

HIGH-RESOLUTION CT PULMONARY CHANGES IN PATIENTS WITH CYSTIC FIBROSIS USING BHALLA SCORE SYSTEM CORRELATED WITH CLINICAL PARAMETERS

Kristina Dimitrijevikj^{1,2}, Nadica Mitreska^{2,3}, Violeta Vasilevska-Nikodinovska^{2,4}

¹University clinic of pulmonology and allergology, Skopje, North Macedonia

²Faculty of Medicine, Ss Cyril and Methodius University in Skopje, North Macedonia

³University Institute of Radiology, Skopje, North Macedonia

⁴University Surgical Clinic "St. Naum Ohridski"- Skopje, North Macedonia

Abstract

Cystic fibrosis (CF), caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, is an inherited, chronic, progressive, and fatal disease. It mainly involves the lungs and pancreas, but also the upper airways, liver, intestine, and reproductive organs.

The aim of our study is to evaluate one of the most used scoring systems, the Bhalla scoring system, in the detection of lung impairment in patients with cystic fibrosis.

A total of 32 patients diagnosed with CF came to our University clinic of pulmonology and allergology-Skopje to perform HRCT for the first time and to detect the degree of the disease. Clinical data, age at application, deep throat and sputum cultures were obtained from medical records. High-resolution computed tomography (HRCT) was performed on a 128-slice PHILIPS INCISIVE CT scanner, using 1 mm slices and a high spatial resolution image reconstruction algorithm using Bhalla score system.

A total of 66% of patients have mild severity of bronchiectasis, 53% of all have mild peribronchial thickening. 41% of all have from 1 to 5 extent of the bronchiectasis and 53% of all have from 1 to 5 extent of mucus plugs as a dominant HRCT findings. Sputum was positive in 44 % of patients.

High resolution computed tomography (HRCT) is well-established and is the current "gold standard" method for monitoring lung anatomical changes in patients with CF. Bhalla HRCT scoring system is useful for pulmonary evaluation of children with CF.

Keywords: cystic fibrosis, HRCT, Bhalla score.

Introduction

Cystic fibrosis (CF), caused by a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, is an inherited, chronic, progressive, and fatal disease [1].

Deletion in CFTR leads to dehydration of the airway surface liquid layer, reduction in mucociliary clearance, and chronic bronchopulmonary infection in the lungs [2].

High resolution computed tomography (HRCT) is well-established and is the current "gold standard" method for monitoring lung anatomical changes in patients with CF. To facilitate evaluation and comparison of quantitative data, investigators have developed quantitative scoring systems based on CT findings [3].

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. [4,5] The Bhalla scoring system, widely used particularly in pediatric and adult patients with CF, is a scoring system that has been demonstrated to correlate HRCT findings with clinical and physiological characteristics [6,7].

The aim of this study is to detect the morphological changes, their distribution along the parenchyma due to CF lung disease in relative young patients according to HRCT findings and to correlate the HRCT scores using the Bhalla scoring system with clinical parameters.

Material and Methods

A total of 32 patients diagnosed with CF came to our University clinic of pulmonology and allergology-Skopje to perform HRCT for the first time and to detect the degree of the disease. Clinical

data, age at application, deep throat and sputum cultures were obtained from medical records Moj Termin. Weight, height and body mass index (BMI) were used for clinical evaluation. Deep throat and sputum cultures were evaluated for the presence of bacteria including *Pseudomonas Aeruginosa*.

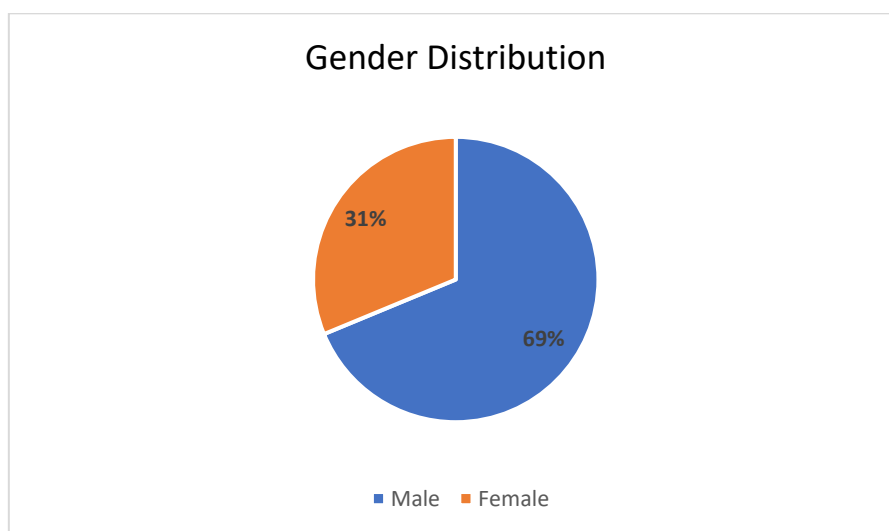
High-resolution computed tomography (HRCT) was performed on a 128-slice PHILIPS INCISIVE CT scanner, using 1 mm slices and a high spatial resolution image reconstruction algorithm. The scoring system proposed by Bhalla et al.[8]for CT evaluates the following: (1) severity of bronchiectasis, (2) extent of bronchiectasis, (3) peribronchial thickening, (4) extent of mucus plugs, (5) abscesses/sacculation, (6) generalities of the bronchial division involved, (7) number of bubbles, (8) emphysema, and (9) collapse/consolidation.

Results

The analysis was conducted on a selected group of 32 patients diagnosed with cystic fibrosis, encompassing variables such as age, gender, body mass index (BMI), and Bhalla scoring parameters.

