The Use of Volumetric Chest Computed Tomography in Determination of Chronic Obstructive Pulmonary Disease Phenotypes

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Summary:

Background: Chronic Obstructive Pulmonary Disease (COPD) represents one of the major causes of chronic morbidity where, airflow limitation is caused by a mixture of small airways disease and parenchyma destruction.

Objective: to correlate the clinical characteristics of patients with COPD with imaging classification into phenotypes.

Patients and Methods: Thirty patients with stable COPD were examined by chest CT. Bronchial wall thickness is evaluated by measuring the wall area percentage by identifying the trunk of the apical bronchus of the right upper lobe, while the extent of emphysema was assessed using the percentage of lung voxels with X-ray attenuation values less than -950 HU {automatically calculated by special software}.

Results: Three phenotypes were found: A phenotype (airway-predominant) , 66.6% of total, E phenotype (emphysema predominant), 20% of total and M phenotype (mixed), 13.3% of total.

Conclusions: Using volumetric chest CT in patients with chronic obstructive pulmonary diseases determine three disease patterns. Airway predominant disease which correlate to patients who have clinical & spirometric pattern of chronic bronchitis rather than emphysema. Emphysema predominant on CT correlated with patients with clinical findings of lung hyperinflation rather than bronchial inflammation. Patients with mixed CT findings combined of both previously mentioned types found to be correlated with those with overlapped clinical patterns of both chronic bronchitis & emphysema.

Key words: chronic obstructive airway disease (COPD), volumetric chest CT, COPD phenotypes.

Introduction:

COPD is characterized by progressive and poorly reversible airflow limitation (1). It results from a combination of at least two pathologic processes: small airway remodeling and a loss of lung elastic recoil due to alveolar destruction. Their relative proportion can vary considerably between individuals with the same degree of airflow limitation, and thus spirometry is inadequate to fully characterize the COPD (2). COPD, including chronic bronchitis (CB), emphysema and forms of CB combined with emphysema (2, 3,4).

The management of COPD depends on the relative distribution and severity of these two pathologic processes; factors that may vary widely even among patients with a similar degree of airflow limitation (5,6,7). Standard pulmonary function tests (PFT) with spirometry is unhelpful for distinguishing the specific contribution of each process (8,9). Volumetric chest CT analyses can help differentiate the COPD phenotypes, which is crucial information for determining the appropriate management strategy (10, 11). For patients with emphysema-

predominant, lung-volume reduction surgery may be effective to improve pulmonary function, in contrast, for patients with airway-predominant, medical treatment of airway disease may be more appropriate (12,13,14,15).

The patients were classified according to the volumetric CT findings as follows:

Airway predominant, which showed none to mild emphysema (LAA % between 0 -25%) with presence of bronchial wall thickening; (A phenotype).

Emphysema predominant, which showed moderate to severe emphysema (in moderate emphysema: LAA% 25%-50% and in severe emphysema: LAA% more than 50%) without presence of bronchial wall thickening; (E phenotype).

Mixed; which showed a combination of moderate to severe emphysema and presence of bronchial wall thickening;(M phenotype) (12, 13).

The purpose of the present study is to correlate the clinical characteristics of patients with COPD with imaging classification into phenotypes.

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Patients and Methods:

The study sample consisted of 30 consecutive patients with clinical diagnosis of COPD, in Baghdad teaching hospital, the study started at

September- 2011 until June- 2012. The mean age of patients was 68 years; age range, 32-88 years, with male: female ratio is 9:1. Twenty patients were current smokers who smoked a mean of 110 packs per year (range, 71-150 packs per year). Fifteen patients fulfilled the criteria for having CB — namely; a history of productive cough on most days for at least 3 months for 2 successive years and 15 did not.

All patients had PFTs and chest x-ray (CXR) before they referred to do emphysema protocol thin-section inspiratory CT.

