

Correlation between Bhalla score and spirometry in children and adolescents with Cystic Fibrosis

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SUMMARY

Objective: to correlate the findings of high resolution computed tomography of the chest based on the Bhalla score with the clinical data and spirometry in children and adolescents with cystic fibrosis, and to study the concordance between two radiologists for the Bhalla score and its categories.

Methods: we evaluated the medical records of 23 patients from the outpatient clinic. The items evaluated included age, weight, height, height/age Z-score, weight/age Z-score, body mass index (BMI), O₂ saturation, spirometry and Bhalla score.

Results: the patients had a mean age of 17.4 years ± 5.7 years, with fifteen females and eight males. There was good correlation between Bhalla score and spirometry (FVC-r =0.718, p<0.001; FEV1-r=0.830, p<0.001; FEF25-75%-r =0.786, p<0.001; FEV1/FVC-r=0.714, p<0.001). It was also noted that some patients with FEF25-75% > 70% already had changes in their final Bhalla score. In the analysis of the concordance between the examiners a Kappa coefficient of 0.81 (p <0.001) was found, and an intraclass correlation coefficient of 0.98.

Conclusion: a good correlation between Bhalla scores with spirometry confirmed its usefulness in evaluating and monitoring patients with cystic fibrosis, given it can be used both in patients who are unable to perform spirometry as well as for a pooled analysis of the two examinations since the HRCT scans show early changes in patients with normal function tests.

Uniterms: cystic fibrosis, tomography, spirometry, child, adolescent.

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INTRODUCTION

Individuals with cystic fibrosis (CF) undergo constant multi-professional monitoring and require standardization of treatment in order for the most subtle improvements or deteriorations in their clinical condition can be noted, with the minimum possible variation between examiners.

In this context, various authors have been interested in developing scores to evaluate the development of the disease, known as scores of the severity of cystic fibrosis and scores for evaluating radiological and tomographic changes.¹⁻⁶ The use of scores enables the longitudinal evaluation of patients and standardized comparisons between them, and is therefore useful both at the clinical and research areas.¹⁻³

Since publication of the classic work by Shwachman and Kulczycki in 1958, various other scores have been developed and published.¹⁻⁶

As pulmonary insufficiency is related to the majority of deaths for patients with CF, a specific evaluation of pulmonary impairment would be recommendable and, given these circumstances, some authors have been interested in developing scores based on radiological findings using chest radiography or tomography.⁷

It is important to reiterate that high resolution computed tomography (HRCT) of the thorax is the ideal method owing to the characteristics of pulmonary impairment

in cystic fibrosis, given that it is recommended for evaluation of the lung parenchyma.

The major concern at present in relation to the use of HRCT relates to the issue of ionizing radiation and especially the amount of radiation to which the patient is exposed throughout their life, resulting from multiple examinations, particularly when considering a chronic pulmonary disease such as Cystic Fibrosis. Within this perspective, studies have been conducted in an attempt to reduce doses while maintaining the quality of the images.^{8,9}

A classic work by Lucaya et al. evaluated the effect of the reduction of this dose on the quality of the images and standards the so-called "low dose HRCT". Low dose HRCT presents a significant reduction in the dose of radiation received by the patient (72% when using 50 mAs and 80% when using 34 mAs) compared to the exam with the usual dose (180 mAs).²³ It is important to note that the said study was conducted with children and young adults submitted to low dose HRCT, and not necessarily suffering from cystic fibrosis.

Monitoring pulmonary changes, however, is not only based on imaging examinations. Tests of pulmonary function have also been used with this objective over the years.²

In the literature it is possible to find works comparing the different clinical/radiological and tomographic scores and pulmonary function tests. In the majority of cases, a positive correlation can be noted between them, with the exception of patients with diseases considered as mild, who may present alterations in the tomography examinations and normal pulmonary function tests.⁸⁻¹⁰ Comparing the different evaluation parameters of pneumonopathy in CF is important for understanding the evolution of the changes and establishing criteria for realizing preliminary and therapeutic interventions at the appropriate time.

In recent years, owing to advancements in nutritional support, appropriate treatment of chronic colonization and exacerbations as well as recent neonatal triage, the survival curve of cystic fibrosis patients has improved. On the other hand, there is no standardized protocol about the age for conducting the first tomography or the frequency at which this should be conducted. This issue is crucial considering the amount of ionizing radiation to which the patient is exposed throughout life, as many of them undergo regular radiological examinations. Therefore, studies that evaluate the correlation between pulmonary function and chest tomography present high clinical applicability.

The objective of this study was to correlate structural pulmonary changes from chest tomography using the Bhalla score with the pulmonary function evaluated using spirometry in children and adolescents with cystic fibrosis.

