Cystic fibrosis in adults: differences between upper and middle versus lower lung lobes in MDCT morphology and correlation with lung function test results

Poster No.: C-2014
Congress: ECR 2013
Type: Scientific Exhibit
Authors: M. Schmitz, E. Coppenrath, R. Fischer, R. Huber, M. F. Reiser, U. Mueller-Lisse; Munich/DE
Keywords: Anatomy, Lung, Respiratory system, CT, CT-High Resolution, Comparative studies, Diagnostic procedure, Physiological studies, Genetic defects, Metabolic disorders, Pathology
DOI: 10.1594/ecr2013/C-2014

Any information contained in this pdf file is automatically generated from digital material submitted to EPOS by third parties in the form of scientific presentations. References to any names, marks, products, or services of third parties or hypertext links to third-party sites or information are provided solely as a convenience to you and do not in any way constitute or imply ECR's endorsement, sponsorship or recommendation of the third party, information, product or service. ECR is not responsible for the content of these pages and does not make any representations regarding the content or accuracy of material in this file.

As per copyright regulations, any unauthorised use of the material or parts thereof as well as commercial reproduction or multiple distribution by any traditional or electronically based reproduction/publication method ist strictly prohibited.

You agree to defend, indemnify, and hold ECR harmless from and against any and all claims, damages, costs, and expenses, including attorneys' fees, arising from or related to your use of these pages.

Please note: Links to movies, ppt slideshows and any other multimedia files are not available in the pdf version of presentations.

www.myESR.org
1. Cystic fibrosis (CF), an inherited, autosomal-recessive metabolic disorder associated with chlorine channel malfunction in exocrine cells and glands, represents the most common inheritable disease among Caucasian populations worldwide [1][2]. Considering the effects in the lung, CF is characterized by both patho-physiologic changes in function and pathologic alteration of morphology.

2. In clinical practice, spirometry serves to perform different lung function tests (LFTs) in CF patients. LFTs provide quantifiable test results that allow for both a cross-sectional assessment of the patient's lung function - compared to, e.g., the general population [3] - and a longitudinal assessment - e.g., demonstrating intrapersonal short-term changes associated with infectious exacerbation of CF, success of certain therapeutic measures, or long-term changes in the course of the disease that determine changes of medical interventions (pharmaceutical or physiotherapeutic). As technical equipment is widely available, easy to apply and to maintain, and LFTs are considered generally harmless in nature, spirometric LFTs are frequently applied in CF patients.

3. Using radiological imaging, several approaches for assessment of lung morphology can be taken: conventional chest radiography (CR), computed tomography (CT) and multi-detector-row CT (MDCT), and even MRI. Although the latter is being considered to be the least harmful procedure, the current lack of generally available lung imaging protocols for MRI and difficulties in interpretation due to inconsistent display of peripheral lung structures still result in inferiority to X-ray-based radiological imaging.

   The superiority of CT over CR regarding the demonstration of normal and pathologic lung structures comes at the price of increased radiation exposure.

   As CF patients require clinical lung imaging regularly and repetitively from an early age on, radiation dose accumulation is of great concern. Two different approaches to depicting lung morphology with high spatial resolution at reasonable radiation exposure (ALARA principle) include

   - high-resolution CT (HRCT), with the acquisition of individual, incremental CT slices of 1-1.5 mm in width every 10-15 mm (i.e. leaving gaps uncovered by imaging), and

   - low-dose MDCT, with coverage of the entire lung volume with a decreased tube current-time product, profiting from the already high inherent contrast between air spaces and soft tissue density matter within the lung [4].
4. Brody and co-workers [1] applied and validated a complex weighted scoring system for CF-related pathologic lung morphology (Table 1), offering the possibility to express structural alterations as a quantitative result.

Brody and co-workers [1] based their study on HRCT scans obtained in both inspiration and expiration in children of 6-10 years of age with a clinical diagnosis of CF. It demonstrated a modest but significant correlation between lung morphology scoring and spirometric LFTs, particularly including forced expiratory volume in one second (FEV1).

