Phenotyping Assessment of Chronic Obstructive Pulmonary Disease by Using Multi-Detector Computed Tomography

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Abstract; Background: Phenotyping of Chronic obstructive pulmonary disease (COPD) is referred to a single or combination of diseases attributes that describe differences between individuals with COPD. An accurate detection of COPD phenotyping by imaging is urgently needed to enable individualized treatment and improve patient's outcome. We aimed to study the role of multi-detector computed tomography (MDCT) in phenotype assessment of COPD. Patients and methods: The study was conducted on 48 patients (35 males and 13 females with age range between 48-75years) from outpatient clinics of our hospitals during the period from November 2014 to October 2015. Results: All patients have had different clinical symptoms such as cough, expectoration and dyspnea. Conventional X-ray and pulmonary function tests (PFTs) and were performed and the results were tabulated. MDCT was performed and measured bronchial wall thickness and emphysema score representing percentage ratio of emphysema tissue volume in relation to the lung volume. Patients were classified into three main groups: bronchitic phenotype (18.75%), emphysematous phenotype (29.17%), and mixed group (52.08%). Conclusion: The measurements of lung physiology through PFTs do not always discriminate between the COPD phenotypes. MDCT scanning have the potential to separate and quantify both emphysema and airway component in COPD patients. [Ghada Abdel monaem, Enass M. Khattab, Ahmad Alsammak, Ayman Ramadan Abdelhai. Phenotyping Assessment of Chronic Obstructive Pulmonary Disease by Using Multi-Detector Computed Tomography. J 2016:12(12):141-151]. ISSN 1545-1003 2375-7264 Am Sci (print): ISSN (online). http://www.jofamericanscience.org. 18. doi:10.7537/marsias121216.18.

Keywords: MDCT in COPD, Pulmonary function tests, phenotyping assessment

1. Introduction:

Chronic obstructive pulmonary disease (COPD) is defined as a disease of progressive limitation of airflow due to inflammation of small airways, destruction and fibrosis of the lung parenchyma. It includes emphysema, chronic asthma, and chronic bronchitis^[1]. COPD is a leading cause of morbidity as well as mortality worldwide. The number of deaths is increasing due to aging population and to higher smoking rates in many countries^{[2].} It resulted in an estimated economic cost of \$2.1 trillion in 2010^[3].

Patients' classification into distinct subgroups which allow us to better determine appropriate therapy and predict the prognosis is important and called phenotyping. Hence the precious goal of phenotyping is to identify patient groups with the same prognostic or therapeutic characteristics. Until now in COPD, the disease characteristics and/or disease severity have been called COPD phenotypes^[4].

The first and the simplest method of phenotyping COPD patients was clinical observation individualizing pink puffer in emphysema subtype from blue bloater in chronic bronchitis subtype. The other phenotyping is the classic Venn diagram describing the underlying diseases: asthma, chronic bronchitis, and emphysema in COPD ^[5]. Many subtypes of COPD have emerged from this

illustrationn. One COPD patient may have multiple phenotypes and multiple etiologies ^[6]. So, those clinical methods are insufficient to characterize all subtypes of COPD patients. The radiologic phenotypes are subdivided into emphysema and airways disease and mandatory for validation of clinical suspicion.

Accurate assessment of parenchymal disease in emphysema can be achieved by computed tomography (CT) scanners. The results of it are good predictors of histopathologic findings and the degree of expiratory airflow obstruction ^[7]. Proximal airway wall thickening measurements by CT are inversely correlated with lung function and relate to the subject's burden of small airway disease ^[8] and the exacerbation frequency ^[9].

In emphysema-predominant COPD patients, lung-volume reduction surgery may be more appropriate in improving pulmonary function. On the other hand, for patients with airway-predominant COPD, medical treatment of airway disease is usually more effective. So, classification is necessary for the planning and management of therapy ^[10].

The aim of this study was to evaluate the role of multi-detector computed tomography (MDCT) in phenotype assessment of COPD.

