Modified shuttle test performance in hospitalized children and adolescents with cystic fibrosis

Narelle S. Cox a, Jennifer Follett a, Karen O. McKay b,c,*

a Department of Physiotherapy, The Children's Hospital at Westmead, Australia
b Department of Respiratory Medicine, The Children's Hospital at Westmead, Australia
c Discipline of Paediatrics & Child Health, The Children's Hospital at Westmead Clinical School, The University of Sydney, Westmead, NSW, Australia

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Abstract

Background: The Modified Shuttle Test (MST) is a valid and sensitive measure of exercise capacity in adult CF patients. Recently, its validity in children has been demonstrated. The aim of this study was to demonstrate the utility of the MST as a measure of responsiveness to hospitalisation for i.v. antibiotic and supportive therapy in children and adolescents with CF.

Methods: 28 children and adolescents (40 admissions) performed a MST and lung function within 48 h of admission and discharge to hospital for administration of intravenous antibiotics. Mean age was 12.7 years and antibiotic therapy length was 14.7 days.

Results: Upon admission, the mean (S.D.) FEV1 was 63 (19)% predicted, FVC was 80 (18)% predicted, FEF25–75 was 43 (29)% predicted and MST distance 718 (232) m. FEV1 increased by 15% (p < 0.001), FVC by 13% (p < 0.001), FEF25–75 by 39% (p < 0.001) and MST distance by 102 m (p < 0.001). The percentage improvement in MST distance at 18% (p < 0.001) was similar to that for FEV1, but could not be predicted by the change in FEV1.

Conclusion: This study demonstrated the utility of the MST to assess the effect of hospitalisation for i.v. antibiotic and supportive therapy in children and adolescents with CF.

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Keywords: Exercise testing; Paediatrics; Exercise tolerance; Physiotherapy; Lung function; Antibiotics

1. Introduction

Declining respiratory function, impaired nutritional status, musculoskeletal complications and other sequelae of cystic fibrosis (CF) impact significantly on exercise tolerance, and ultimately an individuals’ ability to perform normal activities of daily living [1]. Although lung function, in particular the forced expiratory volume in the first second (FEV1), is often viewed as the “Gold Standard” measure of pulmonary disease and expected outcome in CF, predicting exercise tolerance or functional ability from lung function results is not always accurate or possible [2–5].

Exercise testing, to determine exercise tolerance and functional ability, is gaining in importance as a tool for assessing prognosis [5,6], respiratory morbidity [7,8], suitability for transplantation [9] and quantifying impact of disease on quality of life [10]. In addition, exercise testing has been used to assess the effectiveness of intensive therapy in both adults and children [11–14]. Formal exercise testing in appropriate laboratories with exhaled air analysis provides the most accurate means of measuring exercise capacity although informal exercise tests can be a suitable alternative. Informal exercise tests (or field tests), like the Modified Shuttle Test (MST), provide time-conscious and inexpensive forms of exercise assessment which provide a less stressful environment for patients, and can be undertaken outside of formal testing laboratories [15,16], thus minimising the need for repeated visits to major centres for assessment. There is also some evidence...
that children prefer field tests such as shuttle tests to formal exercise assessments such as treadmill tests [16].

The MST is a valid measure of exercise capacity in both adults [17] and children with CF [18]. The MST evokes a symptom-limited exercise response in patients with mild as well as severe pulmonary disease equivalent to that obtained with a treadmill test [17]. This is in contrast to the Three-Minute Step Test, which in children, has been shown to be sub-maximal in nature [19]. The MST is portable and easily administered and can be conducted in limited space. It has been noted that the MST is externally paced, thus providing increased motivation to subjects, removes tester influence and is more representative of patterns of daily childhood activity than formal laboratory-based exercise tests [20].

MST performance in adults with CF has been shown to be highly responsive to intravenous antibiotic-induced changes in disease status [15]. As yet, the accuracy of the MST in detecting changes in exercise tolerance, as a result of intensive therapy such as that occurring during a hospitalisation for intravenous (i.v.) antibiotic treatment in children with CF, has not been determined.

We hypothesized that the MST would be a useful measure of the effect of hospitalisation for i.v. antibiotic and supportive therapy (i.e. airway clearance, dietary optimisation, medication management, social support, intensive medical review, assistance with schooling). As such, the aim of this study was to establish, in children and adolescents with CF, the magnitude of the change in distance travelled during the MST over the course of hospitalisation, as well as the magnitude of change in spirometric lung function. In addition, we sought to ascertain whether the magnitude of improvement in MST distance was dependent on baseline exercise capacity and was related to improvement in FEV1.

