Ventilatory Responses to Six-minute Walk Test, Incremental Shuttle Walking Test, and Cycle Ergometer Test in Patients with Chronic Obstructive Pulmonary Disease

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ABSTRACT
The purpose of this study was to examine the ventilatory responses during a six-minute walk test (6MWT), an incremental shuttle walking test (ISWT), and a cycle ergometer test (CET) in patients with chronic obstructive pulmonary disease. Twelve subjects (11 male, age 72.2 years, with a forced expiratory volume in one second of 53.6% of the predicted normal) took part in the study. Throughout the three exercise tests, oxygen uptake (VO₂), carbon dioxide production (VCO₂), minute ventilation (VE), and heart rate (HR) were measured using a portable breath-by-breath system. Oxygen saturation (SpO₂) and breathlessness were recorded at the end of each minute during the tests. There were no significant differences among the three exercise tests in terms of the peak values for VO₂, VCO₂, VE, HR, and breathlessness. SpO₂ was significantly lower in both walking tests (6MWT: 89.8 ± 3.3%, ISWT: 88.9 ± 3.8%) compared to values in the CET (93.3 ± 2.3%) (p < 0.05). VO₂ during the 6MWT increased sharply for 2 minutes, and then showed a steady-state profile. During the CET and the ISWT, however, VO₂ increased with respect to workload. In conclusion, the three tests clearly measure different aspects of exercise tolerance and should be considered complementary.

The assessment of disability in patients with chronic obstructive pulmonary disease (COPD) usually requires that the practitioner estimate the patient's capacity for exercise. Methods of assessing the performance of whole body exercise include tests of maximal capacity and endurance capacity. To evaluate these capacities, pulmonary gas exchange is usually analyzed.

The six-minute walk test (6MWT) is now the most commonly used timed walk test (11, 24, 28). It is simple, and does not require sophisticated equipment or advanced technical training. In addition, walking is a familiar activity typically performed by even the most severely debilitated patients (24, 28). In the 6MWT, the patient determines the walking speed, and the distance walked will depend on the patient's capacity to pace himself or herself accordingly.

The incremental shuttle walking test (ISWT) is also simple for both the operator and the patient. It should be minimal sets of equipment with easy methods, and data must have reproducibility for general test (27). The two tests therefore differ in terms of protocol, given that the 6MWT is a time-limited walk test and the ISWT is a symptom-limited walk test (17).

Maximal incremental exercise tests are usually performed on a cycle ergometer or a treadmill (15). Testing with cycle ergometers or treadmills enables
collection of essential physiological, metabolic, and ventilatory data. However, such equipment is expensive, sometimes unavailable, and requires training prior to its use. Studies using a cycle ergometer have provided evidence that impairment of muscular energy is a major contributor to the reduced ability and endurance of patients with COPD (8). However, data obtained using a cycle ergometer test (CET) may not adequately reflect the physiological and metabolic functions that occur during routine daily activities that involve walking (20). In particular, frail and elderly patients with severe cardiac or pulmonary disease often become exhausted after only a few minutes of conventional maximal exercise testing. Therefore the patient’s exercise capacity may be underestimated.

Consequently, although the 6MWT, ISWT, and CET have commonly been used to evaluate patients with COPD, the characteristic features and comparative advantages and disadvantages of these respective tests have not been clear. Therefore, the purposes of this study were to examine gas exchange parameters and the workload or distance walked in the three tests; to compare cardiorespiratory responses (heart rate; FR and oxygen saturation; SpO₂) and dyspnea responses among the three tests; and to examine the changes in gas exchange parameters during the 6MWT, ISWT, and CET in patients with COPD.

MATERIALS AND METHODS

Study Subjects. Subjects were recruited from participants in the pulmonary rehabilitation program at Akita City General Hospital. They came to Akita City Hospital every two weeks and underwent a course of pulmonary rehabilitation. Exclusion criteria included unstable pulmonary status, orthopedic or cardiovascular complications affecting exercise performance, difficulty in understanding the required tasks, and the necessity for supplemental oxygen during walking. At the time of the study all patients were clinically stable and were not under steroid treatment. The study protocol was approved by the Ethical Committee of Akita City General Hospital. The subjects were fully informed of any risks involved in participating in the research program, and their written informed consent was obtained.