2. Patients and methods:

2.1 Patients:

These study was designed as a prospective diagnostic study carried out in radiodiagnosis department, of Zagazig University Hospitals between November 2014 and October 2015 and included 48 patients who presented to the out-patient clinics of the Internal medicine department with clinical evidence of COPD (cough, expectoration, difficult breathing) were eligible whatever the etiology. The study was approved by the local ethics committee of our institute. All Patients provided written informed consent before enrollment. Patients were informed by the treating physician about the protocol of the study and follow-up schedules.

Patients were excluded if there were consolidation. collapse, malignancy or pleural abnormalities that might affect the total lung volume; pregnant woman; or patients presenting with critical illness as respiratory failure. At baseline, a structured clinical history and physical examination were carried out in all patients. Demographic and clinical characteristics, including age, heart rate, respiratory rate, blood pressure, and meticulous chest examination of all patients were obtained. Conventional chest Xray (postero-anterior and lateral views) is prerequisite for all patients. Arterial blood gas sampling was performed, and the ratio of arterial oxygen tension to inspired oxygen fraction (PaO2/FiO2) was calculated. Static and dynamic lung volumes and single breath diffusing capacity (DL CO) were measured by a massflow sensor (V6200 Autobox Body Plethysmograph; Sensor Medics, Yorba Linda, CA) according to standard methodology ^[11,12]. All patients were classified into the respective GOLD stage (short for the Global Initiative for Chronic Obstructive Lung Disease)^[13] according to the forced expiratory volume in 1 second (FEV1) and FEV1/ forced expiratory vital capacity (FVC). Pulmonary function test (PFT) was done as the percentage of FEV1/FVC < 70% is a predictive value confirms the presence of airflow limitation (obstructive), then FEV1 will detect severity as following: Stage I Mild if FEV1 ≥80%; Stage II Moderate if FEV1 50-79%; Stage III Severe if FEV1 30-49%; and Stage IV Very severe if FEV1 < 30% or <50%.

2.2. Multi-Detector Computed Tomography:

Non enhanced MDCT was performed on Philips Ingenuity Core 128 MDCT & GE Light speed Ultra 8 slice CT Scanners then post processing was done on Philips Intelli Space portal workstation. Before the MDCT study, patients were instructed that they will be required to take and hold deep inspiration upon request during the study, they were trained on this maneuver 5 min before the scanning starts. The parameters of the CT scan include: Slice thickness: 1.25 mm; KVp and mA per slice: 120 kVp and approximately <240 mA; tube rotation was 0.6-0.9 second (0.75s); detector collimation: 1mm; matrix size: 512 x 512 and Field of view (FOV) was adjusted for small, medium and large patients.

For the quantitative evaluation, again the local software of the MDCT workstation (Advantage Windows 4.4 software) was used for the segmentation and CT emphysema index calculation. So, CT image data were reconstructed with a high spatial frequency algorithm and viewed at a window level of - 450 HU and a window width of 1500 HU. Multi- planar reconstruction of the acquired thin sliced axial images facilitated coronal, sagittal and 3D volume rendering reconstruction technique.

The CT emphysema index is defined as the proportion of the lung affected by emphysema or the percentage of lung pixels with attenuation below specific thresholds ^[14]. It was assessed by determining the area of both lungs, measuring less than -950 Hounsfield units (HU) and (below-900 HU to below-960 HU for patient holding breath at full lung capacity), with various slice thicknesses and reconstruction algorithms. The percentage of lung pixels with attenuation below specific thresholds was used as an emphysema index. ^[15]

The image sequence was then revised for correct segmentation. After image manipulation, the segmented image sequence is saved and transferred to another computer. Image software was used for the calculation of the lung attenuation for emphysema score ^[16].

2.3. Image analysis:

2.3.1 Qualification of pulmonary emphysema:

If present, from the start, pulmonary emphysema divided into three subtypes:

- 1. Centrilobular emphysema (CLE),
- 2. Panlobular emphysema,

3. Paraseptal emphysema (PSE), based on the portion of the primary acinus involved ^[14] as a morphological qualitative interpretation.

