Phillipe Martins[1]

Avaliação por imagem dos Pacientes com Enfisema Pulmonar

Imaging Evaluation of Patients with COPD

RESUMO

A doença pulmonar obstrutiva crônica (DPOC) está entre uma das principais causas de morbidade e mortalidade ao longo do mundo. É definida como obstrução irreversível do fluxo aéreo, com apresentação heterogênea, podendo acometer as vias aéreas ou o parênquima pulmonar. Os pacientes com DPOC frequentemente apresentam outras comorbidades, que se correlacionam e modificam os seus prognósticos. A tomografia computadorizada de tórax se tornou o principal exame de imagem para avaliação do DPOC da forma mais completa, caracterizando os seus múltiplos fenótipos.

PALAVRAS-CHAVE

Tomografia computadorizada de tórax; Doença pulmonar obstrutiva crônica; Enfisema pulmonar; Via aérea; Pulmão.

ABSTRACT

Chronic obstructive pulmonary disease (COPD) is one of the leading causes of morbidity and mortality worldwide. It is defined by irreversible airflow obstruction and is a heterogeneous disease that affects the airways and/or the parenchyma. Comorbidities can often coexist with COPD, worsening the prognosis of both morbid conditions. These distinct aspects of COPD can be addressed through imaging, with computed tomography (CT) being the technique of choice for phenotype-driven characterization.

KEY WORDS

Chest computed tomography; Chronic obstructive pulmonary disease; Pulmonary emphysema; Airway; Lung.

[1] *Mestre em Radiologia - Membro do Colégio Brasileiro de Radiologia - Membro da Sociedade de Radiologia do Rio de Janeiro*

Rua Barão de Flamengo, 24, 101, CEP:22220-080, Flamengo, Rio de Janeiro, Rio de Janeiro, Brasil
Email: phillipe.martins19@gmail.com

ABBREVIATIONS

COPD: Chronic obstructive pulmonary disease
CT: Computed tomography
CXR: Chest x-ray
FEV1: Forced expiratory volume in 1 second
FVC: Forced vital capacity
GOLD: Global Initiative for Chronic Obstructive Lung Disease
HU: Hounsfield unit
PFT: Pulmonary function tests

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is defined by spirometric evidence of airflow obstruction and includes conditions such as emphysema, chronic bronchitis, and reversible or irreversible small airways obstruction[1]. It is a globally distributed condition, given that its primary causal factor is tobacco smoking, a habit in societies worldwide[2,3]. COPD has a prevalence of 11.7 %, leading to approximately three million deaths annually, including its complications[3]. COPD is the fourth leading cause of death in the United States[4]. According to the World Health Organization, COPD is projected to become the third leading cause of death worldwide by the year 2030[5].

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) is the most widely used international classification system for COPD patients. GOLD is subdivided into four grades based on the ratio of forced expiratory volume in 1 second (FEV1) to forced vital capacity (FVC) of less than 0.7 and the FEV1 predictive percentage[1,3]. The treatment goals are to reduce the progression of symptoms, alleviate acute decompensation and provide support, using Beta-2-agonist or antimuscarinic bronchodilators, inhaled corticosteroids, oxygen supplementation, antibiotics, and finally, lung reduction surgery or transplantation[6].

COPD is an insidious disease, with many years between the development of pulmonary function abnormalities and the onset of serious respiratory symptoms[7]. Respiratory symptoms are sometimes erroneously attributed to aging, higher body mass index and other diseases, leading to underrecognition and delayed diagnosis[8]. The two major pathophysiologic features of the COPD are emphysematous destruction of lung structure and morphofunctional airway disease. Pulmonary function tests (PFT) are used for the diagnosis and assessment of COPD, but PFT have limited value in measuring airway obstruction, especially in small airways that are predominantly affected before the onset of emphysema[9]. Furthermore, normal spirometry is now known not to imply an absence of lung or airway injury and patients with normal spirometry who have a history of chronic tobacco smoke exposure might have substantial airway and parenchymal disease detected by CT scan[10].

COPD is also associated with significant extrapulmonary multimorbidity, including cardiovascular, endocrine, and musculoskeletal system abnormalities, all of which impact the quality of life and prognosis of the patient. Additionally, COPD patients are at high risk for lung cancer[11].

Imaging modalities were classically performed primarily to assess lung morphology. However, with the advancement of knowledge about radiogenomics and COPD phenotypes associated with extrapulmonary manifestations, CT takes on a new challenge. The aim of this review is to summarize the current role of CT in the assessment of patients with COPD. Magnetic resonance imaging in COPD patients is beyond the scope of this article due to its limited availability on a large scale in low-resource countries, its high cost for use in research studies and requires validations through several multicenter randomized controlled trials.

