

Validity of a modified shuttle test in adult cystic fibrosis

Judy Bradley, Jennifer Howard, Eric Wallace, Stuart Elborn

Abstract

Background—The purpose of this study was to provide some evidence of the validity of a modified shuttle test (MST) by comparing performance on the MST with peak oxygen consumption ($\dot{V}O_{2peak}$) measured during a treadmill test in a group of adult patients with cystic fibrosis. **Method**—Twenty patients with stable cystic fibrosis performed a ramped maximal treadmill test (STEEP protocol) and the MST using a randomised balanced design.

Results—The relationship between the distance achieved on the MST and $\dot{V}O_{2peak}$ was strong ($r = 0.95$, $p < 0.01$) with 90% of the variance in $\dot{V}O_{2peak}$ explained by the variance in MST distance. The relationship was represented by the regression equation (with 95% confidence intervals) $\dot{V}O_{2peak} = 6.83 (2.85 \text{ to } 10.80) + 0.028 (0.019 \text{ to } 0.024) \times \text{MST distance}$.

Conclusion—This study provides evidence of the construct validity of the MST as an objective measure of exercise capacity in adults with cystic fibrosis.

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Keywords: modified shuttle test; cystic fibrosis

Exercise testing is useful in determining prognosis, exercise prescription, and in the evaluation of new and existing treatments in patients with cystic fibrosis. The most precise method of assessing exercise capacity is by formal laboratory tests with online analysis of expired air. However, formal tests are not widely available to clinicians working in cystic fibrosis centres, and there is debate as to the most appropriate protocol for testing. Furthermore, many patients with cystic fibrosis find these tests excessively stressful and are reluctant to perform such tests on a routine basis. Some centres have attempted to use informal tests to assess and monitor exercise capacity in patients with cystic fibrosis, but some studies have highlighted the controversy surrounding the reliability, validity, and sensitivity of many of these tests.^{1 2}

The shuttle walking test is an incremental externally paced informal exercise test which overcomes many of the problems associated

with existing informal exercise tests. The original authors of the shuttle walking test have shown this test to be a reliable (after just one practice test), valid, and sensitive measure of exercise capacity in patients with chronic obstructive pulmonary disease.³⁻⁵ We have carried out preliminary work with the shuttle walking test in adult patients with cystic fibrosis, and have shown that the walking speeds in the original test (up to a maximum of 2.37 m/s) do not elicit a maximal response in adult patients with cystic fibrosis and minimal disability as well as in patients with more severe disability. On the basis of these preliminary findings the original test was modified by the addition of three levels and, further, by permitting the patients to run. The additional stages to the original 12 stage test were: level 13, 5.63 mph, 15 shuttles; level 14, 6.00 mph, 16 shuttles; and level 15, 6.38 mph, 17 shuttles. It was hypothesised that this modified shuttle test (MST) could be used to measure peak exercise capacity objectively in adult patients with cystic fibrosis. The aim of this study was therefore to compare patients' performance on the MST with peak oxygen consumption ($\dot{V}O_{2peak}$) measured directly during a treadmill test.

Methods

Twenty patients (14 men) of mean (SD) age 25 (7) years, weight 58 (8) kg, height 1.68 (0.08) metres volunteered for the study. All patients had been familiarised with the MST and the treadmill test prior to entry into the study. Patients undertook the treadmill test on one visit to the hospital and the MST on a separate visit. The order of the tests was randomised in a counterbalanced design. The mean (SD) duration between visits was 7 (4) days. The tests were performed at approximately the same time each day. Baseline spirometric measurements (Vitalograph Alpha), resting oxygen saturations and resting heart rate (Ohmeda Sao₂ monitor with ear probe), and rating of perceived breathlessness (Borg scale⁶) were recorded before the exercise test on each study day. The study was approved by the hospital ethical committee and informed consent was obtained from all patients.

TREADMILL TEST

The treadmill test was a symptom limited maximal exercise test performed according to

Sport and Exercise Sciences, University of Ulster at Jordanstown, Co. Antrim BT37 0QB, UK

J Bradley
E Wallace

Adult Cystic Fibrosis Unit, Belfast City Hospital, Belfast, Co. Antrim BT9 7AB, UK

J Howard
S Elborn

Correspondence to:
Dr S Elborn.

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the standardised treadmill exponential exercise protocol (STEEP).⁷ During the treadmill test measures of $\dot{V}O_2$ (ml/min), $\dot{V}CO_2$ (ml/min), and minute ventilation ($\dot{V}E$, l/min) were recorded at 15 s intervals (PK Morgan). The equation forced expiratory volume in one second (FEV_1) \times 35 was used to predict maximum voluntary ventilation (MVV).⁸ The heart rate was measured at one minute intervals using a 12 lead electrocardiogram (Model Marguette Case 15) and SaO_2 was continuously monitored using an Ohmeda SaO_2 monitor. At the end of the test the peak heart rate, SaO_2 , and peak rate of perceived breathlessness were recorded. Reasons for stopping or failing to maintain the correct pace were also recorded.