5. Examination conditions between children and adults may vary due to differences in patient compliance, lung maturation and the airspace/stroma ratio. The Brody score assesses pathologic lung morphology in HRCT images on an equally weighed per-lung-lobe basis with equal weighting for each single lobe, while counting the lingula as an individual lobe.

The Brody score has demonstrated moderate correlations with different lung function tests in our previous study of adult CF patients [5].

According to the suggestion by Brody and co-workers [1], we weighed all individual lung lobes equally at morphologic scoring.

We hypothesized that there was no significant difference in both lung morphology and correlation with lung function tests (LFTs) between upper and middle lung lobes (ULL + MLL) versus lower lung lobes (LLL) in adult CF-patients.
Table 1: The Brody Scoring System according to [1]

© Department of Clinical Radiology, University of Munich - Munich/DE
Methods and Materials

Patients

Adult patients over the age of 18 years with a clinical diagnosis of CF were identified in the clinical and radiology information systems. CF patients who underwent both spirometric LFTs and low-dose MDCT of the chest in our institution within three days of each other between January, 2002, and March, 2011, were included in the analysis (n=81, 36 female, 45 male, age 31+/−8 years).

MDCT Protocol

Unenhanced MDCT of the chest was obtained in inspiration only, at a tube voltage of 120 KVp, with the lowest technically achievable tube current that would still yield diagnostic images.

Examinations performed until January, 2007, applied a 4-channel MDCT scanner, at 35 mA tube current, 0.5 s rotation time, 4x1 mm collimation, 1.75 pitch, 10 mAs effective tube current-time product per slice and 1.3 mm effective slice thickness. The protocol resulted in an average effective dose of 0.50 mSv for an adult female patient of average height and weight [2].

Examinations from February 2007 on were performed on a 64-channel MDCT scanner, at 35 mA tube current, 0.5 s rotation time, 64x0.5 mm collimation, 1.173pitch, 15 mAs effective tube current-time product per slice and 0.625 mm effective slice thickness.

MDCT images were reformatted with 3 mm slice thickness in 3 orthogonal planes and additional images of 1.0 to 1.5 mm in at least one plane and stored in an electronic picture archiving and communication system (PACS).

MDCT Evaluation

MDCT images were displayed on 1k-PACS monitors with one image per screen, window 1,600 HU and level -600 HU (lung window). Evaluation was primarily based on axial and coronal images. In cases where assigning findings to particular lung lobes was not possible, sagittal images were used additionally. All MDCT scans were evaluated by an attending radiologist with 10 years of post-residency clinical experience in chest radiology, including formal evaluation of chest scans in CF patients based on scoring systems. We applied the scoring system according to Brody et al. [1]: it allows for systematic assessment of presence, distribution, and extent of the following CF-specific alterations for each lobe of the lung, central and peripheral, regarding the lingula as the left middle lobe equivalent: bronchiectasis, mucous plugging, peribronchial thickening, parenchymal opacity, and hyperinflation.
Subscores and total score ("Brody score") are expressed numerically, ranging from 0 to 207 (possible maximum), at increments of 0.25. The Brody score increases with increasing CF-related lung structure pathology (Table 1).

In contrast to the study by Brody et al. [1], however, both parenchymal opacity and hyperinflation were assessed in inspiration only.

**Spirometry and Lung Function Tests**

Spirometry was performed according to standardized European guidelines [3]. At least one full LFT test cycle was completed per patient. Results were electronically calculated, documented, and stored by the spirometry system. Predicted values for the different LFTs referred to the respective standard tables of the European Coal and Steel Community (ECSC) [3].

