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Original Article

Six-Minute Walk Test and Maximum Exercise Test in Cycloergometer in Chronic Obstructive Pulmonary Disease. Are the Physiological Demands Equivalent?

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ABSTRACT

Background and objectives: The physiological load imposed by the six minute walk test (SMWT) in chronic obstructive pulmonary disease (COPD) patients come from small studies where the influence of disease severity has not been assessed. The aim of the present study was to compare the SMWT with an incremental cardiopulmonary exercise test (CPET) in patients classified by disease severity according to FEV_1 (cutoff 50% predicted).
Patients and methods: Eighty-one COPD patients (53 with FEV_1 ≥50%) performed both tests on two consecutive days. Oxygen consumption ($\dot{V}O_2$), carbon dioxide production ($\dot{V}O_2$), minute ventilation ($\dot{V}E$), heart rate (HR) and pulse oximetry (SpO_2) were measured during SMWT and CPET using portable equipment. Dyspnea and leg fatigue were measured with the Borg scale.
Results: In both groups, walking speed was constant during the SMWT and $\dot{V}O_2$ showed a plateau after the 3rd minute. When comparing SMWT (6th min) and peak CPET, patients with FEV_1 ≥50% showed a greater $\dot{V}O_2$, but lower values of $\dot{V}O_2$,V_E, HR, dyspnea, leg fatigue, and SpO_2 during walking. In contrast, in those with FEV_1 <50% predicted values were similar. Distance walked during the SMWT strongly correlated with $\dot{V}O_2$ at peak CPET (r=0.78; *P*=0.0001).
Conclusion: The SMWT is a constant load exercise in COPD patients, regardless of disease severity. It imposes high metabolic, ventilatory and cardiovascular requirements, which were closer to those of CPET in severe COPD. These findings may explain the close correlation between distance walked and peak CPET $\dot{V}O_2$.

Prueba de marcha de 6 min y ejercicio máximo en cicloergómetro en la enfermedad pulmonar obstructiva crónica, ¿son sus demandas fisiológicas equivalentes?

Palabras clave:
Enfermedad pulmonar obstructiva crónica
Ejercicio
Prueba de marcha en 6 min

RESUMEN

Introducción y objetivos: La demanda fisiológica impuesta por la prueba de marcha de 6 min (PM6M) se ha estudiado escasamente en la enfermedad pulmonar obstructiva crónica (EPOC) y se desconoce si la gravedad de la enfermedad la afecta. El objetivo del presente estudio fue comparar la PM6M con una prueba de ejercicio cardiopulmonar (PECP) incremental en pacientes categorizados por gravedad y se usó como punto de corte un volumen espiratorio forzado en el primer segundo (FEV_1) del 50% del valor predicho.
Pacientes y método: En 81 pacientes a los que se les realizaron ambos ejercicios se evaluó el consumo de oxígeno ($\dot{V}O_2$), la producción de anhídrido carbónico ($\dot{V}O_2$), la ventilación por minuto, la frecuencia cardíaca (FC) y la oximetría de pulso con un equipo portátil; además, se cuantificó la disnea y la fatigabilidad.
Resultados: Durante la PM6M, la velocidad adoptada fue constante y el $\dot{V}O_2$ ascendió hasta una meseta a los 3 min, independientemente de la gravedad de la EPOC. Comparado con la PECP, en los pacientes con FEV_1 ≥ 50%, el $\dot{V}O_2$ fue mayor, pero la $\dot{V}O_2$, la ventilación por minuto, la FC, la disnea, la fatiga de las piernas y la

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oximetría de pulso fueron significativamente inferiores durante la PM6M. En cambio, en aquellos con FEV_1<50% la $\dot{V}O_2$, la FC y la disnea fueron similares. La distancia recorrida durante la PM6M en el grupo total se correlacionó estrechamente con el $\dot{V}O_2$ de la PECP (r=0,78; p=0,0001).
Conclusión: La PM6M posee las características de un ejercicio de carga constante, independientemente del estadio de la EPOC. Impone una alta exigencia metabólica, ventilatoria y cardiovascular, mayor en los pacientes más graves, lo que explicaría la estrecha correlación entre distancia recorrida (PM6M) y $\dot{V}O_2$ máximo (PECP).

Introduction

The six-minute walk test (6MWT) is commonly used to evaluate exercise capacity in chronic obstructive pulmonary disease (COPD) due to its simplicity and reproducibility.[1] Furthermore, walking is a normal activity for patients and better reflects the capacity for performing the activities of daily life than the standard exercises tests.[2] Lastly, the 6MWT has acquired clinical relevance since it allows for ranking of the severity of COPD and prediction of its survivability.[3,4]

Despite its importance, the physiological characteristics of the test have only been explored in small groups of patients. It is therefore unknown whether the severity of the disease affects these characteristics. In these studies, it has been observed that the 6MWT has the characteristics of a submaximal exercise where the patients assumes a constant walking speed equal to the maximum sustainable load with a plateau of oxygen consumption ($\dot{V}O_2$) after 3 minutes[5,6]. However, the magnitude of the metabolic, ventilatory and cardiovascular demand that it places on the patients is poorly understood.

The metabolic demand of the exercise includes the $\dot{V}O_2$ and the production of carbon dioxide ($\dot{V}O_2$), the latter being proportional to the synthesis of lactic acid and its damping by bicarbonate. The cardiovascular and ventilatory responses required to meet these metabolic demands correspond to additional demands. Consequently, the sum of these constitute the physiological demands requiered by the exercise. In published studies,[5-8] the extent of the physiological demands imposed by the 6MWT has been estimated comparing an incremental cardiopulmonary exercise test (CPET) using a cycle ergometer, even when it is accepted that they are different types of exercise. This is because the CPET is the gold standard test used in the pulmonary function laboratory for estimating exercise capacity. It has been observed that during the 6MWT the $\dot{V}O_2$ may be similar[5,7,9] to or less than,[6,10] that observed during the CPET, while the ventilation per minute ($\dot{V}$), the $\dot{V}CO_2$, the respiratory quotient (RQ = $\dot{V}O_2/\dot{V}O_2$) and the arterial lactate were consistenly lower.[5-7,10] The effects on dyspnoea have been mixed with reported values similar[8] to or less than those reached with CPET.[6,7] The inconsistencies identified may lie in the small number of patients included in these studies and in methodological issues associated with the standardisation of the 6MWT and the use or not of verbal incentive.