2.3.2 Quantification of pulmonary emphysema:

A. Calculation of emphysema (index & score):

tomography (CT) Computed volumetric rendering techniques (VR)3D images of the lung were created. The total lung volume was calculated by using a threshold of L= -750 and W= 1000. The 3D VR of the lung was saved and the volume of the lung tissue was obtained. A threshold of L= -950 and W= 100 was used to measure the emphysematous tissue. These thresholds were selected and manually adjusted. Once the thresholds were set, a 3D VR image of the affected tissue was obtained. Depending on the extent of emphysema and density the VR images had to be manually trimmed and manipulated. The volume of the emphysema tissue was then calculated based on the 3D VR image of the affected tissue. The ratio of

the lung volume and the emphysema volume was an estimate of the percentage of lung affected by emphysema. Then it was graded on a 5-point scale based on the percentage of lung involved ^[15]:

No emphysema=Score 0; up to 25% of lung parenchyma involved=core 1; between 26% and 50% of lung parenchyma involved=Score 2; between 51% and 75% of lung parenchyma involved=Score 3; between 76% and 100% of lung parenchyma involved=Score 4.

Six images in three slices were analyzed in the lungs and an average score of all images was obtained and considered as a representative value of severity of emphysema in each person. This scoring system was first done on the grey scale images. Then this scoring was repeated again after applying a density mask or index to the image sequence. The density mask is a density threshold (-950 to -1024 HU) that highlights voxels within this density range. This level was chosen because it correlated best to the emphysematous changes in the lungs ^[17].

B. Airway measurements:

Only cross-sections perpendicular to the long airway axis have been selected. Regions of interest were traced manually, the bronchial external (D) and internal diameters (L) were assessed by standard software analysis for distance measurement expressed in (mm). After D and L measurements (Figure 1), the wall thickness (WT) with the assumption that the bronchial wall thickness is constant on the cross section: WT = (D - L)/2. Bronchial wall thickness (BWT) also named as T/D ratio, which defined as wall thickness (T) divided by the total diameter of the bronchus (D), were measured at the segmental and subsegmental levels as the following:

NB; Five selected lung levels were analyzed ^[18]:

- 1. Superior margin of the aortic arch (level 1).
- 2. Tracheal carina (level 2).
- **3.** 1 cm below the carina (level 3).
- 4. Inferior pulmonary veins (level 4).
- 5. 2 cm above the diaphragm (level 5).

2.4. Statistical analysis:

All data were analyzed using SPSS 15.0 for windows (SPSS Inc., Chicago, IL, USA) and MedCalc 13 for windows (MedCalc Software bvba). The categorical variables were expressed as a number (percentage), and the continuous variables were expressed as the mean \pm SD and median (range). Continuous variables were checked for normality by using Kolmogorov-Smirnov test. Student t-test was used to compare normally distributed data in two groups. One-Way ANOVA (F) test was used to compare normally distributed variables in three groups. Post-hoc Tamhane's T2 tests were used. Percent of categorical variables were compared using the Chi-square (χ 2) test. Pearson's momentum correlation analysis was done between T/D, FEV1 & emphysema score and all study parameters. p < 0.05 was considered statistically significant (S), p < 0.005 was considered highly statistically significant (HS), and $p \ge 0.05$ was considered non statistically significant (NS).



Figure (1): Measurements of the airway cross section: D - airway external diameter, L - airway luminal diameter, WT - wall thickness^[18]

3. Results:

The study included 35 males (73%) and 13 females (27%). Their age ranged between 48 and 75 years, the overall mean of age for included patients was 60.29 ± 7.13 and the age group between 50 - <60 years old was the most frequently affected (Figure 2). The peak and mean of age was higher in the males patients (75 years, mean= 61.43 ± 7.37) than in females patients (65 years, mean= 57.23 ± 5.64), with (*p* value=0.070).



Figure (2): Age grouping of studied patient

As regard the clinical data of studied patients, (56.3%) & (14.5 %) of patients were smokers & Exsmoker respectively, however, cough (89.6 %) was the main presenting clinical symptom in our study.

The studied patients were subdivided into three groups according to COPD clinical and CT phenotypes criteria. Group I is chronic bronchitis predominant (included 9 patients), group II is emphysema predominant (included 14 patients) and group III is mixed type (included 25 patients).