Twelve subjects (11 male; mean age, 72.2 years) took part in the study. All patients had a history of cigarette smoking, and had spirometric evidence (forced expiratory volume in one second; FEV₁ < 80% predicted, FEV₁/forced vital capacity; FVC < 70%) and a clinical history consistent with COPD (3, 18). All subjects had moderate, stable COPD with a mean ± SD, FEV₁ of 53.6 ± 22.1 % of the predicted normal. The demographic and pulmonary function data are summarized in Table 1. All subjects had stopped smoking in the past, although all had quit prior to starting the program.

Study Design. Over a period of five weeks, subjects performed the 6MWT, the ISWT, and the CET in random order. No more than two tests were undertaken on the same day. Prior to and throughout all the exercise tests, ventilatory and gas exchange parameters were measured using a breath-by-breath system. SpO₂ and breathlessness were recorded before each of the tests, and at the end of each minute during each test. Subjects were instructed to refrain from eating or drinking any caffeinated products for two hours prior to testing.

Six-minute Walk Test (6MWT). This test was carried out in a hospital corridor. Subjects walked along a rectangular track for a length of 88 meters (30 m × 14 m). Subjects were instructed to walk as fast as possible for 6 minutes and to cover as much ground as possible in that time. They were allowed to slow down or stop if necessary, but were required to resume walking as soon as they felt able. Each minute subjects were given feedback on the elapsed time, and were encouraged to continue walking. All subjects were familiar with the 6MWT prior to the study. The test was repeated on the same day with a minimum of 30 minutes of rest. Data from the test in which the maximum distance was covered was used in the analyses.

Incremental Shuttle Walking Test (ISWT). The ISWT was performed using the protocol described by Singh et al. (27). This test required the subject to walk up and down a 10 m course. In order to avoid the need for abrupt changes in direction, the course was marked by two cones placed 0.5 m from either end. The walking speed was controlled by a series of audio-recorded sounds (beeps) given at regular intervals. The initial walking speed was set at 0.50 m/sec, and increased each minute by 0.17 m/sec. The test has 12 levels, each one minute in duration. Before starting the test, the procedure was explained in a standard manner. The operator sat alongside the course and gave no encouragement throughout the test. The end-point of the test was determined by the subject when he became too breathless to maintain
the required speed, or by the operator when the subject failed to complete a shuttle in the time allowed (i.e., being more than 0.5 m away from the cone when the beep sounded). The ISWT was repeated after at least 30 minutes of rest, and data from the test in which the maximum distance was covered was used in the analyses.

**Cycle Ergometer Test (CET).** Subjects cycled on an electrically braked ergometer (Aerobike 800; Combi, Tokyo, Japan) at a constant speed of 50 rpm with an initial load of 0 watts, which was increased each minute by 10 watts to a symptom-limited maximum (15, 20). Each subject, after having been instructed and given a practice trial of pedaling for enough, performed the test once. The test was stopped when the subject was unable to maintain the required speed.

**Equipment.** During all tests, the ventilatory and gas exchange parameters and the HR were measured, using a portable metabolic test system (MetaMax 3B; Cortex, Leipzig, Germany). The MetaMax 3B system consisted of a face mask (attached to a volume transducer), a Polar HR chest strap, a transmitter (with expiratory gas analyzing system), and a receiving unit. The transmitter was placed around the subject's neck, with the two main parts resting on the chest. The equipment, which was carried by the subject, weighed 0.7 kg. The receiver was linked to a personal computer, and the MetaSoft (Cortex, Leipzig, Germany) was used for data analysis. This apparatus had been previously validated against a conventional stationary instrument (12, 23).

Calibration of the volume transducer was performed using a three liter syringe. The oxygen and the carbon dioxide analyzers were calibrated with gas mixtures from a tank of standard gas and room air before each test. The ventilatory and gas exchange parameters were measured in the breath-by-breath mode and subsequently averaged over 20 second intervals, and the peak data represented the last 20-second average obtained during each test. Peak HR (HR peak) was recorded for all three tests.

