

Chronic obstructive pulmonary disease • 4: Imaging the lungs in patients with chronic obstructive pulmonary disease

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The role of chest radiography and computed tomography in the evaluation of pulmonary emphysema and chronic bronchitis is reviewed.

Chronic obstructive pulmonary disease (COPD) is defined in functional terms as a chronic slowly progressive disorder characterised by airways obstruction that does not change markedly over several months.¹ Chest radiography and computed tomography (CT) primarily assess lung morphology, so it is necessary to consider separately the role of imaging in the evaluation of the morphological abnormalities that cause airflow obstruction in smokers. These can be divided into emphysema and chronic bronchitis.

The aim of this review is to summarise the current role of imaging in the assessment of patients with COPD. The review will focus on chest radiography and CT for the evaluation of morphological abnormalities and on the potential role of CT for the evaluation of functional abnormalities.

PULMONARY EMPHYSEMA

Chest radiography

The radiographic appearances of emphysema reflect the presence of lung destruction, bulla formation, and overinflation. The only direct sign of emphysema on the radiograph is the presence of bullae. Because of the limited contrast resolution of the chest radiograph, focal areas of increased lucency due to the presence of lung destruction are difficult to identify. Indirect signs of lung destruction include focal absence of pulmonary vessels and reduction in vessel calibre with tapering towards the lung periphery. Abnormalities in the vascular pattern are highly suggestive of emphysema but have low sensitivity. In the classic study by Thurlbeck and Simon² these findings had a sensitivity of only 40% in detecting emphysema. Findings related to overinflation, particularly flattening of the diaphragm and increased retrosternal airspace, are more common but are not specific.³⁻⁴ In one investigation the combination of signs of hyperinflation and vascular alterations allowed the diagnosis of emphysema in 29 (97%) of 30 necropsy proven and symptomatic cases, but only eight (47%) of 17 necropsy proven but asymptomatic cases.⁵ The combination of signs of hyperinflation and vascular alterations on the radiograph allows diagnosis of emphysema in the majority of patients with moderate to severe disease.³⁻⁴

Limitations of chest radiography in the diagnosis of emphysema include low specificity, low sensitivity in the diagnosis of mild emphysema (Thurlbeck panel score of 25 or less),⁴ considerable interobserver disagreement in the interpretation of findings,⁴⁻⁶⁻⁷ and inability to quantify the severity of emphysema.

Computed tomography

Computed tomography (CT) is superior to chest radiography in demonstrating the presence, distribution, and extent of emphysema. Although in most cases emphysema is evident on conventional or spiral CT scans performed using 5–10 mm thick sections, it is more reliably assessed on high resolution CT (HRCT) images (1–2 mm thick sections reconstructed using an edge enhancing algorithm).⁸⁻⁹

Emphysema is characterised in HRCT scans by the presence of areas of abnormally low attenuation which can be easily contrasted with surrounding normal lung parenchyma.¹⁰⁻¹¹ Centrilobular emphysema of mild to moderate degree is characterised on HRCT scans by the presence of multiple small round areas of abnormally low attenuation, several millimetres in diameter, distributed throughout the lung, but usually having an upper lobe predominance. Areas of lucency often appear to be grouped near the centres of secondary pulmonary lobules.¹¹⁻¹³ Panlobular emphysema is characterised by uniform destruction of the pulmonary lobule leading to widespread areas of abnormally low attenuation.¹³⁻¹⁵ Panlobular emphysema usually involves mainly the lower lobes. Paraseptal emphysema is characterised by involvement of the distal part of the secondary lobule and is therefore seen adjacent to the interlobular septa and the visceral pleura.⁸⁻¹⁶

The accuracy of CT and HRCT scanning in the diagnosis and severity of emphysema has been well documented.⁴⁻⁸⁻¹⁰⁻¹⁷ In a study of necropsic lung specimens, one group of investigators was able accurately to identify centrilobular emphysema, even of a mild degree, using HRCT scanning.¹⁰ The correlation between the in vitro CT emphysema score and the pathological grade was excellent ($r=0.91$). Although it may be possible to obtain a near one to one correlation between CT score and pathological specimens in vitro, it is not possible to obtain such a good correlation in vivo. The correlation between in vivo HRCT assessment of emphysema and the pathological severity in various studies has been in the order of 0.7–0.9,⁸⁻⁹⁻¹⁷ and several groups have pointed out that mild emphysema can be missed on CT scans.⁸⁻¹⁵⁻¹⁸