Regarding the demographic data of the patients in each group; there was a significant difference between male and female involved (p=0.008), while we found no significant difference in the age in each group (p=0.125), the mean ± SD for age were 56.11 ± 5.98, 60.36 ± 7.65, and 61.76 ± 6.88 for groups I, II, and III respectively, with no significant difference between the three groups (table 1). The mean value of FEV1% ± SD in groups I, group II, and group III were 62.67 ± 15.03, 55.36 ± 17.52, and 47.56 ± 16.26;

respectively (Table 1). There was no significant difference for FEV1 between the three groups. The mean value of TDR \pm SD in groups I, group II and group III were 33.16 \pm 1.25, 30.41 \pm 0.49, and 32.78 \pm 0.87; respectively. There was high significant difference for TDR when the three groups were compared (Table 1).

Table (1): (Comparisor	n between t	the studied	groups as regard	demograp	hic data; F	EV_1 ; and C	ГDR
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Demographic data	Group (I)		Group (II)			Group (III)		Test	p
	N=9 (18.75%)		N=14 (29.17%)			N=25 (52.08%)			
	No	%	No	%		No	%		
Age (years)								F	
Mean \pm SD	56.11	± 5.98	60.36 ± 7.65			61.76 ± 6.88		2.176	0.125 (NS)
Range	50-0	65	48-71			48 - 75			
Sex								χ^2	
Male	5	55.6%	7	50%		23	92%	9.707	0.008 (S)
Female	4	44.4%	7	50%		2	8%		
FEV ₁								Test	р
Mean \pm SD	62.67 ± 15.03		55.36 ± 17.52 47		47	47.56 ± 16.26		3.063	0.057 (NS)
Range	41 - 8	85	26-81		23 - 83				
FEV ₁	No	%	No	%	No		%	χ^2	
Mild	1	11.1%	2	14.3%	2		8%	0.386	0.824 (NS)
Moderate	5	55.6%	5	35.7%	7		28%	2.198	0.333 (NS)
Severe	3	33.3%	6	42.9%	12		48%	0.585	0.746 (NS)
Very severe			1	7.1%	4		16%	2.042	0.360 (NS)
TDR								F	Р
Mean \pm SD	33.16 ± 1.25 30.41 ± 0		30.41 ± 0.49	32.78 ± 0		32.78 ± 0.87		40.476	<0.001 (HS)
Range	31.48	- 35.30	29.3 - 31	31.05 - 34.5		4.5			

NS= non-significant; S= significant; HS=highly significant

As regard chest X-Ray; the studied patients depict different findings, 11 patients (22.91%) showing increase broncho-vascular marking (which is non-specific), representing chronic bronchitis group, 10 patients (20.83%) showing hyperinflation and flattening of diaphragm representing emphysema predominant on the level of chest X-Ray, in addition, 21 patients (43.75%), showing both findings who are grouped by CT as group II (emphysema), finally, normal chest X-Ray seen in 6 patients (12.51%)and all demonstrated on (Figure 3).



Figure (3): Chest X-ray finding in each patient

According to the emphysema score and emphysematype which correlate to the studied groups, the mean value \pm SD of emphysema score for groups II, III were (34.54 \pm 15.98 & 41.50 \pm 16.94) respectively. Score 2 is more represented in group III. Centriacinar emphysema is the most represented type demonstrated on (Table 2).

The correlation between FEV1 (%) and TDR versus selected study parameters were demonstrated on (table 3), and revealed high significant correlation between FEV1 and emphysema score in group III with no significant correlation between FEV1 and TDR in any group. Also, it reveals no significant correlation between TDR and emphysema score in any group.

