High-resolution computed tomography features in patients with chronic obstructive pulmonary disease

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ABSTRACT

<u>Introduction</u>: In recent years, there has been increasing interest in diagnosing various components of chronic obstructive pulmonary disease (COPD) using high-resolution computed tomography (HRCT). The present study was undertaken to evaluate HRCT features in patients with COPD.

<u>Methods</u>: 40 male patients with COPD (age 40 years or older) and with a significant smoking history (20 pack-years or more) were included in the study. They were evaluated for HRCT features including vascular attenuation and distortion, mosaic attenuation pattern, directly visible small airways, low attenuation areas of emphysema and measures of hyperinflation of the lungs: tracheal index, sterno-aortic distance, thoracic cage ratio and thoracic cross-sectional area.

<u>Results</u>: The tracheal index ranged from 0.46 to 0.94; Saber-sheath trachea was found in 14 patients. The mean thoracic cage ratio at two levels, carina and 5 cm below carina, were 0.69 (range 0.61–0.78) and 0.73 (range 0.62–0.83), respectively. Sterno-aortic distance at carinal level ranged from 1.43 to 4.55 cm, with a mean of 3.00 cm. Directly visible small airways was the commonest finding (36 patients), followed by vascular attenuation (25 patients), mosaic attenuation pattern (16 patients) and vascular distortion (8 patients). Among various subtypes of emphysema, centriacinar emphysema was commonest (16 patients), followed by paraseptal (13) and panacinar emphysema (11).

<u>Conclusion</u>: There are certain specific HRCT features of emphysema and it is possible on HRCT to identify the subtypes of emphysema, such as centriacinar, panacinar and paraseptal emphysema. Various features of hyperinflation can also be well identified and quantified on HRCT.

INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is a disease state characterised by an airflow limitation that is not fully reversible. The airflow limitation is usually both progressive and associated with an abnormal inflammatory response of the lungs to noxious particles or gases.[1] Various disorders incorporated under COPD include emphysema, peripheral airways disease and chronic bronchitis. As the definition of emphysema is a pathological one, it requires histopathological examination to authenticate the disease, which is not usually carried out and often not consented to by the patient. Moreover, during the early stages of COPD, conventional spirometry does not reveal any abnormality as the earliest changes in these patients involve alveolar walls and small airways, and a modest increase in peripheral airways resistance is not reflected in such spirometric measurements.[2] During the last few decades, with the advent of high-resolution computed tomography (HRCT), there has been increased interest in diagnosing emphysematous and chronic bronchitis components of COPD using HRCT. Many studies have assessed HRCT features in patients with COPD,[3-9] but there was a problem with non-uniformity regarding the included COPD patient population, and the various studies have evaluated for different HRCT features. The present study was undertaken to evaluate stable COPD patients for various HRCT features including vascular attenuation and distortion, mosaic attenuation pattern, directly visible small airways, low attenuation areas of emphysema and measures of hyperinflation of lungs, viz. tracheal index, sterno-aortic distance, thoracic cage ratio and thoracic cross-sectional area.

METHODS

The present study was conducted in the Departments of Respiratory Medicine, Radiodiagnosis and Physiology at

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Table I. HRCT features noted in individual COPD patients.

| HRCT features	No. of patients	Percentage of study subjects
Saber-sheath trachea with tracheal index < 0.67	14	35
Thoracic cage ratio > 0.75 at carina	5	12.5
Thoracic cage ratio > 0.75 at 5 cm below carina	11	27.5
Sterno-aortic distance > 4 cm	5	12.5
Thoracic cross-sectional area/height^2 > 80.00 cm^2/m^2	28	70
Vascular attenuation	25	62.5
Vascular distortion	8	20
Mosaic attenuation pattern	16	40
Directly visible small airways	36	90