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Some investigators have reported no significant difference between the extent of emphysema as judged by the HRCT scan and gross pathological specimens.^{9 10 17} However, the correlation between the CT and pathological emphysema scores in these studies has ranged from 0.7 to 0.9, suggesting that the severity of emphysema was often underscored or overscored on CT scans. Using a computer assisted method for obtaining objective quantification of horizontal paper mounted lung sections as a gold standard, Bankier *et al*¹⁹ compared the HRCT densitometric evaluation of mean lung attenuation with subjective visual assessments by three readers in 62 consecutive patients evaluated before lung resection. They found that subjective grading of emphysema was significantly less accurate than objective CT densitometric results ($r=0.44-0.51$; $p<0.05$ versus $r=0.56-0.62$; $p<0.001$) when correlated with pathological scores. Importantly, analysis of visual scoring data suggested systematic overestimation of emphysema by all three readers.¹⁹ The majority of studies, however, have shown good correlation between the emphysema score on the CT scan and pathological specimens,^{8 9 15 20 21} good agreement between expert readers for assessment of the presence and extent of emphysema,^{8 20 21} and good correlation between the subjective and objective analysis of emphysema.²⁰

Assessment of mild emphysema on CT scanning is improved by using the minimum intensity projection (MinIP) technique.¹⁸ MinIP is a software program that identifies only areas of lung with the lowest attenuation and thus suppresses normal lung and pulmonary vessels. The technique involves obtaining contiguous 1 mm sections through a volume of lung tissue. The 1 mm images are reconstructed individually or as a slab several millimetres in thickness. Comparing MinIP images with high resolution 1 mm sections, Remy-Jardin *et al*¹⁸ found that, in 13 patients with subtle emphysema, MinIP was more sensitive than HRCT (81% versus 62%). Furthermore, in four of 16 cases interpreted as normal on routine 1 mm images, subtle foci of emphysema could be identified on the corresponding minimum intensity projection images.

Objective quantification of emphysema

Given the inherent limitations of subjective visual scoring, the characteristic presentation of emphysema as areas of low CT attenuation values, and the digital nature of the CT data, there is considerable interest in the objective quantification of emphysema on CT scans.^{20 22-31} Three different approaches have mainly been used for objective quantification of emphysema on CT scanning: (1) use of a threshold value below which emphysema is considered to be present (density mask or pixel index (PI)),^{20 24 25} (2) assessment of the range of lung densities represented in a lung slice (histogram analysis),^{23 27} and (3) assessment of overall lung density, often in combination with volumetric imaging.²⁸⁻³¹

Müller *et al*²⁰ first made use of a standard CT software program called density mask that highlights voxels within any preselected range. They showed that, on conventional 10 mm thick sections, a threshold of -910 HU, which highlights all pixels with attenuation values less than -910, correlates best with the extent of emphysema. Using this technique, these authors found good correlation ($r=0.89$) between the extent and severity of emphysema as assessed by CT and pathological assessment with a modified panel grading system. In the same study the correlation between the mean visual scores of two independent observers and the pathological score was 0.90 ($p<0.001$), leading these investigators and others to conclude that visual scoring was nearly as precise and clinically more practical than quantitative assessment.²⁰ Similarly good results using -910 HU have been reported by others.²⁶ Gevenois *et al*^{17 32} have shown that, using 1 mm sections, the optimal threshold for HRCT images when compared with morphometric data is -950 HU.

A second method to quantify emphysema objectively is by computerised analysis of HRCT data, which produces a histo-

gram of the frequency distribution of pixel density values in a given lung region. All areas that have densities lower than the lowest fifth of the histogram or fall within a preselected range of densities may be defined as emphysematous.^{23 33} Using this approach, it has been reported that the lowest fifth percentile of the histogram in patients who have emphysema correlates well with the airspace wall per unit volume (AWUV) where $AWUV = \text{alveolar surface area/lung volume}$.²³ Using a similar approach in 28 patients with emphysema, Gould *et al*³³ found significant correlations between the lowest fifth percentile of Hounsfield number values and both the mean value of the surface area of the walls of distal AWUV ($r=-0.77$) and the extent of emphysema ($r=0.5$).

