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Clinical, physiological, and radiological different phenotypes of COPD patients

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Abstract

Background COPD is a heterogeneous lung disorder with multiple phenotypes and endotypes. This study aimed to identify the diverse clinical, physiological, and radiological phenotypes of COPD. Moreover, to provide whether there was a possible relation between FEV1%, FVC%, and FEV1/FVC ratio, [both before and after broncho-dilation with the diameters of the airway at three diverse levels throughout both inspiratory and expiratory phases of respiration].

Results This study included 50 cases, that were classified according to the radiological phenotypes into 5 groups [29 cases (58%) were mild [centrilobular emphysema) CLE)], 8 cases (16%) were moderate CLE, 5 cases (10%) were [confluent emphysema (CON)], 5 cases (10%) were [advanced destructive emphysema (ADE)] and 3 cases (6%) were [para septal emphysema (PSE)]. There was no considerable variance in the frequency of COPD clinical phenotypes among the diverse radiological phenotypes. There was a moderate positive correlation between the predicted FEV1% and the corresponding inter-luminal diameter at the selected levels (RB1, and LB3) in the inspiratory phase of respiration ($P<0.001$ and $p=0.001$ respectively) ($r=0.58$, 0.46 respectively). and there was a moderate positive correlation in the expiratory phase of respiration between the predicted FEV1% and the equivalent inter-luminal diameter at the selected levels (RB1, and LB3) ($P<0.001$ respectively) ($r=0.62$, 0.51 respectively).

Conclusions We confirmed that COPD is a highly heterogeneous illness, with multiple diverse clinical, physiological, and radiological phenotypes. Furthermore, HRCT can well be allied with pulmonary function tests (PFT).

Keywords COPD, Quantitative MSCT, Pulmonary function test, Phenotypes

Introduction

COPD is a heterogeneous lung disorder categorized by chronic respiratory complaints (shortness of breath, cough, sputum, exacerbations) due to a diversity of the airway's anomalies (bronchitis, bronchiolitis) and/or alveolar (emphysema) that cause constant, commonly progressive airflow limitation [1]. and is nowadays considered as a heterogeneous illness with multiple phenotypes and endotypes [2].

The term phenotype has been presented to aid physicians in the documentation of the diverse types of COPD sub-groups. The description for "phenotype" is considered as [the physical appearance or bio-chemical criteria as a consequence of interaction amid the genotype and environment]. Furthermore, the definition clearly states that a phenotype has to be a subgroup with a great impact on the prognosis (complaints, exacerbations, response to medications, rate of disease progression, or death) [3].

Spirometry was the main evaluation technique in diagnosing the severity of airway obstruction because it is simple, non-invasive, and easily applied. The diagnosis of COPD was built mostly on pulmonary function tests. However, the constant variations in parenchymal and airway pathology added a more diverse analytical urge [4].

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CT imaging has arisen as a non-invasive measure in the phenotyping of COPD, aiming to investigate the changes in the airway wall, lumen, and lung parenchyma, as well as calculations of emphysema degree (EM) and load of small airways illness [5].

This study aimed to identify the diverse clinical, physiological, and radiological phenotypes of COPD. Moreover, to provide whether there was a possible relation between FEV1%, FVC%, and FEV1/FVC ratio, [both before and after broncho-dilation with the diameters of the airway at 3 diverse levels throughout both inspiratory and expiratory phase of respiration].

Patients and methods

Study design

It is a prospective cross-sectional study that was accomplished in the Chest Department, Faculty of Medicine, Aswan University, during the period from October 2021 till October 2022.

Ethical consideration

This study was approved by the ethical committee of the Faculty of Medicine, Aswan University (IBR 522/3/21), and all subjects gave written informed consent prior to participating in the study.

Clinical trial registration number

NCT05747235

Eligible participants

Inclusion criteria

- All COPD cases that are clinically stable (at least 30 days after being recovered from the most recent exacerbation)
- Smoker or former smoker (minimum of 10 packs each year)
- Post-bronchodilator [FEV1/FVC ratio < 0.7 and FEV1 < 80% or pre-bronchodilator FEV1/FVC ratio < 0.7 and FEV1 < 80%]
- Capability to complete the MSCT

Exclusion criteria

- Cases with other chest illnesses: for example, collapse, consolidation, effusion, malignancy, and thoracic cage deformity which have an impact on lung volumes.
- Uncooperative cases.