our institute. The study was approved by the Institutional Board of Studies and by the Ethical Committee. Male patients with COPD aged 40 years or older were included in the study. We included only male patients in our study for two reasons: firstly, in our country, we found that female patients are uncomfortable with declaring their smoking status and providing the exact quantum of smoking, and secondly, many female patients were observed to develop COPD due to reasons other than active smoking, such as using solid biomass fuel for cooking and exposure to passive smoke in enclosed poorly-ventilated houses. In particular, indoor air pollution in poorly-ventilated dwellings has been implicated as a risk factor for the development of COPD among rural women. A quantitative assessment of these types of risk factors is a challenging task. The diagnosis of COPD was based on criteria defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2004 update.[1] All COPD patients gave their written explicit consent for the study. They had a smoking history of at least 20 pack-years and had an airflow limitation that was not fully reversible (post-bronchodilator forced expiratory volume in the first second [FEV$_1$] < 80% of the predicted value in combination with FEV$_1$/forced vital capacity [FVC] < 70%). They had an increase in FEV$_1$ of less than 200 ml or less than 12% of the baseline value that was assessed 20 minutes after two puffs of inhaled salbutamol was administered via a metred dose inhaler using a spacer. The patients were excluded from the study if they had any evidence of coexisting bronchiectasis, cystic fibrosis, tuberculosis, bronchial asthma, interstitial lung disease, bronchogenic carcinoma, previous lung surgery or coronary artery disease. They were also excluded if they had any concomitant disorders like diabetes mellitus, chronic alcoholism, uraemia, or sarcoidosis.

All included patients underwent clinical and laboratory evaluation according to our study protocol, including a complete blood examination, urine examination, chest radiograph, electrocardiography,

echocardiography, and spirometry. The spirometry was carried out on Transfer Test Model 'C' (P K Morgan, Chatham, Kent, UK). All patients were required to withhold inhaled short-acting bronchodilators six hours prior to the test, long-acting β-agonists 12 hours prior to the test and sustained release theophylline 24 hours prior to the test. Spirometric indices were calculated using the best out of three technically-satisfactory performances as per the recommendations of the American Thoracic Society.[10] The following parameters were recorded: peak expiratory flow rate (PEFR), FEV$_1$, FVC, and FEV$_1$/FVC%.

HRCT was carried out using Somatom Plus 4 Volume Zoom Spiral CT scanner (Siemens, Erlangen, Germany). Scanning was performed at a field-of-view large enough to encompass the patient. Images were obtained at full inspiration using 1-mm collimation at 120 kV (p) and 90 mAs with 0.75 sec acquisition time. Scans were taken at 10-mm intervals with the patient in the supine position. Images were reconstructed using a high spatial frequency algorithm and a 512 × 512 matrix. No contrast was used. The following study parameters were evaluated using HRCT:

(1) Tracheal index: a ratio of transverse / anteroposterior diameter at a plane 1 cm above the aortic arch. Saber-sheath trachea is described as when the tracheal index was < 2/3.

(2) Thoracic cage ratio: a ratio of anteroposterior / transverse diameter. It was evaluated at two planes: tracheal carina and 5 cm below the carina.

(3) Sterno-aortic distance: distance from the posterior surface of the sternum to the anterior margin of the aorta at the carinal level.

(4) Vascular attenuation: vascular attenuation was considered when there was a thinning of pulmonary vessels and a reduction in their number.