An additional approach has been used in which the mean lung density of either a given section or entire lung volumes may be computed as a means of defining the presence and extent of emphysema.^{28 34} Good correlation has been reported between these methods and a number of pathological grading systems. The development of sophisticated computer programs, coupled with spiral CT scanners, now allows practical quantitative three dimensional (3D) CT assessment of either select regions or entire lung volumes in a single breath hold period.²⁹⁻³¹ Using 5 mm and 7 mm collimation with a pitch of 1.5, Park *et al*²⁵ found good correlation between 3D assessment of both mean lung attenuation values and frequency distribution histograms of whole lungs compared with routine two dimensional analysis ($r=0.98-0.99$) and visual scoring ($r=0.74-0.82$), respectively.

CT allows measurement of overall and regional lung density and volume. Coxson *et al*²⁶ developed prediction equations that allow quantification of lung surface area and lung surface to volume ratio and surface area. They showed that mild emphysema is associated with an increase in lung volume and a reduction in surface to volume ratio, while surface area and tissue weight are only decreased with severe disease. The CT predicted surface to volume ratio correlated well with the histological findings.²⁶

The introduction of multislice CT scanners now makes it feasible to reconstruct contiguous thin 1-2 mm sections through the entire lung volume. However, whether this will result in more accurate quantification of disease remains to be determined.

In summary, objective quantification allows more consistent assessment of disease extent than subjective analysis. It allows assessment of overall and regional changes, to monitor the progression of emphysematous lung destruction in individual patients and to assess the impact of surgical and medical treatment. It should be noted, however, that lung density measurements on CT scanning can be affected by a number of variables including patient size, depth of inspiration, the type of CT scanner used, collimation, and the reconstruction algorithm. The analysis therefore requires careful attention to technique.

Correlation between CT and functional assessment of emphysema

It is recognised that the sensitivity of HRCT in detecting early emphysematous change is low but its accuracy is higher than that of pulmonary function tests.^{4 35 36} Patients with predominantly upper lobe emphysema and normal lower lobes as identified by HRCT have near normal pulmonary function tests compared with those with predominantly lower lobe emphysema,³⁵ which implies that the anatomical site of the emphysema determines the degree of impairment of lung function.

CHRONIC BRONCHITIS

The role of imaging in the assessment of uncomplicated chronic bronchitis is poorly documented. Even in published series of patients with supposedly "pure" chronic bronchitis it

is likely that co-existent emphysema was often present.^{37–38} The principal radiographic abnormalities attributed to chronic bronchitis are bronchial wall thickening and increased lung markings, often described as the “dirty chest”.^{39–40} These findings have a low sensitivity in the detection of chronic bronchitis, being present in 18% of 119 patients with chronic bronchitis in one study.⁴¹ The findings are also non-specific, and are often seen in healthy non-smokers, in patients with asthma, and in those with bronchiectasis or acute bronchitis of various aetiologies.

Few studies have assessed the diagnostic role of HRCT in chronic bronchitis and the information available is limited.^{42–43} In one investigation of 175 healthy adults (98 current smokers, 26 ex-smokers, and 51 non-smokers) no bronchial wall thickening was found on the chest radiograph in any subject but on the HRCT scan it was considered to be present in 45 cases (33% of smokers, 16% of ex-smokers, and 18% of non-smokers).⁴³ There is, however, considerable inter-observer disagreement in the interpretation of bronchial wall thickness on CT scans. Furthermore, subjective assessment of bronchial wall thickening on HRCT scans is markedly influenced by window settings. There has therefore recently been considerable interest in the development of objective measurements to determine airway wall dimensions.

Objective measurements of airway dimensions

Unlike the parenchyma, the airways have proved very difficult to measure. The first attempts at measuring airways objectively involved manually tracing the airway with a digitiser on the printed image.^{44–47} The airway wall thickness was measured by manually drawing lines from the lumen through the wall.⁴⁸ One drawback to these techniques is that dimensions are very sensitive to the display parameters of the printed image. Optimal measurement of airway lumen using this technique requires the use of a window level of –450 HU^{46–47} and a window width of 1000–1400 HU.⁴⁸ These windows produce images that are too dark for optimal visualisation of the parenchyma or of airways that are less than 3–4 mm in diameter. Furthermore, the technique is cumbersome, time consuming, and associated with considerable intra- and inter-observer variability.