All eligible participants were subjected to the following:

1) *A thorough history* is taken, comprising the following information: age, gender, BMI, occupation, smoking status, smoking index, other special habits (such as experience with biomass fuel), the existence of comorbid conditions, chest complaints, health-related quality of life (HRQoL) evaluation, frequency of exacerbations, requirement for hospitalization in the preceding year, clinical phenotypes of COPD, and GOLD staging.

The patients' breathlessness was categorized according to the modified Medical Research Council scale [6].

With minimal assistance from the researchers, the patients were instructed to complete *the CAT and SGRQ-c questionnaires* independently in order to evaluate their HRQoL. Eight questions make up the CAT questionnaire: a cough (CAT 1), phlegm (CAT 2), tightness in the chest (CAT 3), dyspnea (CAT 4), activity restriction (CAT 5), confidence in leaving the house (CAT 6), sleep (CAT 7), and energy (CAT 8). Each of these items receives a score between 0 and 5, while the overall score ranges from 0 to 40. A healthy subject's overall CAT score is less than six, with a higher score indicating a stronger or worse impact of COPD on HRQoL [7]. Fourteen questions make up the SGRQ-c questionnaire, with questions 1 through 7 focusing on the symptom component, questions 9 and 12 on the activity component, and questions 8, 10, 11, 13, and 14 on the impact component. Each component's score as well as the overall score ranges from 0 to 100%, with a higher score indicating worse HRQoL. The total score in healthy subjects is (6%), the symptom component is (12%), the activity component is (9%), and the effect component is (2%) [8].

Exacerbations in the last year: only moderate and severe exacerbations were taken into account when calculating the total number of exacerbations. A moderate exacerbation was defined as one that required outpatient therapy, whilst a severe exacerbation was classified as one that needed hospital admission [9].

The following clinical phenotypes of COPD were identified using the GesEPOC guidelines: a non-exacerbator phenotype (NON-AE) is one in which there have been no severe exacerbations in the preceding year and less than two episodes of moderate exacerbation. The presence of two or more episodes of mild exacerbation or an event of severe exacerbation in the preceding year was used to identify the exacerbator phenotype (AE). Without taking into account the frequency of exacerbations, the presence of bronchial asthma criteria (ACOS) was used to establish the asthma-COPD phenotype [10].

2) *Six-minutes walking test*:

The patients were asked to walk along a 30-m hallway at sea level for approximately 6 min before the walking distance was measured. Using a pulse oximeter, oxygen saturation was assessed both before and right after the 6MWT [11].

3) *Investigations*

- Spirometry: we measured [FEV1, FVC, and FEV1/FVC ratio pre- and post-bronchodilator] [12].
- *Laboratory assessment:* CBC (complete blood count), LFT (liver function tests), RFT (renal function tests), CRP (C-reactive protein).
- HRCT of the lung

In a supine posture and without the use of contrast material, all cases underwent MSCT chest during both the inspiratory and expiratory phases. A diagnostic radiologist reviewed each CT scan film and watched them all on the same viewer system, a GE Lightspeed Ultra 160 slice CT scanner (GE Healthcare, Milwaukee, WI, USA). The following CT parameters are used: gantry rotation speed of 0.75 s, pitch 0.875, B31f reconstruction kernel, section thickness 1–1.25 mm, collimator width 1 mm, and scan range from lung apex to diaphragm. Additionally, a common technique was used to reconstruct the CT raw data to 1.25 mm section thicknesses.

We distinguished firstly the visually based patterns of COPD as shown in Fig. 1. Moreover, we measured airway internal diameters in some selected zones: the apical bronchus (RB1) of the right upper lobe, the posterior basal bronchus (RB10) of the right lower lobe, and the anterior bronchus (LB3) of the left upper lobe, all of which were upright to the long airway axis. After that, we manually traced it, allowing us to assess the bronchial internal diameters (L) by standard.

Statistical analysis

Data analysis was done using SPSS (Statistical Package for Social Science) software program version 21.0 (SPSS Inc., Chicago, IL, USA).

