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Short Communication

Six minute walk test Z score: Correlations with cystic fibrosis severity markers

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Abstract

Background: The six-minute-walk-test (6MWT) has been increasingly used in cystic fibrosis (CF) patients. However, few studies in children have correlated 6MWT with current parameters used to evaluate CF severity. Moreover, no study transformed the values of distance walked from meters into Z scores to avoid bias like age and gender, which are sources of 6MWT variability.
Methods: A cross-sectional descriptive study was performed to analyze the correlations (Spearman) among forced expiratory volume in one second (FEV_1), body mass index (BMI), chest radiography (CXR), chest tomography (CT), and 6MWT Z score (Z-6MWT). Clinically stable CF patients, aged 6–21 years, were included.
Results: 34 patients, 14F/20M, mean age 12.1±4.0 years were studied. The mean Z-6MWT was −1.1±1.106. The following correlations versus Z-6MWT were found: FEV_1 ($r=0.59$, $r^2=0.32$, $p=0.0002$), BMI Z score ($r=0.42$, $r^2=0.17$, $p=0.013$), CXR ($r=0.34$, $r^2=0.15$, $p=0.0472$) and CT ($r=-0.45$, $r^2=0.23$, $p=0.0073$).
Conclusions: In conclusion there was a significant, but poor, correlation between the six minute walk test Z score and the cystic fibrosis severity markers currently in use.

Keywords: Chest imaging; function tests; minute walk test; fibrosis

1. Introduction

In cystic fibrosis (CF) disease progression is assessed through spirometry, chest radiography and tomography and clinical data [1–3]. In the last decade, the six-minute walk test (6MWT) has been widely used to evaluate global exercise capacity in patients with cystic fibrosis [4–8] and it has been proposed as a simple and reliable test for the periodic evaluation of CF patients' exercise program [4,9]. It is a low cost test, easy to perform, reproducible and may serve as a predictor of mortality and morbidity in patients with cardiopulmonary diseases [4,10,11,12]. It is also useful for longitudinal assessment, to monitor response to treatment and to guide therapy [11,13].

The 6MWT has been increasingly used in young children, for whom performing cardiopulmonary exercise tests is especially problematic, requiring a high degree of cooperation, good coordination and motivation [10,14]. It has to be taken into account that there is a degree of practice bias with the

Abbreviations: CF, cystic fibrosis; CXR, chest radiography; CT, chest computed tomography scan; PFT, pulmonary function tests; 6MWT, six minute walk test; FVC, forced vital capacity; FEV_1, forced expiratory volume in one second; $FEF_{25-75\%}$, forced expiratory flow between 25 and 75% of vital capacity; BMI, body mass index.

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6MWT so that the more the children do it, the better they become [10]. Up to now, few studies in children have correlated 6MWT with current parameters used to evaluate CF severity. Moreover, no study transformed the values of distance walked from meters into Z scores to avoid bias like age and gender, which are sources of 6MWT variability.

In this study we transformed the values of distance walked in the 6MWT from meters into Z scores and investigated the correlations between six minute walk test Z score (Z-6MWT) and other current parameters used to evaluate CF severity, such as forced expiratory volume in one second (FEV_1), body mass index (BMI), chest radiography (CXR) and chest computed tomography (CT).

2. Methods

This was a cross-sectional descriptive study. Between June 2006 and August 2008, we studied 34 CF patients (between 6 and 21 years old) recruited from the outpatient clinic of our hospital. The diagnosis of cystic fibrosis was made according to established criteria [15]. Only patients with stable disease were included in this study. Exclusion criteria were pulmonary exacerbation [16] in the month preceding the tests or a chest CT done in the previous year to avoid another radiation exposure. Spirometry, chest radiography and CT and the 6MWT were all carried out on the same morning.

This study was approved by the Human Ethics Committee of Hospital das Clínicas — Medical School of University of São Paulo, Brazil (approval number 1074/05). Written informed consent was obtained from all subjects or their parents.

2.1. Spirometry

Spirometry was performed by a single technician with experience in pediatric tests, using the standards recommended by the American Thoracic Society (ATS) [17]. A Master Screen spirometer (Multispiro Creative Biometcs) was used. The results were expressed as the percentage of predicted values for forced vital capacity (FVC), FEV_1 and forced expiratory flow between 25 and 75% of vital capacity ($FEF_{25-75\%}$). The equations of Polgar and Promadhat were used as a reference for subjects up to 17 years of age, and the equation of Knudson et al. was used for patients aged between 18 and 21 years [18,19]. The severity of the ventilatory obstruction was classified according to ATS/ERS (European Respiratory Society) [20].