The aim of this study was to compare the 6MWT with the CPET in patients catergorised by COPD severity using a forced expiratory volume in one second (FEV_1) of 50% of the predicted value as the cutoff value. Our hypothesis is that $\dot{V}O_2$is greater during the 6MWT, as a consequence of the greater muscle mass involved in this type of exercise, independent of the severity of the COPD. Neverthless, a greater active muscle mass may contribute to metabolising the lactic acid and, therefore, we postulate that $\dot{V}O_2$ and the ventilatory and cardiovascular requirements will be lower during the walk test. Lastly, it is possible that the limited exercise capacity in severe COPD may reduce the muscle work during CPET and the muscle activity during walking and promote similar CO values and, consequently, a similar physiological demand in both types of exercise.

Methods

Patients

We studied 81 patients with mild to very severe COPD, as defined by GOLD.[11] These patients were part of a follow-up cohort that agreed to perform a 6MWT and a CPET on random and on consecutive days and were in a stable phase of the disease, i.e. no exacerbations in the last two months. Fifty-three patients had an FEV_1 greater than or equal to 50% and 28 patients had an FEV_1 below 50%. Drug treatment was not modified during the study. In the patient group with FEV_1 greater than or equal to 50%, 30 used short-acting beta-adrenergics, 15 used short-acting anticholinergics, 22 used long-lasting beta-adrenergics, 10 used tiotropium and 23 used inhaled corticoids. All patients with FEV_1 less than 50% used a combination of long-lasting beta-adrenergics, tiotropium and inhaled corticoids and 4 also used theophylline. None of the patients were using systemic corticoids. None had participated in a fitness training program. All signed an informed consent approved by the Ethics Committee of our institution. The recruitment criteria for this cohort were the following: a) older than 45 years, b) smoking history greater than 20 packs/year, c) FEV_1/FVC (forced vital capacity) less than 70% after receiving 200 mg of salbutamol, d) no history of asthma or other chronic lung disease, and e) absence of comorbidities that would prevent the patient from performing an exercise test. For this study, we also excluded patients that used home oxygen therapy and those who could not perform the walk test without stopping.

Measurements

Pulmonary Function

Spirometry and maximal voluntary ventilation were obtained using a Sensor Medics 2100 spirometer (Yorba Linda, California, USA) according to the standards of the American Thoracic Society (ATS) and the European Respiratory Disease Society,[12] through the use of Hankinson et al[13] reference values. Lung volumes were measured in the same session using a body plethysmograph (Sensor Medics Auto Box 6200) according to the standards of the ATS and the European Respiratory Disease Society[14] through the use of Quanjer et al.[15] theoretical values.

Exercise Tests

The 6MWT was performed in a 20-metre corridor according to the standards of the ATS.[16] The patients were asked to walk at a maximum tolerated speed and were encouraged verbally every minute.[17] Although the patients had previous experience with this type of exercise, they performed two tests on the day of the study in a random manner and separated by at least 30 minutes. One of these was done without instrumentation and the other one with the use of a portable telemetric device (Oxycon Mobile, Viasys Healthcare GmbH, Hoechberg, Germany). This system is lightweight (950g) and compact and includes a face mask with dead space of less than 30

Table 1
Clinical and functional characteristics in 81 patients with chronic obstructive pulmonary disease

Characteristic	Mean ± 1SD	Range
Male/female	49/32	–
Age, years	67 ± 8	50-83
BMI, kg/m²	26.8 ± 4	19-38
GOLD stages, n		
Mild-1	21	–
Moderate-2	32	–
Serious-III	20	–
Very serious-III	8	–
FEV_1, theoretical %	64 ± 24	19-116
FEV_1/FVC, %	48 ± 14	16-69
RV/TLC, %	45 ± 10	25-64
FRC, theoretical %	127 ± 34	90-208
ApO_2; mmHg	75 ± 10	57-100
$ApCO_2$, mmHg	40 ± 4	30-52

SD: standard deviation; FEV1: forced expiratory volume in one second; FRC: functional residual capacity; FVC: forced vital capacity; BMI: body mass index; $ApCO_2$: arterial carbon dioxide partial pressure; ApO_2: arterial oxygen partial pressure; RV: residual volume; TLC: total lung capacity.

ml, heart rate and pulse oximetry (SpO_2) monitor, battery, transmitter unit with O_2 and CO_2 analysers connected through a chest harness, and a receiving unit connected to a computer for remote data storage. The gas analysers and the turbine that measures volume were calibrated before each test. The $\dot{V}O_2$, CO_2, $\dot{V}_E$, heart rate (HR) and SpO_2 were thus measured continuously. Dyspnoea and leg fatigue were measured at the end of the test using the Borg scale.

In patients with FEV_1 greater than or equal to 50%, the distance covered with or without telemetry was 514 ± 85 m versus 512 ± 80 m, the difference between both tests was 1.8 ± 22 m. For those with FEV_1 less than 50%, the distance with and without telemetry was 416 ± 87 m versus 430 ± 87 m, that is, 14 ± 24 m greater during the 6MWT without telemetry. In both groups, these differences were lower than those reported for two consecutive 6MWT,[18] probably due to the patients' previous experience with this type of exercise.