SpO₂ was measured using a pulse oximeter and finger sensor (Pulsox-M24; Teijin, Tokyo, Japan) every minute. This device, designed for ambulatory use and weighing 45 g, was attached to the subject's wrist. Breathlessness was measured using the Borg 0–10 dyspnea scale (5). During the tests, subjects described the intensity of breathlessness by pointing to a descriptor on the scale every minute.

**Statistical analysis.** Statistical analysis was performed using the SPSS statistical package (Version 91; SPSS Japan Inc. Tokyo). The one-way repeated measures analysis of variance was used to analyze the gas exchange parameters, the performance, HR,
SpO₂, and dyspnea responses. Relationships between variables (maximum power and peak oxygen uptake (VO₂ peak), distance walked and VO₂ peak) were assessed by the application of Pearson's correlation and linear regression analysis. A p value of < 0.05 was considered significant.

RESULTS

All patients completed the study. No subjects rested during the 6MWT. The ISWT was terminated in all subjects because of an inability to maintain the required speed. The CET was terminated because of dyspnea in nine subjects. In the remaining three subjects the test was terminated because of leg fatigue. Results are expressed as mean ± SD. Predicted values at maximal exercise were obtained from published equations (13, 14).

Changes in ventilation and gas exchange indexes during exercises

Figures 1–4 summarize oxygen uptake (VO₂), carbon dioxide production (VCO₂), minute ventilation (VE), and HR responses during the 6MWT, the ISWT, and the CET. VO₂, VCO₂, VE, and HR increased sharply during the first 2 minutes of the 6MWT, then showed a steady-state profile from minute 3 to 6 of the 6MWT. VO₂, VCO₂, and VE increased gradually in the ISWT and CET. The slopes of VCO₂ and VE in the ISWT were steeper than those in the CET.

Peak exercise data

Performance and ventilatory results at peak exercise in the study are shown in Table 2. Among the three tests, VO₂ peak was highest in the ISWT. SpO₂ was significantly lower at the end of both walking tests.
compared to that in the CET (p < 0.05).

There were significant, moderate positive correlations between the maximum power output in the CET and the distance walked in the 6MWT (r = 0.64, p = 0.024), and between the maximum power output in the CET and the distance walked in the ISWT (r = 0.79, p = 0.002). A strong correlation (r = 0.87, p < 0.001) was observed between the distance walked in the 6MWT and that walked in ISWT. The distance walked during the 6MWT was significantly further than that walked during the ISWT (p < 0.01).

Relationship between maximum power or distances walked and oxygen consumption

There were significant, strong positive correlations between the maximum power output and V̇O₂ peak in the CET (r = 0.91, p < 0.001), and between the distance walked and V̇O₂ peak in the ISWT (r = 0.85, p < 0.001) (Fig. 5). A moderate correlation (r = 0.69, p = 0.013) was observed between the distance walked and V̇O₂ peak in the 6MWT (Fig. 6).

DISCUSSION

At present, there are few studies analyzing gas exchange during field walking tests (19, 20, 26). To the best of our knowledge, this is the first study to compare ventilatory responses during the 6MWT, ISWT, and CET in the same patients with chronic obstructive pulmonary disease.

The incremental increases in V̇O₂ observed during the ISWT and the CET in this study confirm that these tests, by providing exercise of increasing intensity, provoke gradual physiological responses (15, 26). The slopes of V̇O₂, V̇CO₂, and V̇E during the ISWT were steeper than those during the CET, suggesting that ventilatory responses were more increased during the ISWT than during the CET. These increased ventilatory responses during the ISWT could be explained by the difference in the rate of increase in work per minute between the

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Table 2  Peak exercise data in 12 subjects