IMAGING

Radiographic

Chest X-ray (CXR) has been used in the examination of patients with emphysema in the past. Signs of COPD were described, including the presence of air-filled bubbles, rectification and lowering of the diaphragm, focal reduction of pulmonary vasculature, and increased retrosternal space[2,3,12]. The only direct radiographic sign of emphysema is the presence of bullae[9].

Despite the low cost and widespread availability of CXR, the limiting drawbacks of radiography include low specificity, reduced sensitivity in assessing mild disease, substantial inter-observer variability in findings interpretation, and the inability to quantify the severity of emphysema[9].

Computed tomography

The growing availability of CT worldwide position it as the most precise imaging method compared to CXR for characterization of COPD[1]. Moreover, the enhanced resolution achieved with modern CT scanners with multiple rows of detectors allows for the thinnest sections possible, and imaging findings correlate well with anatomopathological findings[13,14].

CT is a well-recognized imaging approach for identification and quantification of emphysema and bronchial wall thickness, using a combination of visual and quantitative automatic methods. Importantly, the extension of emphysema and bronchial wall thickness are independent markers of the degree of airflow obstruction and the risk of exacerbation. Emphysema is also associated with an increased risk of all-cause mortality in COPD patients[1,15]. The spatial distribution of imaging findings serves as a crucial prognostic factor, with lower lobe emphysema indicating worse outcomes[15].

Simple unenhanced thin-section volumetric acquisition is recommended when utilizing chest CT for COPD patients[16]. CT scans should be evaluated with lung window settings (usually with window level – 700 UH and window width 1500 UH). Expiration acquisition is advisable and post-processing features should always be included, such as minimum intensity projection (MinIP) reconstruction, for better visualizations of subtle emphysema and other lower attenuation changes[1,9].

A Statement of the Fleischner Society for CT-Definable Subtypes of Chronic Obstructive Pulmonary Disease recommend a setting for scan parameters (table 1)[1].

Table 1. Standard CT parameters for evaluation of COPD

Parameter	Value
CT configuration	Multidetector row CT ≥ 16 detectors
Pitch	1 – 14
Colimattion	≤ 1 mm
Kilovolt peak	120
Effective milliampere second	40 – 200
Reconstruction algorithms	Smooth and sharp
Reconstruction section	0.625 – 1 mm

Modified to Fleischner Society1.

There is a visual phenotype CT classification system for stratifying COPD patients based on the predominance of imaging findings. Patients are classically categorized into emphysematous or airway disease predominant with substantial overlapping[1] (figure 1).

Pulmonary emphysema is identified by areas of low attenuation on CT, corresponding to abnormal permanent dilatation of the air spaces distal to the terminal bronchioles in the pathological specimens, accompanied by alveolar wall destruction[3,9,13]. The emphysematous group is classified into centrilobular, paraseptal and panlobular types based on a visual approach (figure 1).

The centrilobular form of emphysema (figure 1A) is the type most closely associated with tobacco and is upper lung predominant[9]. Centrilobular types are trace with minimal centrilobular

lucencies occupying < 0.5% of a lung zone; mild with scattered centrilobular lucencies involving 0.5 – 5% of a lung zone; moderate with many well-defined centrilobular lucencies occupying > 5% of any lung zone; confluent with coalescent centrilobular lucencies that compromise multiple secondary pulmonary lobules without distortion architecture; advanced destructive emphysema with panlobular lucencies, with hyperexpansion of secondary pulmonary lobules and distortion of pulmonary architecture. The panlobular pattern (figure 1B) is classically described in patients with alpha1-antitripsin deficiency that show lower lobe predominant lucencies involving generalized destruction of all acini. Paraseptal are subdivided into two groups, mild paraseptal emphysema and substantial paraseptal emphysema, the former exhibit small (≤ 1 cm), well-demarcated rounded juxtapleural lucencies aligned in a row along a pleural margin, while the latter exhibit large (> 1 cm) juxtapleural cyst-like lucencies or bullae, involving more than one lung apex aligned in a row along a pleural margin[1] (figure 1A).