Emphysema score	Group I (n=9)		Group II	(n=14)	Group III (n=25)			
	No	%	No	%	No	%		
Emphysema score (%)								
Mean \pm SD			34.54 ± 15.98		41.50 ± 16.94			
Median			33.07	33.07		41.45		
Range			18.45 - 77		15.51 – 78			
Emphysema score								
Score 0	9	100%						
Score 1			6	42.9%	7	28%		
Score 2			6	42.9%	11	44%		
Score 3			1	7.1%	5	20%		
Score 4			1	7.1%	2	8%		
Emphysema subtypes								
No emphysema	9	100%						
Centroacinar			9	64.3%	10	40%		
Para-acinar			4	28.6%	8	32%		
Panacinar			1	7.1%	7	28%		

 Table (2): Emphysema score & emphysema type in studied groups



Fig. (4): Centrilobular emphysema (score: 2) categorized as Group III (phenotype M) in 70 years old male patient, heavy smoker presented by cough, expectoration, dyspnea and wheeze with PFTs: - FEV/FVC < 70% and FEV1 \approx 46%. (A): Chest x-ray (PA view) shows hyperinflation of both lung fields with distortion of the pulmonary vessels. (B) Axial scan CTcut shows hypodense multiple areas of air trapping in both lung with emphysematous bullae in right middle lobe medially. (C) Axial CT cut through level 2 (Tracheal carina) shows WT= (D - L)/2 =1.77 & TDR= WT/D= 34 %.): Emphysema (obtained from ELC/TLC= 37.36%) and TDR: 33.15% (obtained from TDR mean from 5 levels). (D) 3D surface rendering volumetry shows total lung capacity (TLC) of 6448 cc.(E)Axial cut shows area of air trapping (blue colour).(F)3D surface rendering volumetry shows emphysematous lung capacity (ELC) of 2409 cc.

	All patients (n=48) [r(p)]	Group (I) (n=9) [r(p)]	Group (II) (n=14) [r(p)]	Group (III) (n=25) [r(p)]
Age Versus FEV ₁	-0.293 (0.043	-0.183 (0.638)	-0.171 (0.558)	-0.258 (0.213)
Emphysema score Versus FEV ₁	-0.603 (<0.001)		-0.653 (0.011)	-0.617 (0.001)
TDR Versus FEV ₁	-0.238 (0.104)	-0.562 (0.115)	-0.260 (0.369)	-0.305 (0.138)
Age Versus TDR	-0.041 (0.782)	0.264 (0.493)	0.134 (0.647)	-0.176 (0.399)
Emphysema score Versus TDR	-0.075 (0.612)		0.305 (0.289)	0.182 (0.384)

Table (3): Correlation between FEV_1 (%) and TDR versus selected study parameters

S= <0.05; NS=>0.05; and HS=<0.01



Fig. (5): Panlobular emphysema (score: 3) categorized as Group II (phenotype E) with multiple emphysematous bullae affected the RT lung in 58 years old male patient, ex- smoker, complaining of cough and wheeze with PFTs: FEV/FVC < 70% and $FEV1 \approx 26\%$. (A) Chest x-ray (PA view) shows hyperinflation of both lung fields with distortion of the pulmonary vessels, flattened cupolas, barrel shaped chest, widening of intercostal spaces & multiple variable sized bullae in both lungs. (B) & (C) Axial & coronal CT cuts shows hypodense multiple areas of air trapping in both lung with multiple emphysematous bullae more in right lung.(D) 3D surface rendering volumetry shows total lung capacity (TLC) of 6892 cc.(E) Axial cut shows area of air trapping (blue colour). (F) 3D surface rendering volumetry shows emphysematous lung capacity (ELC) of 3648 cc.



Fig. (6): No emphysema (score: 0) categorized as Group I (phenotype A) in 56 years old female patient, non-smoker, complaining of cough and wheeze with PFTs: FEV/FVC < 70% and FEV1 \approx 85%. (A) Chest x-ray (PA view) shows increase broncho-vascular markings. (B) Axial CT cut through level 1 (Superior to aortic arch) shows WT= (D - L)/2 = 1.8 & TDR= WT/D= 34 %. (C) Axial CT cut through level 2 (Tracheal carina) shows WT= 1.9 & TDR= 32%. (D) Axial CT cut through level 3 (1 cm below carina) shows WT= 1.9 & TDR= 34.52 %. (E) Axial CT cut through level 4 (level of inferior pulmonary vein) shows WT= 1.9 & TDR= 35.50 %. (F) Axial CT cut through level 5 (2 cm above diaphragm) shows WT= 1.7 & TDR= 33.30 %.



