Original Paper

The Correlation Between HRCT Phenotypes and Spirometric Indices in Patients with COPD

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) is a preventable and controllable inflammatory respiratory disease that is a leading cause of morbidity and mortality worldwide.
Objectives: The current study aimed to investigate COPD phenotypes by high resolution computed tomography (HRCT) and compare these phenotypes and other CT findings with the severity of Spirometric variables.
Patients and Methods: A cross-sectional study was performed on 56 patients with COPD of any duration and smoking history referred to the radiology department of Al-Imamain Al-Kadhimain Medical city, during the period from May 1 to December 31, 2019. Spirometry was performed at the same visit during which chest HRCT was imaged, and two independent radiologists and findings interpreted these images were evaluated according to the modified Bhalla scoring system.
Results: From 56 patients included in the study, 47 (83.9%) patients exhibited morphological CT changes. Patients with HRCT changes were classified into three phenotypes: Emphysema dominant (n=19), airway dominant (n=18), and mixed phenotype (n=10). Except for forced expiratory volume in 1 second to forced vital capacity ratio (FEV1/FVC), other spirometric variables, including severity stages termed the global initiative for chronic obstructive lung disease (GOLD), showed no significant correlation to the correspondent phenotypes. In contrast, HRCT findings, including those scored according to the modified Bhalla system, were significantly correlated to the CT phenotypes. On the other hand, GOLD severity showed no correlation with the presence or severity of morphological lung changes detected on HRCT.
Conclusion: The GOLD stages of COPD severity based on spirometry are not correlated with radiological phenotypes recognized on HRCT or the severity of those morphological changes. In contrast, a significant correlation was found between COPD phenotypes characterized on CT and the severity of morphological abnormalities.

Keywords: COPD, CT phenotypes, GOLD scoring, CT scoring.

Introduction

Chronic obstructive pulmonary disease (COPD) is a preventable and controllable inflammatory respiratory disease characterized by airflow limitation that is not fully reversible [(1)]. It is now the third leading cause of death globally, according to studies published by the World Bank/World Health Organization [(2-4)].

The diagnosis of COPD is conventionally based upon pulmonary function testing (PFT). Spirometry is a simple, important, and the most generally used PFT in clinical practice to distinguish variations from the norm in lung volumes and airflow [(5,6)]. With both the Global Initiative for Chronic Obstructive Lung Disease (GOLD) guidelines and the combined American Thoracic Society and the European Respiratory Society, COPD guidelines recommend using the

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fixed cutoff for the diagnosis of COPD is forced expiratory volume in one second (FEV1) to forced vital capacity (FVC) ratio (FEV1/FVC) <0.70 [2, 7, 8].

According to the GOLD 2017 scoring system, patients with an (FEV1/FVC) ratio of less than 0.7 are classified into: GOLD I patients, with preserved FEV1 (mild COPD), GOLD II with FEV1 <80% predicted (moderate), GOLD III FEV1 <50% predicted (severe) and GOLD IV FEV1 <30% predicted (very severe). Those having the same GOLD category may have very different morphologic CT appearances [9].

High-resolution computed tomography (HRCT) phenotypes of COPD may reflect the pathological basis of COPD indirectly by evaluating the small airway inflammation and emphysema and is aimed to classify patients into distinct subgroups according to response to therapy and prognosis so that better selection of the appropriate treatment that can optimize clinically meaningful outcomes for patients [10-12].

This study was designed to investigate COPD phenotypes by HRCT and compare these phenotypes and other CT findings with the severity of Spirometric variables.

Patients and methods

A cross-sectional study was performed on patients with COPD of any duration and smoking history in the respiratory outpatient clinic of Al-Imamain Al-Kadhimain Medical City in Baghdad during the study period from 1st of May 2019 to 31st of December 2019.

Exclusion criteria were in-cooperative patients (inability to perform pulmonary function tests or CT scan) and those known to have secondary pulmonary deposits, tuberculosis sequelae, active chest infection, or recent major trauma to the chest.

Verbal informed consent has been taken for all patients before participating in the study.

Spirometry was performed at the same visit during which chest HRCT was imaged. Initially, a brief history was taken about demographic information, occupation, presenting symptoms and duration, amount of smoking and duration, whether previous chest imaging was available, and a quick clinical examination, including general look, presence of respiratory distress, and patient's activity.