METHODS

The study was planned with a review of all of the medical record for patients being monitored at the Cystic Fibrosis Outpatient Clinic at the Federal University of Minas Gerais (AFC/UFMG). In the AFC/UFMG service protocol, the realization of the first tomography is recommended at six years, an age at which the majority of children are also able to undertake spirometry.

The inclusion criteria were defined as the realization of at least one chest tomography examination and one spirometry examination in the same month. The exclusion criteria were the interval between the tomography and spirometry with an interval of over 1 month, spiral CT, without high resolution or non-recovery of examinations, given that the study was retrospective.

High Resolution Computed Tomography

The HRCT examinations were conducted at the Federal University of Minas Gerais Hospital das Clínicas using Somatom AR-T (*Siemens*) and Auklet (*Toshiba*) devices. The images were obtained during inhalation for all patients and upon exhalation for some, using 1.5 to 2.0 mm collimation, 10 mm intervals and 120 kV and 160 mAs. The images were reconstructed using a high resolution algorithm and documented with appropriate windows for evaluation of pulmonary parenchyma.

As not all patients had been submitted to cross sections during exhalation, only images acquired during inhalation were considered.

HRCT evaluation score

The HRCTs were evaluated independently by two radiologists, using the Bhalla score.⁶ The items evaluated were: a) severity of bronchiectasis; b) peribronchial thickening; c) extent of bronchiectasis (number of lung segments); d) extent of mucus plugs (number of lung segments); e) abscesses or sacculations (number of lung segments); f) generalities of the bronchial division involved (bronchiectasis/plug); g) number of bubbles; h) emphysema (number of lung segments); i) collapse/consolidation.

The points in each category vary from zero to three and the final result can be subtracted from 25 to adapt the score to inclusion in the Shwachman-Kulczycki score. The initial P is added to the final result when mucous plugs are present, and T when there is peribronchial thickening. The Bhalla score is presented in Table 1. Results are classified as excellent when between 21 and 25 points, good when between 20 and 16 points, mild between 11 and 15 points, moderate between 6 and 10 points, and serious between 0 and 5 points.

TABLE 1 Bhalla Score

Category	0	1	2	3
Severity of bronchiectasis	absent	Mild (light subtly greater than the adjacent vessel)	Moderate (light 2 to 3 times higher than the adjacent vessel)	Severe (light 3 times higher than the adjacent vessel)
Peribronchial thickening	absent	Mild (thickening of the wall equal to the vessel)	Moderate (greater thickening/doubling of the vessel)	Severe (thickening 2 times greater than the vessel)
Extent of the bronchiectasis (number of lung segments)	absent	1 - 5	6 - 9	>9
Extent of mucus plugs (number of lung segments)	absent	1 - 5	6 - 9	>9
Abscesses or sacculations (number of lung segments)	absent	1 - 5	6 - 9	>9
Generalities of the bronchial division involved (bronchiectasis /plug)	absent	Over the 4 th generation	Over the 5 th generation	Over the 6 th generation and distal
Number of bubbles	absent	Unilateral (none > 4)	Bilateral (none > 4)	>4
Emphysema (number of lung segments)	absent	1 - 5	>5	
Collapse/consolidation	absent	Subsegmental	Segmental/lobar	

Clinical evaluation

Weight, height, BMI, height/age and weight/age Z-scores and O₂ were used for clinical evaluation.

Pulmonary function tests

The pulmonary function tests were conducted at the Pulmonary Function Laboratory at the Federal University of Minas Gerais Hospital das Clínicas and the following data was used in the analysis: a) forced vital capacity (FVC); b) forced expiratory volume in one second (FEV1); c) forced expiratory flow between 25 and 75% (FEF 25-75%); d) FEV1/FVC ratio x 100. The recommendations of the American Thoracic Society and Polgar, Knudson and Pereira equations were used as reference values.¹¹⁻¹⁴

Statistical analysis

The concordance between the two radiologists for the final Bhalla score, as well as for each category it composes was analyzed by calculating the kappa coefficient.

The correlation between the Bhalla score and its components, the pulmonary function tests and other characteristics of interest were tested using the Spearman correlation coefficient, given that the assumption of normality was violated.

The average evaluation by the two radiologists was used for the Bhalla score.

RESULTS

The records of 144 patients were analyzed. After analyzing the data collected, 53 patients had realized tomography and spirometry. Patients that had conducted spiral chest tomography, without high resolution (N=3), patients whose films were not available for analysis and patients whose interval between tomography and spirometry was greater than 30 days (N=27) were excluded from the 53 eligible patients (N=27). The final sample was therefore constituted by 23 patients.

The clinical characteristics of the population studied are presented in Table 2.