2. Materials and methods

The study population consisted of children and adolescents with CF admitted to The Children’s Hospital at Westmead for i.v. antibiotic and supportive therapy for a period of at least 10 days. All were admitted due to respiratory exacerbations characterised by signs and symptoms including decreased pulmonary function, new infiltrates on chest X-ray, increased cough, breathlessness, change in sputum production (colour and/or quantity), malaise and weight loss. None of the admissions were for routine scheduled courses of IV antibiotics. All participants had been diagnosed with CF by way of a newborn screening programme and only one was pancreatic sufficient. Only those who had previously performed an exercise test, lung function testing and who did not require supplemental oxygen were invited to join in the study. Ethics approval for this study was obtained from The Children’s Hospital at Westmead Ethics Committee, which advised that individual written consent was not necessary for this study as exercise testing by means of the MST and spirometry were part of the existing care plan for CF.

All subjects performed lung function testing, and completed a MST within 48 h of admission to and discharge from hospital. The i.v. antibiotic therapy consisted of two antibiotics (one usually being an aminoglycoside), the particular antibiotics being chosen based upon the sensitivity patterns of bacteria obtained from sputum cultures and prior clinical improvement. The participant with MRSA was treated with a combination of three i.v. antibiotics (vancomycin, meropenem and tobramycin). The duration of the course was generally 14 days, except when there had been insufficient improvement in the opinion of the respiratory consultant involved and an extension of up to 7 days occurred. During the admission, each participant received review by a dietician and social worker as well as daily physiotherapy consisting of both an airway clearance technique and an exercise session. All subjects performed positive expiratory pressure (PEP) as their airway clearance technique. Exercise sessions were undertaken by all participants and performed under the supervision of a physiotherapist. Exercise sessions were of 20–30 min duration and comprised aerobic activity (particularly treadmill) and low load upper and lower limb strengthening exercises.

Lung function was measured by an experienced scientific officer using a Vmax 22D spirometer coupled to an Autobox V62J Body Plethysmograph and Spectra software (Sensormedics Corp., Yorba Linda, CA, USA) in accordance with American Thoracic Society guidelines, and the results were expressed as a percentage of that predicted by Polgar and Promadhat [21]. All participants had been performing lung function frequently since the age of 5 and were technically proficient in terms of the required manoeuvres.

The MST was administered by a physiotherapist familiar with the test as described by Bradley et al. [15]. The modified test has 15 levels and allows subjects to run as necessary. The test requires participants to move around two markers over a 10 m course in time with “beeps” from a pre-recorded tape. Each level in the test lasts for 1 min, with the speed of the test increasing by 0.61 km/h each minute. There are a maximum of 15 levels. The test is concluded when participants state subjectively that they are unable to continue or fail to make the course marker on two consecutive beeps.

Heart rate (HR) and oxygen saturation (by pulse oximetry, SaO2) were measured before and after the MST using a finger probe (Datex, Ohmeda TuffSat, Madison, WI, USA). Participants were also asked to give a rating of their perceived exertion (RPE) using The Children’s Hospital RPE scale (Fig. 1). This is a validated six-point scale, which ranges from 0 (not tired at all) to 5 (absolutely exhausted, could not possibly continue with exercise) [22]. In addition to numerical and written prompts, the scale has visual cues...
in the form of a teddy bear in various levels of comfort/distress.

The age of subjects ranged from 7.6 to 17.6 years (mean 12.7 years). As with most CF subjects, the participants were below average height with a mean height $z$-score of $-0.02$ (range 3.71 to 0.96) and were also below average weight with a mean weight $z$-score of $-0.04$ (range 2.86 to 0.26).

Seventy-eight percent of those participating isolated *Pseudomonas aeruginosa* upon sputum culture at the time of admission to hospital and 11% grew *Staphylococcus aureus* (all of whom had repeatedly isolated *P. aeruginosa* upon sputum culture within the previous 12 months). The remainder of the participants had neither of these bacteria but had *Stenotrophomonas maltophilia* (this participant had isolated *P. aeruginosa* repeatedly upon sputum culture within the previous 6 months), *MRSA* or a coliform species (this participant had isolated *P. aeruginosa* upon sputum culture one month prior to admission). The mean length of hospitalisation for i.v. antibiotic and supportive therapy was 14.7 days (range 10–22 days).