Inclusion criteria: adult patients had previously diagnosed as COPD patients. CT Examination: Thin-section CT examination is performed with Brilliance 64scanner, Philips medical systems, (Best, the Netherlands), and consisted of sequential acquisitions of 1-mm thick sections at 120 kilovolt, 250 milliamp, resolution (standard) ,increment 0.5 ,collimation 64*0.625, pitch 1.172, rotation time 0.75, filter: standard B, window (c) 60, window (w) 360, matrix 512,and time of scan 5.26 s.

No intravenous contrast material was administered. The CT scans were reconstructed using both a low spatial frequency reconstruction algorithm (standard) for density measurements, and a high spatial frequency algorithm (bone) for airway measurements.

Image Analysis: Airway evaluation: for airway evaluation, CT scans were reconstructed by using high resolution chest CT (HRCT) algorithm.

The trunk of the apical bronchus of the right upper lobe is usually sliced in cross section. With the bronchus identified, the following parameters were measured manually: short radius (SR), and long radius (LR) of the lumen (Fig.1) In brief, the following procedures were performed:

Assuming that, in a cross-sectional plane, the airway lumen is a true circle, the total diameter of the bronchus was calculated as (D), while Bronchial lumen diameter was calculated as (L).

The outer area of the bronchus (Ao) has been calculated from the following equation; $Ao = \pi (D/2)^2$.

The area of bronchial lumen (Ai) has been calculated from the following equation; $Ai = \pi (L/2)^2$.

Wall area (WA) was calculated as $(Ao - Ai) / A_O$.

The percentage wall area $[WA\% = \{(Ao - Ai) / A_O\} \times 100]$

Analysis of LAA: The extent of emphysema was assessed using the percentage of lung voxels with X-ray attenuation values (LAA %) less than -950 HU. LAA % was calculated automatically by special dedicated soft ware.
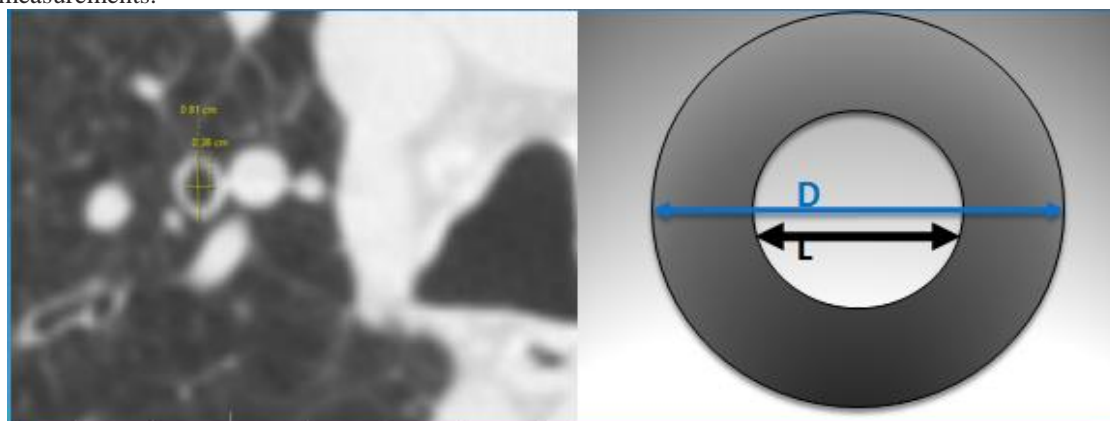

Fig.1 demonstrating the method of measuring bronchial wall thickness

Results:

Population of COPD phenotypes: A total of 30 patients with COPD were classified into three phenotypes according to volumetric CT findings, (Table 1), number of males 27 while the number of female is 3, mean age 68years old and male: female ratio is 9:1.

Table 1 .Volumetric chest CT Characteristics of COPD according to Phenotypes

| COPD phenotypes	Emphysema (LAA %)	BWT (WA %)	Percentage of each phenotype
Phenotype E	Moderate to severe	Without BWT	20 %
Phenotype A	None to mild	With BWT	66.6 %
Phenotype M	Moderate to severe	With BWT	13.3 %

Definition of abbreviations: LAA%; percentage of lung voxels with attenuation values less than -950 HU. BWT; bronchial wall thickness. WA%; percentage of bronchial wall area.