Several groups of investigators have assessed the use of automated image analysis for measurement of airway dimensions. McNitt-Gray *et al*⁴⁹ reported that the airway lumen area could be accurately measured using a threshold cut off of –500 HU. The lumen area is calculated by counting the number of voxels within the –500 HU boundary. King *et al*⁵⁰ used an excised fixed pig lung and found that a threshold cut off of –577 HU produced the least error in lumen measurements.

A popular method for measuring airway wall thickness is the full width at half maximum method (“half-max”). This approach casts rays from the airway centroid through the airway wall and measures the x ray attenuation curve along the ray as it passes from the airway lumen through the wall and into the lung parenchyma. The technique assumes that the image gray level at the true airway wall will be half way between the minimum and maximum gray levels. However, Reinhardt *et al*⁵¹ pointed out that the scanning process introduces blurring and partial volume effects and may therefore not be uniform across structures of different sizes. They showed that the airway lumen will be underestimated and the airway wall thickness overestimated with this technique. They therefore developed a technique known as “maximum likelihood method” to estimate the wall thickness.⁵¹ This approach casts rays out from the centroid of airway lumen and matches the attenuation threshold along each ray to an ideal calculated ray. The wall thickness was found to be predicted with greater accuracy using the maximum likelihood method than with the half-max method.

King and co-workers have recently developed a technique known as the “score guided erosion algorithm” for the measurement of airway dimensions.⁵⁰ This consists of an edge finding algorithm that assumes that airways are circular and have a relatively high density compared with the surrounding parenchyma. Using this approach, a density map of the image is shifted and subtracted from the previous image. A pixel that has a large change after this shift can therefore be assumed to be an edge. Using this technique, these authors were able to calculate the wall area with much greater precision than has previously been possible.

Airway measurements are influenced by the airway angle relative to the plane of section, airway size and beam collimation.^{46–50} Optimal measurements require use of sections 2 mm or less in thickness and are currently limited to airways 2 mm or more in diameter. Most studies which assess airway measurements have limited the analysis to airways coursing perpendicular to the plane of the CT section—that is, airways cut in cross section. These airways are round and have even wall thickness and are therefore relatively easy to measure. Airways coursing obliquely are oval in shape so assessment of these airways requires correction for the angle of orientation.^{46–50} King *et al*⁵⁰ assessed the angle of orientation of the airways by determining the position of the centroid in three adjacent CT slices. Using a combination of a “score guided erosion algorithm” and an angle correction factor these authors were able to obtain accurate measurements of airway luminal dimensions and airway wall thickness in airways coursing perpendicular or obliquely to the cross-sectional plane.⁵⁰

In summary, several studies have shown that airway dimensions can be objectively quantified on HRCT scans. However, these measurements have been largely experimental and limited to phantoms, isolated lung specimens, normal subjects, and patients with asthma. The only quantitative study that has examined the airway dimensions in patients with COPD was recently published by Nakano *et al*.⁵² The authors evaluated the apical right upper lobe bronchus of 114 smokers using the half-max method. They chose this airway because it is usually cut in cross section on CT scanning and is consistently and reliably identified on CT scans. The thickening in this large airway was found to be correlated with abnormalities in lung function. The correlation with forced expiratory volume in 1 second (FEV₁) % predicted, forced vital capacity (FVC) % predicted, and residual volume/total lung capacity (RV/TLC) observed in this study suggests that airway wall thickening and lumen narrowing of large airways results in airflow obstruction.⁵² Furthermore, multiple regression analysis suggested that, for a given FEV₁, subjects with more extensive emphysema had less airway wall thickening than those with less extensive emphysema. However, all symptomatic smokers had thicker walls than asymptomatic smokers.⁵²

Airway wall dimensions are very important measurements since they have been shown to be the major site of airflow limitation. However, further studies are required to determine the potential role of CT scanning in the evaluation of the severity of airway wall inflammation and airway obstruction in patients with COPD.

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