Early View

Research letter

Impact of chest computed tomography scan on the management of patients with chronic cough

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This manuscript has recently been accepted for publication in the ERJ Open Research. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJOR online.

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Impact of Chest Computed Tomography Scan on the Management of Patients with Chronic Cough

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Disclosure of interest: None for all authors
Take home message: one quarter of CC patients have abnormal chest CT-scan but its on CC management is limited. Chest CT-scan should not be routinely performed in CC particularly in patients with dry cough.
To the Editor,

Chronic cough (CC), defined as cough lasting for more than 8 weeks, is a common reason for consultation in general and respiratory medicine. CC is a complex entity with potential multiple causes. CC management has been described in American and European guidelines\(^1\)\(^2\). Lung function tests and chest X-ray are mandatory as first-line diagnostic work-up in CC. However, the usefulness of chest computed tomography (CT) scan in CC management has not been clearly identified. According to European guidelines, clinicians should not routinely perform a chest CT scan in CC patients presenting normal chest X-ray and physical examination\(^1\). On the other hand, considering American guidelines, chest CT-scan has to be taken into account in patients with normal chest X-ray and after ruling out common causes of CC\(^2\). However, no criteria regarding chest CT scan in CC patients have been clearly established. In order to bring data on chest CT scan in CC management, our study aims to determine the impact of chest CT-scan on the management of patients with CC.

A retrospective observational study was carried out in the Department of Respiratory Medicine at Toulouse University Hospital Center for research from 2002 to 2018. Inclusion criteria were 1) patients aged of 16 years old or older, 2) chronic cough was the main reason for consulting, 3) both normal chest X-Ray and physical examination of the lungs and 4) chest CT-scan was performed as investigation of CC. Exclusion criteria were 1) No smoking cessation or no discontinuation of drugs being drug-induced cough within the last 4 weeks prior the inclusion. 2) Underlying conditions associated with a history of abnormal CT scan. Patients’ characteristics have been previously published\(^3\). Productive cough was defined as cough with a production of more than 100 mL of sputum per day. As a consequence, dry cough was defined as the no production of sputum over than 100 ml per day. The use of patients’ medical data was approved by the Institutional Review Board of the French Society for Respiratory Medicine (CEPRO 2018-036).
CC patients were divided into 2 groups according to normal or abnormal chest CT-scan. Abnormalities were determined according to an established consensus by two clinicians blinded to clinical and functional data. The Fleischner Society Glossary was used for the definition of normal chest X-Ray and chest CT-scan⁴. A nodule was considered benign if a biopsy rule out a malignant proliferation or if they disappeared or were stable during a minimal follow-up of 2 years. In order to assess the impact of chest CT-scan, three outcomes were considered: an “overall impact” (if investigations and/or treatments regardless the underlying lung disease were initiated according to chest CT-scan), an “impact on cough management” (if investigations and/or treatments were initiated for cough according to chest CT-scan) and an “impact on cough” (if a treatment was initiated thanks to chest CT-scan and led to cough improvement). All CT-scan patterns were included in the group “overall impact”, even if there was no impact on cough. Treatment response was determined as subjective improvement of cough according to a consensus of two cough specialists based on data from medical records. The outcomes were determined by two other clinicians blinded to the chest CT scan.

Regarding statistical analysis, continuous data and categorical data were expressed as median and interquartile range, and as number of patients and/or percentages, respectively. Univariate and multivariate analysis were performed according to logistic regression (abnormal chest CT scan and overall impact were the dependent variables). Logistic regression is classically used to predict the categorical dependent variable with the help of independent variables. Statistical significance was defined as a p-value <0.05. Negative predictive values of chest X-ray were calculated according to the formula True Negatives/(True negatives+False negatives).

A total of 653 CC patients were included in the study. Among them, a chest CT scan was performed in 595 patients, 71.6% were females and median age was 61 [51-68] years old. A total of 145 out of 595 (24.4%) showed abnormalities on chest CT scans. The most frequent
patterns were as follows: bronchiectasis (46.9%), nodules (35.2% of which only 3.9% were malignant), bronchial wall thickening (26.2%), and interstitial lung diseases (ILD) (20.7%).

