Pulmonary complications in adult patients with humoral primary immunodeficiencies: validation of a chest HRCT scoring system predicting the results of function tests

Poster No.: C-2500
Congress: ECR 2018
Type: Scientific Exhibit
Authors: E. Zanelli, L. Cereser, P. D'Angelo, M. De Carli, C. Zuiani, R. Girometti; Udine/IT
Keywords: Lung, Respiratory system, CT, Diagnostic procedure, Congenital
DOI: 10.1594/ecr2018/C-2500

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 is 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
Aims and objectives

BACKGROUND

Humoral Primary Immunodeficiencies (hPIDs) include various diseases characterized by impaired antibody production, related to both a molecular defect intrinsic to B cells or to a failure in interactions between B and T cells (1). This condition characteristically leads to recurrent, often severe, upper and lower respiratory tract infections, and to diffuse lung parenchymal diseases, such as "Granulomatous and Lymphocytic Interstitial Lung Disease" (GLILD). Selective IgA deficiency is the most frequent subtype, affecting about 1:700 individuals worldwide, and it is often asymptomatic (1,2) while common variable immunodeficiency disorders (CVID) is the most common symptomatic condition, with a prevalence of 1:25.000-1.50.000 subjects (3).

Thoracic complications manifest in about 60% of patients with hPIDs, and represent the leading causes of morbidity and mortality. Chest High-resolution Computed Tomography (HRCT) is the imaging technique of choice for detection, characterization and quantification of pulmonary abnormalities (PA), and for monitoring response to therapy (4-6). The most common PA detected on HRCT in hPIDs patients comprehend: non-infective airway disorders (i.e., bronchiectasis, airway wall thickening and air trapping), airways and pulmonary infective conditions (i.e., consolidations, ground glass opacities and tree-in-bud opacities), diffuse lung parenchymal diseases (i.e., GLILD and organising pneumonia), and thoracic neoplasms (i.e., lymphoma and thymoma) (6-9).

Currently there is no complete consensus on the selection of patients to be submitted to HRCT monitoring and on the timing of follow-up (6-8, 10).

To the best of our knowledge, various visual HRCT score systems have been established in order to quantify PA in hPIDs and to evaluate their correlation with pulmonary function test (PFT) results. Nevertheless, these score systems were applied only to paediatric hPIDs patients or adult subjects with CVID (4,10-14).

AIM

To validate a modified version of a dedicated HRCT visual scoring system (13,14) in order to predict PFT results in adult patients with different subtypes of h-PIDs, which demonstrated to be clinically and functionally similar, namely CVID and others conditions grouped in the collective term "CVID-like" (including selective IgA deficiency and IgG subclass deficiency).
Methods and materials

STUDY POPULATION

Our referring Ethical Committee approved the study. The need for informed consent was waived due to the retrospective design.

Between 2012 and 2016, 56 adult patients with diagnosis of hPIDs in accordance with European Society for Immunodeficiencies criteria (15) underwent HRCT and PFTs as baseline evaluation for morphological and functional pulmonary involvement, respectively. Four of 56 patients were excluded because of infectious respiratory disease at the time of HRCT or because PFT results were not available. Therefore, a total of 52 baseline HRCT of clinically stable patients (38 with CVID and 14 with CVID-like conditions, namely 11 with IgG subclass deficiency + 3 with selective IgA deficiency) were evaluated. Clinical and demographic data and PFT results were extracted from the patient records.

PULMONARY FUNCTION TESTS

All patients underwent PFTs performed within one month from the HRCT scan. Lung function was evaluated according to the criteria of the European Respiratory Society / American Thoracic Society task force (16). Pulmonary function variables included forced vital capacity (FVC), forced expiratory volume in one second (FEV1), vital capacity (VC), peak expiratory flow (PEF), and total lung capacity (TLC), measured with a spirometer (Vmax 29c; Sensor Medics, Yorba Linda, CA, USA). The severity of ventilatory defects was assessed using a six-point scale (absent, mild, moderate, moderately severe, severe, and very severe) (17). For the purposes of the present study, patients either with obstructive or restrictive defect were classified in two groups, the first one including patients with absent-to-mild defects (i.e., >70% of predicted values), the second one comprehensive of patients having moderate-to-severe defects (i.e., <70% of predicted values).

CT SCANNING PROTOCOL

All HRCT examinations were performed volumetrically with a 64-slices MDCT scanner (LightSpeed HD Discovery 750, General Electrics, Milwaukee, USA), with the patient in the supine position at suspended full inspiration. Scanning parameters are reported in Table 1. If inspiratory scans showed signs of airway disease, additional end-expiratory scan was acquired (32/52 patients).
IMAGING ANALYSIS

All HRCTs were reviewed by one experienced radiologist (8 year of experience in pulmonary imaging), without prior knowledge of patient history or lung function. Readings were performed twice, at 6-month distance. All scans were evaluated on a picture archiving and communication system workstation (Suitestensa Ebit srl, Esaote Group Company, Genoa, Italy), using mediastinal (width, 350 HU; level, 50 HU) and lung window (width, 1500 HU; level, -500 HU) settings. Post-processing techniques, including Multiplanar Reconstruction (MPR), Maximum Intensity Projection (MIP) and Minimum Intensity Projection (MinIP) were routinely used.