The CPET consisted of a progressive exercise test limited by symptoms performed on a ER 800® cycle ergometer (Erich Jaeger, GmbH, Hoechberg, Germany). The patients stayed at rest for 3 minutes pedaling without a load at 60-70 revolutions/min and then the external load was progressively increased by 5-10 watts every minute up to their tolerance limit. The patients were encouraged verbally for the duration of the test. The maximum tolerated load was that which could be sustained for more than 30 seconds. During the maximum

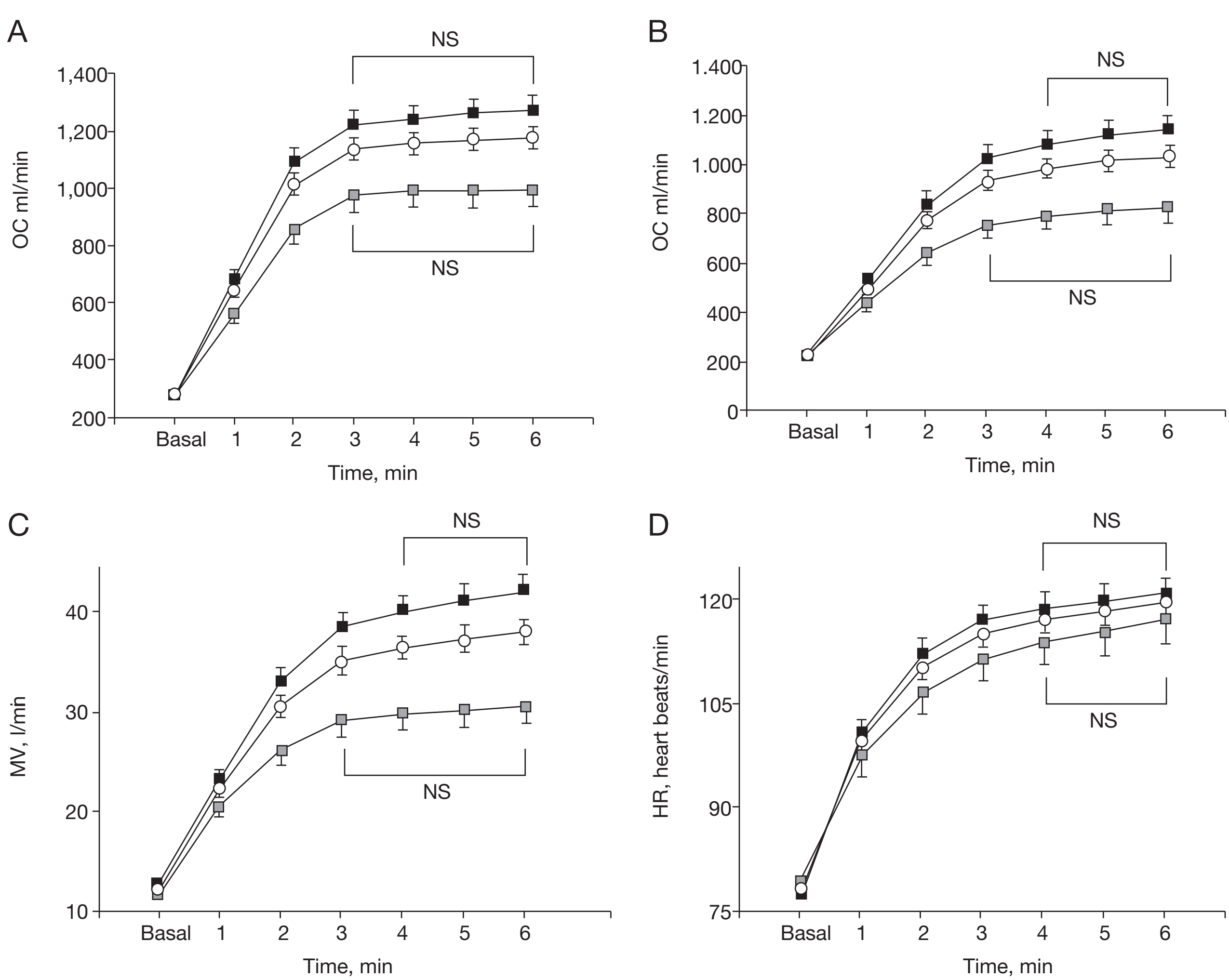

Figure 1. A) Temporal changes in oxygen consumption. B) Temporal changes in carbon dioxide production. C) Temporal changes in minute ventilation. D) Temporal changes in heart rate during the 6-minute walk test in patients with chronic obstructive pulmonary disease. It includes the whole group (white circles), the patients with forced expiratory volume in one second greater than or equal to 50% of the theoretical value (black rectangles) and the patients with forced expiratory volume in one second less than 50% (grey rectangles). The lines indicate the time period in which changes in the four variables were not significant. HR: heart rate; NS: not significant; MV: minute ventilation; OC: oxygen consumption.