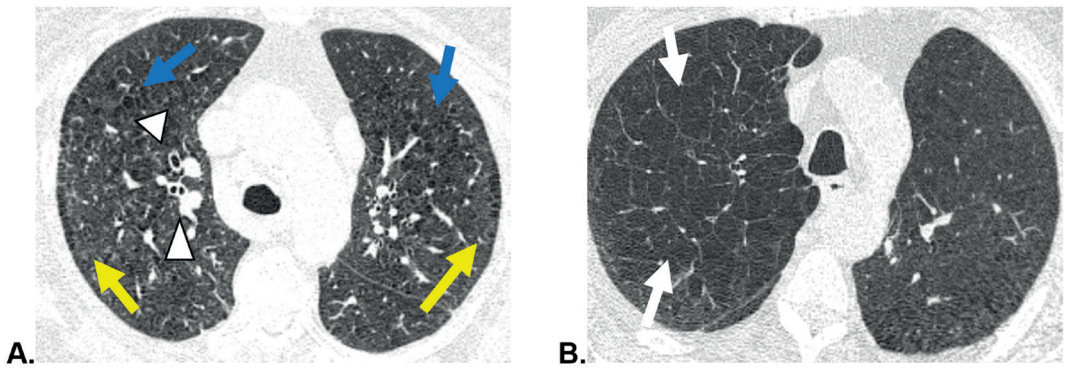

Figure 1. Subtypes of emphysema and bronchial wall thickness depicted in axial chest CT lung window images of different patients (A - B). In (A), bronchial wall thickness is indicated by the white arrowhead, while paraseptal (yellow arrow) and centrilobular (blue arrow) emphysema are also visible. Panlobular emphysema (white arrow) is shown in another patient (B). Courtesy Dr. Pedro Augusto Gama Carpentieri Primo.

Objective quantification of emphysema using CT involves automated tool employing mathematic approaches (also called metric) by computer assisted methods, measuring emphysema area at full inspiration image through threshold density value, histogram mapping, or overall CT density of the lung parenchyma. There is some divergence in the literature regarding the best Housfield unit (UH) density value to define emphysema, but most software utilize a value bellow -950 UH[13,17,18]. Quantitative CT analysis is useful in evaluating mild emphysema, as it may go unnoticed on visual analysis. Nevertheless, quantitative CT may present a false positive rate of emphysema and cannot describe emphysema distribution relative to secondary lobar[9].

Airway disease pattern types are bronchial disease and small airway disease. Bronchial disease reveals thickening of walls of segmental and subsegmental airways (figure 1A and 2C) but lacks consensus regarding technique and measuring cutoff value[3]. Small airway disease shows peripheral micronodular inflammatory centrilobular opacities, associated or not gas trapping[1]. Abnormal air trapping is a hallmark of small airway disease. Air trapping pathophysiology is understood by prolonged lung emptying due to bronchiolar narrowing and emphysematous destruction with loss of the elastic recoil force needed to drive air out of the lungs as an indirect sign of peripheral airway obstruction, predominantly seen on expiratory images[1,15].

Data suggests that small airways abnormality (e.g. air trapping) precedes emphysema development[3,8,19]. Resistance to flow through tubes is inversely related to the reduction in the radius rai-

sed to the fourth to fifth power[20]. A Mc Donough et al study with 78 patients with COPD indicates that narrowing and loss of terminal bronchioles precede emphysematous destruction in COPD[20]. Autopsy studies have showed that up to one-third of the lung can be destroyed by emphysema before respiratory function becomes impaired[9].

Respiratory symptoms typically precede airflow limitation. Furthermore, patients without spirometry abnormalities may demonstrate emphysema, thickening of airway walls and air entrapment[3]. Substantial heterogeneity exists among patients with COPD with respect to clinical presentation, physiological characteristics, imaging characteristics, response to therapy, disease progression, and, ultimately, survival[21]. Thus, Chest CT has the potential to identify early disease in individuals without airflow obstruction[7,8].

Additional visual features on CT include trachea abnormalities and cylindrical bronchiectasis. The trachea may adopt a characteristic morphology in CT exams such as outpouching/diverticula, tracheobronchomalacia, and the trachea "in sabre", which increases anteroposterior diameter and shorten transverse diameter, but is not a pathognomonic sign[3].

The classical bronchiectasis definition is a dilated bronchial lumen relative to the adjacent artery, lack of bronchial tapering, or the presence of bronchi within 1 cm of the pleural surface. Of note, bronchiectasis is associated with more severe airflow obstruction and with hospital admission for exacerbation[1].

COPD patients experience exacerbations during the natural course of disease that worsen prognostication. One of the causes of exacerbation is infectious agents and viral is more common. Of note, therapy with corticosteroid inhalator is associated with increased risk of infection occurrence, higher glucose level and osteopenia. CT is a good option in the setting of COPD exacerbation wherever it shows consolidation or ground glass infiltrates for infection[6].