Graph.1 Gender distribution

- Male patients constituted 22 (69%), while females accounted for 10 (31%).



Age Distribution

- The average age of all patients is 22 years. The oldest patient is 44 years old, while the youngest is 11 years old.

- 15 (47%) of the patients belong to the age group from 10 to 19 years range, 11 (34%) from 20 to 29 years range, 5 (16%) from 30 to 39 years range, and 1 (3%) from 40 to 49 years range.

Table 1. Age range distribution

Age range distribution	1-10	20-29	30-39	40-49
In absolute amount	15	11	5	1
% of total	47%	34%	16%	3%

BMI Analysis

- The average body mass index (BMI) of all patients is 20.39.
- The average BMI of patients by age group is 19.91 (for 10-19 years range), 20.43 (for 20-29 years range), 21.6 (for 30-39 years range), and 22.77 (years 40-49 years range).

Table 2. Average BMI analysis by age range distribution

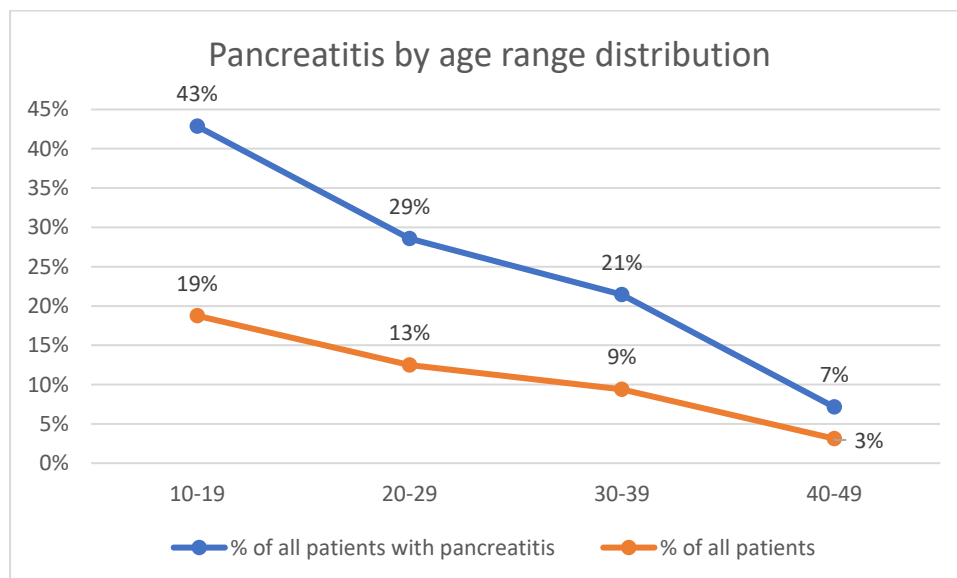
Average BMI by age range distribution	10-19	20-29	30-39	40-49
Average BMI	19,91	20,43	21,26	22,77

Clinical parameters

- Insufficiency Pancreatitis
 - o Present in 14 patients (44% of all).
 - o Distribution across age groups: 19% (10-19 years range), 13% (20-29 years range), 9% (30-39 years range), and 3% (40-49 years range).

Table 3. Pancreatitis by age range distribuiton

Pancreatitis by age range distribution	10-19	20-29	30-39	40-49	Total
Number of patients with presence	6	4	3	1	14
% of all patients with pancreatitis	43%	29%	21%	7%	
% of all patients	19%	13%	9%	3%	44%



Graph.1. Pancreatitis by age range distribuiton

Sputum Characteristics

- o 88% of all patients exhibited at least one type of sputum.
- o Predominant types included *Pseudomonas Aeruginosa* whose presence was found in 44% and MRSA with the same representation of 47%. Less prevalent occurrences of *Aspergillus Fumigatus* (9%), *Aspergillus Flavus* (3%), *Escherichia coli* (3%), and *Staphylococcus Aureus* (3%). As a basis for calculating the percentages, the total number of patients is taken into account.

Table 4. Sputum Characteristics

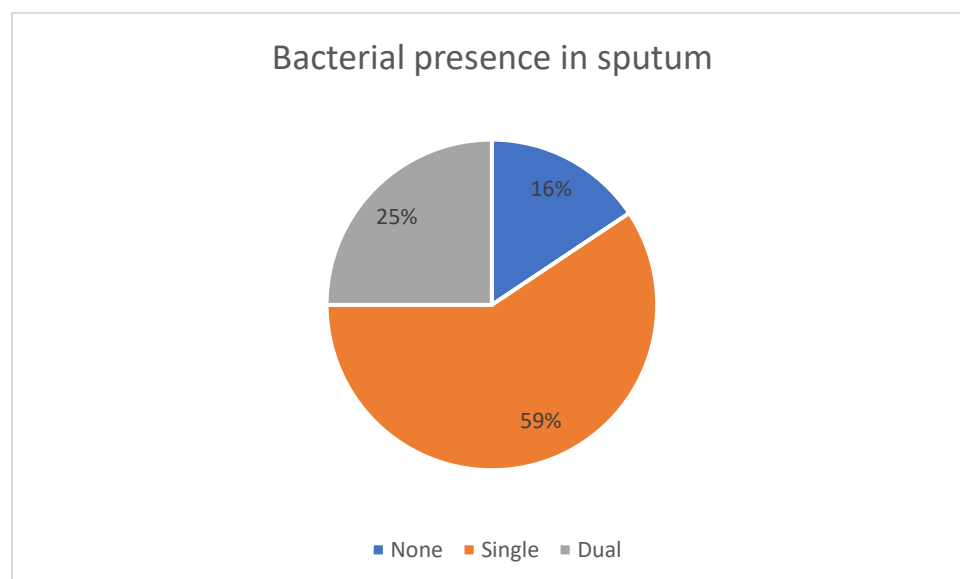
Sputum	# Male	% of all males	% of total	# Female	% of all females	% of total	# Total	% of Total
Candida Species	1	5%	3%	0	0%	0%	1	3%
Pseudomonas Aeruginosa	9	41%	28%	5	50%	16%	14	44%
Escherichia coli	1	5%	3%	0	0%	0%	1	3%
MRSA	11	50%	34%	4	40%	13%	15	47%
Aspergillus Flavus	0	0%	0%	1	10%	3%	1	3%
Aspergillus Fumigatus	2	9%	6%	1	10%	3%	3	9%

Bacterial Diversity in Sputum

Dual bacterial presence was identified in 10 patients (31% of all), while 12 (69%) manifested a single bacterial type.