Twenty patients were classified into the A phenotype. In the A phenotype group, 20 patients (66.6% of the total) showed the presence of bronchial wall thickness (BWT) with none to mild emphysema, Fig.2 show CT of one of the 20 patients with A phenotype.
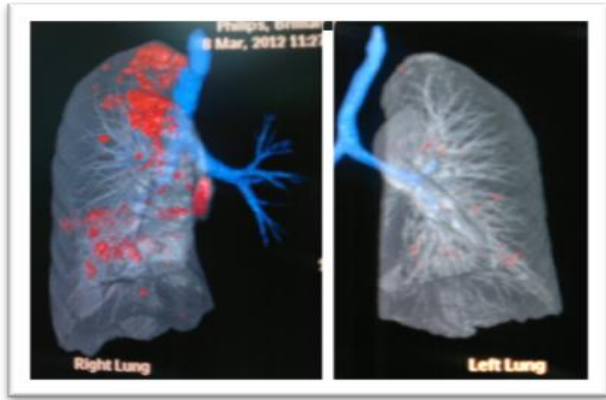
Fig.2. 61years old female, classified as phenotype A (LAA%=10%, D=5.2mm, L=2.2mm, WA%=82.2%): Volumetric chest CT, Red areas on volumetric CT represent LAA%.

Six patients were classified into the E phenotype. In the E phenotype group, 6 patients (20% of the total) showed moderate to severe emphysema without presence of BWT, Fig.3 show CT of one of the 6 patients with E phenotype.
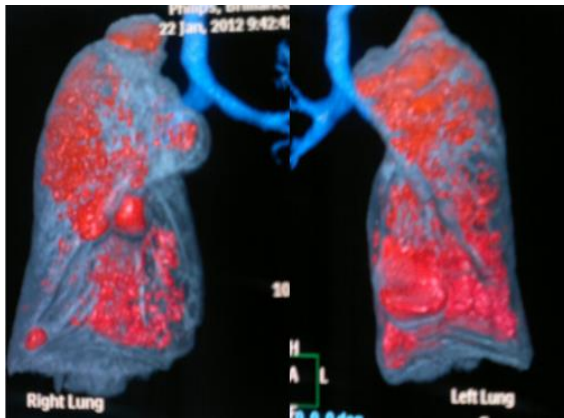
Fig.3. 60 years old COPD male patient present with phenotype E (LAA%=28%,L=2.7mm

,D=6mm,WA%=80%), volumetric chest CT. Red areas on volumetric CT represent LAA%.

Four patients were classified into the M phenotype. In the M phenotype group, 4 patients (13.3% of the total) showed moderate to severe emphysema with presence of BWT, Fig.4 show CT of one of the 4 patients with M phenotype.

Fig.4. 55 years old COPD male patient present with phenotype M. (LAA%=70%,L=6.8mm,D=10.3mm,WA%=65.4%), volumetric chest CT, Red areas represent LAA%.

Pulmonary function test of each phenotype: there were no significant differences, Significance was set at p<0.05, in age and smoking history. The A phenotype group show increased FEV1/FVC% and was significantly higher as compared with those in the other phenotype groups, although there was no significant difference in FEV1% predicted and FVC% predicted values between all phenotypes groups (Table 2).

Table 2: Age and Pulmonary function data in three phenotypes of chronic obstructive pulmonary disease

	E phenotype	**M** Phenotype	**A** phenotype	**P value** between E and M types	**p value** between E and A types	**p value** between M and A types
Age (years)	68.1± 1.1	68.4 ±1.7	68.3 ± 1.8	0.07	0.49	0.49
FVC (% of pred.)	73± 15.5	76± 20	77±21	0.46	0.25	0.11
FEV1 (% of pred.)	45.4±15.1	42.0± 17	48.5± 16.8	0.46	0.17	0.32
FEV1/FVC (%)	44.1±13.5	43.5±16.2	51.6 ±9	0.29	**0.03**	**0.04**

Values are means ±SD (standard deviation), pred.: predicted, FVC: Forced vital capacity, FEV1: forced expiratory volume in one second

Results of CT measurements: the data for airway measurements suggest that the airway wall is thicker and the luminal area smaller in patients who have more severe airflow obstruction. There were no correlations between LAA % and WA %. Therefore we adopted WA % as a primary measurement of airway abnormality and LAA % as an index of emphysema (Table 3).