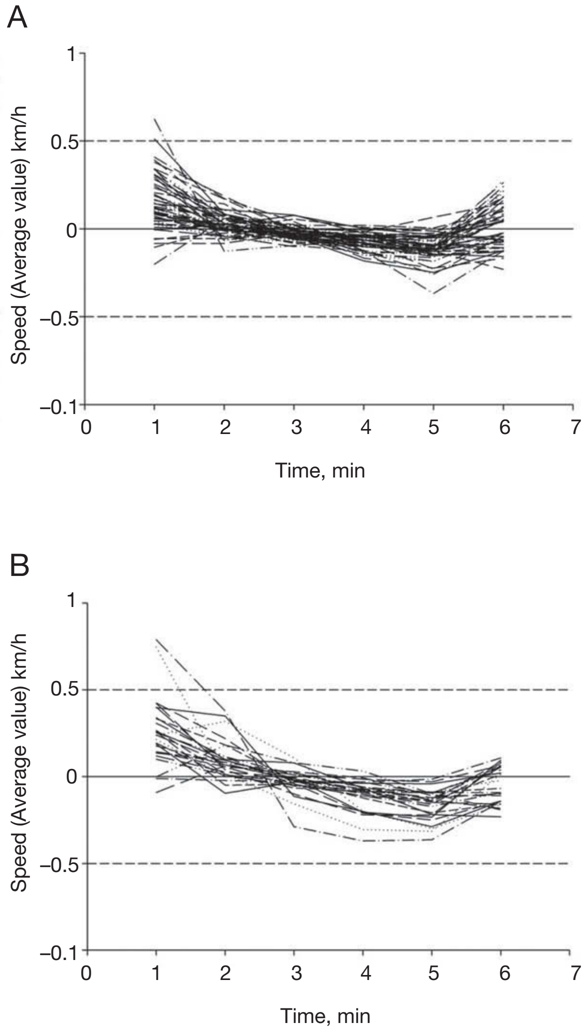

Figure 2. Individual speeds observed during the 6-minute walk test in patients with chronic obstructive pulmonary disease. A) With forced expiratory volume in one second greater than or equal to 50% of the theoretical value. B) With forced expiratory volume in one second less than 50%. The data are expressed as the difference between the observed velocity and the average value. The dotted reference lines identify changes of ± 0.5 km/h.

load reached, the data for the last 30 seconds were averaged for the analysis. We used the same portable telemetry device used for the 6MWT and took identical measurements. Blood pressure was monitored using a Dinamap™ Plus vital signs monitor (Critikon, Tampa, Florida, USA). Dyspnoea and leg fatigue were measured at the end of the test using the Borg scale. The Jones et al.[19] equations were used to determine the theoretical $\dot{V}O_2$ and HR values.

Statistical Analysis

The data are expressed as means with ± 1 SD in the text and tables and as means ± 1 SE in the figures. The normality of the variables was analysed with the Shapiro-Wilk test. The temporal analysis of the variables measured during the 6MWT was performed with one-way repeated measures ANOVA with the non-parametric Friedman test and the multiple comparisons were performed with the Tukey test. The variables obtained at the end of both exercises were compared using the Wilcoxon test. These comparisons were carried out in two subgroups: those with FEV_1 greater than or equal to 50% of the predicted value (GOLD stages 1 and 2) and those with FEV_1 less than 50% of the predicted value (GOLD stages 3 and 4). Values of $p<0.05$ were considered statistically significant.

Results

The characteristics of the entire group are described in table 1. As shown, the study group was heterogeneous with the following distribution, according to the GOLD classification: stage 1 (n = 21; FEV_1: 96 ± 12%), stage 2 (n = 32; FEV_1: 66 ± 8%), stage 3 (n = 20; FEV_1: 41 ± 5%) and stage 4 (n = 8; FEV_1: 29 ± 8%). Both the 6MWT and the CPET were well tolerated and no adverse events were reported.

Physiological Characteristics of the 6-minute Walk Test

The temporal changes in $\dot{V}O_2$, $\dot{V}O_2$, $\dot{V}_E$ and HR observed during the 6MWT in the whole group and the subgroups are decribed in figure 1. In patients with FEV_1 less than 50%, the $\dot{V}O_2$, $\dot{V}O_2$, $\dot{V}_E$ and HR showed a similar behaviour, with a plateau between 3-6 minutes. In patients with FEV_1 greater than or equal to 50%, $\dot{V}O_2$ showed the same temporal profile, but $\dot{V}O_2$ and $\dot{V}_E$ reached a stable state much later, between 4-6 minutes. The HR also reached plateau at 4 minutes in both subgroups.

Table 2
Physiological responses at the end of a cardiopulmonary exercise on the cycle ergometer and during the last minute of the 6-minute walk test in 53 patients with chronic obstructive pulmonary disease and forced expiratory volume in one second greater than or equal to 50% of the predicted value (GOLD states 1 and 2)

	CPET (maximum values)	6MWT (last minute)	P value
External load (watts)	78 ± 33	–	–
Distance (m)	–	514 ± 85	–
$\dot{V}O_2$, (mL/min)	1.207 ± 345	1.275 ± 366	0.003
$\dot{V}O_2$ (theoretical %)	86 ± 21	90 ± 21	0.004
$\dot{V}O_2$ (mL/kg/min)	16.5 ± 4	17.4 ± 4	0.012
$\dot{V}O_2$ (mL/min)	1.292 ± 420	1.141 ± 375	0.0001
RQ	1.06 ± 0.09	0.89 ± 0.07	0.0001
$\dot{V}_E$ (L/min)	48 ± 16	42 ± 12	0.0001
$\dot{V}_E$/VVM (%)	61 ± 16	53 ± 15	0.0001
$\dot{V}_E/\dot{V}O_2$	40 ± 7	33 ± 6	0.0001
$\dot{V}_E/\dot{V}CO_2$	38 ± 6	37 ± 6	0.52
HR, (beats/min)	124 ± 21	121 ± 17	0.02
HR, (theoretical %)	81 ± 12	78 ± 11	0.02
O_2 (pulse, mL/beat)	9.7 ± 2	10.6 ± 3	0.0001
SpO_2, %	93 ± 6	91 ± 7	0.0001
Dyspnoea, (Borg)	5 ± 2	3.3 ± 2	0.0001
Leg fatigue, (Borg)	6.5 ± 2	2.9 ± 2	0.0001

Values are expressed as mean ± 1 SD.
SD: standard deviation; HR: heart rate; CPET: cardiopulmonary exercise test; 6MWT: 6-minute walk test; SpO_2: oxygen saturation pulse oximetry; RQ: respiratory quotient; $\dot{V}_E$: minute ventilation; $\dot{V}O_2$: carbon dioxide production; $\dot{V}_E/\dot{V}O_2$: equivalent ventilation for carbon dioxide; $\dot{V}_E/\dot{V}O_2$: equivalent ventilation for oxygen; $\dot{V}O_2$: oxygen consumption; MVV: maximum voluntary ventilation.

