses to the 6MWT and ICET in subjects with IPF.

Two recent studies in Caucasian subjects with COPD report equations to estimate P_{peak} from 6MWD.^{16,17} However, regression equations to estimate P_{peak} derived in individuals of Caucasian origin are not appropriate for an Asian population due to differences in body anthropometry. Specifically, compared to Caucasians, Asians are usually shorter, have a lower body mass and a higher percentage of body fat relative to their BMI.^{18,19} Since patients with COPD comprise the greatest proportion of individuals referred to PRPs, there is a need for specific regression equations to estimate P_{peak} for an Asian population with COPD.

The primary aims of this study were to: (i) compare the heart rate (HR), oxygen saturation (SpO_2) and symptom responses to the 6MWT and ICET and, (ii) determine whether P_{peak} measured from an ICET could be estimated from 6MWD in Asian subjects with IPF and COPD. As some studies in subjects with COPD have shown that the association between P_{peak} and 6-minute walk work (6MWW [6MWD x body weight]), which represents the work of walking²⁰, is stronger than the association with 6MWD,^{17,21} a secondary aim was to determine the proportion of variance in P_{peak} accounted for by including 6MWW in a regression equation.

METHODS

A prospective cross-sectional study design was utilized. All subjects completed the 6MWT and ICET, and measurements of body anthropometrics, lung function, arterial blood gas tensions and quadriceps muscle strength during a two-week period. The study was approved by the Human Ethics Review Committee of Nagasaki University Graduate School of Biomedical Sciences. Written, informed consent was obtained from all subjects prior to participation.

Subjects

We recruited 45 consecutive patients with IPF and 45 patients with COPD who were referred to the PRP at Nagasaki University Hospital. The diagnosis of IPF²² and COPD²³ was made according to established criteria. Medical management was optimized prior to inclusion in the study and subjects were required to be clinically stable with no changes in medication for at least four weeks prior to recruitment. Exclusion criteria comprised very mild symptoms (Medical Research Council, MRC, grade 1)²⁴ and comorbid conditions affecting exercise performance (e.g. musculoskeletal or neurological impairment, cardiac disease, severe cognitive impairment).

Lung function and arterial blood gas tensions

Lung function (spirometry, static lung volumes and DL_{CO}) and arterial blood gas tensions were measured.^{23,25}

Quadriceps muscle force

Quadriceps force (QF) was measured as the peak force (kg) developed during a maximal isometric knee extension maneuver using a hand-held dynamometer with

fixing-belt (μ Tas F-1; Anima Corporation; Tokyo, Japan) in accordance with a standard protocol that has demonstrated good test-retest reliability (intraclass correlation coefficient 0.94).²⁶ The highest value from three attempts on the dominant side was recorded.

Exercise tests

Subjects completed two 6MWTs and a laboratory-based, symptom-limited ICET in random order. None of the subjects had prior experience of the exercise tests. Subjects receiving long-term oxygen therapy (LTOT) performed the tests breathing oxygen supplied at their prescribed flow rate for exercise. Standardized instructions and encouragement were used with the aim of maximizing performance. Oxygen saturation was monitored continuously throughout both tests (Konica Minolta Pulsox Me Oximeter, Osaka, Japan) and the tests were terminated if SpO₂ fell to below 80%. Dyspnea was measured prior to, at the end of each minute during both tests, and on test completion.²⁷ Leg fatigue was assessed at test completion.²⁷

The 6MWT was performed according to published guidelines along a 30m corridor.²⁸ The test was performed twice, on consecutive days, and the 6MWD achieved on the second test was used in the analysis. Heart rate was monitored continuously using telemetry (Polar Electro, Oy, Finland).

The ICET (step protocol, 1 minute stages) was performed on an electrically braked cycle ergometer (Rehcor version 2.21; Lode BV; Groningen, the Netherlands) and was separated from the 6MWT by \geq 24 hours. After a period of rest followed by 2 minutes of unloaded pedaling, work rate was increased by 5 W/min for subjects with MRC grade 4, and 10 W/min for those with MRC grades 2 and 3. Subjects pedaled between 40-50 rpm throughout the test. Heart rate was monitored continuously using

single lead electrocardiography. P_{peak} was recorded as the highest work rate maintained for at least 30 seconds.

Statistical analysis

The effect of familiarisation on 6MWD was examined using paired t-tests and by calculating the coefficient of variation (CV).

Paired t-tests were used to compare pre-exercise and peak measurements of HR, and dyspnea, and pre-exercise SpO_2 with nadir SpO_2 . Independent t-tests and Chi-squared test were used to compare subgroups within the IPF cohort.