A 256 slice SIEMENS, SOMATOM, Definition Edge, Germany, was used for imaging. Non-contrast-enhanced study with volumetric acquisitions and reconstruction 0.6 mm slice thickness, in high spatial resolution algorithm, using 120 Kv and auto-adjusted Care-dose mAs. The scans were performed in the supine position, with the breath held at full inspiration.

The imaging features searched and assessed on HRCT were emphysema, bronchial wall thickness, tracheal index (TI): ratio of transverse to AP diameter of trachea 1 cm above the aortic arch, thoracic cage ratio (TCR): ratio of AP to transverse diameter of the chest 5 cm below carina, Sterno-aortic distance (SAD): distance from the posterior surface of the sternum to anterior margin of the aorta at the level of the carina, vascular attenuation (thinning and decreased the number of pulmonary vessels), the presence of bronchiectasis, bullae, pulmonary artery dilatation (when pulmonary artery diameter≥ 3cm or when the pulmonary artery to aortic ratio ≥ 1), evidence of fibrosis, tree-in-bud, air trapping, and mucous plugs.

As analyzing and scoring each CT study, patients were classified as having just emphysema (EMP) when the emphysema score one or more, just airway dominant (AWD) when the peribronchial thickening score is one or more, or mixed (EMP and AWD) when both emphysema and peribronchial thickening scores are one or more.

All study protocols were approved by Iraqi Board for medical specialization/ Diagnostic Radiology. Patients names and personal information were kept confidential.

Data were entered and analyzed using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 27 was used. Quantitative variables

were presented as mean ± standard deviation (SD), and qualitative variables were presented in frequencies and percentages. Chi-square, t, or ANOVA test was used accordingly for statistical analysis, and a P value of less than 0.05 was considered significant.

Results

Fifty-six COPD patients were included in this study with a mean age of 57.6± 10.4 years; 51 (91.1%) were males, and 5 (8.9%) were females. Sixty-four percent of the candidates were current smokers, while 35.7% were not smokers at the survey time, with mean pack-year smoking for the previous and current smokers 28.38 ± 14.4.

COPD severity according to GOLD scoring categorize patients into GOLD I =8 (14.3%), GOLD II= 22 (39.3%), GOLD III= 15(26.8%), and GOLD IV = 11(19.6%).

Nineteen patients (33.9%) showed emphysema dominant phenotype, 18 patients (32.1%) showed airway dominant phenotype, mixed phenotype seen in 10 (17.9%) of the patients, while 9 (16.1%) of them showed no CT findings that we sought. The mean emphysema score on CT was found to be 1.8 ± 2.1, seen in 29 patients (including both emphysema dominant and mixed phenotypes).

Emphysematous bullae were seen in 11 (19.6 %) with a mean score of 0.23± 0.50. Tree-in-bud was seen in 17 (30.4%) patients with mean scoring 0.37 ± 0.64, vascular attenuation and mucous plug noticed in 16 (28.6%) patients, and the mean score of the mucous plug was 0.39 ± 0.67.

While 24(42.9%) showed air trapping with a score mean 0.67± 0.91. Peribronchial thickening was seen in 28 (50%) patients, with a mean score of 2.0± 2.5. Bronchiectasis has seen in 20 (35.7%) subjects with a mean score of 1.5± 3.4. While fibrotic collapse/ consolidation was noticed in 19 (33.9%) and score mean 0.37 ± 0.55, which were segmental or sub-segmental, pulmonary artery dilatation was seen in 6 (10.7%) of them.

The mean overall CT score was 7.4± 6.98. Nine (16.1%) of patients had normal score (0), 36 (64.3%) of them had mild score (1-9), 7 (12.5%) had moderate score (10-14), and 4 (7.1%) had very severe score (>18), while none of them had the severe range (15-18). All CT findings included in Bhala scoring system were mentioned in (Table 1).

Indicators of hyperinflation were also checked, as thoracic cage ratio 5cm bellow carina (TCR) mean found 0.66± 0.08, and 2 (3.57%) showed to have a barrel chest (TCR > 0.9).