Table 5. Bacterial Diversity in Sputum

Bacterial presence	Number of patients	% of all
None	5	16%
Single	19	59%
Dual	8	25%



Graph.2 Bacterial presence in sputum

Radiological study and HRCT findings

HRCT was performed on a 128-slice PHILIPS INCISIVE CT scanner, using 1 mm slices and a high spatial resolution image reconstruction algorithm.

The Bhalla scoring system serves as a methodology for assessing computed tomography (CT) findings (Table 1, below). The score considers nine specific parameters:

- Severity of Bronchiectasis: This assesses the extent and severity of the bronchiectasis present.
- Extent of Bronchiectasis: It evaluates how widespread the bronchiectasis is within the lung.
- Peribronchial Thickening: This parameter assesses the thickening of the tissue surrounding the bronchi.
- Extent of Mucus Plugs: It evaluates the presence and distribution of mucus plugs within the bronchi.
- Abscesses/Sacculation: This aspect considers the presence of abscesses or sacculation in the lung.
- Generalities of the Bronchial Division Involved: It assesses the specific bronchial divisions affected by the pathology.
- Number of Bubbles: This parameter counts the number of air-filled spaces or "bubbles" within the lung.
- Emphysema: It evaluates the presence and extent of emphysematous changes in the lung.
- Collapse/Consolidation: This assesses the collapse or consolidation of lung tissue.

Scores from 0 to 3 were assigned to each of the first seven categories (severity of bronchiectasis, peribronchial thickening, extent of bronchiectasis, extent of mucus plugging, sacculation, generations of bronchi involved, and number of bubbles) while from 0 to 2 are assigned for the last two categories (emphysema and collapse/consolidation). The total score may have a maximum value of 25 and was calculated by adding individual scores for each item. The total points were then subtracted from 25 to obtain the Bhalla score. The maximum points that can be obtained in a Bhalla score is 22 (prior to subtracting from 25).

Table 6				
Category	Score			
	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 4th generation	Over the 5th generation	Over the 6th 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	

The total range for the Bhalla score is from 3-25, where a lower score indicates more severe HRCT findings. This score was subdivided into mild (16-25), moderate (9-15), and severe (3-8).

- The average Bhalla score from all patients is 18.31 which belongs to the mild range.
- 25 patients (78% of all) belong to the mild range, 6 (19% of all) belong to the moderate range, and 1 (3%) belong to the severe Bhalla score range.

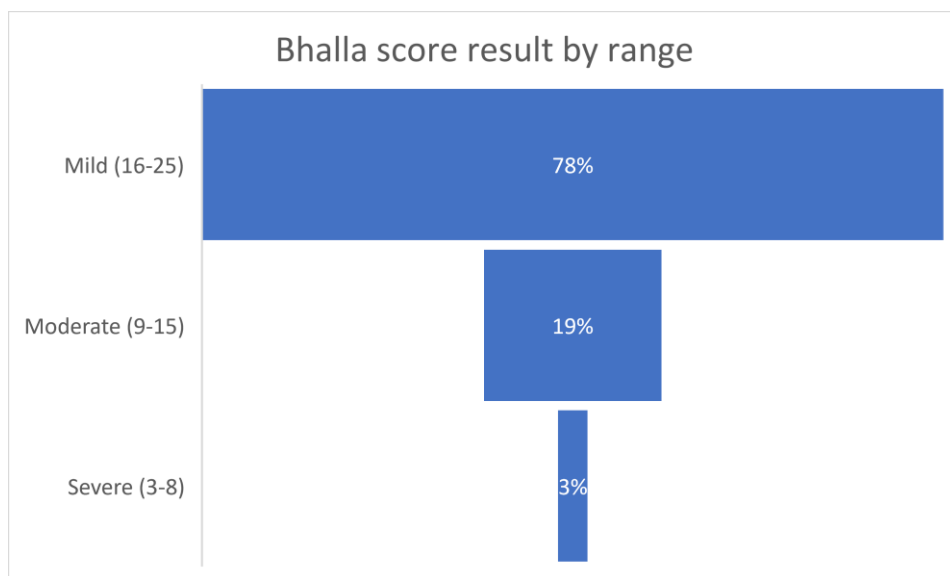
Statistical analysis

In the pursuit of a comprehensive examination, sophisticated statistical analyses were applied utilizing tools such as SPSS and Microsoft Excel. The focus was the distribution of Bhalla scores, meticulously categorized into predetermined Bhalla score baskets. The analysis unfolded in dual dimensions, presenting findings both in absolute numerical values and relative terms as percentages relative to the total.