Pearson product moment correlation coefficients (r) were calculated between P_{peak} and 6MWD, 6MWW, anthropometry, lung function and QF data.

Linear regression analysis was performed using 6MWD or 6MWW, lung function and QF data to determine their contribution to P_{peak} and to develop the predictive equations for estimating P_{peak} . The bias and limits of agreement between the estimated and measured P_{peak} were calculated.²⁹

Data are expressed as mean \pm SD. All data were normally distributed. The level of significance was set at $P < 0.05$. Analyses were performed using SPSS software (Version 17, Chicago, IL, USA).

RESULTS

In the IPF cohort, 14 exercise tests (nine 6MWTs, five ICETs) in 10 subjects, all of whom were receiving LTOT, were prematurely terminated due to profound oxygen desaturation ($\text{SpO}_2 < 80\%$). These subjects had greater impairment in FVC (57 ± 12

vs 72 ± 17 %pred, $P < 0.05$) and D_{LCO} (31 ± 15 vs 41 ± 19 %pred, $P = 0.15$) compared to the remaining 35 subjects with IPF. Anthropometric, lung function, arterial blood gas tensions and QF data of the 80 subjects (IPF $n=35$, COPD $n=45$) who completed both exercise tests are shown in Table 1. QF was lower in the 13 IPF subjects who were receiving oral corticosteroids (14 ± 9 vs 22 ± 10 kg, $P = 0.03$).

Exercise tests

The increase in 6MWD on the repeat test was 11 ± 13 m and 13 ± 18 m (both $P < 0.001$) in the IPF and COPD cohorts respectively. The CV for repeat tests was 8.3% (IPF) and 7.3% (COPD).

Responses to the 6MWT and ICET

In the IPF cohort, peak HR, dyspnea and leg fatigue were significantly greater at the end of the ICET compared to the 6MWT (Table 2). Leg fatigue at the end of the 6MWT was significantly greater in the 13 subjects receiving oral corticosteroids (4.0 ± 0.8 vs 3.1 ± 1.1 , $P = 0.04$). A similar proportion of subjects showed a decrease in SpO_2 to $\leq 88\%$ during both tests (6MWT, $n=24$, 69%; ICET $n=20$, 57%).

In the COPD cohort, peak HR and scores for dyspnea and leg fatigue were significantly greater at the end of the ICET compared to the 6MWT (Table 2). A greater proportion of subjects showed a decrease in SpO_2 to $\leq 88\%$ on the 6MWT ($n=11$, 24%) compared to the ICET ($n=2$, 4%, $P = 0.04$).

Associations between 6MWD, 6MWW, and P_{peak}

P_{peak} was associated with all measures of lung function, QF, 6MWD and 6MWW in

the IPF cohort (Table 3). In the COPD cohort, P_{peak} was associated with anthropometric data, FEV₁ (L), FVC %pred, FRC %pred, QF, 6MWD and 6MWW (Table 3). Figures 1 and 2 illustrate the relationships between 6MWD and 6MWW with P_{peak} and include the 95% prediction intervals to show the precision of an individual estimate of P_{peak} .

The predictive equations that accounted for the highest proportion of variance in P_{peak} were:

IPF: $P_{\text{peak}} (W) = (0.122 \times 6\text{MWD}, m) + (0.387 \times \text{FVC \%pred}) - 21.474, R^2=0.70$.
6MWD alone accounted for 63% of the variance in P_{peak} : $P_{\text{peak}} (W) = (0.153 \times 6\text{MWD}, m) - 3.831, R^2=0.63$. When 6MWW was used in the analysis, the best predictive equation was: $P_{\text{peak}} (W) = (1.008 \times 6\text{MWW}, \text{kmxkg}) + (0.748 \times \text{TLC \%pred}) - 20.595, R^2=0.59$.

COPD: $P_{\text{peak}} (W) = (0.168 \times 6\text{MWD}, m) - 4.085, R^2=0.64$. The same amount of variance was accounted for when 6MWW was used in the equation: $P_{\text{peak}} (W) = (2.310 \times 6\text{MWW}, \text{kmxkg}) + 8.820, R^2=0.64$.

The bias and limits of agreement between the estimated and measured P_{peak} were IPF: 0.04 (-21.9 to 22.0W) and COPD: -0.03 (-25.5 to 25.4W).