COPD is not a single-organ disease[10]. While prevalence of COPD is higher in elderly people, multimorbidity is common in these individuals, being that tobacco is a common risk factor for both conditions. Multimorbidity influences mortality and hospitalizations regardless of the severity of airflow obstruction and deserves specific treatment[22]. Therefore, routine chest CT during follow up can aid in identifying comorbid conditions and certain CT features may serve as surrogate markers of comorbidity in COPD patients[4].

The cardiovascular system can be affected in COPD patients[1]. Cardiovascular disease has a greater prevalence in COPD, and the risk of cardiovascular events is heightened after an acute exacerbation of COPD. Coronary artery calcifications depicted on routine CT is considered evidence of high risk for coronary events and raised mortality in COPD. Even a non-ECG-gated CT done in clinical COPD context could assess coronary calcification besides ECG-gated CT. This important finding suggests that clinically available chest CT scans may provide information about heart disease risk that can then guide further cardiac evaluation and optimization of cardiac risk reduction strategies in patients with COPD[4,19] (figure 2A and B).

In regions with reduced ventilation, hypoxic vasoconstriction occurs leading to increased pulmonary arterial resistance and, secondary to adaptive processes, pulmonary hypertension, and right ventricular dysfunction. Pulmonary hypertension is an independent predictor of hospitalization and death in COPD patients. Pulmonary artery-aorta ratio of more than 1 was shown to be an independent risk factor for exacerbations in patients with COPD[3].

The incidence of vertebral fractures on chest CT is increased in individuals with COPD. Evaluation of the lung parenchyma and thoracic vertebrae on chest CT imaging may provide critical insight into osteoporosis risk, suggesting that chest CT imaging may facilitate selection of those high-risk patients that should be referred for further bone mineral density assessment, especially men with COPD not contemplated for general osteoporosis screening guidelines. Moreover, sarcopenia in COPD patients exhibits a high prevalence with a worse prognosis. Skeletal muscle area measured at CT has been associated with clinical outcomes and exacerbations in COPD patients[4,19].

In addition, lung cancer is also frequently observed in individuals with COPD and is a major cause of mortality. COPD patients have various risk factors for osteoporosis, such as low BMI, decreased activity, tobacco smoking, age, systemic inflammation, and use of corticosteroids. Annual low-dose CT scans are recommended for lung cancer screening in individuals with COPD due to smoking, following guidelines for the general population[22]. There is a growing demand for CT scans in middle-aged to elderly patients in lung cancer screening, including those with COPD. CT scans for lung cancer screening and COPD monitoring provide a valuable opportunity for risk stratification for comorbidities in these patients[4,23] (figure 2).

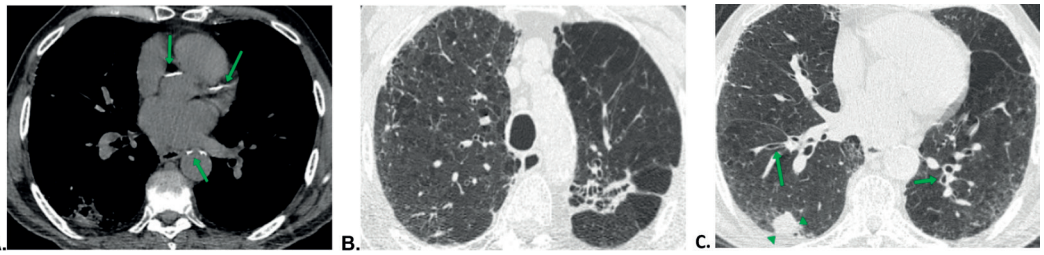

Figure 2. COPD patients with additional features in chest CT (A – C). In A and B, CT image of the same patient show emphysematous destruction of lung parenchyma and calcification in the aorta and coronary arteries. In C, CT image reveals a suspicious lung nodule (green arrowhead), as well as emphysema and bronchial wall thickness (green arrow). Courtesy Dr. Pedro Augusto Gama Carpentieri Primo.

CONCLUSION

COPD is a significant public health problem; however, it is also a common, preventable, and treatable disease. Extensive underdiagnosis and misdiagnosis result in patients receiving no treatment or incorrect treatment.

Given the heterogeneity of COPD with various patient phenotypes, variable symptom progression, and response rates to treatment, CT imaging aids physicians in making specific individual diagnoses that better characterize the patient's chronic lung disease profile. This facilitates a more personalized approach to medicine. Additionally, CT helps identify the presence of frequent comorbidities that may be overlooked in regular clinical practice, deserving proper treatment. There is a wealth of information that can be extracted from a single, full-inspiration CT image.

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