(5) Vascular distortion: an increased branching angle and/or excessive straightening of pulmonary vessels was described as vascular distortion.
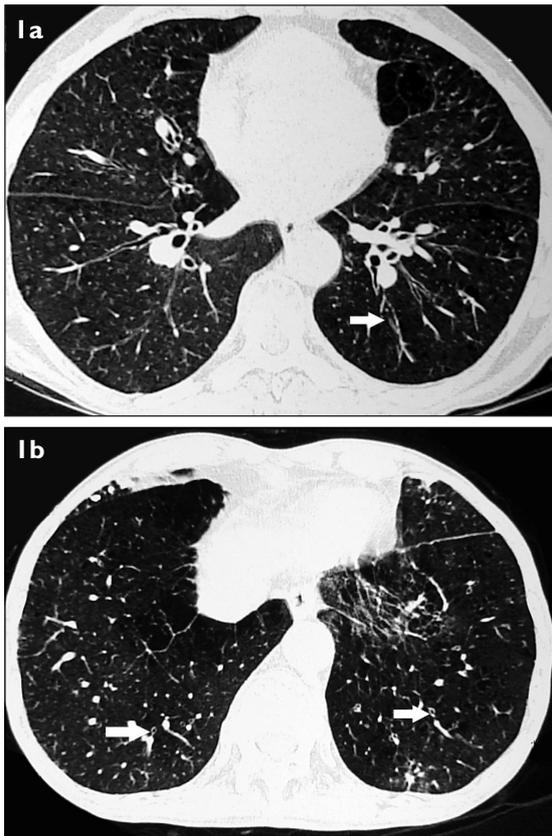
Fig. 1 Axial HRCT images show directly visible small airways as (a) air-filled and branching tubular structures, and (b) ring-like structures.
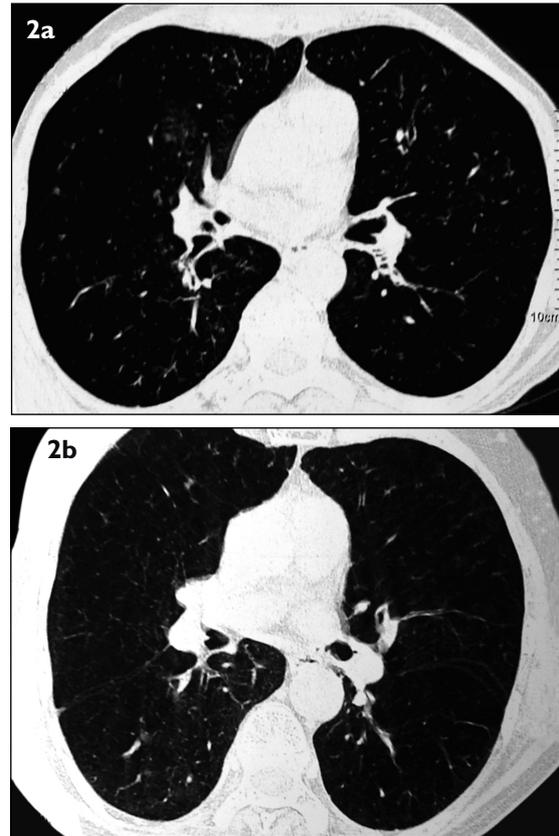
Fig. 2 Axial HRCT images show vascular attenuation characterised by the thinning of pulmonary vessels at the peripheral lung field along with a reduction in their number.

(6) Mosaic attenuation pattern: mosaic attenuation meant non-homogeneous lung density that later was described as areas that remain relatively lucent, interspersed with areas of normal higher lung density.

(7) Directly-visible small airways: the airways with an internal diameter of less than 2 mm.

(8) Thoracic cross-sectional area: thoracic cross-sectional area (TCSA) was measured on HRCT images made 1 cm below the top of the aortic arch. The ratio of TCSA over square of height (TCSA/height^2) was calculated for each patient.

(9) Low attenuation areas of emphysema were assessed on HRCT. These focal areas of decreased attenuation present differently in different types of emphysema:

(a) In centriacinar emphysema, focal areas of decreased attenuation with no discernable wall are found in association with respiratory bronchioles, and usually have a focal arteriole at or near the centre of the lesion.

(b) Panacinar emphysema is characterised by large areas of decreased lung density with poorly-defined margins and these abnormally-enlarged air spaces are evenly distributed within and across acinar units.

(c) Paraseptal emphysema, where the enlarged air spaces are along the edge of the acinar unit but only where it abuts against a fixed structure, such as the pleura or a vessel.

For statistical analyses, the mean and standard deviation for each variable was calculated for the entire COPD group. Individual patients having abnormal values compared to the normal reference range were identified as having significant HRCT features. All statistical analysis was carried out using the Statistical Package for Social Sciences version 10.0 (SPSS Inc, Chicago, IL, USA).