DISCUSSION

The main finding of this study is that 6MWD accounts for a large proportion of the variance in P_{peak} achieved during an ICET in a cohort of Japanese subjects with IPF. The addition of FVC %pred, a measure of lung restriction, in the regression equation increased the amount of variance in P_{peak} accounted for to 70%. Consistent with previous studies in Caucasian subjects with COPD, we showed that 6MWD

accounted for a large proportion of the variance in P_{peak} .^{16,17} The regression equations derived in this study will enable clinicians to prescribe the initial intensity of cycle ergometry training based on a percentage of P_{peak} estimated from the 6MWD. However, further studies are needed to prospectively test the estimates of P_{peak} derived from the regression equations in different cohorts of Japanese patients with IPF and COPD, and to determine whether specific equations are required for other Asian populations. Limitations of this study include the relatively small sample size and in particular the small number of females.

In some subjects there were large discrepancies between the estimated and measured P_{peak} . Contributing to this discrepancy could include day-to-day variation in exercise performance because the ICET and 6MWT were performed on different days.³⁰ Another possible explanation is the different effect of quadriceps muscle dysfunction during walking and cycling. The greater loading on the quadriceps muscles during cycling is likely to be associated with poorer exercise performance in subjects with more marked quadriceps impairment.³¹

The equations we present should only be used to derive initial training loads in the absence of a direct measure of P_{peak} . For an individual patient, the estimated P_{peak} could under- or over-estimate P_{peak} (Figures 1 and 2) by an amount that would significantly influence the duration of cycling exercise that the patient could tolerate. Further, unlike $VO_{2\text{peak}}$, the P_{peak} achieved during an ICET is dependent on the rate and magnitude of the increments in power (W/min) used in the testing protocol³² and this has implications for the ability of patients to tolerate training loads prescribed at a percentage of P_{peak} .³³ In clinical practice it will be necessary to adjust the training loads derived using these equations based on the patient's symptoms and physiologic responses.¹⁰ Specifically, monitoring of SpO_2 is essential in patients with

IPF during cycling training in order to determine the need for supplementary oxygen therapy and to titrate oxygen flow rate

To our knowledge this is the first study to develop a regression equation to estimate P_{peak} in a cohort with IPF. In these subjects, all measures of lung function and QF demonstrated moderate to strong correlations with P_{peak} . In contrast, no significant correlations between age and anthropometric measures with P_{peak} were found thus explaining why the substitution of 6MWW for 6MWD in the regression equation did not increase R^2 . Although D_{LCO} was associated with P_{peak} , it was not an independent predictor in the regression model that retained 6MWD and FVC. In the COPD subjects, 6MWD and 6MWW accounted for a similar proportion of the variance in P_{peak} consistent with other studies.¹⁶

Our COPD subjects were shorter in stature by up to 8cm, weighed 15kg less and had lower 6MWDs and P_{peak} than the Caucasian subjects with COPD in studies that reported predictive equations to estimate P_{peak} .^{16,17} These differences highlight the importance of specific equations for the Japanese population.

The magnitude of the increase in 6MWD on the repeat 6MWT was similar to that reported by others in IPF³⁴ and COPD³⁵ subjects. Consistent with previous research, a single ICET was performed as studies have reported acceptable reproducibility of P_{peak} in both subject cohorts.³⁶⁻³⁸ We did not collect any metabolic or ventilatory data during the ICET because our aim was to measure P_{peak} and to replicate the manner in which patients perform cycle-based exercise during a PRP. The absence of a mask or mouthpiece ensured that subjects did not prematurely terminate exercise as a result of discomfort or problems of excessive saliva or claustrophobia caused by these attachments.

The significant oxygen desaturation in the IPF cohort during exercise is most likely explained by the impairment in D_{LCO} and the restrictive defect.³⁹ A similar proportion of subjects with IPF desaturated to $\leq 88\%$ during the 6MWT and ICET.³⁴ This contrasts with our findings in the COPD cohort and other studies that have shown greater desaturation during walking tests in this population.^{16,40-42} In subjects with COPD, the difference in the magnitude of desaturation is related to the higher ventilatory response to cycle based exercise tests.⁴²

In conclusion, this study provides regression equations to estimate P_{peak} from the 6MWT in Japanese subjects with IPF and COPD that may provide clinicians with a method of prescribing the intensity for cycle-based training in the absence of a direct measure of P_{peak} .

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FIGURE LEGENDS

Figure 1 (a) Relationship between 6MWD and peak power (P_{peak}) measured on incremental cycle ergometry test (ICET) and (b) 6-minute walk work (6MWW) and P_{peak} in 35 subjects with IPF. The figure shows the regression line together with the 95% confidence intervals (solid lines) and 95% prediction intervals (dashed lines).

Figure 2 (a) Relationship between 6MWD and peak power (P_{peak}) measured on incremental cycle ergometry test (ICET) and (b) 6-minute walk work (6MWW) and P_{peak} in 45 subjects with IPF. The figure shows the regression line together with the 95% confidence intervals (solid lines) and 95% prediction intervals (dashed lines).