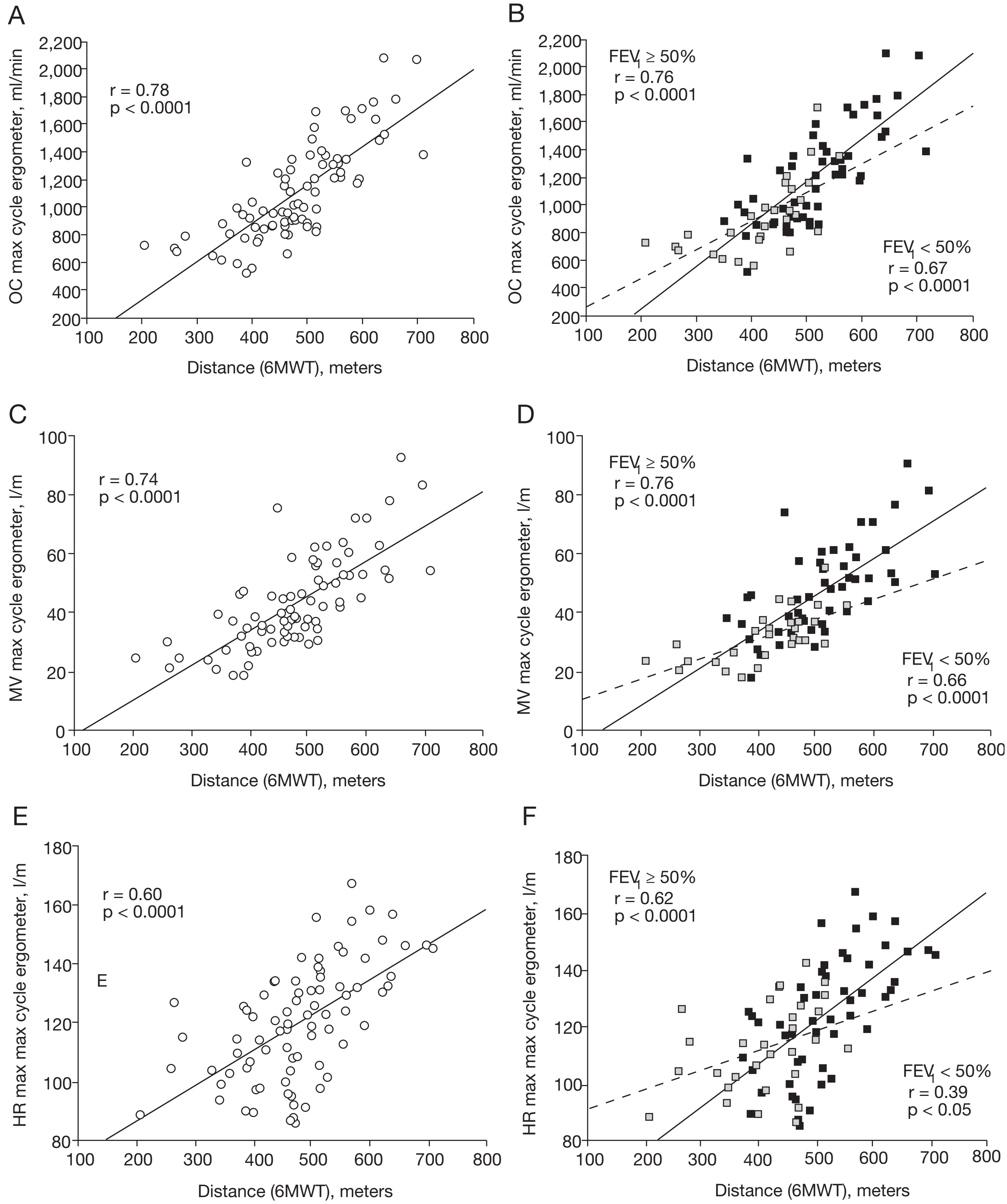

Figure 3. A) Correlation between the distance covered in the 6-minute walk test and the peak oxygen consumption measured in the cycle ergometer exercise in the whole group. B) Correlation between the distance covered in the 6-minute walk test and the peak oxygen consumption measured in the cycle ergometer exercise in the patient subgroups. C) Correlation between the distance covered in the 6-minute walk test and the maximum minute ventilation measured in the cycle ergometer exercise in the whole group. D) Correlation between the distance covered in the 6-minute walk test and the maximum minute ventilation measured in the cycle ergometer exercise in the patient subgroups. E) Correlation between the distance covered in the 6-minute walk test and the maximum heart rate measured in the cycle ergometer exercise in the whole group. F) Correlation between the distance covered in the 6-minute walk test and the maximum heart rate measured in the cycle ergometer exercise in the patient subgroups. HR: heart rate; FEV_1: forced expiratory volume in one second; 6MWT: six-minute walk test; $\dot{V}_E$: minute ventilation; $\dot{V}O_2$: oxygen consumption. It includes the whole group (white circles), the patients with forced expiratory volume in one second greater than or equal to 50% of the theoretical value (black rectangles) and the patients with forced expiratory volume in one second less than 50% (grey rectangles). In graphs B, D and F, the continuous lines represent the regression lines of those patients with $FEV_1 \geq 50\%$ and the dotted lines represent the regression lines of those with $FEV_1 < 50\%$.