RESULTS

The present study included 40 male patients with COPD. Their mean age was 58.55 (range 50–69) years. Total duration of illness due to COPD ranged 2–25 years, with a mean of 12.63 years. All subjects were significant smokers with a mean smoking history of 33.25 (range 20–74) pack-years. In 21 patients, chest radiographs showed one or more features of COPD: low flat diaphragm, hyperinflated lungs, attenuated peripheral blood vessels and tubular heart on the posteroanterior view, and large
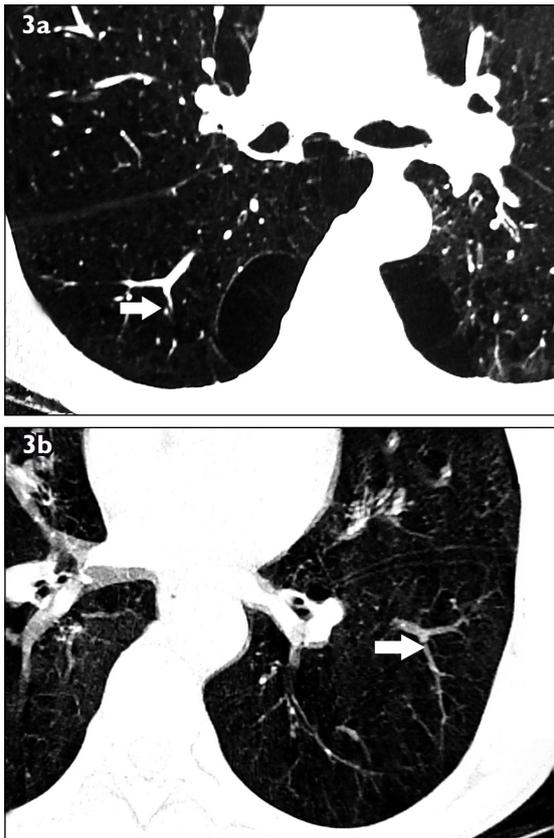
Fig. 3 Axial HRCT images from two different patients show vascular distortion characterised by increased branching angles and excessive straightening of pulmonary vessels.
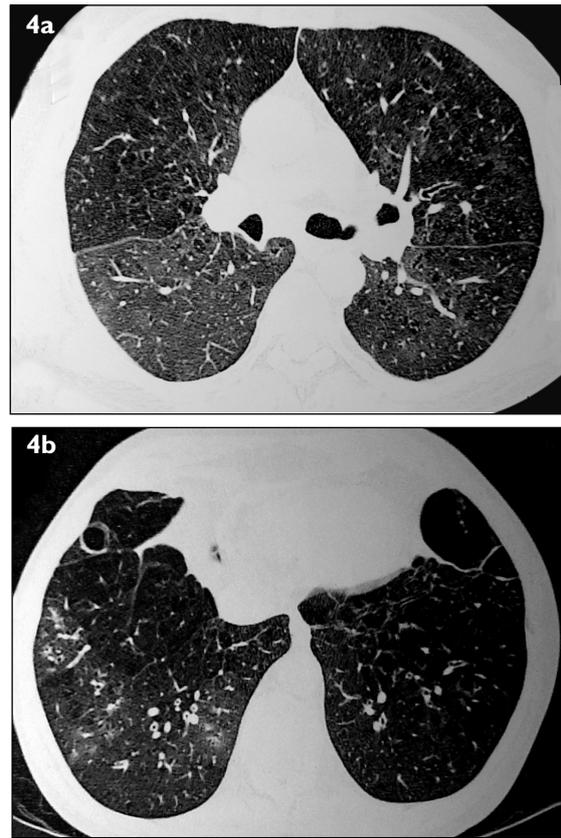
Fig. 4 Axial HRCT images show non-homogeneous lung density – a cardinal feature of the mosaic attenuation pattern.

retrosternal space and barrel chest on the left lateral view. Four patients who had no features suggestive of emphysema on chest radiographs were found to have emphysema on HRCT. Individual COPD patients with characteristic HRCT features are shown in Table I. Overall, 28 COPD patients had one or more HRCT findings suggestive of hyperinflation of the thoracic cage, altered tracheal index, sterno-aortic distance or thoracic cross-sectional area/height[2].