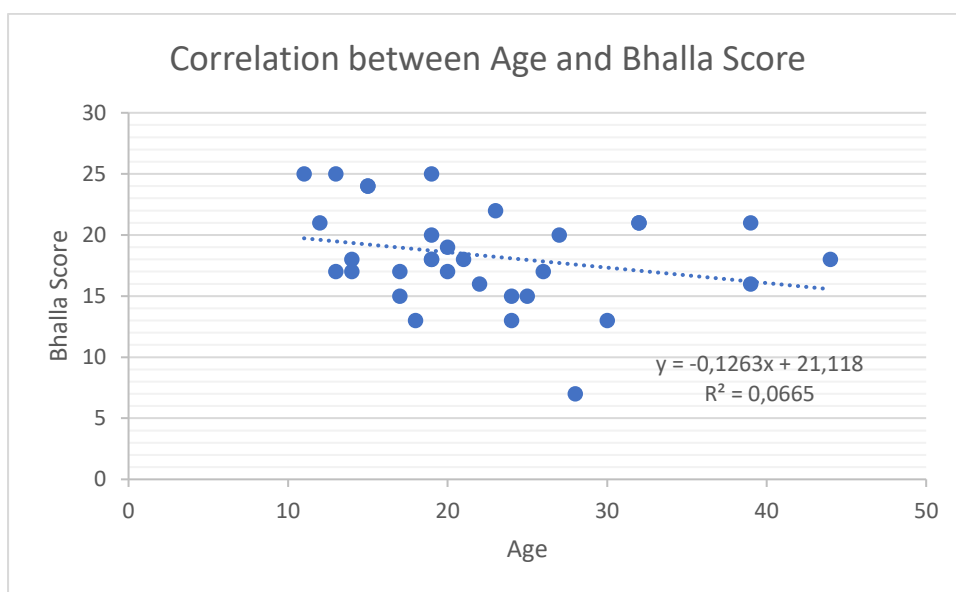
Additionally, correlations between Bhalla scores and pivotal variables, including age, Body Mass Index (BMI), and various Bhalla score parameters were explored.

Table 7. Bhalla score by age range distribution

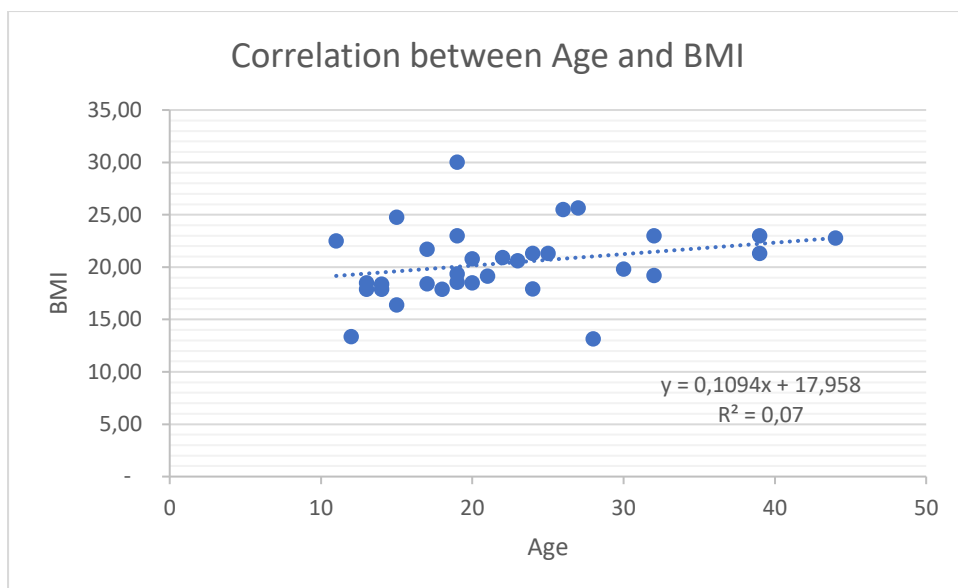
Bhalla score by age range distribution	10-19	% of all	20-29	% of all	30-39	% of all	40-49	% of all	# Total	% of all
Mild (16-25)	13	41%	7	22%	4	13%	1	3%	25	78%
Moderate (9-15)	2	6%	3	9%	1	3%	0	0%	6	19%
Severe (3-8)	0	0%	1	3%	0	0%	0	0%	1	3%



- No significant correlation was found between the age and Bhalla scores ($r = -0.26$), Age and body mass index (BMI) ($r=0.26$), and body mass index (BMI) and Bhalla scores ($r = 0.27$).