Results are expressed as mean values with ranges or standard deviations. The percentage change in parameters measured at admission and discharge were computed as follows: $100 \times \left( \frac{\text{value discharge} - \text{value admission}}{\text{value admission}} \right)$. Percentage maximal heart rate was calculated as follows: $100 \times \left( \frac{\text{HR} - [220 - \text{age in years}]}{\text{HR}} \right)$. The relationship between pulmonary function measured by spirometry and exercise capacity measured by the MST, at admission and discharge, as well as the relationship between the magnitude of improvement in MST distance and baseline MST distance, were assessed by calculating the Pearson’s correlation coefficient and the related statistical significance of these values. The proportion of individuals with a clinically relevant improvement in FEV$_1$ (defined as an improvement from baseline of $\geq 10\%$) and an improvement in MST distance (of at least 10% from baseline) was compared using crosstabs and chi-squared analysis. Differences in mean values were analysed for statistical significance using paired two-tailed Student’s $t$-tests. The software package utilised was SPSS for Windows version 11.5.1 (SPSS Inc., Chicago, IL, USA). A value of $p < 0.05$ was considered significant.

### 3. Results

Twenty-eight children and adolescents (6 male) provided 40 sets of complete data. At the commencement of hospitalisation, the mean (S.D.) FEV$_1$ was $63\%$ predicted with a range of 36% to 114%, forced vital capacity (FVC) was $80\%$ predicted and forced expiratory flow$25–75$ (FEF$_{25–75}$) was $43\%$ predicted. The mean MST distance was $718\ (232)\ m$ ranging from $340\ m$ to $1530\ m$ (see Table 1). Admission MST distance correlated significantly with FEV$_1$ and % predicted FEV$_1$ ($r=0.663$, $p<0.001$ and $r=0.416$, $p<0.01$, respectively), FVC and % predicted FVC ($r=0.590$, $p<0.001$ and $r=0.360$, $p<0.05$, respectively), as well as FEF$_{25–75}$ and % predicted FEF$_{25–75}$ ($r=0.489$, $p\leq 0.001$ and $r=0.360$, $p<0.05$, respectively).

### Table 1

Lung function and MST distance at admission to and discharge from hospital

<table>
<thead>
<tr>
<th></th>
<th>Admission mean (range)</th>
<th>Discharge mean (range)</th>
<th>% Change$^a$ mean (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV$_1$ (l)</td>
<td>1.52 (0.81–3.13)</td>
<td>1.74 (0.94–4.25)**</td>
<td>15 (–9 to 58)</td>
</tr>
<tr>
<td>FEV$_1$ (% predicted)</td>
<td>63 (36–114)</td>
<td>71 (42–118)**</td>
<td>15 (–13 to 57)</td>
</tr>
<tr>
<td>FVC (l)</td>
<td>2.10 (0.91–4.36)</td>
<td>2.33 (1.22–5.37)**</td>
<td>13 (–9 to 144)</td>
</tr>
<tr>
<td>FVC (% predicted)</td>
<td>80 (43–127)</td>
<td>87 (56–136)**</td>
<td>11 (–35 to 107)</td>
</tr>
<tr>
<td>FEF$_{25–75}$ (l/s)</td>
<td>1.13 (0.24–3.32)</td>
<td>1.43 (0.54–3.94)**</td>
<td>39 (–41 to 221)</td>
</tr>
<tr>
<td>FEF$_{25–75}$ (% predicted)</td>
<td>43 (9–121)</td>
<td>51 (20–142)*</td>
<td>33 (–43 to 122)</td>
</tr>
<tr>
<td>MST distance (m)</td>
<td>718 (340–1530)</td>
<td>820 (500–1530)**</td>
<td>18 (–26 to 118)</td>
</tr>
</tbody>
</table>

Significant changes between discharge and admission are shown: $^*p<0.005$, $^{**}p<0.001$ paired two-tailed Student’s $t$-test.

$^a$ Change from admission to discharge $= 100 \times \left( \frac{\text{value discharge} - \text{value admission}}{\text{value admission}} \right)$.
There were statistically significant improvements in all lung function parameters, as well as MST distance over the period of hospitalisation (Table 1 and Fig. 2). Mean FEV\(_1\) improved by 15% (range of improvement –9% to 58%, \(p \leq 0.001\)). FVC increased by 13% (range of improvement –9% to 144%, \(p \leq 0.001\)), while small airway function, as measured by FEF\(_{25-75}\), also improved significantly (39% increase, range of improvement –41% to 221%, \(p \leq 0.001\)).