TABLE 2 Characteristics of the population studied

Characteristics	n	Mean	SD
Age (years)	23	17.45	5.75
Weight (kg)	23	43.42	13.66
Height (cm)	23	152.1	14.8
Height/age Z-score	23	-1.3	1.5
Weight/age Z-score	23	-1.6	2.6
BMI	23	18.5	3.1
O2 Saturation	23	95.3	2.1
Shwachman - Kulczycki Score	23	80	16.1
Bhalla Score (R1)	23	16.8	7
Bhalla Score (R2)	23	17	6.6
Bhalla Score (R1 R2 average)	23	16.9	6.7
FVC%	23	87.1	20.5
FEV1%	23	74.2	23.7
FEF 25-75%	23	54.9	32.8
FEV1/FVC x 100	23	74.2	12.6

SD: standard deviation.
The median age of the population studied was 16.5 years.

Cultures

Nine of the patients studied (39.1%) were colonized by *Pseudomonas aeruginosa*, being three (13%) by the mucoid strain, fifteen (65.2%) by *Staphylococcus aureus*, and three (13%) were not colonized.

Concordance between radiologists

A very good concordance between radiologists was found for the Bhalla score, with a kappa coefficient of 0.81 and an intraclass correlation coefficient (ICC) of 0.98, which classified it as adequate (ICC equal to or greater than 0.80).

Relationship between Bhalla scores and pulmonary function tests

A statistically significant positive correlation was identified between the Bhalla score and pulmonary function tests.

TABLE 3 Correlation between the Bhalla score and pulmonary function tests

Characteristics	Bhalla Score	
	r	P-value
FVC%	0.718	<0.001
FEV%	0.830	<0.001
FEF 25-75%	0.786	<0.001
FEV1/FVC x 100	0.714	<0.001

DISCUSSION

The results found in this study prove the hypothesis that the Bhalla score represents a good correlation with pulmonary function tests and can be an ally in the evaluation of pulmonary structural changes.

In a study using the same score, Demirkazik *et al.* evaluated 14 patients from a group of 40 that had HRCTs compared to the clinical and radiographic categories of the Shwachman-Kulczycki score and pulmonary function tests. The age range varied from five months to 18 years, with all patients undergoing pulmonary function tests aged over six years. A good correlation was found between the Bhalla score and FVC ($r = 0.71$ and $p = 0.004$) and the FEV1 ($r = 0.66$ and $p = 0.01$). These findings correspond to the present study, which presented a strong and positive correlation for FVC ($r = 0.718$, $p < 0.001$) and FEV1 ($r = 0.830$, $p < 0.001$).¹⁰

On the other hand, Helbich *et al.* evaluated the tomography of 107 patients with an average age of 14.5 ± 7.3 years at four different times. There was a weak correlation ($r = 0.25$ and $p < 0.0001$) between the tomography and the pulmonary function tests, and while the HRCT showed significant structural changes, the spirometry manifested minimal progression or slight improvement on the standard.¹⁵

More recently, with the objective of investigating the relationship between non-invasive inflammatory markers, function tests and pulmonary structural changes, Robroeks *et al.* studied 34 patients with average age of $12.6 \text{ years} \pm 4.4$ using the score described by Brody *et al.*⁹ and found a strong correlation between the final score and the FVC ($r = -0.73$, $p < 0.001$), FEV1 ($r = -0.77$, $p < 0.001$) and FEV1/FVC ($r = -0.43$, $p < 0.001$).¹¹ Likewise, in 22 patients with an average age of $22 \text{ years} \pm 5.9$ and using a modified Bhalla score, Dodd *et al.* found a significant correlation between the final score and the FEV1 ($r = -0.40$, $p < 0.05$).¹⁸ Furthermore, Marchant *et al.*, in an evaluation of 16 patients aged under 12 years with the objective of comparing the Bhalla and Nathanson scores found a significant correlation between the final Bhalla score and the FEV1 ($r = -0.65$, $p = 0.012$) and FVC ($r = -0.57$, $p = 0.032$).¹⁹

However, analyzing the scores and function tests of each patient in isolation and taking into consideration that the FEF 25-75% is the parameter that causes most early changes in CF, it was verified that 11 of the 23 patients studied presented an FEF 25-75% above 70%. Despite the final Bhalla score being over 16 in these cases or being classified as good or excellent, the letter T was added to the final score of 7 patients, indicating the presence of peribronchial thickening, and bronchiectasis was recorded in 4

patients by the two radiologists.^{16,17} The findings in this study are reflected in the literature and a study by Marchant *et al.*, given that all of the 16 patients had bronchiectasis, including 5 who presented normal pulmonary function tests, showing that the examinations should be complementary and should not substitute one another.¹⁹

Within the same perspective, De Jong *et al.* evaluated the HRCTs and pulmonary function tests of 48 patients that were conducted when they had an average age of 11.05 years \pm 3.30 and repeated after a two year interval. The HRCTs were evaluated using five different scores (Castile, Brody, Helbich, Santamaria and Bhalla).¹⁹ The authors verified that while there was deterioration in the HRCT findings in all scores used, the function tests remained unchanged or showed improvements. Furthermore, some patients with normal pulmonary function tests presented structural changes in the HRCT.