Tracheal index (TI); mean 1.9± 0.26, with Saber sheath trachea (TI< 0.5) was seen in one (1.78%) of them. In comparison, Sterno-aortic distance (SAD) was found to be >4 cm in one patient. As seen in (table 2 and 3).

Regarding the severity of CT findings based on CT score, 3(33.3%) of patients with normal CT score had GOLD I, 3 (33.3%) were GOLD II, 2(22.2%) were GOLD III, and 1 (11.1%) had GOLD IV.

Table 1. HRCT findings of all patients (n=56)

CT finding	Frequency (%)	mean ± SD
Bronchiectasis (score range 0–30)	20 (35%)	1.53 ± 3.49
Peribronchial thickening (score range: 0–18)	28 (50%)	2.03 ± 2.52
Tree-in-bud (score range: 0–6)	17 (30.4%)	0.37 ± 0.64
Mucous plugging(score range:0–6)	16 (28.6%)	0.39 ± 0.67
Air trapping (score range: 0–6)	24 (42.9%)	0.67 ± 0.91
Bullae (score range: 0–3)	11 (19.6%)	0.23 ± 0.5
Emphysema (score range: 0–6)	29 (51.8%)	1.85 ± 2.12
Fibrotic consolidation/ collapse (score range: 0–2)	19 (33.9%)	0.37 ± 0.55
CT total score (score range: 0–77)		7.48 ± 6.98

Table 2. Demographic, spirometric, and CT findings comparisons and correlations among patients with EMP only, AWD only, and mixed types of COPD severity, as GOLD score with COPD phenotype detected by CT.

Patient characteristics / phenotype		Emphysema dominant (n=19)	Airway dominant (n=18)	Mixed phenotype (n=10)	Norma (n=9)	P-value
Age in year	Mean	61.15	52.8	62.1	54.8	0.032
	SD	9.8	9.3	12.5	6.8	
Pack Year	Mean	34.9	26.6	31	15	0.176
	SD	14.2	13.02	14.9	6.9	
Currently smoker	N	10	14	7	5	0.393
	%	27.8%	38.9%	19.4%	13.9%	
FEV1 (L)	Mean	1.1	1.3	1.2	1.5	0.151
	SD	0.42	0.48	0.4	0.3	
EVC (L)	Mean	2.01	2.1	2.09	2.5	0.151
	SD	0.5	0.6	0.5	0.3	
FEV1/ FVC	Mean	0.54	0.61	0.5	0.68	0.04
	SD	0.08	0.07	0.08	0.08	
Peribronchial thickening	Mean	0	4.1	4	0	<0.001
	SD	0	1.7	2.7	0	
Bronchiectasis	Mean	0	2.2	4	0	0.007
	SD	0	3.3	6.03	0	
Tree-in-bud	Mean	0.2	0.4	0.9	0	0.008
	SD	0.4	0.6	0.9	0	
Air trapping	Mean	0.6	0.9	0.9	0	0.060
	SD	0.8	1.05	0.9	0	
Fibrotic collapse/ consolidation	Mean	0.4	0.2	0.7	0.1	0.105
	SD	0.5	0.4	0.8	0.33	
Mucous plug	Mean	0.3	0.5	0.7	0	0.124
	SD	0.67	0.7	0.82	0	
EMP score	Mean	3.68	0	3.4	0	<0.001
	SD	1.66	0	1.42	0	
Bullae	Mean	0.2	0	0.8	0	<0.001
	SD	0.45	0	0.78	0	
CT score	Mean	5.5	8.5	15.4	0	<0.001
	SD	2.16	5.8	9.57	0	
Vascular attenuation	N	5	5	6	0	0.033
	%	31.3%	31.3%	37.5%	0.0%	
SAD >4 cm	N	0	0	1	0	0.195
	%	0	0	1	0	
Pulmonary artery dilatation	N	1	3	2	0	0.354
	%	16.7%	50.0%	33.3%	0.0%	
TCR	Mean	0.6	0.6	0.67	0.63	0.513
	SD	0.09	0.09	0.09	0.07	
TI	Mean	0.94	1.009	0.89	0.92	0.543
	SD	0.31	0.28	0.22	0.103	

Table 3. Demographic, Spirometric, and CT findings: Comparisons and Correlations among patients with GOLD severity.