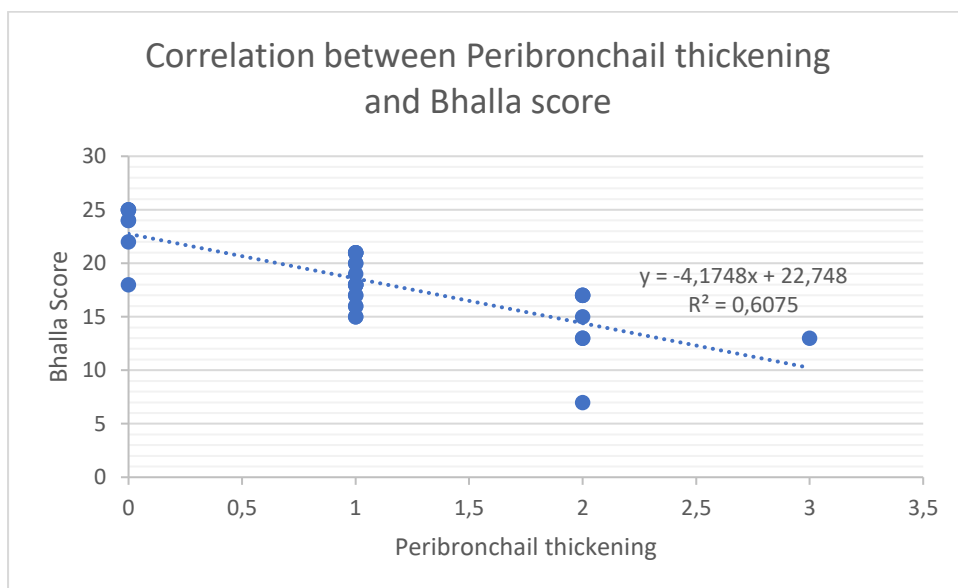


Graph. 3 Correlation between age and Bhalla Score

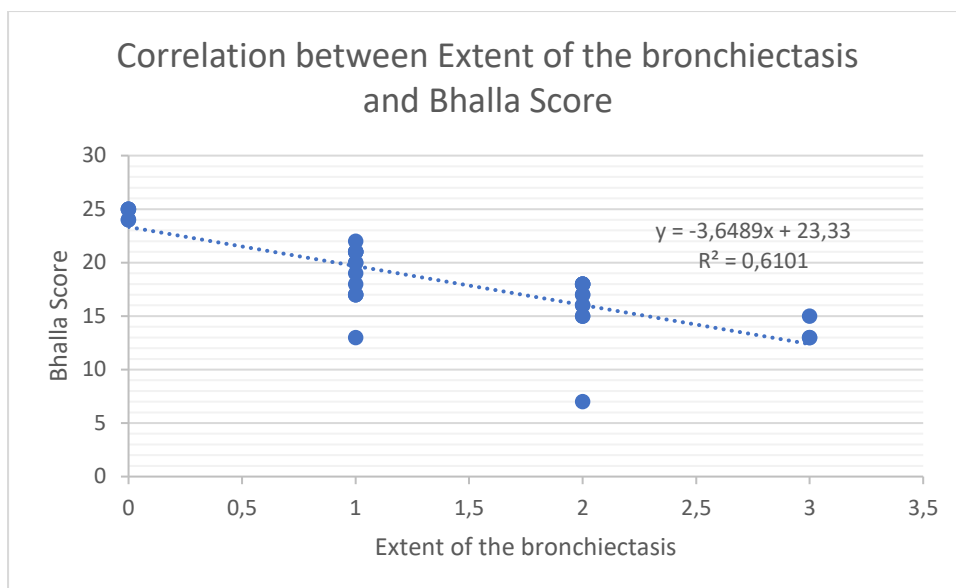


Graph. 4. Correlation between Age and BMI

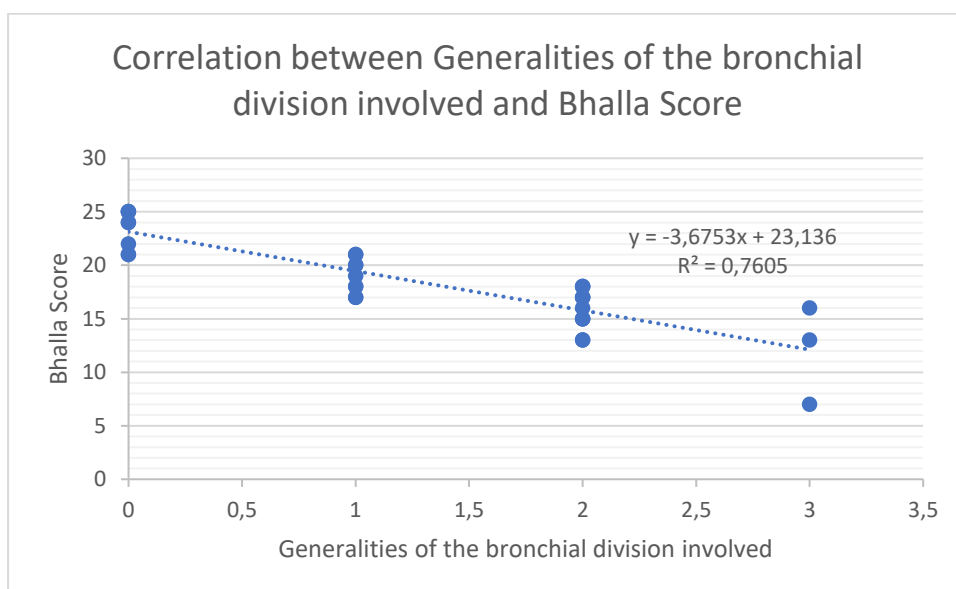
• Significant correlations were found between Peribronchail thickening and Bhalla score ($r=-0.78$), Extent of the bronchiectasis and Bhalla Score ($r=-0.78$), and Generalities of the bronchial division involved and Bhalla Score ($r=-.87$).



Graph 5. Correlation between Periobronchail thickkening and Bhalla score



Graph 6. Correlation between Extent of the bronchiectasis and Bhalla Score



Graph 7. Correlation between Generalities of the bronchial division involved and Bhalla Score

Given that we are talking about relatively young patients (whose average age is 22 years), below we will highlight the most significant results of Bhalla scoring:

- 66% of all have mild (light subtly greater than the adjacent vessel) severity of bronchiectasis.
- 53% of all have Mild (thickening of the wall equal to the vessel) peribronchial thickening.
- 41% of all have from 1 to 5 extent of the bronchiectasis (number of lung segments).
- 53% of all have from 1 to 5 Extend of mucus plugs (number of lung segments).
- Abscesses of sacculation is confirmed as absent for 81% of all patients.
- Generalities of the bronchial division involved (bronchiectasis/plug): 28% Over the 4th generation and 38% Over the 5th generation.
- Bubbles (measured in numbers) are absent for 84% of patients.
- Emphysema (number of lung segments) is absent in 97% of patients.
- Collapse/consolidation is absent in 78% of patients.