The tracheal index ranged 0.46–0.94, with a mean and standard deviation of 0.669 ± 0.0947. None of the patients had a transverse diameter more than the anteroposterior diameter at this level. The majority of patients (30/40) had a value < 0.70. At the carina, the mean thoracic cage ratio was 0.69 (range 0.61–0.78); 30 patients had a ratio of 0.65:0.75. At a point 5 cm below the carina, the mean thoracic cage ratio was 0.73 (range 0.62–0.83), and 28 patients had a ratio between 0.70 and 0.80. Distributive analysis showed that the thoracic cage ratio was greater at 5 cm below the carina. The TCSA at 1 cm below the aortic arch, described as aortic arch area/(height in metre)^2 ranged from 61.8 to 104.5 cm^2/m^2, with a mean of 87.57 cm^2/m^2. A TCSA/height^2 of more than 80 cm^2/m^2

was present in 28 patients. Sterno-aortic distance at the carinal level ranged from 1.43 to 4.55 cm, with a mean of 3.00 cm. A sterno-aortic distance of more than 4 cm was observed in only five (12.5%) patients.

Directly-visible small airways were detectable as air-filled and branching tubular structures or ring-like structures (Fig. 1); this feature was observed in 36/40 patients. Other features (vascular attenuation, vascular distortion and mosaic attenuation) indicative of abnormal lung parenchyma were seen in 25 patients. Vascular attenuation was characterised by a thinning of pulmonary vessels at the peripheral lung field, along with a reduction in their absolute number (Fig. 2). This was seen in 25 patients. Vascular distortion was seen in eight patients; it was characterised by increased branching angles and excessive straightening of pulmonary vessels (Fig. 3). A HRCT appearance of non-homogeneous lung density, considered as a cardinal feature of the mosaic attenuation pattern (Fig. 4), was observed in 16 patients. Seven out of eight patients with vascular distortion also had mosaic attenuation pattern. Vascular distortion and mosaic attenuation pattern were noticeable in patients who had vascular attenuation. Vascular distortion was

Fig. 5 Axial HRCT images in patients with centriacinar emphysema show multiple, round lucent regions of various sizes surrounded by normal parenchyma.
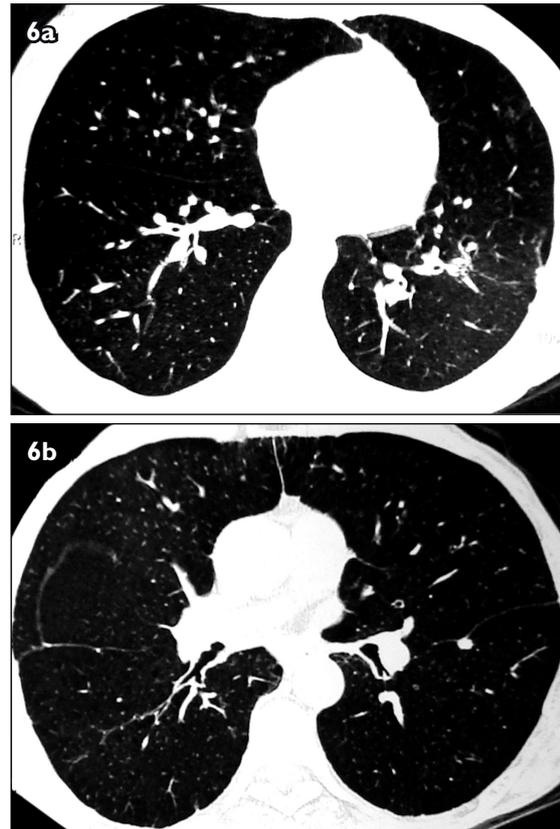
Fig. 6 Axial HRCT images show diffuse low attenuation lung parenchyma – typical of panacinar emphysema.

not observed in 20 patients who were having FEV_1/FVC of more than 50%; all patients with FEV_1/FVC less than 40% had vascular attenuation. 16/22 patients with FEV_1/FVC in the range of 41%–60% had vascular attenuation and only one out of ten patients with FEV_1/FVC over 60% had vascular attenuation.