The speed at which the walk was performed was relatively constant, as described in figure 2, where individual changes in velocity are represented through the test in relation to the average achieved. The variations were no greater than ± 0.5km/h, as previously noted.[5]

Comparision Between the 6-minute Walk Test and the Cardiopulmonary Exercise Test

The features observed at the end of both exercises in the two groups of patients are described in tables 2 and 3. While the $\dot{V}O_2$ in both groups was significantly greater during the 6MWT, other variables showed different behaviours. In patients with FEV_1 greater than or equal to 50% (table 2), $\dot{V}O_2$, QR, $\dot{V}_E$, HR, dyspnoea and leg fatigue were greater during the CPET. However, patients with FEV_1 less than 50% reported no differences in the $\dot{V}O_2$, HR and dyspnoea at the end of both types of exercise and the difference in $\dot{V}_E$ was only marginal, as shown in table 3.

In both types of exercise, $\dot{V}_E$ correlated closely with $\dot{V}O_2$ and the correlation coefficients were similar for the entire group (r = 0.92 in the 6MWT and r = 0.91 in the CPET, p<0.0001 in both cases) and for the subgroups. Furthermore, the distance walked during the 6MWT was closely correlated with the physiological variables measured at the end of the cycle ergometer exercise (fig. 3).

Discussion

The most important findings of this study are the following: a) the $\dot{V}O_2$ achieved during the 6MWT was greater that that achieved during CPET, regardless of the severity of the COPD, and b) the distance covered during the 6MWT was closely correlated with the maximm $\dot{V}O_2$ of the CPET. Additionally, our results confirm that the patients adopt an almost constant speed during the 6MWT and reach $\dot{V}O_2$ plateau at around 3 minutes. These characeristics are consistent with exercise that has constant and submaximal load, given that a stable state is achieved, and are independent of the severity of the COPD. Furthermore, the present data confirms that the physiological demands in terms of $\dot{V}O_2$, RQ, $\dot{V}_E$, HR and dyspnoea are lower when walking, especially in patients with less severe COPD. In patients with FEV_1 less than 50%, $\dot{V}O_2$, HR and dyspnoea were similar at the end of both tests. On the other hand, the walk test induced greater oxygen desaturation than the cycle ergometer exercise, regardless of the severity of the COPD.

Physiological Characteristics of the 6-minute Walk Test

During the 6MWT, the patients achieved a stable state around 3 minutes, as shown by the behaviour of $\dot{V}O_2$ (fig. 1), characteristic of a submaximal exercise. Also, it is reasonable to assume that the workload imposed by the 6MWT was constant given that its energy requirements depend largely on body weight and the speed adopted,[5] which essentially did not vary during the test (fig. 2). This supports previous data that indicate that the 6MWT is a submaximal and sustainable exercise.[5,6]

On the other hand, although the ?O_2 profile was not affected by the severity of COPD, its absolute values were lower in patients with FEV_1 less than 50%, which is due at least in part to the combined effects of a mechanical restriction limiting the $\dot{V}_E$ early on (fig. 1) and to the marked arterial oxygen desaturation (table 3).

Physiological Characteristics of the 6-minute Walk Test Compared with the Cardiopulmonary Exercise Test

The $\dot{V}O_2$ reached during the 6MWT was significantly higher than that observed during the CPET in contrast to previous data that showed that, when walking, one achieves a $\dot{V}O_2$ similar to or less than that achieved on a cycle ergometer. This indicates that the ?O_2 achieved depends on the muscle mass used, which is higher in the 6MWT due to the contribution of the muscles of the trunk and upper limbs. The discrepancies with previous studies may be due to the lower number of patients in these earlier studies. It is also possible that the increase in the external load used during our study's CPET was inappropriate and prevented a linear relationship with the $\dot{V}O_2$, which may cause an early increase in lactate and a lower peak $\dot{V}O_2$.[20,21] This alternative seems unlikely since the range of increase chosen has not been shown to affect peak $\dot{V}O_2$ in COPD[22] and because it does not differ from protocols used in similar studies.[5,7,8] Furthermore, the results of the CPET do not differ from those previously published on a similar population.[23] Another possible explanation is that the length of the corridor used (20m) may have been too short and thus reduced the efficacy of the exercise, which could result in a disproportionate increase in $\dot{V}O_2$ for the given distance.[6] Although we can not rule out this possibility with certainty, there is evidence that the use of corridors between 15-50 m does not affect the test's characteristics.[24]

Despite the increased $\dot{V}O_2$ achieved during the 6MWT, the values for $\dot{V}O_2$, RQ, $\dot{V}_E$ and HR were consistently higher for the cycle

Table 3
Physiological responses at the end of a cardiopulmonary exercise on the cycle ergometer and during the last minute of the 6-minute walk test in 28 patients with chronic obstructive pulmonary disease and forced expiratory volume in one second less than 50% of the predicted value (GOLD states 3 and 4)

	CPET (maximum values)	6MWT (last minute)	P value
External load (watts)	50 ± 19	–	–
Distance, m	–	416 ± 87	–
$\dot{V}O_2$, (mL/min)	915 ± 271	997 ± 317	0.009
$\dot{V}O_2$ (theoretical %)	62 ± 17	67 ± 21	0.019
$\dot{V}O_2$ (mL/kg/min)	13 ± 2.9	14 ± 3.8	0.007
$\dot{V}C0_2$, (mL/min)	867 ± 308	826 ± 295	0.27
RQ	0.94 ± 0.08	0.82 ± 0.06	0.0001
$\dot{V}E$ (L/min)	33 ± 9	30 ± 9	0.041
$\dot{V}E$/VVM (%)	82 ± 19	76 ± 20	0.024
$\dot{V}E/\dot{V}O_2$	36 ± 5	31 ± 3	0.0001
$\dot{V}E/\dot{V}CO_2$	39 ± 6	38 ± 5	0.27
HR (beats/min)	113 ± 15	117 ± 19	0.19
HR, (theoretical %)	74 ± 10	76 ± 12	0.18
O_2 (pulse, mL/beat)	8.1 ± 2	8.5 ± 2	0.032
SpO_2 (%)	86 ± 6	82 ± 6	0.0001
Dyspnoea (Borg)	6.5 ± 2	5.8 ± 2	0.096
Leg fatigue (Borg)	6.5 ± 2	3.6 ± 3	0.001

Values are expressed as mean ± 1 SD.