**Correlation of MDCT and Spirometry Findings**

Brody scores and respective subscores for bronchiectasis, mucous plugging, peribronchial thickening, parenchymal opacity, and hyperinflation were compared between ULL+MLL and LLLs (with double-scores for LLL; two-tailed Student's-t-test, p<0.05) and Pearson-correlated with measured-to-predicted (mp) values for 1-second-forced-expiratory-volume (mpFEV1) and forced-vital-capacity (mpFVC), according to the respective standard tables of the European Coal and Steel Community (ECSC) [3].
Table 1: The Brody Scoring System according to [1]

© Department of Clinical Radiology, University of Munich - Munich/DE
Results

Brody scores, bronchiectasis-subscores, mucous-plugging-subscores, and peribronchial-thickening-subscores (Table 1) were higher for ULL+MLL versus LLL (doubled). However, parenchymal-opacity-scores and hyperinflation-scores were similar (Table 2).

Figure 1 shows a Bland-Altman-plot of the Brody overall score for both groups.

Values along the x-axis represent both each patient's individual Brody score for the entire lung and the overall distribution of Brody scores among our patients.

Values along the y-axis represent the respective differences between the Brody score for (ULL+MLL) x 1.5 and the Brody score for the entire lung (blue diamonds), and the Brody score for LLL tripled and the Brody score for the entire lung (red squares), respectively. Y-values higher than zero therefore mark results morphologically worse in relation to the entire lung, while y-values smaller than zero represent results better in relation to the entire lung.

In a minority of patients, affection of the LLL was equal or worse than affection of the ULL and MLL (Figure 2).

However, the majority of our patients showed results typical of CF-induced pathologic lung morphology, i.e. a higher affection of upper lung areas (blue trendline in Figure 1), and a lower affection of the lower lung areas (red trendline in Figure 1) (Figure 3).

Pearson-correlation coefficients between LFTs and Brody-scores and different subscores, respectively, were higher for LLL than for ULL+MLL. For the Brody score and the subscores for bronchiectasis, mucous plugging and peribronchial thickening, respectively, LFT correlations were higher for the LLL than for ULL+MLL or the entire lung, respectively (Figures 4 and 5).
### Table 1: The Brody Scoring System according to [1]

© Department of Clinical Radiology, University of Munich - Munich/DE
Table 2: Differences between upper and middle lung lobes (ULL + MLL, and lower lung lobes (LLL), respectively, in results of the Brody score and its different subscores in adult patients with CF-related lung disease

© Department of Clinical Radiology, University of Munich - Munich/DE

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean, +/- SD (ULL+MLL)</th>
<th>Mean, +/- SD (LLL x 2)</th>
<th>Two-sided t-test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brody overall score</td>
<td>53.4 +/- 25.5</td>
<td>45.0 +/- 27.3</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>24.0 +/- 11.6</td>
<td>20.2 +/- 12.4</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Mucous plugging</td>
<td>8.3 +/- 5.0</td>
<td>7.2 +/- 5.0</td>
<td>p = 0.008</td>
</tr>
<tr>
<td>Peribronchial thickening</td>
<td>15.9 +/- 8.8</td>
<td>12.3 +/- 8.4</td>
<td>p &lt; 0.001</td>
</tr>
<tr>
<td>Parenchymal opacity</td>
<td>2.7 +/- 3.0</td>
<td>2.4 +/- 3.6</td>
<td>p = 0.2834</td>
</tr>
<tr>
<td>Hyperinflation</td>
<td>2.4 +/- 2.8</td>
<td>2.9 +/- 3.2</td>
<td>p = 0.0968</td>
</tr>
</tbody>
</table>

Fig. 1: Bland-Altman-plot of the Brody overall score for both groups. Values along the x-axis represent both each patient's individual Brody score for the entire lung and the overall distribution of Brody scores among our patients. Values along the y-axis represent
the respective differences between the Brody score for (ULL+MLL) x 1.5 and the Brody score for the entire lung (blue diamonds), and the Brody score for LLL tripled and the Brody score for the entire lung (red squares), respectively. Y-values higher than zero therefore mark results morphologically worse in relation to the entire lung, while y-values smaller than zero represent results better in relation to the entire lung.

© Department of Clinical Radiology, University of Munich - Munich/DE

**Fig. 2:** In a minority of patients, affection of the LLL was equal or worse than affection of the ULL and MLL, as demonstrated in this patient's low-dose MDCT of the chest with images displayed showing lung levels 5 cm above (2A), at (2B), 5 cm below (2C), and 10 cm below (2D) the tracheal carina, respectively.