Results

This study included 50 cases. According to the clinical findings, we classified the study population into 3 clinical phenotypes (ACOS, AE, and non-AE) and according to the radiological phenotypes into 5 groups [29 cases (58%) were mild CLE, 8 cases (16%) were moderate CLE, 5 cases (10%) were CON, 5 cases (10%) were ADE and 3 cases (6%) were PSE] as disclosed in Fig. 2.

There was considerable variance between the 5 radiological phenotypes regarding both the smoking index ($p=0.046$) and the need for hospitalization in the last year ($p=0.001$) as shown in Table 1.

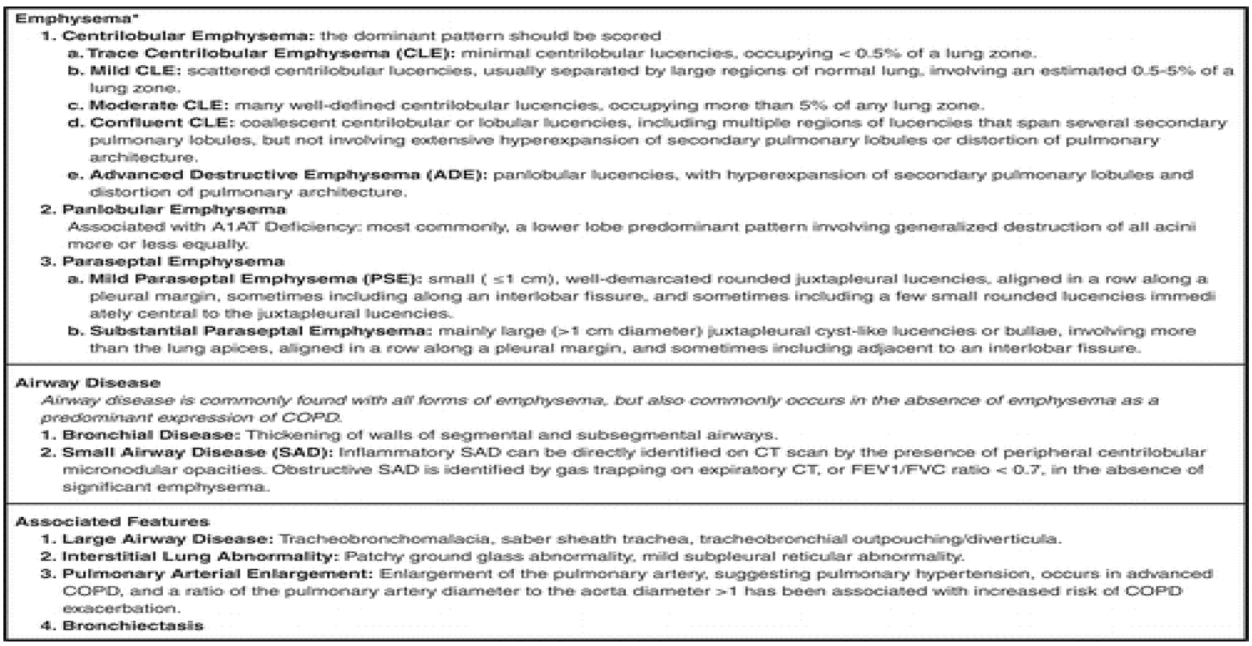

Fig. 1 Visually defined forms of COPD at CT [7]. Abbreviations: CLE: centrilobular emphysema; ADE: advanced destructive emphysema; CON: confluent emphysema; PSE: parastatal emphysema

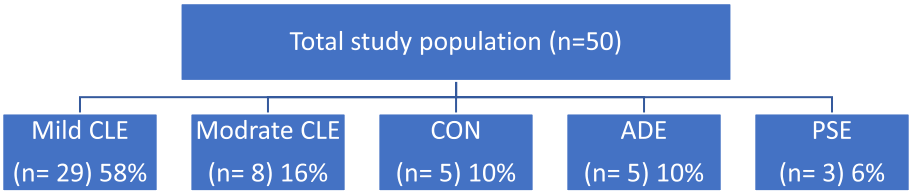

Fig. 2 Distribution of the diverse emphysema phenotypes identified among the study population based on MSCT examination

Table 1 Demographic and clinical characteristics of the study population ($n=50$)