In our study, we found cardinal features of emphysema in 25 out of 40 COPD patients. Among the three subtypes of emphysema, centriacinar emphysema, described in the presence of multiple, round lucent regions of various sizes surrounded by normal parenchyma (Fig. 5), was the commonest (16 patients). HRCT features of diffuse low attenuation lung parenchyma (Fig. 6) typical of panacinar emphysema were detectable in 11 patients. Paraseptal emphysema was seen in 13 patients (Fig. 7). 25 patients had at least one type of emphysema. Vascular attenuation and directly visible small airways were observed in all these 25 patients. In the present study, emphysema was characteristically seen in the upper lobes. Table III shows the correlations between spirometric indices (PEFR, FEV_1, FVC and FEV_1/FVC ratio) and the features of the hyperinflation of the lungs including the tracheal index, thoracic cage ratio at carina, thoracic cage ratio at 5 cm

below carina, sterno-aortic distance and thoracic cross-sectional area. All these features of the hyperinflation of the lungs had significant correlations with PEFR, FEV_1 and FEV_1/FVC ratio. However, FVC had a significant correlation (a negative one) with thoracic cross-sectional area only.

DISCUSSION

At first glance, this study seems like one of many studies that assessed the characteristic HRCT features in patients with COPD;[3-9] only when we consider the clinical implications of this study do the differences become obvious. The present study included patients who were attending outpatients at our institute, where the clinical features and chest radiographs were suggestive of chronic airflow obstruction and the spirometry revealed irreversible or partly-reversible airflow obstruction indicative of COPD. Further subtyping of COPD as emphysema, chronic bronchitis or peripheral airways disease is not confidently possible through these conventional methods. Confirmation of emphysema, which is defined pathologically, requires a histopathological assessment. Practically, it is difficult to find any patient, or even a
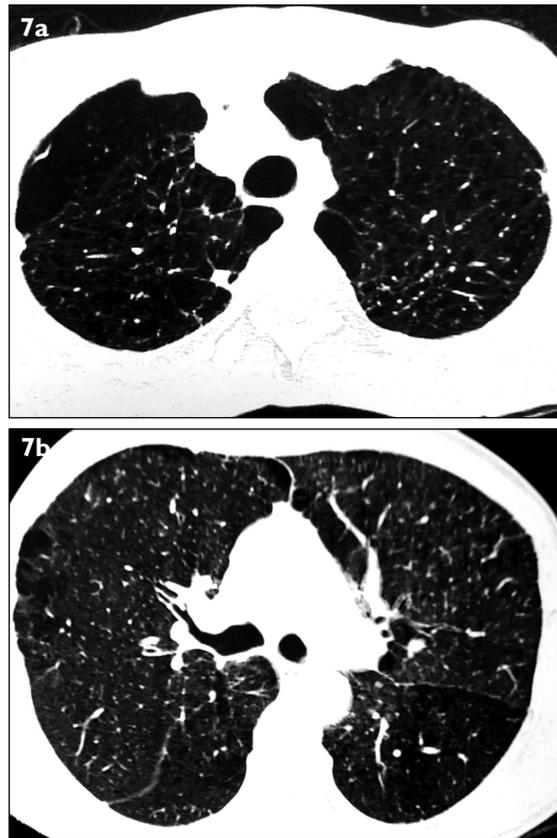
Table II. Detection of emphysema and its subtype in COPD patients using HRCT.

Type of emphysema	No. (%) of patients
Centriacinar emphysema	16 (40)
Panacinar emphysema	11 (27.5)
Paraseptal emphysema	13 (32.5)
Any type of emphysema	25 (62.5)

Fig. 7 Axial HRCT images show small subpleural areas of hyperlucency – characteristic of paraseptal emphysema.

treating physician convinced by lung biopsy, to confirm emphysema. In this scenario, the role of a noninvasive test like HRCT becomes apparent. At present, HRCT is not recommended for diagnosis by various international guidelines on COPD. However, the benefits of HRCT are too many to ignore: (1) Patients with early emphysema may present with clinical findings such as shortness of breath and decreased diffusion capacity without evidence of any airway obstruction on spirometry. (2) HRCT may be used to have a preoperative assessment of patients with bullous emphysema who are being considered for bullectomy or lung volume reduction surgery. The presence of diffuse emphysema obviates bullectomy.[11] (3) HRCT is helpful in evaluating other coexisting smoking-induced lung diseases including respiratory bronchiolitis, bronchogenic carcinoma, Langerhans histiocytosis, and desquamative interstitial pneumonia.[12] (4) Recent advances in alpha-1 antitrypsin therapy in patients with alpha-1 antitrypsin deficiency and the possibility of retinoic acid therapy as a treatment for emphysema have further increased the utility of HRCT in patients with COPD to confirm panacinar emphysema during the early course of the disease.[12]