<table>
<thead>
<tr>
<th></th>
<th>CET</th>
<th>6MWT</th>
<th>ISWT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Workload</td>
<td>(W)</td>
<td>77.5 ± 31.9</td>
<td></td>
</tr>
<tr>
<td>Distance</td>
<td>(m)</td>
<td>—</td>
<td>490.6 ± 93.0</td>
</tr>
<tr>
<td>HR peak</td>
<td>(bpm)</td>
<td>111.7 ± 16.1</td>
<td>108.6 ± 18.9</td>
</tr>
<tr>
<td>% predicted</td>
<td>(%)</td>
<td>75.4 ± 8.9</td>
<td>73.5 ± 12.4</td>
</tr>
<tr>
<td>SpO₂</td>
<td>(%)</td>
<td>93.3 ± 2.3</td>
<td>89.8 ± 3.3*</td>
</tr>
<tr>
<td>Dyspnea peak</td>
<td>(%)</td>
<td>6.8 ± 2.3</td>
<td>6.0 ± 2.7</td>
</tr>
<tr>
<td>V̇O₂ peak</td>
<td>(ml/min/kg)</td>
<td>13.86 ± 3.62</td>
<td>14.47 ± 2.13</td>
</tr>
<tr>
<td>% predicted</td>
<td>(%)</td>
<td>67.7 ± 14.0</td>
<td>71.5 ± 11.0</td>
</tr>
<tr>
<td>V̇CO₂ peak</td>
<td>(ml/min/kg)</td>
<td>14.55 ± 5.45</td>
<td>12.56 ± 2.02</td>
</tr>
<tr>
<td>V̇E peak</td>
<td>(L/min)</td>
<td>28.5 ± 11.1</td>
<td>25.5 ± 6.9</td>
</tr>
<tr>
<td>% MVV</td>
<td>(%)</td>
<td>65.7 ± 17.5</td>
<td>62.3 ± 20.8</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. Prediction values were obtained from following equations. male: V̇O₂ max/kg = 60 – 0.55 × age (ml/min/kg), female: V̇O₂ max/kg = 48 – 0.37 × age (ml/min/kg), V̇E max = 26.3 × VC – 34 (L/min), MVV = FEV₁ × 35 (L/min), HR max = 220 – age

CET: cycle ergometer test; 6MWT: six minute walk test; ISWT: incremental shuttle walking test; HR peak: peak heart rate; SpO₂: oxygen saturation; V̇O₂ peak: peak oxygen uptake; V̇CO₂ peak: peak carbon dioxide production; V̇E peak: peak minute ventilation; MVV: maximal voluntary ventilation; *: p < 0.05 compared to CET
ISWT and the CET (8, 15, 26). It could be speculated based on the current study that the increase in walking speed (by 0.17 m/sec every minute) in the ISWT is larger (a bigger increment of work) than the increase in work rate (by 10 watts every minute) in the CET. This difference could be partly explained by the supposition that the increase in neurogenic stimuli from the extremities to the respiratory centers was greater during the walking test than during the CET (9, 10).

In contrast, VO\textsubscript{2} during the 6MWT increased sharply for about 2 minutes and showed a steadystate VO\textsubscript{2} profile from minute 3 to 6 in the 6MWT. Since the walking speed chosen by the patients is almost constant throughout an encouraged 6MWT, as indicated by the current result (Fig. 1) and earlier data (6, 30), it seems reasonable to assume that the work rate (walking speed) is constant throughout a 6MWT. It can be speculated that the walking speed is set by the patient to achieve a sustainable work rate and VO\textsubscript{2} throughout the test. In these circumstances, the physiological data from the test is highly relevant, since it may reflect the integrated response of the organ systems involved in oxygen transport/oxygen utilization, which allows a high but sustainable level of whole-body exercise. Onorati et al. (19) suggested that ISWT was preferable to 6MWT in the assessment of maximal exercise capacity and ventilatory limitation in patients with moderate COPD.