© Department of Clinical Radiology, University of Munich - Munich/DE
Fig. 3: The majority of our patients showed results typical of CF-induced pathologic lung morphology, i.e. a higher affection of upper lung areas, and a lower affection of the lower lung areas, as demonstrated in this patient's low-dose MDCT of the chest with images displayed showing lung levels 5 cm above (3A), at (3B), 5 cm below (3C), and 10 cm below (3D) the tracheal carina, respectively.

© Department of Clinical Radiology, University of Munich - Munich/DE
Fig. 4: Pearson correlations of the Brody score and its different subscores with the mean-to-predicted (mp) values for the forced vital capacity (FVC) of the lung in adult patients with CF-related lung disease. Correlation coefficients are highest for the lower lung lobes when correlating mpFVC with the Brody score, the bronchiectasis score, the mucous plugging score, and the peribronchial thickening score, respectively.

© Department of Clinical Radiology, University of Munich - Munich/DE
Fig. 5: Pearson correlations of the Brody score and its different subscores with the mean-to-predicted (mp) values for the forced expiratory volume in one second (FEV1) of the lung in adult patients with CF-related lung disease. Correlation coefficients are highest for the lower lung lobes when correlating mpFVC with the Brody score, the bronchiectasis score, the mucous plugging score, and the peribronchial thickening score, respectively.

© Department of Clinical Radiology, University of Munich - Munich/DE
Conclusion

In applying the Brody scoring system for HRCT in adult patients with CF, we corroborated previously accepted knowledge that the upper and middle lung lobes (ULL+MLL) are usually more seriously affected by CF-related morphologic change than the lower lung lobes (LLL).

However, while Brody and co-workers [1] demonstrated moderate correlations between the Brody score and different lung function tests (LFTs) in children aged 6-10 years affected with CF, our results imply that the uneven distribution of CF-induced lung disease between the upper and middle lung lobes on the one hand and the lower lung lobes on the other has some bearing on lung function.

It appears that lower-lung-lobe morphology is more closely correlated with both mpFEV1 and mpFVC than upper-and-middle-lung-lobe morphology in adult CF patients.

This in turn implies that for an adult CF patient affection of the lower lung lobes with CF-related lung disease is of particular importance for lung function.
Table 1: The Brody Scoring System according to [1]

© Department of Clinical Radiology, University of Munich - Munich/DE
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean, +/- SD (ULL+MLL)</th>
<th>Mean, +/- SD (LLL x 2)</th>
<th>Two-sided t-test p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brody overall score</td>
<td>53.4 +/- 25.5</td>
<td>45.0 +/- 27.3</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Bronchiectasis</td>
<td>24.0 +/- 11.6</td>
<td>20.2 +/- 12.4</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Mucous plugging</td>
<td>8.3 +/- 5.0</td>
<td>7.2 +/- 5.0</td>
<td>p=0.008</td>
</tr>
<tr>
<td>Peribronchial thickening</td>
<td>15.9 +/- 8.8</td>
<td>12.3 +/- 8.4</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Parenchymal opacity</td>
<td>2.7 +/- 3.0</td>
<td>2.4 +/- 3.6</td>
<td>p=0.2834</td>
</tr>
<tr>
<td>Hyperinflation</td>
<td>2.4 +/- 2.8</td>
<td>2.9 +/- 3.2</td>
<td>p=0.0968</td>
</tr>
</tbody>
</table>

**Table 2:** Differences between upper and middle lung lobes (ULL + MLL, and lower lung lobes (LLL), respectively, in results of the Brody score and its different subscores in adult patients with CF-related lung disease

© Department of Clinical Radiology, University of Munich - Munich/DE
References


Personal Information

Parts of the work presented herein are based on results of doctoral thesis work in preparation by Marco Schmitz at the Medical Faculty, Ludwig-Maximilian-University of Munich, Germany.