Patient characteristics		GOLD Score				
		I (n=8)	II (n=22)	III (n=15)	IV (n=11)	P- value
Age (years)	Mean	50.2	57	62.06	58.2	0.071
	SD	9.45	9.59	11.15	9.52	
Pack Year	Mean	34.9	26.6	31	26.5	0.042
	SD	14.2	13.02	14.9	16.20	
Currently smoker	N	7	14	8	7	0.441
	%	0.19	0.38	0.22	0.19	
FEV1(L)	Mean	1.8	1.19	1.2	1.14	<0.001
	SD	0.18	0.35	0.42	0.46	
EVC(L)	Mean	2.82	2.	2.17	1.9	0.002
	SD	0.24	0.49	0.48	0.62	
FEV1/ FVC	Mean	0.66	0.59	0.57	0.52	0.033
	SD	0.03	0.07	0.09	0.09	
Peribronchial thickening	Mean	2.25	2.59	1.13	2	0.391
	SD	3.49	2.59	1.95	2.28	
Bronchiectasis	Mean	1.75	2.45	0.6	0.36	0.272
	SD	4.2	4.74	0.98	0.5	
Tree-in-bud	Mean	0.62	0.45	0.2	0.27	0.413
	SD	0.74	0.80	0.41	0.46	
Air rapping	Mean	0.37	1.22	0.53	0	0.001
	SD	0.74	1.06	0.63	0	
Fibrotic collapse/ consolidation	Mean	0.25	0.27	0.4	0.6	0.312
	SD	0.70	0.45	0.50	0.67	
Mucous plug	Mean	0.25	0.54	0.2	0.3	0.585
	SD	0.46	0.80	0.7	0.5	
EMP score	Mean	1.7	1.2	2.5	2.2	0.277
	SD	2.54	1.71	2.09	2.49	
Bullae	Mean	0.5	0.13	0.26	0.18	0.368
	SD	0.75	0.35	0.59	0.40	
CT score	Mean	7.7	8.9	5.86	6.09	0.555
	SD	10.59	8.22	4.03	4.06	
Vascular attenuation	N	2	7	5	2	0.837
	%	12.5%	43.8%	31.3%	12.5%	
SAD >4 cm	N	0	1	0	0	0.656
	%	0	1	0	0	
Pulmonary artery dilatation	N	0	3	1	2	0.565
	%	0.0%	50.0%	16.7%	33.3%	
TCR	Mean	0.63	0.68	0.64	0.6	0.422
	SD	0.07	0.08	0.09	0.10	
TI	Mean	0.93	0.87	1.04	0.96	0.316
	SD	0.2	0.18	0.34	0.27	

Patients with mild CT score severity, 3(8.3%) of them had GOLD I, 15 (41.7%) were GOLD II, 10 (27.8%) were GOLD III, and 8 (22.2%) had GOLD IV. See (Table 4).

One (14.3%) of patients with moderate CT score had GOLD I, 1 (14.3%) were GOLD II, 3 (42.9%) were GOLD III, and 2 (28.6%) had GOLD IV. Patients with a very severe range of CT score; 1 (25%) of them had GOLD I, 3 (75%) were GOLD II. No significance concluded in this correlation (P- value= 0.4); (Table 5). While the highly significant correlation was found between CT, score severity with COPD phenotype with P-value< 0.001 (Table 6).

Table 4. Correlation of COPD severity as GOLD score with COPD phenotype detected by CT.

GOLD severity		EMP	AWD	Mixed	Normal	P- value
I	N	2	2	1	3	0.430
	%	25.0%	25.0%	12.5%	37.5%	
II	N	6	10	3	3	
	%	27.3%	45.5%	13.6%	13.6%	
III	N	8	2	3	2	
	%	53.3%	13.3%	20.0%	13.3%	
IV	N	3	4	3	1	
	%	27.3%	36.4%	27.3%	9.1%	
Total	N	19	18	10	9	
	%	33.9%	32.1%	17.9%	16.1%	

Table 5. Correlation between severity of CT findings based on CT score with GOLD severity.