Fig. (7): Panlobular emphysema (score: 2) categorized as Group III (phenotype M) in 60 years old female patient, nonsmoker, complaining of cough and dyspnea with PFTs: FEV/FVC < 70% and FEV1 \approx 42%. (A) Chest x-ray (PA view) shows relative hyperinflation of both lung fields with distortion of the pulmonary vessels. (B) Axial CT cut shows hypodense multiple areas of air trapping in both lung. (C) Axial CT cut through level 3 (1 cm below carina) shows WT= 1.8 & TDR= 32.65 %. (D) 3D surface rendering volumetry shows total lung capacity (TLC) of 2825 cc. (E) Axial cut shows area of air trapping (blue colour). (F) 3D surface rendering volumetry shows emphysematous lung capacity (ELC) of 913 cc.



Fig. (8): Centrilobular emphysema (score: 1) categorized as Group II (phenotype E) in 70 years old male patient, ex-smoker, presented by cough, expectoration & wheeze with PFTs: FEV/FVC < 70% and FEV1 \approx 62%. (A) Chest x-ray (PA view) shows hyperinflation of both lung fields with distortion of the pulmonary vessels. (B) & (C) Axial & coronal CT scans shows hypodense multiple areas of air trapping in both lung with emphysematous bullae in right middle lobe medially.(D) 3D surface rendering volumetry shows total lung capacity (TLC) of 4036 cc.(E) Axial cut shows area of air trapping (blue colour). (F) 3D surface rendering volumetry shows emphysematous lung capacity (ELC) of 867 cc.



Fig. (9): Panlobular emphysema (score: 2) categorized as Group II (phenotype E) in 51 years old female patient, non-smoker, complaining of cough, expectoration & dyspnea with PFTs: FEV/FVC < 70% and FEV1 \approx 55%. (A) Chest x-ray (PA view) shows hyperinflation of both lung fields with obvious other emphysematous. (B) & (C): Axial & coronal CT scans shows hypodense multiple areas of air trapping in both lung.(D) 3D surface rendering volumetry shows total lung capacity (TLC) of 2934 cc.(E) Axial cut shows area of air trapping (blue colour). (F) 3D surface rendering volumetry shows emphysematous lung capacity (ELC) of 1670 cc.

4. Discussion:

Chronic obstructive pulmonary disease (COPD) is defined as "a disease state characterized by airflow limitation that is not fully reversible". Remodeling of small airway with varying levels of emphysematous affection is the underlying mechanism of airflow limitation in obstructive lung diseases. PFT results can not differentiate between these two pathologies. The differentiation is clinical important because of therapeutic intervention selection ^[19]. Kitaguchi et al.^[20] proposed classifying COPD patients according to their CT findings into Phenotype A (nor minimal emphysema with or without airway disease), Phenotype E (emphysema without airway disease) and Phenotype M (mixed airway and emphysema disease). A similar approach was also proposed by Han *et al.*^[6] where they suggested that CT could be used to discriminate between patients with the same spirometric results. Although spirometry is a noninvasive and gives a global evaluation of the lung function, it does not evaluate the emphysema distribution through the lung. In contrast, lung assessment including parenchyma, airways, and vessels can be obtained by CT^[21].

Chest radiography is an inexpensive, valuable meanin diagnosing moderate-to-severe emphysema. However, it is less sensitive than CT in detecting mild emphysema and less accurate in evaluating regional distribution of emphysema, its quantification and extent, rather than the affected airway ^[22].

With the continuous development in disease management, researchers have developed new quantification methods for the evaluation of the different chest MDCT findings in COPD patients. Airway changes are quantified by several parameters, e.g. wall thickness, total airway count and square root of wall area ^[23]. Airspace (emphysematous) changes are also quantified by some parameters, e.g. emphysema index and semi-quantitative visual scoring system. The airspace and airway measures were, when co-existent, negatively correlate in COPD patients ^[24].