In our study, SpO\textsubscript{2} decreased during the three tests, and the magnitude of desaturation in patients with COPD was significantly greater in both walking tests compared to that in the CET. Measurement of SpO\textsubscript{2} during exercise is used to assess the severity of gas exchange impairment. Desaturation during the walking tests is common in patients with COPD because VO\textsubscript{2} during the walking is caused by a larger amount of muscle mass at work than that at work during the cycling (16). Palange et al. (20) showed that the partial pressure of arterial oxygen (PaO\textsubscript{2}) values were lower during the ISWT than during the CET. In addition, they observed higher the physiological dead space/tidal volume ratio (VD/VT) during the ISWT than during the CET. They suggested that this decreased lung gas exchange efficiency was related to pronounced hypoxemia during the walking test. Poulain et al. (21) also reported that desaturation during the 6MWT is significantly larger than that during the CET. Incremental cycling protocols are recommended to evaluate the exercise tolerance in COPD patients because they allow an appropriate analysis of the relationships between VO\textsubscript{2} and the work rate (15, 28). However, walking may be a more efficient type of
movement, especially in elderly subjects who are not used to cycling; in this regard, the 6MWT may be more suitable than the CET or the ISWT for evaluating everyday physical demands. This observation supports the use of the 6MWT as a valuable test in the assessment of exercise-induced desaturation in COPD patients. It sometimes happens that SpO₂ decreases suddenly during the walking exercise (2), and SpO₂ has slightly to do with breathlessness (22). Therefore, it is essential to monitor SpO₂ during the walking test, as suggested in the American Thoracic Society guidelines (2).

This study showed that peak values for VO₂, VCO₂, and VE measured during the CET, the 6MWT, and the ISWT in patients with COPD were not significantly different. Further, no significant differences were observed in the HR peak and dyspnea scores. In COPD patients, Swinburn et al. (29) and Alison et al. (1) reported that VO₂ peak and peak VE (VE' peak) were similar in the CET and the 12-minute walking test. Troosters et al. (30) reported that VO₂ peak and HR peak showed no differences between the CET and the 6MWT, though VE' peak, peak VCO₂ (VCO₂ peak), and arterial lactate concentration at the peak exercise were lower in the 6MWT than in the CET. Palange et al. (20) reported that VO₂ peak, VE' peak and HR peak were similar between the CET and the ISWT, but VCO₂ peak and arterial lactate concentration at the peak exercise were lower in ISWT. The fact that VO₂ levels were similar at the peak of walking and cycling can be partly explained by the high oxygen cost of ventilation experienced by COPD patients (25). In our study, VCO₂ peak values were not higher during the CET than in the walking tests, in contrast to findings in other studies (20, 30). The reason for the lack of any significant difference in the VCO₂ peak values, as Palange et al. (20) remarks, might be that a larger muscle mass is used during the walking tests than during the CET. Because contracting muscles may degrade lactate, it could be postulated that more lactate was removed during the walking (4, 30).

During the field walking test, we directly measured ventilation and gas exchange parameters using a portable metabolic system. In some reports in which the relationship between walking distance and VO₂ peak has been discussed, VO₂ peak has been measured during a CET. Cahalin et al. (7) reported that the distances walked during the 6MWT to VO₂ peak during the CET produced a coefficient of determination of 0.50 (r² = 0.50) in patients with end-stage lung disease. Singh et al. (26) reported that the relationship between the distances walked on the ISWT and VO₂ peak measured on the treadmill in COPD patients produced r² = 0.77. According to such reports, the r² with the 6MWT was much lower than that with the ISWT. In our study, significant relationships with moderate to strong correlations were also observed. In the relationship between distance walked and VO₂, r² was 0.48 with the 6MWT and 0.72 with the ISWT. Contributing to the stronger r² with the ISWT is the fact that a much broader range of distance was walked (160–670 m); in contrast, the range of distance walked in the 6MWT was relatively narrow (338–616 m).

In summary, no significant differences in the peak values in ventilation, gas exchange parameters, HR, or dyspnea responses were observed among the 6MWT, ISWT, and CET. However, the SpO₂ value was significantly lower in both walking tests compared to that in the CET. VO₂ during the 6MWT increased sharply for 2 minutes, then showed a steady-state profile. The 6MWT may be more suitable than the ISWT for evaluating the physical demands of everyday activities, in terms of evaluation for everyday life and ease of administration. In our study, a significant, strong positive correlation was observed between the distance walked and VO₂ peak in the ISWT. In the 6MWT, however, the correlation between the distance walked and VO₂ peak was significant, moderate, and positive. The results of the present study have identified the 6MWT, the ISWT, and the CET as a strenuous protocol that imposes a significant, but sustainable, load on the exercising body. The 6MWT differs from the ISWT and the CET in that it evaluates a steady state exercise performance. The three tests clearly measure different aspects of exercise tolerance, and should be considered complementary.

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