Airway and parenchymal-interstitial PA were defined according to the Fleischner Society glossary (18). Applying a modified version of a well-established HRCT visual scoring system (13), the reader scored for each pulmonary lobe the extent and severity of both airway and parenchymal-interstitial PA, as resumed in Table 2 and Table 3. Two composite scores were assessed for all findings and were normalized to a 0-100% scale, the first one including all airway scores ($A$-score = Bronchiectasis score + Airway wall thickening score + Mucus plugging score + Tree-in-bud score and Air trapping score), and the second one including all parenchymal-interstitial scores ($PI$-score = Consolidation / Ground glass opacities score + Septal thickening / Linear opacities score + Parenchymal nodules score + Bullae / Cysts score).

We modified the cited original scoring system by including the score referable to Bullae / Cysts in the $PI$-score (since they are common in adult population). Moreover, when expiratory scan was not available, we adjusted the normalization of $A$-score to the absence of the Air trapping score ($A$-score = Bronchiectasis score + Wall-thickening score + Mucus plugging score * 100/300, instead of * 100/400).

DATA ANALYSIS

Receiver operating characteristic (ROC) analysis was performed to determine the accuracy of $A$-score and $PI$-score in predicting moderate-to-severe obstructive or restrictive defects on PFTs, respectively. Intra-reader agreement was tested using Cohen's kappa statistic. All analyses were performed with a commercially available software (MedCalc version 12.5.0.0, MariaKerke, Belgium). The # level was set 0.05.
**Table 1:** HRCT protocol in our Institution, with a 64-slice multidetector CT scanner.

© Institute of Radiology, University Hospital of Udine - Udine/IT

© Institute of Radiology, University Hospital of Udine - Udine/IT
<table>
<thead>
<tr>
<th>PARENCHYMAL / INTERSTITIAL ABNORMALITIES</th>
<th>SCORES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
</tr>
<tr>
<td>Consolidation – extent</td>
<td>Absent</td>
</tr>
<tr>
<td>Ground-glass opacity – extent</td>
<td>Absent</td>
</tr>
<tr>
<td>Nodules – number</td>
<td>Absent</td>
</tr>
<tr>
<td>Septal thickening / linear and/or irregular opacities – extent</td>
<td>Absent</td>
</tr>
<tr>
<td>Bullae / cyst – extent</td>
<td>Absent</td>
</tr>
</tbody>
</table>

Notes: values/numbers refer to the volume of the interested lobe and they are calculated for each lobe (includ lingula).


© Institute of Radiology, University Hospital of Udine - Udine/IT
Results

We report the results of the reading session with highest overall accuracy.

A-score showed an area under the curve (AUC), sensitivity and specificity for moderate-to-severe defects on PFT of 0.854 (95% CI 0.725-0.938), 88.9%, and 80.5%, with threshold value of 12.5. Patients with A-score # 12.5 had a significantly higher extension and severity score for almost all airway PA compared to patients with lower A-score (p<0.05) (Table 4).

PI-score showed an area under the curve (AUC), sensitivity and specificity for moderate-to-severe defects on PFT of 0.833 (95% CI 0.701-0.924), 100% and 77.8%, with threshold value of 9.7. The prevalence of almost all parenchymal-interstitial PA was significantly greater in the PI-score score group # 9.7 compared to patients with lower PI-score (Table 5).

As further evidence of the significance of our results we observed that intra-reader agreement was excellent for both A-score (k=0.830) and PI-score (k=0.915), with no significant changes between readings (p>0.05).

Example cases taken from our series are presented in Figures 1 and 2.
### Table 4: Prevalence of airway abnormalities and of their severity / extension scores according to A-score values below or above the threshold value (12.5).