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Table 3: CT data in three phenotypes of chronic obstructive pulmonary disease

	phenotype E (n=6)	phenotype M (n=4)	phenotype A (n=20)
WA%	60±7	67±8	69±8
LAA%	40±20	30±11	16± 7

Definition of abbreviations: LAA% = percentage of the low attenuation area to the corresponding lung area; WA%=percentage of the wall area, n: number of patients

Discussion:

High-resolution CT (HRCT) is an established tool for the in vivo assessment of emphysema, mainly used to investigate populations with advanced lung disease. (16). Quantitative information on the subclinical parenchymal lung disease, obtained by volumetric chest CT, can be correlated to pulmonary functional alterations (17)

In the present study, there was no significant difference in age between the patients of different phenotypes. Our results are similar to study done by Bosken and coworkers (18). In the present study, the 30 patients, who are already diagnosed as COPD, classified into 3 phenotypes according to the volumetric chest CT findings and the most common phenotype was A, followed by E and M phenotypes. Our results are similar to a study done by Fujimoto et al (14).

While Massimo Pistolesi, classify the COPD cases into 2 phenotype either airways obstructive or a parenchymal destructive COPD phenotype, based on nine variables and this identification of the predominant phenotype may permit to clinically characterize COPD beyond its unifying spirometric definition, while in our study, the classification depend mainly on the findings of volumetric chest CT (19). In the present study, the A phenotype group show increased FEV1/FVC% and was significantly higher as compared with those in the other phenotype groups, although there was no significant difference in FEV1% predicted and FVC% predicted values between all phenotypes groups. Our results are similar to that obtained by a study done by Fujimoto K (14). In the present study, the data obtained from volumetric chest CT for each phenotype, suggest that the WA% was higher in A phenotype than E phenotype, and there is mild difference between A phenotype and M phenotype, while the LAA% was higher in E phenotype than A phenotype, and there was no large difference between E phenotype and M phenotype. So airway wall is thicker and the luminal area smaller in patients who have more severe airflow obstruction, while the LAA % is higher with more severe emphysematous changes, and there are no correlations between LAA % and WA %. The results of the stepwise multiple regression analysis in the present study, suggests that WA % and LAA % are measuring independent aspects of pulmonary pathophysiology: the airway and parenchymal components, respectively. In our study, found that the percentage of low attenuation area and WA % independently contributed to the prediction of FEV1, FVC, and FEV1/FVC, this result confirms the results obtained by Nakano and colleagues (11). Other studies had shown that COPD patients present with airway wall thickening on HRCT have greater reversibility of airflow obstruction in response to inhaled bronchodilators and corticosteroids than those with emphysema without bronchial wall thickening (4,14,20).These data, taken together, suggest that expiratory airflow limitation is mainly associated to airways pathology in COPD patients with predominant features of chronic bronchitis, while it is mainly associated to parenchymal destructive changes in COPD patients with predominant features of emphysema and in those patients ,the lung-volume reduction surgery may be effective to improve pulmonary function.

Conclusion:

Using volumetric chest CT in patients with chronic obstructive pulmonary diseases determine three disease patterns. Airway predominant disease which correlate to patients who have clinical & spirometric pattern of chronic bronchitis rather than emphysema. Emphysema predominant on CT correlated with patients with clinical findings of lung hyperinflation rather than bronchial inflammation. Patients with mixed CT findings combined of both previously mentioned types found to be correlated with those with overlapped clinical patterns of both chronic bronchitis & emphysema.

Author contribution:

Dr. Atheer Adnan Fadhil: Study design, interpretation of data, drafting of manuscript & critical revision.

Dr. Mustafa Nema: Study design, acquisition of clinical data & critical revision.

Dr. Shaymaa A. Abdalrazak: Acquisition of radiological data, interpretation of data & drafting of manuscript.

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