CT Score		GOLD Score					p- value
		I	II	III	IV	Total	
0	N	3	3	2	1	9	0.421
	%	33.3%	33.3%	22.2%	11.1%	100.%	
Mild (1-9)	N	3	15	10	8	36	
	%	8.3%	41.7%	27.8%	22.2%	100.%	
Moderate (10-14)	N	1	1	3	2	7	
	%	14.3%	14.3%	42.9%	28.6%	100.%	
Severe(15-18)	N	0	0	0	0	0	
	%	0.0%	0.0%	0.0%	0.0%	0.0%	
Very severe (>18)	N	1	3	0	0	4	
	%	25.0%	75.0%	0.0%	0.0%	100.%	

Table 6. Correlation between severity of CT findings based on CT score with CT phenotypes.

CT score severity		CT Phenotyping					p-value
		EMP	AWD	Mixed	Normal	Total	
Normal	N	0	0	0	9	9	<0.001
	%	0.0%	0.0%	0.0%	100.0%	100.0%	
Mild	N	19	15	2	0	36	
	%	52.8%	41.7%	5.6%	0.0%	100.0%	
Moderate	N	0	1	6	0	7	
	%	0.0%	14.3%	85.7%	0.0%	100.0%	
Severe	N	0	0	0	0	0	
	%	0.0%	0.0%	0.0%	0.0%	0.0%	
Very severe	N	0	2	2	0	4	
	%	0.0%	50.0%	50.0%	0.0%	100.0%	
total	N	19	18	10	9	56	
	%	33.9%	32.1%	17.9%	16.1%	100.0%	

Cases from our study

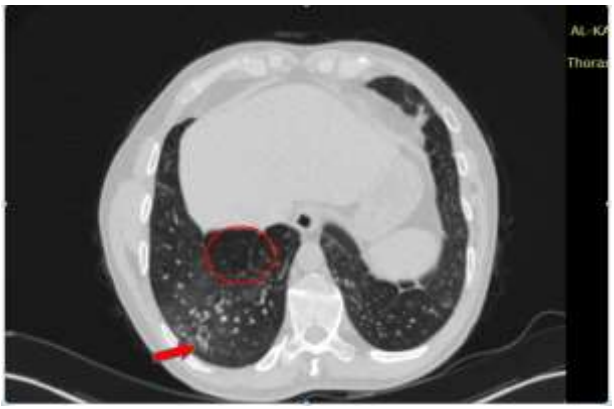

Figure 1. Axial chest CT scan of 70 years old male with COPD shows area air trapping with vascular attenuation (red circle) and tree in bud appearance (arrow); he had AWD type of COPD, GOLD III score, and CT score of 10.

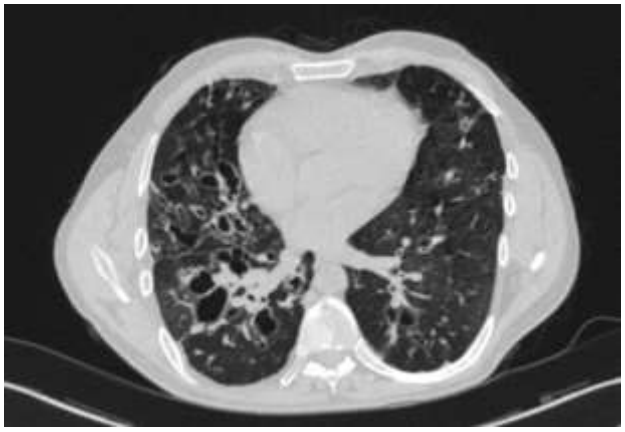

Figure 2. HRCT for 66 years old age male with COPD of mixed phenotype showing widespread bronchiectasis, peribronchial thickening, and small areas of centrilobular emphysema, he had AWD type of COPD, GOLD II score, and CT score of 20.