<table>
<thead>
<tr>
<th>Condition</th>
<th>A-Score ≥12.5 (n=17)</th>
<th>A-Score &lt;12.5 (n=35)</th>
<th>p-value (chi square)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRONCHIECTASIS ²</td>
<td>88.2% (15/17)</td>
<td>74.3% (26/35)</td>
<td>NS</td>
</tr>
<tr>
<td>SEVERITY SCORE&gt;1 ²</td>
<td>22.2% (20/90)</td>
<td>2.6% (4/156)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>EXTENSION SCORE&gt;1 ²</td>
<td>26.7% (24/90)</td>
<td>0% (0/156)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>AIRWAY WALL THICKENING ²</td>
<td>88.2% (15/17)</td>
<td>62.8% (22/35)</td>
<td>NS</td>
</tr>
<tr>
<td>SEVERITY SCORE&gt;1 ²</td>
<td>60% (54/90)</td>
<td>2.3% (3/132)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>EXTENSION SCORE&gt;1 ²</td>
<td>60% (54/90)</td>
<td>14.4% (19/132)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>TREE IN BUD ²</td>
<td>47% (8/17)</td>
<td>5.7% (2/35)</td>
<td>p = 0.0015</td>
</tr>
<tr>
<td>EXTENSION SCORE&gt;1 ²</td>
<td>18.7% (9/48)</td>
<td>0% (0/12)</td>
<td>NS</td>
</tr>
<tr>
<td>MUCOID PLUGS ²</td>
<td>58.8% (10/17)</td>
<td>37.1% (13/35)</td>
<td>NS</td>
</tr>
<tr>
<td>EXTENSION SCORE&gt;1 ²</td>
<td>36.7% (22/60)</td>
<td>2.6% (2/78)</td>
<td>p &lt; 0.0001</td>
</tr>
<tr>
<td>AIR TRAPPING ⁶</td>
<td>81.8% (9/11)</td>
<td>33.3% (7/21)</td>
<td>p = 0.0255</td>
</tr>
<tr>
<td>EXTENSION SCORE&gt;1 ²</td>
<td>72.2% (39/54)</td>
<td>28.6% (12/42)</td>
<td>p = 0.0002</td>
</tr>
</tbody>
</table>

¹ percentage (number of positive patients/number all patients); ² percentage (number of lobes with max score/number of pathologic lobes)
<table>
<thead>
<tr>
<th></th>
<th>PI-score ≥9.7 (n=18)</th>
<th>PI-score &lt;9.7 (n=34)</th>
<th>p-value (chi square)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CONSOLIDATION</td>
<td>55.5% (10/18)</td>
<td>11.8% (4/34)</td>
<td>p = 0.0023</td>
</tr>
<tr>
<td>EXTENSION SCORE&gt;1##</td>
<td>18.3% (11/60)</td>
<td>4.2% (1/24)</td>
<td>NS</td>
</tr>
<tr>
<td>GROUND GLASS OPACITY#</td>
<td>61.1% (11/18)</td>
<td>5.9% (2/34)</td>
<td>p = 0.0001</td>
</tr>
<tr>
<td>EXTENSION SCORE&gt;1##</td>
<td>31.8% (21/66)</td>
<td>0% (0/12)</td>
<td>NS</td>
</tr>
<tr>
<td>NODULES#</td>
<td>77.8% (14/18)</td>
<td>32.3% (11/34)</td>
<td>p =0.0046</td>
</tr>
<tr>
<td>EXTENSION SCORE&gt;1##</td>
<td>38.1% (32/84)</td>
<td>4.5% (3/66)</td>
<td>p&lt;0.0001</td>
</tr>
<tr>
<td>SEPTAL THICKENING/LINEAR OPACITIES#</td>
<td>55.6% (10/18)</td>
<td>5.9% (2/34)</td>
<td>p=0.0002</td>
</tr>
<tr>
<td>EXTENSION SCORE&gt;1##</td>
<td>20% (12/60)</td>
<td>8.3% (1/12)</td>
<td>NS</td>
</tr>
<tr>
<td>BULLAE /CYST#</td>
<td>22.2% (4/18)</td>
<td>2.9% (1/34)</td>
<td>NS</td>
</tr>
<tr>
<td>EXTENSION SCORE&gt;1##</td>
<td>25% (6/24)</td>
<td>16.7% (1/6)</td>
<td>NS</td>
</tr>
</tbody>
</table>

# percentage (number of positive patients/number all patients); ## percentage (number of lobes with max score/number of pathologic lobes)

**Table 5:** Prevalence of parenchymal / interstitial abnormalities and of their extension scores according to PI-score values below or above the threshold value (9.7).

© Institute of Radiology, University Hospital of Udine - Udine/IT
**Fig. 1:** Airway abnormalities in a 58-year-old woman with IgG subclass deficiency. (a, b) HRCT images show mild bronchiecstasy in the upper right lobe and tree-in-bud opacities in the upper left lobe. An A-score of 7.3 was assigned, lower than the threshold value (12.5), in accordance with no obstructive defects at PFTs.

© Institute of Radiology, University Hospital of Udine - Udine/IT
**Fig. 2:** Parenchymal-interstitial abnormalities in a 40-year-old woman with CVID. (a, b, c) HRCT images show septal thickening and linear opacities, patchy ground glass opacities, nodules, and mild bronchiectasis in both lower lobes. A PI-score of 48.8 was assigned, much higher than the threshold value (9.7), in accordance with a moderate restrictive defect at PFTs. A final diagnosis of GLILD was made by mean of biopsy.

© Institute of Radiology, University Hospital of Udine - Udine/IT
Conclusion

In conclusion, the proposed modified HRCT scoring system is highly accurate in predicting PFT results when applied to adult hPIDs patients at the time of baseline evaluation. Further studies on follow-up patients might support our results, in order to select patients at higher risk of progression of respiratory disease and to adapt the timing of functional and HRCT monitoring accordingly.
Personal information

Elisa Zanelli, MD
Institute of Radiology, Departments of Medical and Biological Sciences
University of Udine
33100 UDINE
ITALY
elisazanelli@hotmail.it
References