Although the airspace damage is irreversible, many researchers have found that the pre-operative quantitative CT assessment of emphysema and its distribution predicted a better post-operative outcome. For example, some authors suggested that upper lobe emphysema had a better outcome after lung volume reduction surgery (LVRS) than patients with predominantly lower lobe emphysema ^[25].

The goal of COPD phenotyping is to identify patient groups with similar prognostic or therapeutic characteristics, however, significant variation and confusion surrounds the use of the term "phenotype" in COPD. Our study was done on 48 patients where 73% were males and 27% were females and peak-age was 50 - <60 years which represented 90.9% of our cases. This agreed with Grydeland *et al.*^[26] who found that the number of peak-years in COPD cases was higher in males than females. Laniado-Laborín ^[27] found that people whom were lifelong smokers about 50% have gotten COPD. Rennard and Stephen^[28] found that in United States and United Kingdom, of those with COPD 80-90% were either current smokers or Ex-smoker. Our study showed almost the same results where 56.3% were smoker and 14.5% were Ex-smoker (70.8% were current and previously smoked). Chronic cough is the first and more frequent symptom in patients of COPD ^[29]. Our series confirmed that statement showing that 89.6% had cough and 47.9% had dyspnea.

In our study by chest radiography there were 12.51% of patients diagnosed as normal and appeared by CT as emphysema, these findings were consistent with the findings reported in a study by Yilmaz *et al.*^[30] who reported that even when conventional radiographic findings are normal, HRCT could be a useful examination, because it provides a high degree of anatomic details and can indirectly confirm airway remodeling. It has been used to study overall bronchial and parenchymal damage, also this agreed with Miniati et al. ^[22] who suggested in his study for the comparison between the chest X ray and CT in that chest radiography couldn't detect trace or mild emphysema that was easily detected on CT. The rate of false-positive cases was very low.

We use MSCT as standard HRCT scanning with single-slice CT that produce images of different thickness from data acquired by contiguous thin slice scanning during a single breath- hold. In our study we used threshold (-950 HU) of emphysema were used according to 10th centile of normal individuals based on correlations with pathological measures and pulmonary function tests ^[31]. The mean T/D ratio of 31% was considered as cut off point comparing our patients to each other's.

The big section of the three phenotypes in our patients was the mixed form (52.08%) while the chronic bronchitis type represents (18.75%) and emphysematous type represents (29.17%) of the patients which is not far from other studies in this concern such as Kitaguchi *et al.*^[20] in which the percentage of emphysematous group was 31% and the bronchitic group represented 12.9 % of total patients. In our work we found no significant correlation between FEV1 and bronchial wall thickening percentage, Devecia and Teyfik^[32] found that T/D ratio correlate relatively negative with abnormalities of FEV1 of predicted. Also suggests that wall thickening and airway narrowing influence airflow obstruction. Our study revealed that there is significant

correlation between emphysema score and FEV1 in group II and III, this finding in similar to Makita *et al.*^[33] who stated that there is significant relationship between FEV1 percentage predicted observed in this study and severity of emphysema, unlike Tulek et al.^[34] who found that there is inverse correlation between emphysema score and FEV1.

Also Patel *et al.*^[35] reported that while there were independent functional correlations between emphysema and airway disease with FEV1, there was a statistically significant negative but weak correlation between measures of these two disease processes.

Finally, although FEV1 is an essential measure in COPD research, its importance is limited by its inability to reveal regional variations in disease within the lungs or to distinguish between wide ranges of pathophysiological processes, including inflammation, smooth muscle hypertrophy, mucous metaplasia, fibrosis, and loss of bronchiolar tethering with destructed alveoli. All of gross pathologies of the lung can be analyzed quantitatively using MDCT and classified to airway-predominant, emphysema-predominant, or mixed and this classification is very beneficial for proper therapy ^{[10].}

Conclusion:

Airway-related COPD and emphysema are distinct phenotypes and the assessment of lung physiology through PFTs do not accurately discriminate between the abnormalities resulting from predominant airway disease from those resulting from predominant emphysema. Advances in HRCT have the potential to separate and quantify both airway component and emphysema in COPD patients.

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