



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

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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 radiography are mandatory as first-line diagnostic work-up in CC. However, the usefulness of chest computed tomography (CT) 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 radiography and physical examination [1]. On the other hand, considering the American guidelines, a chest CT scan has to be taken into account in patients with normal chest radiography 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 provide data on chest CT scans in CC management, our study aims to determine the impact of chest CT scans 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) CC was the main reason for the consultation; 3) both normal chest radiography and physical examination of the lungs; and 4) chest CT scan was performed as an investigation of CC. Exclusion criteria were: 1) no smoking cessation or no discontinuation of drugs causing drug-induced cough within the past 4 weeks prior the inclusion; and 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 production of more than 100 mL of sputum per day. Consequently, dry cough was defined as no production of sputum over the 100 mL per day threshold. 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 two 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 radiography and chest CT scan [4]. A nodule was considered benign if a biopsy ruled 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 the chest CT scan, three outcomes were considered: an "overall impact" (if investigations and/or treatments regardless the underlying lung disease were initiated according to the chest CT scan), an "impact on cough management" (if investigations and/or treatments were initiated for cough according to the chest CT scan), and an "impact on cough" (if a treatment was initiated thanks to the 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 the 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 (IQR), and as number of patients and/or percentages, respectively. Univariate and multivariate analyses were performed according to logistic regression (abnormal chest CT scan and overall



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A quarter of chronic cough (CC) patients have an abnormal chest CT scan but the effect of this on CC management is limited. Chest CT scan should not be routinely performed in CC, particularly in patients with dry cough. <https://bit.ly/3Bl3EeE>

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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 (NPVs) of chest radiography 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 (IQR) 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 the 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 nine (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 leiomyoma (n=1) and bronchiectasis with recurrent infection (n=1). In nine patients with CC improvement, seven had bronchiectasis and among them one patient had cough improvement with physiotherapy and six with azithromycin. The specific management of each patient with ILD (hypersensitivity pneumonia) and adenocarcinoma led to cough improvement. Given these results, chest radiography has an NPV of 75.6%, 95.0%, 96.8% and 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 <40 years or presenting with dry cough (OR 0.30, 95% CI 0.10–0.71, p=0.013 and OR 0.33 95% CI 0.21–0.52, p<0.0001) (table 1). The combination of patients being aged <40 years and presenting with dry cough lowered the risk of having an abnormal chest CT scan (OR 0.28, 95% CI 0.08–0.71, p=0.017). After multivariate analysis, the risk of presenting an abnormal chest CT scan remained statistically significant only for dry cough (OR 0.34 95% CI 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 an abnormal chest CT scan represents approximately one quarter of CC patients with normal chest radiography. The role of chest CT scan in CC patients has been poorly studied in the literature. A retrospective study specifically assessed chest CT scan in 59 CC patients and showed that abnormalities relevant for CC appear on the chest CT scan in 36% [5]. In another study, chest CT scan found abnormalities in 59% of CC patients [6]. The main difference between those studies

TABLE 1 Univariate and multivariate logistic regression analyses of risk variables for abnormal chest computed tomography (CT) scan and overall impact in patients with chronic cough

	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-value	OR	95% CI	p-value
Abnormal chest CT scan[#]						
Age <40 years	0.30	0.10–0.71	0.013	0.19	0.01–1.17	0.13
Female	0.87	0.56–1.37	0.55	0.84	0.52–1.38	0.49
Active or former smokers	1.39	0.90–2.13	0.13	1.34	0.85–2.1	0.21
Cough duration ≤1 year	0.77	0.48–1.23	0.26	0.83	0.51–1.37	0.45
Dry cough	0.33	0.21–0.52	<0.0001	0.34	0.21–0.55	<0.0001
Nocturnal cough	1.00	0.66–1.51	0.99	1.00	0.65–1.55	0.99
Age <40 years and dry cough	0.28	0.08–0.71	0.017	1.87	0.21–41.20	0.61
Overall impact[¶]						
Female	0.50	0.21–1.19	0.11	0.42	0.17–1.06	0.06
Active or former smokers	1.33	0.54–3.09	0.52	1.16	0.46–2.80	0.74
Cough duration ≤1 year	0.93	0.38–2.63	0.88	1.05	0.41–3.10	0.92
Dry cough	0.46	0.20–1.14	0.08	0.49	0.21–1.22	0.11
Nocturnal cough	1.54	0.65–3.88	0.34	1.57	0.66–4.01	0.32

No patients aged <40 years had an overall impact of chest CT scan. For this reason, no statistical analysis has been made for this category of patients. Bold font indicates statistical significance. [#]: number of patients was 145 out of 595 (24.4%); [¶]: number of patients was 30 out of 595 (5.0%).

and ours relies on the fact that we only included patients with a normal physical examination and chest radiography. Interestingly, in our study, only 30 (5.0%) CC patients underwent overall investigations or treatments according to abnormalities present on the 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% of patients, 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 CC [7] and is not recommended in CC patients apart from those who have chronic bronchitis [1]. However, according to our study, a decrease in cough has been observed in some patients with bronchiectasis [8, 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 with nodules, mosaic lung pattern and CC could have been misdiagnosed.

In conclusion, according to our study, one quarter of CC patients have an 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.

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References

- 1 Morice AH, Millqvist E, Bieksiene K, *et al.* ERS guidelines on the diagnosis and treatment of chronic cough in adults and children. *Eur Respir J* 2020; 55: 1901136.
- 2 Irwin RS, French CL, Chang AB, *et al.* Classification of cough as a symptom in adults and management algorithms: CHEST guideline and expert panel report. *Chest* 2018; 153: 196–209.
- 3 Descazeaux M, Brouquières D, Didier, A, *et al.* Obesity predicts treatment response to proton pump inhibitor therapy in patients with chronic cough. *Lung* 2020; 198: 441–448.
- 4 Hansell DM, Bankier AA, MacMahon H, *et al.* Fleischner Society: glossary of terms for thoracic imaging. *Radiology* 2008; 246: 697–722.
- 5 Truba O, Rybka A, Klimowicz K, *et al.* Is a normal chest radiograph sufficient to exclude pulmonary abnormalities potentially associated with chronic cough? *Adv Respir Med* 2018; 86: 113–120.
- 6 McGarvey LP, Heaney LG, MacMahon J. A retrospective survey of diagnosis and management of patients presenting with chronic cough to a general chest clinic. *Int J Clin Pract* 1998; 52: 158–161.
- 7 Hodgson D, Anderson J, Reynolds C, *et al.* The effects of azithromycin in treatment-resistant cough: a randomized, double-blind, placebo-controlled trial. *Chest* 2016; 149: 1052–1060.
- 8 Martin MJ, Lee H, Clayton C, *et al.* Idiopathic chronic productive cough and response to open-label macrolide therapy: An observational study. *Respirology* 2019; 24: 558–565.
- 9 Saiman L, Anstead M, Mayer-Hamblett N, *et al.* Effect of azithromycin on pulmonary function in patients with cystic fibrosis uninfected with *Pseudomonas aeruginosa*: a randomized controlled trial. *JAMA* 2010; 303: 1707–1715.