There were significant differences in the patients' characteristics between previous studies and the present study. Some of these studies have either included only emphysema patients,[6,9] chronic bronchitis patients or patients diagnosed as COPD on the basis of guidelines other than GOLD.[3-5,7,8] Our inclusion criteria for COPD patients were based on GOLD guidelines;[1] all subjects included were significant smokers (20 pack-years or more) and all had an irreversible airflow obstruction. Moreover, it is probable that we have assessed more exhaustive HRCT parameters, viz. vascular attenuation and distortion, mosaic attenuation pattern, directly visible small airways, low attenuation areas of emphysema and measures of hyperinflation of lungs: tracheal index, sterno-aortic distance, thoracic cage ratio and TCSA.

The tracheal index was originally defined as the ratio of coronal length, measured on lateral view of a radiograph, to sagittal length, measured on the posteroanterior view.[13] On radiographs, however, the dimensions of an image are not the same as those of an actual one because the image is enlarged in proportion to the subject-film distance. Using HRCT images, it has become possible to precisely evaluate the size of the trachea on the transaction plane.[3] The suggested mechanism of Saber-sheath trachea is hyperinflation associated in patients with COPD. In a study by Tsao and Shieh, Saber-sheath trachea was found as a specific radiographical diagnostic parameter for the diagnosis of COPD (specificity 92.9%), although the sensitivity (39.1%) was low.[4] In our study, we found Saber-sheath trachea in 14 out of 40 patients (sensitivity 35%). We calculated the thoracic cage ratio at two levels: at the carina and 5 cm below the carina, by measuring internal thoracic diameters in HRCT sections. By measuring the internal thoracic diameters, we excluded possible errors caused by chest wall thickness. A ratio of over 0.75 was found in five patients (at the carinal level) and in 11 patients (at 5 cm below the carina). In late stages of COPD, the chest is barrel-shaped with increased anteroposterior diameter and the ribs become less oblique due to entrapment of air and chronic overinflation of the lungs.

Table III. Correlation between HRCT features and spirometry variables.

Parameters	Tracheal index		Thoracic cage ratio at carina		Thoracic cage ratio at 5 cm below carina		Sterno-aortic distance		Thoracic cross-sectional area	
	r-value	p-value	r-value	p-value	r-value	p-value	r-value	p-value	r-value	p-value
PEFR	0.399*	0.011	−0.400*	0.011	−0.439**	0.005	−0.337*	0.034	−0.537**	< 0.001
FEV₁	0.545**	< 0.001	−0.667**	< 0.001	−0.674**	< 0.001	−0.619**	< 0.001	−0.752**	< 0.001
FVC	0.159	0.328	−0.265	0.098	−0.297	0.063	−0.230	0.153	−0.429**	0.006
FEV₁/FVC ratio	0.844**	< 0.001	−0.925**	< 0.001	−0.875**	< 0.001	−0.934**	< 0.001	−0.855**	< 0.001

PEFR: peak expiratory flow rate; FEV₁: forced expiratory volume in the first second; FVC: forced vital capacity
*The correlation was statistically significant.
**The correlation was statistically highly significant.