Figure 2

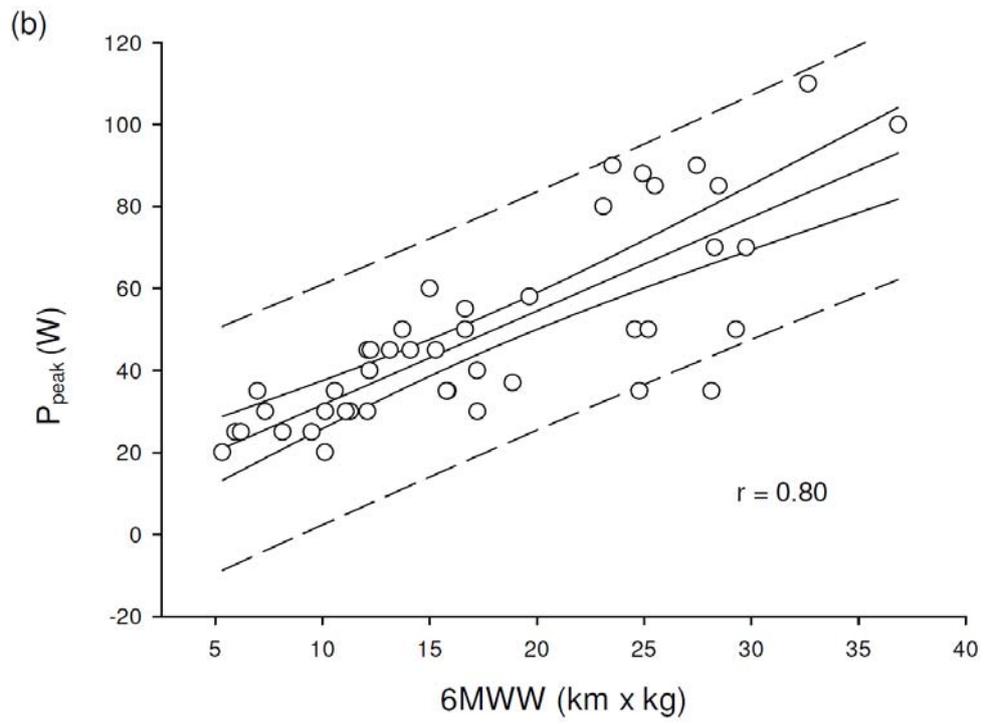
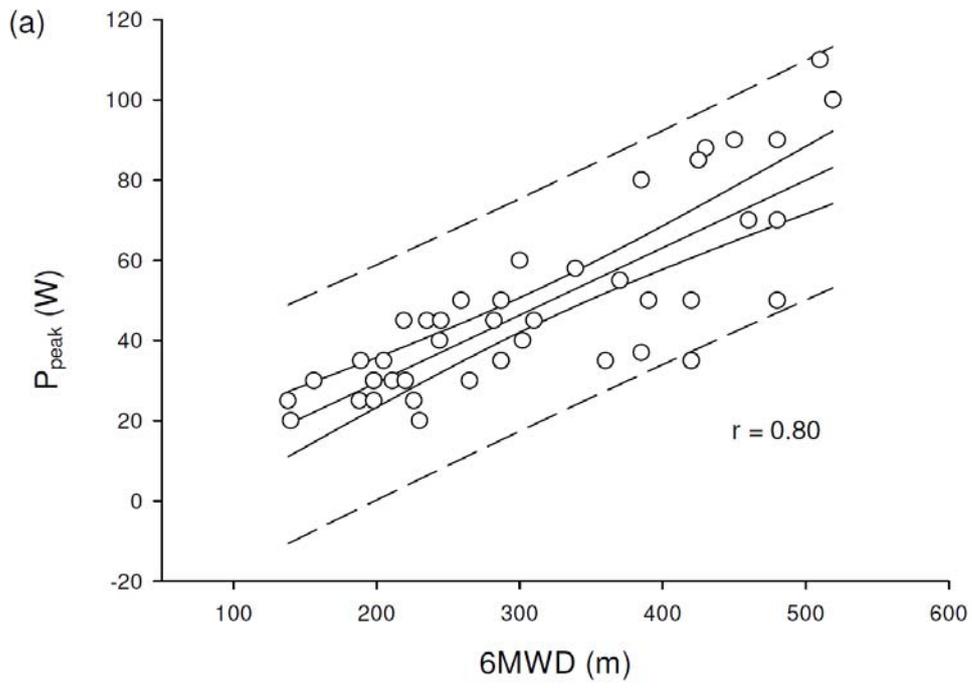