SHUTTLE TEST

Using the 15 level MST, patients were required to walk/run at increasing speeds back and forth on a 10 metre course.³ They were accompanied by an operator during the first minute of the test to help them pace themselves with the audiosignal. At the end of each level the patients were also told to go a little faster and were reminded that they were permitted to run at any time during the test. Patients continued with the test until they were unable to do so or failed to maintain the set pace.³ Heart rate was measured at 15 s intervals using a short range telemetry device (Polar Sports Tester) and SaO_2 was continuously monitored using an Ohmeda SaO_2 monitor. At the end of the test the peak heart rate, SaO_2 , and peak rating of perceived breathlessness were recorded. Reasons for stopping or failing to maintain the correct pace were also recorded.

Results

Lung function (FEV_1) ranged from 17% to 96% predicted normal, indicating that the patients exhibited a wide variety of disease impairment. Table 1 shows that there were no significant differences between study days in baseline test parameters (FEV_1 , resting heart rate, resting rating of perceived breathlessness, resting SaO_2). Furthermore, there were no significant differences between tests in comparable physiological responses to exercise.

Table 1 Mean (SD) baseline characteristics and physiological responses to exercise testing of patients

Parameter	Shuttle test	Treadmill test	p value
Baseline characteristics			
Age (years)	25 (7)	—	—
Weight (kg)	58 (8)	—	—
Height (m)	1.67 (0.008)	—	—
FEV_1 (% pred)	49 (23)	48 (25)	0.31
SaO_2	94 (3)	94 (3)	0.39
Resting heart rate (beats/min)	95 (12)	97 (17)	0.56
Resting heart rate (% pred max)	49 (7)	50 (8)	0.46
Resting rating perceived breathlessness	0 (1)	0 (1)	0.89
Physiological responses			
$\dot{V}O_{2peak}$ (ml/kg/min)	32.85 (10.36)	—	—
$\dot{V}O_{2peak}$ (% pred)	73.45 (26.27)	—	—
$\dot{V}Emax$ (l/min)	57.76 (20.01)	—	—
$\dot{V}E$ (% pred)	101 (40)	—	—
MST distance (m)	—	929 (335)	—
Max heart rate (beats/min)	171 (23)	169 (24)	0.90
Max heart rate (% pred)	87 (10)	86 (11)	0.95
Peak rate perceived breathlessness	6 (1)	6 (1)	0.90
End SaO_2	89 (7)	88 (7)	0.10

FEV_1 = forced expiratory volume in one second; SaO_2 = oxygen saturation; $\dot{V}O_{2peak}$ = peak oxygen consumption; $\dot{V}E$ = minute ventilation; MST = modified shuttle test.

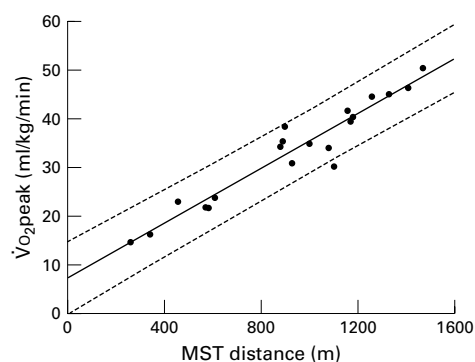


Figure 1 Regression line (with 95% confidence intervals) for the relationship between performance on the modified shuttle test (MST) and peak oxygen consumption ($\dot{V}O_{2peak}$) measured during treadmill testing.

A significant and moderately strong relationship was found between the distance achieved on the MST and lung function (MST vs FEV_1 % predicted: $r = 0.70$, $p = 0.001$) and between $\dot{V}O_{2peak}$ and lung function ($\dot{V}O_{2peak}$ vs FEV_1 % predicted: $r = 0.78$, $p < 0.001$). The relationship between the distance achieved on the MST and directly measured $\dot{V}O_{2peak}$ was strong ($r = 0.95$, $p < 0.00$) with 90% of the variance in $\dot{V}O_{2peak}$ explained by the variance in the MST distance. Using methods adopted from the authors of the original test,⁴ regression analysis was used to further describe the nature of the relationship between $\dot{V}O_{2peak}$ and MST performance. The relationship was represented by the regression equation and 95% confidence intervals:

$$\dot{V}O_{2peak} = 6.83 (2.85 \text{ to } 10.80) + 0.028 (0.019 \text{ to } 0.024) \times \text{MST distance (fig 1)}.$$