Table 7. Severity of bronchiectasis

Severity of bronchiectasis	# Male	% of all males	% of total	# Female	% of all females	% of total	# Total	% of Total
Absent	2	9%	6%	1	10%	3%	3	9%

Mild	16	73%	50%	5	50%	16%	21	66%
Moderate	3	14%	9%	3	30%	9%	6	19%
Severe	1	5%	3%	1	10%	3%	2	6%

Peribronchail thickening	# Male	% of all males	% of total	# Female	% of all females	% of total	# Total	% of Total
Absent	5	23%	16%	2	20%	6%	7	22%
Mild	13	59%	41%	4	40%	13%	17	53%
Moderate	4	18%	13%	3	30%	9%	7	22%
Severe	0	0%	0%	1	10%	3%	1	3%

Extent of the bronchiectasis (number of lung segments)	# Male	% of all males	% of total	# Female	% of all females	% of total	# Total	% of Total
Absent	3	14%	9%	2	20%	6%	5	16%
1-5	9	41%	28%	4	40%	13%	13	41%
6-9	9	41%	28%	2	20%	6%	11	34%
>9	0	0%	0%	0	0%	0%	0	0%

Extend of mucus plugs (number of lung segments)	# Male	% of all males	% of total	# Female	% of all females	% of total	# Total	% of Total
Absent	7	32%	22%	3	30%	9%	10	31%
1-5	13	59%	41%	4	40%	13%	17	53%
6-9	2	9%	6%	2	20%	6%	4	13%
>9	0	0%	0%	0	0%	0%	0	0%

Abscesses of sacculation (number of lung segments)	# Male	% of all males	% of total	# Female	% of all females	% of total	# Total	% of Total
Absent	18	82%	56%	8	80%	25%	26	81%
1-5	3	14%	9%	2	20%	6%	5	16%
6-9	1	5%	3%	0	0%	0%	1	3%
>9	0	0%	0%	0	0%	0%	0	0%

Generalities of the bronchial division involved (bronchiectasis/plug)	# Male	% of all males	% of total	# Female	% of all females	% of total	# Total	% of Total
Absent	5	23%	16%	3	30%	9%	8	25%
Over the 4th generation	8	36%	25%	1	10%	3%	9	28%
Over the 5th generation	7	32%	22%	5	50%	16%	12	38%
Over the 6th generation and distal	2	9%	6%	1	10%	3%	3	9%

Number of Bubbles	# Male	% of all males	% of total	# Female	% of all females	% of total	# Total	% of Total
Absent	19	86%	59%	8	80%	25%	27	84%
Unilateral (none>4)	0	0%	0%	1	10%	3%	1	3%
Bilateral (none>4)	3	14%	9%	1	10%	3%	4	13%
>4	0	0%	0%	0	0%	0%	0	0%

Emphysema (number of lung segments)	# Male	% of all males	% of total	# Female	% of all females	% of total	# Total	% of Total
Absent	21	95%	66%	10	100%	31%	31	97%
1-5	1	5%	3%	0	0%	0%	1	3%
>5	0	0%	0%	0	0%	0%	0	0%

Collapse / consolidation	# Male	% of all males	% of total	# Female	% of all females	% of total	# Total	% of Total
Absent	16	73%	50%	9	90%	28%	25	78%
Subsegmental	3	14%	9%	1	10%	3%	4	13%
Subsegmental/lobar	0	0%	0%	0	0%	0%	0	0%

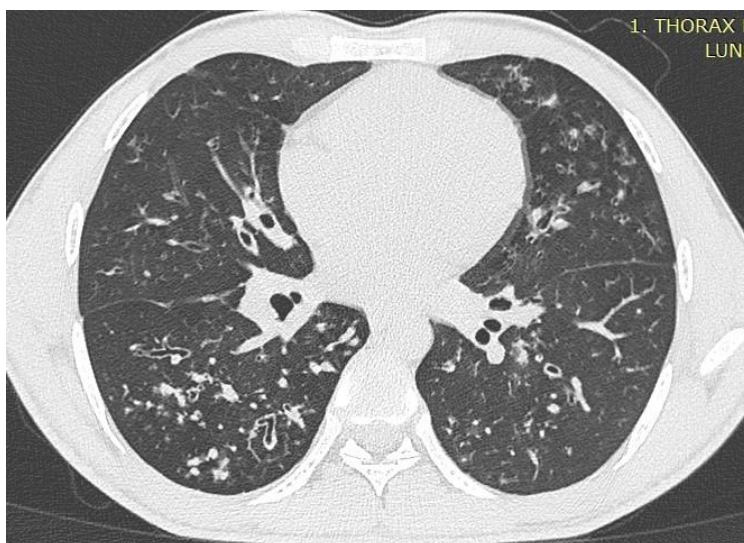


Figure 1. Mild bronchiectatic changes in a patient with cystic fibrosis. The striking abnormality is the widespread nodular “tree-in-bud” pattern reflecting exudative small airways involvement.

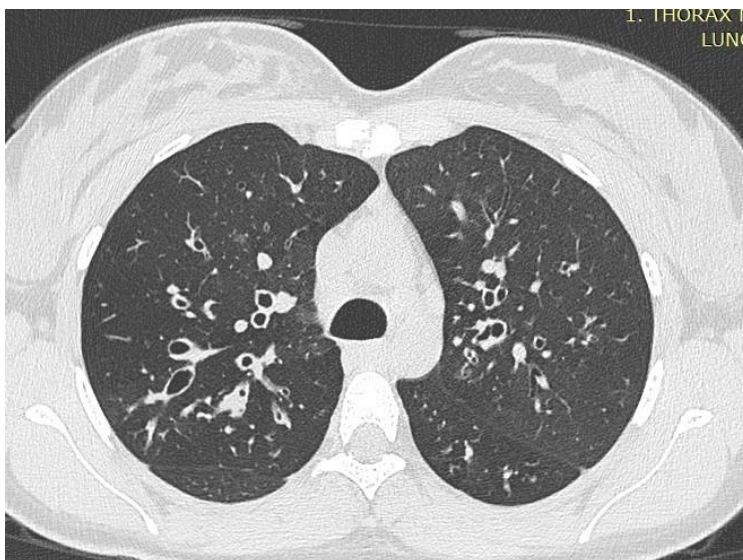


Figure 2. HRCT scan through the upper lobes of an individual with cystic fibrosis showing cylindrical bronchiectasis and bronchial wall thickening.