Mean distance covered in the MST improved by 18% or 102 m (range of improvement –26% to 118%, \(p \leq 0.001\)) over the course of hospitalisation. There was a statistically significant negative correlation between the % improvement in MST distance and baseline MST distance (\(r = -0.455, p < 0.05\)) such that those with higher baseline MST distances had lower improvements in their MST distance from admission to discharge and, conversely, those with lower exercise performance at baseline had a greater improvement over the course of their admission (Fig. 2).

An improvement of at least 5% in MST distance from baseline was seen in 75% of the study cohort, while an improvement of at least 10% from admission to discharge was seen in 60%. Of the 23 occasions on which a subject had an improvement in FEV\(_1\) of ≥10%, there were 15 occasions when the subject also had an improvement in MST distance of at least 10% (Fig. 3). Chi-squared analysis of these frequencies indicated that they were not statistically significantly related.

Measurement of HR, SaO\(_2\) and RPE indicated that the MST elicited a significant elevation in HR and RPE during this exercise test (Table 2). HR on admission increased from a mean of 104 bpm at rest immediately prior to the MST to 141 bpm at the end of exercise. A similar increase was seen at discharge and these heart rates were such that children were exercising at approximately 2/3 (68% admission and 70% discharge) the maximal rate predicted for their age. Similarly, the mean RPE score at the end of exercise was 2.8 on admission and 3.2 at discharge (‘very tired’) a significant increase from that at baseline, which was 0.7 on admission and 0.6 on discharge (between ‘not tired at all’ and ‘a little bit tired’). The safety of the MST was demonstrated by the finding that the mean SaO\(_2\) at end of the MST was only 1% lower than that at baseline, although this was a statistically
Table 2

<table>
<thead>
<tr>
<th></th>
<th>Admission</th>
<th>Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>End-exercise</td>
</tr>
<tr>
<td>SaO2 (%)</td>
<td>96 (1.4)</td>
<td>95 (3.5)**</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>104 (16)</td>
<td>141 (28)**</td>
</tr>
<tr>
<td>HR (%max*)</td>
<td>50 (8)</td>
<td>68 (14)**</td>
</tr>
<tr>
<td>RPE</td>
<td>0.7 (0.7)</td>
<td>2.9 (1.0)**</td>
</tr>
</tbody>
</table>

Significant changes between rest and end-exercise values are shown:

* p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001—paired two-tailed Student’s t-test.

Significant changes between admission and discharge values are shown:

† p ≤ 0.05—paired two-tailed Student’s t-test.

a Calculated from 220 – age.

significant decrease. While there was a trend for resting HR, resting RPE, end-exercise HR and end-exercise RPE to decrease from admission to discharge (Table 2), none of these decreases were statistically significant. There was a statistically significant increase in end-exercise SaO2 between admission and discharge although resting SaO2 did not change significantly.

4. Discussion

This study has clearly demonstrated improvement in both MST distance and lung function after hospitalisation for i.v. antibiotic and supportive therapy. Improvement in MST distance was dependent on baseline exercise capacity in that those with lower MST distances at baseline had proportionally greater increases in MST distance from admission to discharge. The magnitude of the increase in MST distance could not however be predicted by the increase in FEV1.

The mean increase in FEV1 of 15% demonstrated in this study is almost identical to the 14% increase observed by Pike et al. after a 10–14-day course of intravenous antibiotics [13], thus suggesting that our cohort of subjects were similar to some of those previously studied. In addition to the statistically significant increase in all lung function parameters, however, we have also shown for the first time, a concomitant increase in MST distance. Where spirometry is an assessment of airway function and thus flow limitation, the MST assesses functional capacity, which is influenced by not only ventilatory function but also cardiovascular, muscular and metabolic factors. Thus, it would seem that while there are presently no reference values for assessing an individual MST result, change in MST performance may be a suitable measure of the effect of hospitalisation for i.v. antibiotic and supportive therapy.