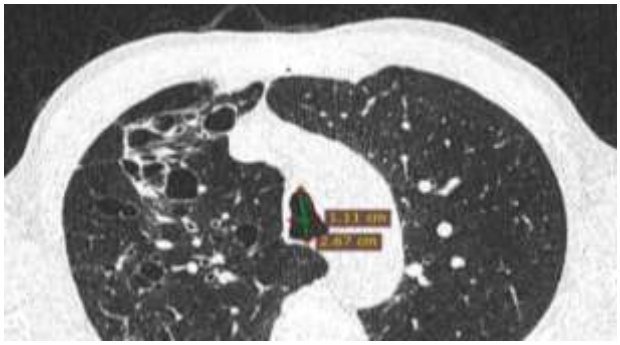

Figure 3. CT scan of 59 years old age male with COPD shows Saber sheath trachea with an area of cystic bronchiectasis in the right upper lobe is also seen, and he had mixed type of COPD, GOLD III score, and CT score of 7.

Discussion

Chronic obstructive airway disease is a greatly heterogeneous condition and includes several pathological processes whose clinical manifestations and systemic effects vary widely depending on individual susceptibility. Grading the severity of COPD by only the FEV1 is misleading. This heterogeneity reflects the pattern and intensity of patient response to therapeutic measures [14].

The 2011 Spanish COPD Guide was the first to indicate that treatment should be guided according to the phenotype and clinical characteristics of the patient, rather than being based on the severity of airflow limitation, and that COPD phenotypes are closely correlated to clinical outcomes [15].

In our study, COPD severity according to GOLD criteria categorize patients into GOLD I =8 (14.3%) patients, GOLD II= 22 (39.3%), GOLD III= 15(26.8%), and GOLD IV = 11(19.6%), having pulmonary functions parameters FEV1 mean 1.3 ±0.44, FVC mean 2.16 ± 0.55, and FEV1/FVC mean 0.59 ± 0.83.

We found that Nineteen patients (33.9%) showed emphysema dominant phenotype (EMP), 18 patients (32.1%) showed airway dominant phenotype (AWD), mixed phenotype seen in 10 (17.9%) of the patients, while 9 (16.1%) of them showed no CT findings, these percentages are close to that of Dogra et al. study [16].

The number of patients having emphysema on CT is 29 (involving emphysema dominant and mixed phenotypes), and the Centrilobular emphysema type is seen twice more common than the paraseptal emphysema subtype, which is expected as the former is typical for smokers.

In correlation with the number of patients between phenotypes and GOLD severities,

although a higher number of those with normal CT studies showed lower GOLD stage, no statistically significant correlation was found (P-value =0.43) as mentioned in Table (3-2). Therefore, GOLD stages depending on spirometry cannot predict the COPD phenotype, da Silva et al. [17] and Dogra et al [16] found similar results, while He et al [18] found GOLD severity to be correlated to COPD phenotypes.

All patients with EMP showed mild severity based on the CT score severity, while mixed phenotype tended to have more severe scoring. The mean CT score in airway phenotype is 8.2 ± 5.8, in emphysema phenotype 6.1 ± 2.9, and in mixed phenotype 15.6 ± 9.8, P-value <0.001.

Significant correlation with high significance found between the severity of individual CT finding with COPD phenotype, which is expected as deciding what phenotype the patient has is related to the presence or absence of emphysema or airway or both contributors to the overall CT score. This result is similar to what Tulek et al. [19] have found.

Regarding the severity of CT findings based on CT score, we found no correlation between the severity of CT findings and the severity of pulmonary function score as GOLD stages (P- value= 0.4, Table (3-5). GOLD severity showed to have no correlation with the presence or severity of morphological lung changed detected on HRCT, and this agrees with Tulek et al. findings ([19].

Mean of FEV1/ FVC in airway phenotype is 0.54 ± 0.08, in emphysema phenotype 0.61 ± 0.07, in mixed phenotype 0.5 ± 0.08, the p-value = 0.04 (significant correlation). While mean FEV1 in GOLD I= 0.66 ± 0.03, in GOLD II= 0.59 ± 0.07, in GOLD III= 0.57 ± 0.09 and in GOLD IV= 0.52 ±0.09, P- value= 0.031, which is significant as well. These findings in agreement with previous studies including da silva et al [17], Dogra et al [16], and Tulek et al [19].

Conclusion

The GOLD stages of COPD severity based on spirometry do not correlate with radiological phenotypes recognized on CT or the severity of the morphological changes; conversely, a close relationship was found between COPD phenotypes characterized on CT and the severity of morphological abnormalities.

Adding HRCT to the routine examinations for selected COPD patients is recommended to provide effective management options.

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