SD: standard deviation; HR: heart rate; CPET: cardiopulmonary exercise test on cycle ergometer; 6MWT: six-minute walk test: RQ; respiratory quotient; SpO_2: oxygen saturation pulse oximetry; $\dot{V}CO_2$: carbon dioxide production; $\dot{V}_E$: minute ventilation; $\dot{V}_E/\dot{V}CO_2$: equivalent ventilation for carbon dioxide; $\dot{V}_E/VO_2$: equivalent ventilation for oxygen; $\dot{V}O_2$: oxygen consumption; MVV: maximum voluntary ventilation.

ergometer in those patients with mild to moderate COPD. These differences were less evident in patients with FEV_1 less than 50% and indicated that as COPD severity increases, the metabolic, ventilatory and cardiovascular stress imposed by both tests tend to resemble each other.

In both types of exercise, $\dot{V}_E$ was closely correlated with ?CO_2. As a consequence, the higher $\dot{V}_E$ observed during the CPET would represent the physiological response to the higher $\dot{V}O_2$ induced by this type of exercise,[25] attributable to a higher lactacidemia.[5,26,27] The lower lactacidemia and, consequently, the lower $\dot{V}O_2$ associated with the walk test as compared to the cycle ergometer exercise are well documented. They do not seem to depend on differences in the extent of the workload between the two types of exercise,[28,29] but on the muscle massed involved. The lower muscle mass used in the CPET increases the work per fibre and exceeds the muscle oxidative machinery.[30] Furthermore, the greater number of muscles used during the 6MWT not only generates lactate, but would also likely participate simultaneously in its removal and degradation, and would thus reduce its plasma levels.[31,32] It is reasonable to attribute the higher dyspnoea observed during the CPET to this higher $\dot{V}_E$ (tables 2 and 3). This would thus explain why the dyspnoea was similar in patients with FEV_1 less than 50% since in this latter group there was less difference in $\dot{V}_E$ at the end of both types of exercise (table 3).

The ventilatory equivalent for CO2, i.e. the relationship $\dot{V}_E/\dot{V}CO_2$, was similar in the two tests, in contrast with the findings of Palange et al.[26] These authors found significantly higher $\dot{V}_E/\dot{V}CO_2$ values at the end of an incremental shuttle test when compared with the cycle ergometer exercise. They attributed this response to an less efficient pulmonary gas exchange when walking, which would also explain the greater hypoxemia associated with this test. Coincidentally, the arterial desaturation in our study was also greater during the 6MWT, but our data indicated that this could be due to a lower ventilatory response for a given $\dot{V}O_2$ ($\dot{V}_E/\dot{V}CO_2$) during the walk test, as Hsia et al.[29] have recently reported.

Clinical Relevance

The CPET is the standard method for determining maximal exercise capacity in COPD. Nevertheless, the 6MWT is easier to perform, reproducible, well standardised and patients with COPD walk at a speed close to their maximum capacity.[6] Nonetheless, the correlation between the distance walked and peak $\dot{V}O_2$ has been poor in previous studies[27,33] and this contrasts with our results. These differences could be due to the inclusion in those studies of patients who could stop during the test,[33] who did not perform a walk test[27] or who did not receive verbal incentive.[27] Under the standardised conditions under which the 6MWT was carried out in this study, there was a high metabolic, ventilatory and cardiovascular demand that probably explains the close correlation between the distance covered during the walk and the peak $\dot{V}O_2$, the maximum $\dot{V}_E$ and the maximum HR obtained on the cycle ergometer.

As a consequence, our data corroborates, with a substantially larger population than that of previous studies, that the 6MWT and the CPET are not interchangeable exercise tests from a physiological point of view. However, from the clinical point of view, when the 6MWT is performed in a standardised manner and verbal incentive is used, it shows the maximum sustainable exercise capacity and efficiently reflects the maximum capacity obtained from the cycle ergometer. Probably, this may explain its strength when staging the severity of the disease and forecasting disease prognosis. Due to the design of the study, those patients that used oxygen therapy were excluded, as well as those who had to stop during the test. These statements do not necessarily apply to all patients with COPD.