Table 1 Characteristics of the subjects (n=80)

Variable	IPF (n=35)	COPD (n=45)
Age (years)	67.2 ± 7.7	67.3 ± 5.1
Males / Females	30 / 5	38 / 7
Height (m)	1.57 ± 0.1	1.63 ± 0.1
Weight (kg)	53.0 ± 11.2	51.6 ± 9.5
BMI (kg/m ²)	21.4 ± 3.6	20.8 ± 2.2
Smokers / ex smokers	3 / 26	5 / 39
LTOT	16 (46%)	10 (22%)
Oral corticosteroids	13 (37%)	6 (13%)
Dose, mg/day	21.4 ± 7.2	11.7 ± 4.1
MRC Grade 2 / 3 / 4	14 / 11 / 10	14 / 15 / 16
Pulmonary function		
FEV ₁ (L)	1.66 ± 0.48	1.10 ± 0.50
FEV ₁ %pred	81 ± 16	45 ± 12
FVC %pred	72 ± 17	81 ± 22
FRC %pred	66 ± 15	146 ± 22
TLC %pred	63 ± 15	109 ± 14
D _{LCO} (ml/min/mmHg)	6.2 ± 2.5	12.9 ± 6.1
D _{LCO} %pred	41 ± 19	59 ± 24
Blood gas data		
PaO ₂ (mmHg)	74.3 ± 8.1	73.3 ± 8.0
PaCO ₂ (mmHg)	39.9 ± 4.3	40.6 ± 4.4
QF (kg)	19.0 ± 10.3	22.0 ± 9.0

Values are mean ± SD or numbers (percentages) of subjects. LTOT, long term oxygen therapy; MRC, Medical Research Council; QF, quadriceps force.

Table 2 Comparison of exercise test data in the subject cohorts

Variable	IPF (n=35)		COPD (n=45)	
	6MWT	ICET	6MWT	ICET
6MWD (m)	325 ± 113		315 ± 110	
P _{peak} (W)		46 ± 22		49 ± 23
6MWW (km x kg)	17.4 ± 7.1		17.5 ± 8.0	
Pre-exercise HR (bpm)	86 ± 8	87 ± 7	84 ± 10	86 ± 12
Peak HR during test (bpm)	119 ± 12	125 ± 10**	115 ± 12	119 ± 19**
Pre-exercise SpO ₂ (%)	95 ± 2	94 ± 2*	96 ± 1	97 ± 1*
Lowest SpO ₂ during test (%)	85 ± 5	87 ± 4**	91 ± 5	93 ± 3**
Pre-exercise dyspnea score	0.2 ± 0.4	0.2 ± 0.4	0.2 ± 0.3	0.2 ± 0.4
Peak dyspnea score during test	4.9 ± 1.3	6.6 ± 1.1**	4.4 ± 1.2	5.7 ± 1.1**
Leg fatigue score on test completion	3.4 ± 1.1	6.0 ± 1.1**	2.6 ± 1.4	5.1 ± 0.9**
Rests during test due to dyspnea	2 (6%)		8 (18%)	

* $P < 0.05$, ** $P < 0.01$ 6MWT vs ICET

Values are mean ± SD or numbers (percentages) of subjects. 6MWT, 6-minute walk test; ICET, incremental cycle ergometry test; P_{peak}, peak power measured during the incremental cycle ergometry test; 6MWW, 6-minute walk work; HR, heart rate; SpO₂, percutaneous oxygen saturation; W, watts; bpm, beats per minute.

Table 3 Correlations between peak power achieved during the incremental cycle ergometry test and other variables

Variable	P_{peak}	
	IPF (n=35)	COPD (n=45)
Age (years)	- 0.06	0.12
Height (m)	0.18	0.35*
Weight (kg)	0.04	0.54**
BMI (kg/m ²)	-0.07	0.55**
FEV ₁ (L)	0.44**	0.34*
FEV ₁ %pred	0.47**	0.25
FVC %pred	0.65**	0.42*
FRC %pred	0.52**	- 0.33*
TLC %pred	0.73**	- 0.38
D _{LCO} (ml/min/mmHg)	0.53**	0.17
D _{LCO} %pred	0.51**	0.21
QF (kg)	0.54**	0.64**
6MWD (m)	0.80**	0.80**
6MWW (km x kg)	0.66**	0.80**

* $P < 0.05$, ** $P < 0.01$

Values are correlation coefficients (r). P_{peak} , peak power; %pred, percent predicted; QF, quadriceps force; 6MWW, 6-minute walk work.