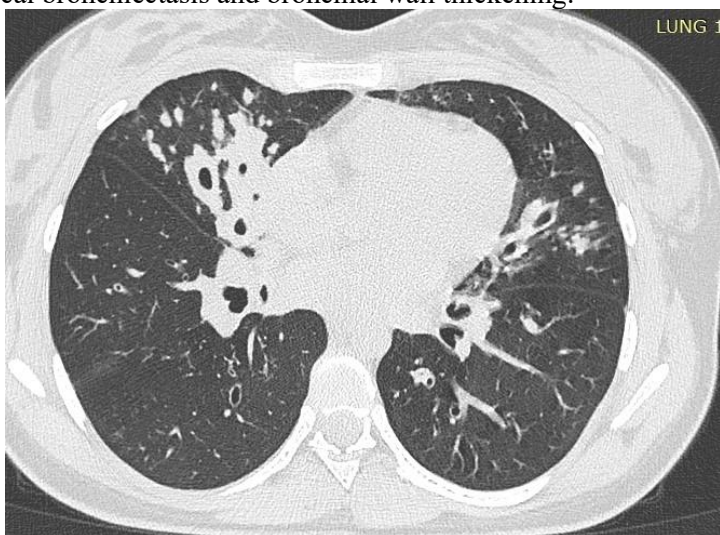


Figure 3. Peribronchial thickening in lower lobes with mucus plugs

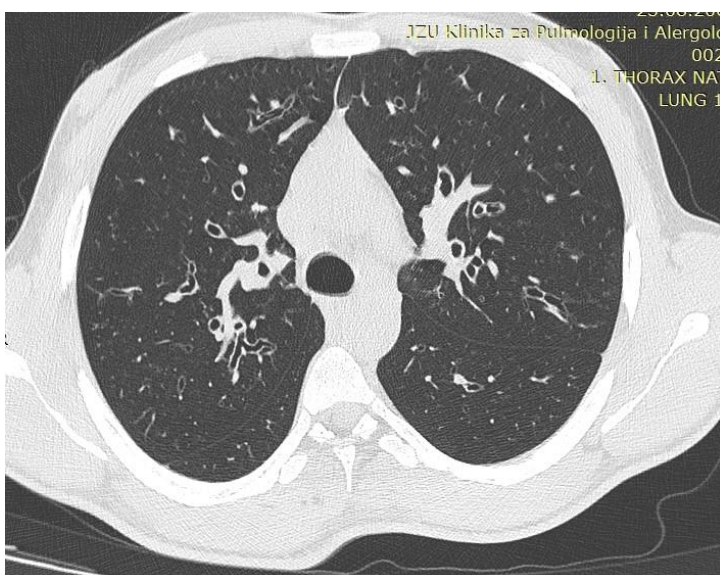


Figure 4. Bronchiectasis in patient with CF in early stage

Discussion

The main cause of mortality in patients with CF is lung disease. For this reason, it is critical to improve pulmonary diagnosis in patients to better predict adverse events and monitor therapies [11]. Currently, different variables, including HRCT scores, sputum cultures, and clinical examinations, are used to assess pulmonary changes in patients with CF [12].

The rationale for performing HRCT in patients with cystic fibrosis is to obtain additional information with prognostic significance that should be used to modify clinical approach and treatment. For this purpose, standardization of the radiologic evaluation through a scoring system is crucial to obtain correlation with clinical outcome and for reproducibility [10].

In this study no significant correlation was found between the age and Bhalla scores ($r = -0.26$), age and body mass index (BMI) ($r = 0.26$), and body mass index (BMI) and Bhalla scores ($r = 0.27$). These results are probably due to the fact that the most patients were younger up to ten years old. Significant correlations were found between peribronchial thickening and Bhalla score ($r = -0.78$), extent of the bronchiectasis and Bhalla Score ($r = -0.78$), and generalities of the bronchial division involved and Bhalla Score ($r = -0.87$).

This is because of the fact that the main HRCT findings to establish CF diagnose are bronchial wall and/or peribronchial interstitial thickening especially early in the disease [13].

Mucous plugging is of particular importance as it is thought to precede infective exacerbations and thus identification of such plugging may be used to trigger changes in therapy [14].

In our case 53% of all patients have from 1 to 5 extent of mucus plugs (number of lung segments) and dual bacterial presence was identified in 10 patients (31% of all), while 12 (69%) manifested a single bacterial type. *Pseudomonas aer.* infection is considered a risk factor for the development of bronchiectasis in children with CF [15]. In our study 44 % of all patients had *Pseudomonas aer.* in their sputum. Acute recurrent pancreatitis (ARP) and chronic pancreatitis (CP) are described as relatively rare manifestations of CF. They have been associated with minimal or mild respiratory disease and pancreatic sufficiency [16].