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References

1. Butland RJ, Pang J, Gross ER, Woodcock AA, Geddes DM. Two-, six-, and 12-minute walking tests in respiratory disease. Br Med J (Clin Res Ed). 1982;284:1607-8.
2. Solway S, Brooks D, Lacasse Y, Thomas S. A qualitative systematic overview of the measurement properties of functional walk tests used in the cardiorespiratory domain. Chest. 2001;119:256-70.
3. Celli BR, Cote CG, Marin JM, Casanova C, Montes de Oca M, Méndez RA, et al. The body-mass index, airflow obstruction, dyspnea, and exercise capacity index in chronic obstructive pulmonary disease. N Engl J Med. 2004;350:1005-12.
4. Cote CG, Pinto-Plata V, Kasprzyk K, Dordelly LJ, Celli BR. The 6-min walk distance, peak oxygen uptake, and mortality in COPD. Chest. 2007;132:1778-85.
5. Troosters T, Vilaro J, Rabinovich R, Casas A, Barbera JA, Rodríguez-Roisin R, et al. Physiological responses to the 6-min walk test in patients with chronic obstructive pulmonary disease. Eur Respir J. 2002;20:564-9.
6. Casas A, Vilaro J, Rabinovich R, Mayer A, Barbera JA, Rodríguez-Roisin R, et al. Encouraged 6-min walking test indicates maximum sustainable exercise in COPD patients. Chest. 2005;128:55-61.
7. Luxton N, Alison JA, Wu J, Mackey MG. Relationship between field walking tests and incremental cycle ergometry in COPD. Respirology. 2008;13:856-62.
8. Turner SE, Eastwood PR, Cecins NM, Hillman DR, Jenkins SC. Physiologic responses to incremental and self-paced exercise in COPD. Chest. 2004;126:766-73.
9. Swinburn CR, Wakefield JM, Jones PW. Performance, ventilation, and oxygen consumption in three different types of exercise test in patients with chronic obstructive lung disease. Thorax. 1985;40:581-6.
10. Van Helvoort HAC, Heijdra YF, De Boer RCC, Swinkels A, Thijs HMH, Dekhuijzen PNR. Six-minute walking-induced systemic inflammation and oxidative stress in muscle-wasted COPD patients. Chest. 2007;131:439-45.
11. Rabe KF, Hurd S, Anzueto A, Barnes PJ, Buist SA, Calverley P, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2007;176:532-55.
12. Miller MR, Hankinson J, Brusasco V, Burgos F, Casaburi R, Coates A, et al. Standardisation of spirometry. Eur Respir J. 2005;26:319-38.
13. Hankinson J, Odencrantz J, Fedan K. Spirometric reference values from a sample of the general US population. Am J Respir Crit Care Med. 1999;159:179-87.
14. Wanger J, Clausen JL, Coates A, Pedersen OF, Brusasco V, Burgos F, et al. Standardisation of the measurement of lung volumes. Eur Respir J. 2005;26: 511-22.
15. Quanjer P, Tammeling G, Cotes J, Pedersen O, Peslin R, Yernault J. Lung volumes and forced ventilatory flows. Report work party: Standardization of lung function testing. Eur Respir J. 1993;6:5s-40s.
16. ATS Statement: Guidelines for the six-minute walk test. Am J Respir Crit Care Med. 2002;166:111-7.
17. Guyatt G, Pugsley S, Sullivan M, Thompson P, Berman L, Jones N, et al. Effect of encouragement on walking test performance. Thorax. 1984;39:818-22.
18. Sciurba F, Criner GJ, Lee SM, Mohsenifar Z, Shade D, Slivka W, et al. Six-minute walk distance in chronic obstructive pulmonary disease: Reproducibility and effect of walking course layout and length. Am J Respir Crit Care Med. 2003;167:1522-7.
19. Jones N, Makrides L, Hitchcock C, Chypchar T, McCartney N. Normal standards for an incremental progressive cycle ergometer test. Am Rev Respir Dis. 1985;131: 700-8.
20. Buchfuhrer MJ, Hansen JE, Robinson TE, Sue DY, Wasserman K, Whipp BJ. Optimizing the exercise protocol for cardiopulmonary assessment. J Appl Physiol. 1983;55:1558-64.
21. ATS/ACCP Statement on cardiopulmonary exercise testing. Am J Respir Crit Care Med. 2003;167:211-77.
22. Benzo RP, Paramesh S, Patel SA, Slivka WA, Sciurba FC. Optimal protocol selection for cardiopulmonary exercise testing in severe COPD. Chest. 2007;132:1500-5.
23. Pinto-Plata VM, Celli-Cruz RA, Vassaux C, Torre-Bouscoulet L, Mendes A, Rassulo J, et al. Differences in cardiopulmonary exercise test results by American Thoracic Society/European Respiratory Society-Global Initiative for Chronic Obstructive Lung Disease stage categories and gender. Chest. 2007;132:1204-11.
24. Salzman SH. The 6-min walk test. Chest. 2009;135:1345-52.
25. Casaburi R, Whipp BJ, Wasserman K, Beaver WL, Koyal SN. Ventilatory and gas exchange dynamics in response to sinusoidal work. J Appl Physiol. 1977;42: 300-1.
26. 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;88:1715-20.

27. Onorati P, Antonucci R, Valli G, Berton E, De Marco F, Serra P, et al. Non-invasive evaluation of gas exchange during a shuttle walking test vs. a 6-min walking test to assess exercise tolerance in COPD patients. Eur J Appl Physiol. 2003;89:331-6.
28. Mathur RS, Revill SM, Vara DD, Walton R, Morgan MD. Comparison of peak oxygen consumption during cycle and treadmill exercise in severe chronic obstructive pulmonary disease. Thorax. 1995;50:829-33.
29. Hsia D, Casaburi R, Pradhan A, Torres E, Porszasz J. Physiological responses to linear treadmill and cycle ergometer exercise in COPD. Eur Respir J. 2009;34:605-15.
30. Miles DS, Critz JB, Knowlton RG. Cardiovascular, metabolic, and ventilatory responses of women to equivalent cycle ergometer and treadmill exercise. Med Sci Sports Exerc. 1980;12:14-9.
31. Van Hall G, Jensen-Urstad M, Rosdahl H, Holmberg H-C, Saltin B, Calbet JAL. Leg and arm lactate and substrate kinetics during exercise. Am J Physiol Endocrinol Metab. 2003;284:E193-205.
32. Beneke R, Leithauser RM, Hutler M. Dependence of the maximal lactate steady state on the motor pattern of exercise. Br J Sports Med. 2001;35:192-6.
33. López J, Montes de Oca M, Ortega Balza M, Lezama J. Enfermedad pulmonar obstructiva crónica. Evaluación de la tolerancia al ejercicio utilizando tres tipos diferentes de pruebas de esfuerzo. Arch Bronconeumol. 2001;37:69-74.