	Patients with COPD with CT scan data ($n=50$)					*P* value
	Mild CLE ($n=29$)	**Moderate CLE ($n=8$)**	**CON ($n=5$)**	**ADE ($n=5$)**	**PSE ($n=3$)**	
Age (years), (mean ± SD)	61.79 ± 15.19	68.25 ± 10.91	64.00 ± 8.97	61.40 ± 11.90	50.67 ± 5.50	0.431¥
Gender, *n* (%)						0.533*
Male	25 (54.3)	8 (17.4)	5 (10.9)	5 (10.9)	3 (6.5)	
Female	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Body mass index (kg/m.^{2}) (mean ± SD)	28.14 ± 5.51	25.63 ± 5.96	26.63 ± 5.33	28.58 ± 8.03	26.20 ± 4.32	0.804¥
Smoking status, *n* (%)						0.501*
Non-smoker	4 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	
Ex-smoker	8 (66.7)	3 (25.0)	0 (0.0)	1 (8.3)	0 (0.0)	
Current smoker	17 (50.0)	5 (14.7)	5 (14.7)	4 (11.8)	3 (8.8)	
Smoking index, mean ± SD	424.04 ± 138.2	484.38 ± 108.0	386.60 ± 72.5	548.20 ± 143.4	233.33 ± 49.3	0.046¥
Biomass fuel exposure, *N* (%)						0.428*
	7 (70.0)	1 (10.0)	2 (20.0)	0 (0.0)	0 (0.0)	
Need for hospitalization last year, *n* (%)						< 0.001*
	3 (17.6)	3 (17.6)	5 (29.4)	4 (23.5)	2 (11.8)	
Associated comorbidities, *n* (%)						
DM	5 (55.6)	3 (33.3)	0 (0.0)	1 (11.1)	0 (0.0)	0.428*
HTN	4 (36.4)	3 (27.3)	1 (9.1)	3 (27.3)	0 (0.0)	0.120
Cardiac	3 (50.0)	2 (33.3)	0 (0.0)	1 (16.7)	0 (0.0)	0.601
Renal	1 (50.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	0.403
Liver	4 (57.1)	1 (14.3)	1 (14.3)	1 (14.3)	0 (0.0)	0.938
History of asthma	2 (66.7)	0 (0.0)	0 (0.0)	1(33.3)	0 (0.0)	0.592
Chest symptoms, *n* (%)						
Cough	29 (58.0)	8 (16.0)	5 (10.0)	5 (10.0)	3 (6.0)	0.123*
Sputum	28 (57.1)	8 (16.3)	5 (10.2)	5 (10.2)	3 (6.1)	0.440
Dyspnea	29 (58.0)	8 (16.0)	5 (10.0)	5 (10.0)	3 (6.0)	0.420
Wheezes	19 (65.5)	6 (20.7)	2 (6.9)	1 (3.4)	1 (3.4)	0.602
Chest pain	2 (33.3)	2 (33.3)	0 (0.0)	1 (16.7)	1 (16.7)	0.403
Hemoptysis	1 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0.422

CLE centrilobular emphysema, *ADE* advanced destructive emphysema, *Con* confluent emphysema, *PSE* paraseptal emphysema

* Pearson Monte Carlo test; ¥ANOVA test

Table 2 illustrates the frequency of COPD clinical phenotypes among the diverse radiological phenotypes with no considerable variance between them ($p=0.65$).

The clinical characteristics of the COPD patients according to their CT phenotypes, where there was considerable variance between the diverse groups regarding the following: the frequency of severe exacerbations ($p=0.022$), 6 min walking test distance ($p=0.026$), Modified Medical Research Council Scale ($p=0.003$), CAT Questionnaire [regarding total score, chest tightness (CAT 3), walking uphill (CAT 4), home activity (CAT 5), leaving home (CAT 6) and energy (CAT 8)] [$p=0.040$,

Table 2 Frequency of COPD clinical phenotypes among the diverse radiological phenotypes in the study group

Clinical phenotypes	Patients with COPD with CT scan data ($n=50$), n (%)					*P* value*
	Mild CLE $n=29$	Moderate CLE $n=8$	CON $n=5$	ADE $n=5$	PSE $n=3$	
ACOS	3 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0.654
AE	18 (51.4)	7(20.0)	5 (14.3)	3 (8.6)	2 (5.7)	
NON-AE	8 (66.7)	1 (8.3)	0 (0.0)	2 (16.7)	1 (8.3)	

Row percent was used * Pearson Monte Carlo test

ACOS Asthma-COPD overlap syndrome phenotype, *AE* exacerbator phenotype, *NON-AE* non-exacerbator phenotype, *CLE* centrilobular emphysema, *ADE* advanced destructive emphysema, *CON* confluent emphysema, *PSE* paraseptal emphysema

$p=0.011$, $p=0.013$, $p=0.041$, and $p=0.002$ respectively] as displayed in Table 3.