In our case pancreatic insufficiency was found in 14 patients (44%). In 1991, two independent publications by Nathanson et al. [17] and Bhalla et al. [18] proposed two distinct scoring systems for the evaluation of CF lung disease in children and adults. In a study comprising 16 patients aged < 12 years, Marchant et al. [19] compared these two scoring systems and showed that the Bhalla method was superior to the Nathanson method in young children with CF. Given that we are talking about relatively young patients (whose average age is 22 years), our most significant results of Bhalla scoring are that 66% of all patients have mild severity of bronchiectasis, 53% of all have mild peribronchial thickening and 41% of all have from 1 to 5 extent of the bronchiectasis. Mucus plugs were found in 53%. In our study abscesses of sacculation, bubbles, emphysema and collapse/consolidation were found in minority of patients and the average Bhalla score from all patients is 18.31 which belongs to the mild range, but slightly approaching to moderate range.

One of the limitations of this study is the small number of patients. A prospective and larger study is needed to confirm these results and would help in further understanding CF progression and disease management. Another limitation of the study is the relatively small number of different clinical parameters measured and the relatively young age of patients. For instance, the number of exacerbations were not evaluated in this study. Future studies are needed to assess the relationships between these variables.

Conclusion

This study showed the usefulness of chest HRCT Bhalla scoring system in the pulmonary evaluation of young patients with CF. High resolution computed tomography (HRCT) is well-established and is the current “gold standard” method for monitoring lung anatomical changes in patients with cystic fibrosis (CF). To facilitate evaluation and comparison of quantitative data, investigators have developed quantitative scoring systems based on computed tomography findings. Bhalla chest HRCT scoring system is useful for pulmonary evaluation of children with CF [7].

References

1. National Heart, Lung and Blood Institute. Facts about Cystic Fibrosis. Bethesda (MD): National Institutes of Health, 1995.
2. Bradbury NA. CFTR and cystic fibrosis: a need for personalized medicine. In: Hamilton KL, Devor DC, eds. *Ion Channels and Transporters of Epithelia in Health and Disease*. Kolodziej M, de Veer MJ, Cholewa M, Egan GF, Thompson BR. Lung function imaging methods in cystic fibrosis pulmonary disease. *Respir Res* 2017;18:96. New York: Springer, 2016;773–802.
3. Kolodziej M, de Veer MJ, Cholewa M, Egan GF, Thompson BR. Lung function imaging methods in cystic fibrosis pulmonary disease. *Respir Res* 2017;18:96.
4. Shwachman H, Kulczycki LL. Long-term study of one hundred five patients with cystic fibrosis; studies made over a five- to fourteen-year period. *AMA J Dis Child*. 1958;96(1):6-15.
5. Bhalla M, Turcios N, Aponte V, Jenkins M, Leitman BS, McCauley DI et al. Cystic fibrosis: scoring system with thin-section CT. *Radiology*. 1991;179(3):783-8.
6. Judge EP, Dodd JD, Masterson JB, Gallagher CG. Pulmonary abnormalities on high-resolution CT demonstrate more rapid decline than FEV1 in adults with cystic fibrosis. *Chest* 2006;130:1424–1432.
7. A S Sasihuseyinoglu, D U Altıntaş, S Soyupak, D Dogruel, M Yılmaz, M Serbes, G Duyuler. Evaluation of high resolution computed tomography findings of cystic fibrosis. *Korean J Intern Med* 2019;34(2):335-343. Published online: July 6, 2018
8. Bhalla M, Turcios N, Aponte V, et al. Cystic fibrosis: scoring system with thin-section CT. *Radiology* 1991;179:783–788.
9. Brody AS, Kosorok MR, Li Z, et al. Reproducibility of a scoring system for computed tomography scanning in cystic fibrosis. *J Thorac Imaging* 2006;21:14–21.
10. Cademartiri F, Luccichenti G, Palumbo AA, E, Maffei E, Pisi G, Zompatori M, Krestin GP. Predictive Value of Chest CT in Patients with Cystic Fibrosis: A Single-Center 10-Year Experience. *AJR* 2008; 190:1475–1480.
11. Carpio C, Albi G, Rayon-Aledo JC, et al. Changes in structural lung disease in cystic fibrosis children over 4 years as evaluated by high-resolution computed tomography. *Eur Radiol*. 2015;25:3577–3585.
12. Helbich TH, Heinz-Peer G, Eichler I, et al. Cystic fibrosis: CT assessment of lung involvement in children and adults. *Radiology*. 1999;213:537–544
13. Naidich DP, Srichai MB, Krinsky GA. *Computed tomography and magnetic resonance of the thorax*. Lippincott Williams & Wilkins. (2007) ISBN:0781757657.
14. Helbich TH, Heinz-peer G, Fleischmann D et-al. Evolution of CT findings in patients with cystic fibrosis. *AJR Am J Roentgenol*. 1999;173 (1): 81-8
15. Stick SM, Brennan S, Murray C, et al. Bronchiectasis in infants and preschool children diagnosed with cystic fibrosis after newborn screening. *J Pediatr*. 2009;155:623–628.
16. Ooi CY, Durie PR. Cystic fibrosis transmembrane conductance regulator (CFTR) gene mutations in pancreatitis. *J Cyst Fibros*. 2012;11:355–362
17. Nathanson I, Conboy K, Murphy S, Afshani E, Kuhn JP. Ultrafast computerized tomography of the chest in cystic fibrosis: a new scoring system. *Pediatr Pulmonol*. 1991;11:81–86.
18. Bhalla M, Turcios N, Aponte V, et al. Cystic fibrosis: scoring system with thin-section CT. *Radiology*. 1991;179:783–788.
19. Marchant JM, Masel JP, Dickinson FL, Masters IB, Chang AB. Application of chest high-resolution computer tomography in young children with cystic fibrosis. *Pediatr Pulmonol*. 2001;31:24–29.