Our findings of an increase in exercise performance after in hospital therapy are by no means the first. In 1984, Cerny et al. showed that exercise capacity, as measured by cycle ergometry, increased significantly in a group of subjects with moderate to severe lung disease [11]; in 1988, an improvement in the 2-min walking distance was reported [14], while more recently, Pike et al. have also shown an improvement in exercise tolerance as measured by the 3-min step test [13]. As the MST constitutes an inexpensive, portable and easily administered test, which can be conducted in limited space, we believe that MST distance could be utilized as an adjunct or alternative outcome measure to pulmonary function testing where formal exercise testing equipment is unavailable.

The MST was selected as the exercise test of choice ahead of other validated field tests, for a number of reasons including those mentioned above. Previous work with the 20-m shuttle in children with CF has been in stable, non-hospitalized subjects [16]. Space restrictions and a concern that the 20-m shuttle run test [23] would prove too taxing for children experiencing a pulmonary exacerbation precluded the use of that test. The MST also provides a single test to be used across all ages and disease severity, where the 20-m shuttle is suggested for use in older healthier children [16,24]. The 6-min walk test [25] and step test [4] are both valid exercise test measures in children with CF. However, the self-paced nature of the 6-min walk makes it sub-maximal and prone to variable motivation, while the step test is not reflective of a normal functional task and is unable to measure aerobic capacity. Our observation of a statistically significant increase in heart rate to at least two thirds of the maximal rate predicted for age and a three- (on admission) to five-fold (at discharge) increase in RPE indicated that the MST elicited a change in the parameters usually indicative of a maximal exercise and thus confirming that the MST has overcome the lack of maximal response elicited in adult CF patients undertaking the original 12-level shuttle walk test [17].

The progressive nature of the MST and the option to run are characteristics of the MST, which suggest that it may be suitable for assessing response in patients with a range of disease severity. This facet is particularly pertinent in children and adolescents many of whom have little functional impairment. We did not detect significant changes in resting HR, RPE or SaO2 from admission to discharge in our group and, although the subjects were able to exercise to a greater extent at discharge, only the end-exercise SaO2 was improved significantly at discharge. In the present study, baseline FEV1 % predicted ranged from 36% to 114% predicted upon admission. While about 25% of our subjects had moderately severe lung disease (as indicated by a FEV1 less than 50% predicted on admission), our group was, as a whole, less impaired than those children studied previously where these indicators of exercise capacity have improved after therapy [11]. Moreover, while those in our cohort with lower exercise capacity on admission did improve more than those with good exercise tolerance on admission, we did measure increases in MST performance in children with well-preserved lung function.

In an earlier study in adults with CF, a change in MST distance of at least 40 m was considered clinically significant [15]. A clinically significant improvement in FEV1 is generally considered to be that of greater than or
equal to 10% and this was achieved for 60% of the hospitalisations in our study. We thus reasoned that an increase in MST distance of at least 10% may also constitute a clinically significant improvement in exercise capacity. In our study population, we found that 60% of the subjects had such an increase. Interestingly, however, there were only 37.5% of occasions when subjects had a 10% or greater improvement in both parameters. This fact highlights the important point that the magnitude of improvement in MST distance could not be predicted from the improvement in FEV₁. It also indicates that, although not the subject of this study, ascertainment of what constitutes a clinically significant improvement in exercise capacity is required.

Participants in the current study were all experienced in performing the MST. As such, a practice test was not undertaken in accordance with the findings of previous work [15], which suggested adult CF patients would be less likely to comply with testing procedures if additional practice tests were required. Consequently, although in our study, the MST took 20–25 min to complete (including preparation and patient recovery time), in centres where this test is not established, and where patients are naïve to the test, a practice test is likely to be necessary, and thus the time required for testing, at least initially, may be considerably longer. The participants in this study all enjoyed performing this test and our study population included a reasonable proportion of adolescent females who are often loathe to undertake such activities. Nevertheless, the test is motivation dependent and may not be as useful in populations where motivation is sub-optimal or where the children are much sicker than our cohort and thus reluctant to perform the test. In addition, as the MST requires movement of the subject and any accompanying equipment, unlike formal exercise tests where the equipment is stationary, the MST is not a suitable test for any patient requiring oxygen or respiratory support, such as non-invasive ventilation, for exercise.

The results of our study show that MST distance is a useful measure of exercise capacity and improves after hospitalisation for i.v. antibiotic and supportive therapy in children and adolescents with CF. It provides an alternative clinical outcome measure when formal exercise testing is not possible and is a complimentary measurement to lung function testing procedures in paediatric populations.

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References