2.2. Chest radiography and chest CT scan

The Brasfield score [21] was used to evaluate chest radiography. Five categories were scored: air trapping, linear marks, nodular cystic lesions, large lesions, and overall severity. Chest roentgenograms showing more severe changes received a lower score.

The CT scans were scored using the scoring system described by Bhalla et al. [22]. In 25 patients chest CT during expiration was also performed and it was possible to calculate a modified Bhalla score [23]. Bhalla score was used instead of the modified Bhalla score for the correlation analysis because it was applied in all patients and a significant correlation between the modified Bhalla score and the Bhalla score was found ($r=0.97$, $p<0.0001$).

Scanning was performed with a GE LightSpeed Ultra CT Scanner. Thin-section CT scans were obtained using a beam current automatically adjusted by the machine (70–100 mA), an exposure time of 0.5 s, a beam potential of 120 kV from lung apex to lung base at 10 mm intervals using 1.25 mm thick single slices, non volumetric, and a field of view of 15–40 cm. Mean CTDI vol was 1.3 mGy. All scans were reconstructed with a high spatial frequency algorithm (bone) and printed with window settings appropriate for the imaging of pulmonary parenchyma (window width—600 HU; window level—1.500 HU).

The radiographic and tomographic scores were calculated independently in a blinded manner by three radiologists (two pediatric radiologists and a chest radiologist). The final score was the average of the three radiologists' scores.

2.3. Six-minute walk test

All 6MWTs were done using a lap 30 m in length, on a flat, hard surface, according to the ATS guidelines [10]. Two tests were performed on the same day with an interval of at least 30 min and after all clinical variables had returned to their basal values. The patients were asked to walk as far as possible for 6 min up and down the measured lap, but not to run. Standardized encouragement was given by the same person after every 1 min ("You are doing well!", "Keep up the good work!"). The distance was measured in meters and the test with the greatest distance was selected. The values were transformed into Z scores based on Geiger et al. data [24], using the following formula: value found − normal value/standard deviation.

2.4. Statistical analysis

Data were expressed as number of cases, mean and standard deviation or median. Mean ± SD was used for parametric data (age, BMI, 6MWT, spirometry) and median was used for non-parametric data (Bhalla and Brasfield scores). Linear regression (Spearman's correlation coefficient) was used for analysis of correlations between the tests, calculated by the GraphPadPrism 5 program. The significance level considered was $p<0.05$.

It was calculated that a minimum sample size of 30 patients was needed in order to estimate correlations with a level of significance of $\alpha=0.05$ and a statistical power (1-ß) of 95% (MedCalc software version 10.0.0).

The BMI of patients was calculated and transformed into Z scores (Z-BMI) using the program Nutrition Epi Info™, version 3.3.2 on the CDC website.

3. Results

Thirty-four patients were evaluated, 14 females and 20 males, mean age of 12.1 ± 4 years. The descriptive characteristics of patients are shown in Table 1. The mean distance walked was 596 ±

Table 1
Characteristics of the CF patients (n=34).

	Mean±sd	Range
Age (years) male/female: 20/14	12.1±4.0	6.0–20.9
Z-BMI	−0.6±1.2	−2.9–2.1
BMI (Kg/m^2)	17.0±2.4	13.7–22
Z-6MWT	−1.1±1.106	−4.07–0.6
6MWT (m)	595.9±68.8	431.0–743.0
FVC (% predicted)	70.4±25.9	20.4–126.0
FEV_1 (% predicted)	59.2±26.0	13.3–134.0
$FEF_{25-75\%}$ (% predicted)	47.4±35.8	4.8–172.4
Bhalla score (median)	10.8	2.7–19.0
Brasfield score (median)	15.7	6.0–23.7

Z-BMI, body mass index Z score; Kg, kilogram; m, meters; Z-6MWT, six-minute walk test Z score; FVC, forced vital capacity; FEV_1, forced expiratory volume in 1 s; $FEF_{25-75\%}$, forced expiratory flow between 25 and 75% of vital capacity.

69 m and the Z-6MWT was −1.1±1.106. Regarding the nutritional status the average BMI was 17±2.4 Kg/m^2. Spirometry showed 11 children with mild obstructive lung disease ($FEV_1 \geq 70\%$) or normal FEV_1 ($FEV_1 \geq 80\%$), seven moderate (FEV_1 between 60 and 69%), five moderately severe (FEV_1 between 50 and 59%), six severe (FEV_1 between 35 and 49%) and five very severe ($FEV_1 < 35\%$).

For all patients the correlations between Z-6MWT and FEV_1, Z-BMI, Brasfield score and Bhalla score were calculated. A significant correlation between all parameters was observed (Figs. 1A, B, C and D).