In patients with emphysema, on lateral chest radiographs, there is an increased retrosternal lucency, and increased distance from the posterior sternal surface to the anterior margin of the ascending aorta.[14] We evaluated the sterno-aortic distance on HRCT by measuring the sterno-aortic distance at the level of carina in the transverse plane. In our study, a sterno-aortic distance over 4 cm was found in five out of 40 patients. Hagen and Kolbenstvedt found increased sterno-aortic distance (≥ 4 cm) in 16/22 emphysema patients.[6] The variation was due to differences in patient population between these studies; Hagen and Kolbenstvedt had included patients with emphysema due to alpha-1-antitrypsin deficiency who had panacinar emphysema.[6] TCSA was measured on HRCT at 1 cm below the top of the aortic arch. TCSA/height² over 80.00 cm²/m² was found in 28 patients. Nine out of 12 patients with a ratio of less than 80.00 cm²/m² had FEV₁/FVC ratio over 60%. In another study, the authors observed that TCSA/height² ratios were significantly greater in a group with grade IV dyspnoea than those in the groups with grade II and III dyspnoea.[15]

Vascular attenuation was present in 25 out of 40 patients (62.5%). All these patients had focal emphysema of at least one type: centriacinar, panacinar or paraseptal. Vascular attenuation had an upper lung field predominance. Vascular distortion in emphysema occurs due to hyperinflation of the lungs. In the present study, this feature was observed in eight patients; these patients also had vascular attenuation, directly visible small airways and low attenuation areas of emphysema. Seven of these patients also had mosaic attenuation pattern on HRCT. Vascular distortion was absent in all 20 patients who had FEV₁/FVC ratio over 50%. It appears that vascular distortion is seen in advanced cases of emphysema and in patients with severely-deranged pulmonary functions. A mosaic attenuation pattern is more pronounced on scans obtained at end-exhalation instead of the more conventional end-inspiration technique.[7] This may be the reason for the presence of a mosaic attenuation pattern in

only 16/40 patients in our study. All these 16 patients had the associated features of vascular attenuation and directly visible small airways. Copley et al have suggested that the mosaic attenuation pattern in addition to other HRCT features is helpful in distinguishing between different entities grouped under COPD.[8]

Normal small airways are not visible on HRCT. As there is a small airways component in heterogeneous entities grouped under COPD, these diseased airways are visible near the lung periphery on HRCT.[16] These diseased bronchioles are visible on HRCT as dilated, air-filled, branching, ring-like or tubular structures in the lung periphery due to wall thickening and dilation. When the airways are obliterated by submucosal or peribronchial fibrosis, nodular, linear or branching peripheral opacities are also seen.[17] In the present study, directly-visible small airways were noticed in 36/40 patients. A high percentage of our patients with this feature support the suggestion that intrinsic changes in the airways themselves may be far more important than has been previously thought.[18] Hogg et al showed that, despite a decreased radius of small airways, airflow resistance is actually not increased because of the greater overall number of these peripheral bronchioles.[19] Because most airflow resistance occurs at the level of the larger airways, significant disease must be present at the level of the peripheral airways to be detected on standard pulmonary function tests.[17] HRCT hence has a definite edge in the diagnosis of small airways disease.

Low attenuation areas of emphysema are visible on HRCT; these focal areas are present at different sites in various sub-types of emphysema. In the present study, these lesions were observed in 25/40 patients. Centriacinar emphysema was present in 16 patients. Smoking is usually associated with centriacinar emphysema, the emphysematous subtype predominantly observed in our patient. However, we also observed panacinar emphysema in significant numbers, because as the process of centriacinar emphysema which advances the focal lesions becomes confluent, it may appear as

panacinar emphysema. Panacinar emphysema as a large area of decreased lung density or decreased attenuation was present in 11 patients. Paraseptal emphysema as focal areas of subpleural emphysema was present in 13 patients; all patients had coexisting centriacinar or panacinar emphysema. All three types of emphysema had upper lobe predominance – a cardinal feature of smoking-induced emphysema. Panacinar emphysema due to alpha-1 deficiency is usually more evident in the lower lobes.

To conclude, there are certain cardinal HRCT features of emphysema that can be well-documented. It is possible on HRCT to identify the subtypes like centriacinar, panacinar and paraseptal emphysema. Various features of hyperinflation can also be well-identified over HRCT and the severity of COPD can be assessed authentically. It will definitely change our perceptions regarding various heterogeneous groups of diseases included under COPD, their relative contributions to the disease and to suspect possible risk factors. This will be helpful in the management of COPD patients on an individual basis according to the disease subtype.

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