Among those 595 CC patients, an impact of chest CT-scan was identified on the overall management in 30 (5.0%) patients, on CC management in 19 (3.0%) and on the initiation of drugs leading CC improvement in 9 (1.5%). Overall management consisted of physiotherapy (n=4) and azithromycin (n=12) for bronchiectasis, ILD management (n=4), nodule biopsy or follow-up (n=2), adenocarcinoma management (n=1) and investigations for diaphragmatic dysfunction (n=2), pleural plaques (n=2), aortic calcification (n=1), oesophageal leymomyoma (n=1) and bronchiectasis with recurrent infection (n=1). In 9 patients with CC improvement, 7 had bronchiectasis and among them one patient had cough improvement with physiotherapy and 6 with azithromycin. The specific management of each patient with ILD (hypersensitivity pneumonia) and adenocarcinoma led to cough improvement. Given those results, chest X-ray has an NPV of 75.6%, 95.0%, 96.8%, 98.5% for abnormal chest CT scan, overall impact, impact on cough management and impact on cough, respectively.

The risk of presenting an abnormal chest CT scan was lower in patients aged of less than 40 years or presenting dry cough (OR 0.30, CI95% 0.10-0.71, p=0.013 and OR 0.33 CI95% 0.21-0.52, p<0.0001) (Table 1). The combination between patients being aged less than 40 years and those presenting dry cough lowered the risk of having abnormal chest CT scan (OR 0.28, CI95% 0.08-0.71, p=0.017). After multivariate analysis, the risk of presenting an abnormal chest CT scan remains statistically significant only for dry cough (OR 0.34 CI95% 0.21-0.55, p<0.0001). Regarding the risk of overall management according to chest CT scan in patients with CC, no statistical difference was observed. The number of patients who present an impact on CC management and an improvement of cough according to chest CT scan was too low to analyse the risk factors regarding these two outcomes.
In our study, the proportion of patients with abnormal chest CT scan represents approximately one quarter of CC patients with normal chest X-ray. The role of chest CT scan in CC patients has been poorly studied in literature. Indeed, a retrospective study specifically assessed chest CT scan in 59 CC patients and showed that abnormalities relevant for CC appear on chest CT scan in 36%⁵. In another study, chest CT scan found abnormalities in 59% of CC patients⁶.

The main difference between those studies and ours relies on the fact that we only included patients with normal physical exam and chest X-Ray. Interestingly, in our study, only 30 (5.0%) CC patients underwent overall investigations or treatments according to abnormalities present on CT scan. Moreover, for the first time, we found that chest CT scan had an impact on cough management and cough improvement in only 3.0% and 1.5%, respectively. The main pattern leading to investigations or treatments in CC were bronchiectasis with initiation of physiotherapy or azithromycin. Azithromycin does not seem to be effective in one study on chronic cough⁷ and is not recommended in CC patients apart from those who have chronic bronchitis¹. However, according to our study, a decrease in cough has been observed in some patients with bronchiectasis⁸,⁹. Therefore, further studies on the effect of azithromycin in CC patients with bronchiectasis should be warranted. We have also found that chest CT scan may not be helpful in CC patients with dry cough.

This study shows limitations mainly driven by its retrospective design. Most of the nodules did not lead to investigations due to their benign aspect. Consequently, diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) which associates nodules, mosaic lung pattern and chronic cough could have been misdiagnosed.

In conclusion, according to our study, one quarter of CC patients have abnormal chest CT-scan; however its impact on overall management or CC management or the initiation of drugs leading to CC improvement seems to be limited. Chest CT-scan should not be routinely performed particularly in patients with dry cough.
Table 1: Univariate and multivariate logistic regression analyses of risk variables for abnormal chest CT scan and overall impact in patients with chronic cough. No patients aged less than 40 years had an overall impact of chest CT scan. For this reason, no statistical analysis has been made for this category of patients.

<table>
<thead>
<tr>
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<th>Abnormal chest CT scan</th>
<th>Overall impact</th>
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<tbody>
<tr>
<td>Number of patients</td>
<td>145/595 (24.4%)</td>
<td>30/595 (5.0%)</td>
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<tr>
<td></td>
<td>Univariate analysis</td>
<td>Multivariate analysis</td>
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<tr>
<td></td>
<td>OR</td>
<td>CI95%</td>
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<td>Age&lt;40 yo</td>
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<td>0.10-0.71</td>
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<td>Female</td>
<td>0.87</td>
<td>0.56-1.37</td>
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<td>Active- or former-smokers</td>
<td>1.39</td>
<td>0.90-2.13</td>
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<td>Cough duration ≤ 1 year</td>
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<td>0.48-1.23</td>
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<td>Dry cough</td>
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<tr>
<td>Nocturnal cough</td>
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<tr>
<td>Age&lt;40 yo and dry cough</td>
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<td>0.08-0.71</td>
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