4. Discussion

In the present study, the Z-6MWT correlated significantly with current parameters used to evaluate CF severity such as FEV_1, Z-BMI, chest radiography and tomography. Despite the statistically significant correlation that was found the correlation coefficients and plots did not show a very tight correlation and this may reflect that the 6MWT is affected by other extra pulmonary domains [10].

Although reference values for 6MWT in Brazilian children have recently been published [25] we decided to use Geiger et al. [24] reference values because our sample consisted of patients up to 21 years old and the Brazilian data only included patients younger than 12 years of age. Nevertheless, the Brazilian data on reference values for the 6MWT strongly correlated with the data of Geiger et al. (r=0.87).

Previous studies in CF patients did not show significant correlations between 6MWT and pulmonary function tests [4,26,27], BMI [8,26] and chest radiography [8]. Different from these studies we decided to transform the values of distance walked from meters into Z score based on reference values from healthy population to avoid bias like age and gender, which are sources of 6MWT variability [10,24,28,29]. The use of the Z score to represent the distance walked was able to render uniform the data of the population studied, which had a wide age range (6 to 21 years old).

Only two studies found significant correlations between 6MWT and FEV_1 (r=0.53 to r=0.75), but one evaluated CF

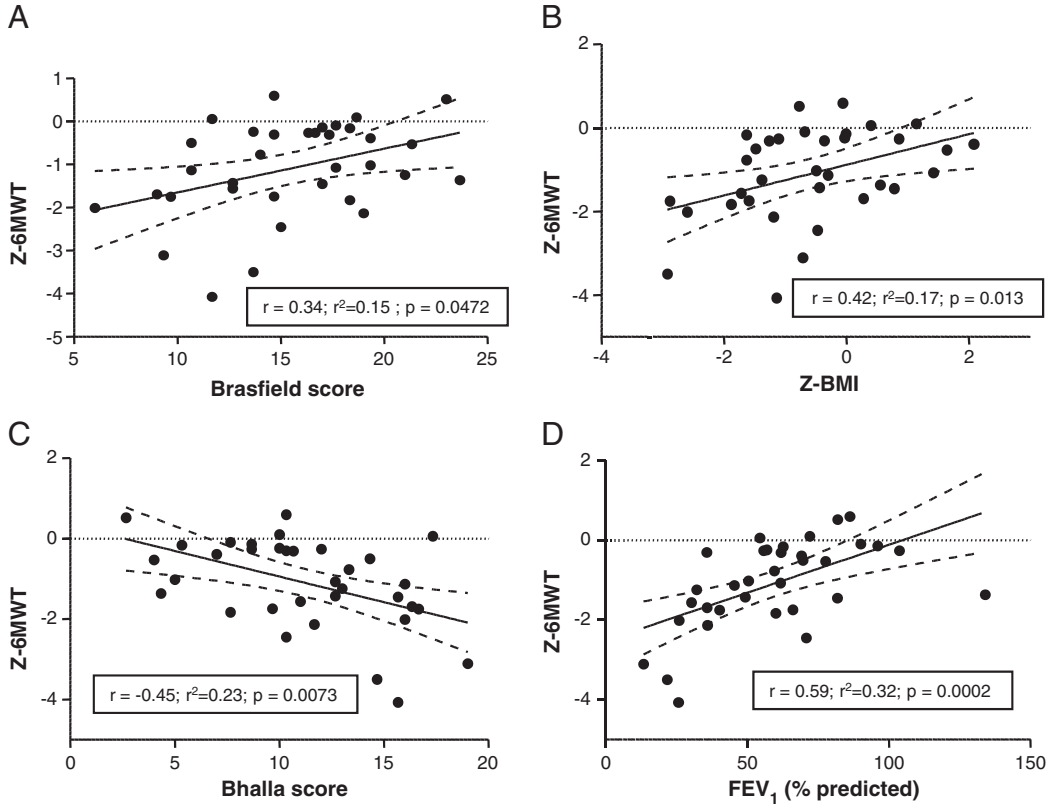

Fig. 1. A) Correlation between Brasfield score and six minute walk test Z score (Z-6MWT); B) Correlation between body mass index Z score (Z-BMI) and Z-6MWT; C) Correlation between Bhalla score and Z-6MWT; D) Correlation between forced expiratory volume in 1 s (FEV_1) and Z-6MWT.

adolescents and adults [8] and in the other patients with CF and other obstructive lung disease were included [30].

The poor correlation we found between the Brasfield and Bhalla scores and the Z-6MWT may be due to the fact that the 6MWT reflects the overall status of both lungs while CXR and CT can help identify abnormalities that affect only a small portion of the lung. The correlation between 6MWT and chest CT has not been described before.

One limitation of our study is that it is a cross-sectional study and this precludes a longitudinal evaluation. It was not possible to assess whether or not the parameters (CXR, CT, FEV_1, 6MWT) would change in a similar way.

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