Discussion

The purpose of this study was to determine the validity of the MST as a measure of exercise capacity in adults with cystic fibrosis. The results show that there was a strong relationship between $\dot{V}O_{2peak}$ and MST performance in patients with cystic fibrosis and varying degrees of lung function impairment. Ninety percent of the variation of directly measured $\dot{V}O_{2peak}$ is explained by the variation in MST performance. This compares very favourably with the original test in which the shuttle walking test performance explained 77.4% of the variance in directly measured $\dot{V}O_2$. Many cystic fibrosis clinicians have no access to formal exercise testing equipment and the regression analysis used in this study provides additional information to such individuals on the nature of the relationship between $\dot{V}O_{2peak}$ and MST performance. There was no significant difference between peak heart rate and peak rating of perceived breathlessness recorded during both exercise tests, which indicates the effectiveness of the MST to evoke a symptom limited exercise response in both mildly and more severely compromised adults with cystic fibrosis.

Most of the patients in the present study encroached on their pulmonary reserve during exercise testing (mean peak $\dot{V}E > 70\%$ MVV). None of the patients reached their maximum predicted heart rate, as determined by the age related equation ($220 - \text{age}$), and "shortness of

breath" and "fatigue" were the most common reasons reported for stopping the exercise test. These findings support the assertion that ventilatory factors rather than cardiovascular factors limit exercise tolerance in cystic fibrosis.⁹

The relationship between lung function and $\dot{V}O_{2peak}$ was moderate. This finding supports previous work which indicated that impaired pulmonary function limits exercise capacity.¹⁰ Lung function is not a good predictor of exercise capacity because of wide intersubject variability of exercise capacity in patients with comparable lung function. In the present study oxygen desaturation (more than 5% fall in SAO_2)¹¹ occurred in all patients with FEV_1 less than 35% predicted, and in two of the patients with FEV_1 of 43% and 50%. Exercises tests to establish if exercise induced desaturation occurs are therefore a necessary prerequisite to exercise prescription in cystic fibrosis. Oxygen saturation should also be intermittently monitored during exercise programmes and, if necessary, supplemental oxygen should be used to avoid oxygen desaturation.

This study has shown that there is a strong relationship between MST performance and $\dot{V}O_{2peak}$ in adults with cystic fibrosis and thus provides evidence of the validity of this test as a measure of peak exercise capacity in adult

cystic fibrosis. Further work is required to establish the intertest reliability, test-retest reliability, and the sensitivity to change of the MST in adult patients with cystic fibrosis.

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Collagen degrading activity associated with *Mycobacterium* species

F Massó, A Paéz, E Varela, L Díaz de León, E Zenteno, L F Montaña

Departamento de Biología Celular, Instituto Nacional de Cardiología "Ignacio Chávez", Juan Badiano 1, Tlalpan 14080, Mexico
F Massó
A Paéz
E Varela
L F Montaña

Departamento de Biología Desarrollo, Instituto de Investigaciones Biomédicas, UNAM, Mexico
L Díaz de León

Departamento de Bioquímica, Instituto Nacional Enfermedades Respiratorias, Tlalpan, México
E Zenteno

Correspondence to:
Dr L F Montaña.

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Abstract

Background—The mechanism of *Mycobacterium tuberculosis* penetration into tissues is poorly understood but it is reasonable to assume that there is a contribution from proteases capable of disrupting the extracellular matrix of the pulmonary epithelium and the blood vessels. A study was undertaken to identify and characterise collagen degrading activity of *M tuberculosis*.

Methods—Culture filtrate protein extract (CFPE) was obtained from reference mycobacterial strains and mycobacteria isolated from patients with tuberculosis. The collagen degrading activity of CFPE was determined according to the method of Johnson-Wint using ³H-type I collagen. The enzyme was identified by the Birkedal-Hansen and Taylor method and its molecular mass determined by SDS-PAGE and Sephacryl S-300 gel filtration chromatography using an electroelution purified enzyme.

Results—CFPE from *Mycobacterium tuberculosis* strain H37Rv showed collagenolytic activity that was four times

higher than that of the avirulent strain H37Ra. The 75 kDa enzyme responsible was divalent cation dependent. Other mycobacterial species and those isolated from patients with tuberculosis also had collagen degrading activity.

Conclusions—*Mycobacterium* species possess a metalloprotease with collagen degrading activity. The highest enzymatic activity was found in the virulent reference strain H37Rv.

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Keywords: *Mycobacterium tuberculosis*; collagenase; metalloprotease

An increasing number of microorganisms, many of which are putative human pathogens, produce enzymes which degrade collagen.¹ The mechanism of penetration of *Mycobacterium tuberculosis* into the tissues and bloodstream is poorly understood but, as with other lung diseases,^{2,3} gastrointestinal infections,⁴ and necrotic conditions,⁵ it is reasonable to assume that there is a contribution from proteases capable of disrupting the