This last finding reinforces the importance of HRCT in monitoring patients with CF, suggesting its use in order to detect early structural changes regardless of the results of pulmonary function tests.

The concordance between examiners for the total Bhalla score in the present study was considered very good by the kappa coefficient (0.81, $p < 0.001$) and the ICC was considered adequate (0.98). These are similar results to those of Cademartiri *et al.*, in which the Bhalla score was used to independently evaluate 145 tomographies by three radiologists.²¹ The average age of patients was 15.6 years \pm 8.4. The ICC was 0.99 between observers 1 and 2, 1 and 3, 2 and 3 and between all three observers, with $p = 0.001$ for all analyses.

CONCLUSION

The evaluation of pulmonary disease in patients with CF should include different clinical and preliminary methods, enabling an improvement in the effectiveness of treatment aiming at containing the progression of the disease.

In recent years, greater ease of access to computed tomography has enabled this test to be incorporated into the routine assessment of patients, presenting essential information about the structural changes that occur in the airways and pulmonary parenchyma, with greater accuracy than assessment by plain radiography. However, the high dose of ionizing radiation, mainly due to the repetition of examinations, raises questions regarding the best time to start implementation, as well as its frequency.

We should reiterate the finding of peribronchial thickening and mucous plugs in patients with preserved lung function (FEF 25-75 $>$ 70%), confirming the need for a

joint analysis between high-resolution CT and spirometry for better monitoring and early intervention.

In regards to frequency, it is reasonable to infer that patients with stable and unchanged pulmonary function could repeat the tests at longer intervals than those showing a decrease in spirometry values. And this is undoubtedly a result with great clinical applicability. It is important to stress that spirometry should not replace the realization of HRCT.

Furthermore, good concordance between examiners for the Bhalla score demonstrates its usefulness as an evaluation criterion for tomographic changes during longitudinal follow-up of patients with CF.

In relation to the limitations of the study it is important to note that this is a retrospective study in a single referral service with a relatively small number of patients, which may limit the generalization of results. Nevertheless, based on the results, we cannot definitively exclude the extrapolation of the findings in this study, though it certainly should be a matter to be explored further in future studies with a prospective design.

Finally, the notion of complementarity of clinical, radiological and functional information will contribute to the development of more discerning monitoring protocols aimed at the overall wellbeing of individuals with CF. These protocols, should consider patients with CF as well as other chronic diseases, who will be submitted to numerous radiological tests and must therefore be protected from the effects of ionizing radiation, either by reducing the dose during the exams or more careful requests for such. It should be noted that the standardization of the frequency should not be instituted by service protocols and that each patient should be evaluated on an individual basis, although spirometry could be an important ally in the decision making regarding the time to perform examination.

RESUMO

Correlação entre escore de Bhalla e espirometria em crianças e adolescentes com fibrose cística

Objetivo: correlacionar os achados da tomografia computadorizada de alta resolução (TCAR) do tórax, com base no escore de Bhalla, com os dados clínicos e a espirometria em crianças e adolescentes com fibrose cística (FC), além de estudar a concordância entre dois médicos radiologistas para o escore de Bhalla e suas categorias.

Métodos: foram avaliados os prontuários e os exames de 23 pacientes do ambulatório. Os itens avaliados foram idade, peso, altura, escore Z altura/idade, escore Z peso/idade, índice de massa corpórea (IMC), saturação de O₂, espirometria e escore de Bhalla.

Resultados: os pacientes avaliados tinham média de idade de 17,4±5,7 anos, sendo 15 do sexo feminino e 8 do sexo masculino. Houve boa correlação entre o escore de Bhalla e a espirometria (CVF-r = 0,718, p < 0,001; VEF₁-r = 0,830, p < 0,001; FEF 25-75%-r = 0,786, p < 0,001; VEF₁/CVF-r = 0,714, p < 0,001). Nota-se, ainda, que alguns pacientes com FEF 25-75% > 70% já apresentavam alterações na nota final do escore de Bhalla. Na análise da concordância entre os examinadores, foi encontrado coeficiente *kappa* de 0,81 (p < 0,001) e coeficiente de correlação intraclasse de 0,98.

Conclusão: a boa correlação do escore de Bhalla com as provas de função pulmonar confirma a sua utilidade na avaliação e no acompanhamento dos pacientes com FC, podendo ser utilizado tanto para pacientes que são incapazes de realizar a espirometria quanto para uma análise em conjunto dos dois exames, uma vez que a TCAR mostra alterações precoces em pacientes com espirometrias normais.

Unitermos: fibrose cística; tomografia; espirometria; criança; adolescente.

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