Table 4 illustrates the intra-luminal diameters at selected levels (RB1, RB10, and LB3) during both inspiration and expiration among the diverse radiological phenotypes where there was statically considerable variance between groups in both [Insp-RB1, Exp-RB1, and EXP-LB3] ($P=0.044$, 0.046 and 0.043 respectively).

Table 5 displays the pulmonary function tests among the diverse radiological phenotypes where there was considerable variance between the included groups in FEV1 values in both pre- and post-broncho-dilator tests ($p=0.001$, $p=0.043$ respectively).

Table 6 disclosed that there was a moderate positive correlation between the predicted FEV1% and the corresponding inter-luminal diameter at the selected levels (RB1, and LB3) in the inspiratory phase of respiration ($P=<0.001$, and $p=0.001$ respectively) ($r=0.58$, 0.46 respectively). While there was a mild positive correlation in the inspiratory phase of respiration between the predicted FEV1% and the corresponding inter-luminal diameter at the selected levels (RB10) ($p=0.007$) ($r=0.38$).

There was a moderate positive correlation in the expiratory phase of respiration between the predicted FEV1% and the equivalent inter-luminal diameter at the selected levels (RB1 and LB3) ($P=<0.001$ respectively) ($r=0.62$, 0.51 respectively) while there was a strong positive correlation in expiratory phase of respiration between the predicted FEV1% and the equivalent inter-luminal diameter at the selected levels (RB10) ($P=<0.001$) ($r=0.72$) as demonstrated in Table 7.

Discussion

A variety of different phenotypes make up the complicated, heterogeneous disorder known as COPD, which has varied clinical characteristics. The prevalence of COPD among hazardous personnel in Egypt was assessed to be about 10% according to GOLD, as well as cumulative disease and morbidity rates [13].

This study included 50 cases with stable GOLD stage I or II COPD, which was categorized according to the visual CT findings into five radiological phenotypes comprising [mild CLE, moderate CLE, CON, ADE, and PSE] based on Fleischner Society and inspiratory HRCT [14, 15], that was classified rendering to the percent of the lung's overall emphysematous zone. Among the five radiological phenotypes examined in this study, mild CLE was the most frequent phenotype. In harmony with our study, earlier research has shown that the most prevalent type of emphysema in smokers with COPD, particularly in the right upper lobe, is centrilobular emphysema [16].

We found that there was considerable variance between the five radiological phenotypes regarding the need for hospitalization in the previous year. When compared to patients who are not hospitalized, individuals who are hospitalized may also have more severe disease, which is manifested by more severe blockage, more impaired gas exchange, higher muscle weakness, increased anxiety, and social isolation [17]. In contrast, a previous study had reported, that there were no substantial variances in respiratory-related hospitalizations between the diverse CT-based groups [18].

In this study, concerning the clinical features of the COPD cases rendering to their CT phenotypes, there was a substantial variance between the diverse groups regarding the following: the frequency of severe exacerbations, 6-min walking test distance, mMRC score, and CAT Questionnaire. In accordance, several studies have reported that there was a relationship between emphysema and the hazard of exacerbation [14, 19, 20]. Similarly, Zhu et al. disclosed that there were significant variances in age, gender, body mass index (BMI), mMRC score, acute exacerbation frequency, and PFTs between enrolled patients of the diverse sub-groups (all $p<0.01$) [21], which is reliable with the prior results [14, 22, 23]. However, Han et al. reported a non-linear relation between emphysema and exacerbation [24]. Furthermore, Karayama et al. reported that there is

Table 3 Clinical characteristics of the COPD patients according to their CT phenotypes ($n=50$)

	Patients with COPD With CT scan data ($n=50$)					*P* value
	Mild CLE ($n=29$)	Moderate CLE ($n=8$)	CON ($n=5$)	ADE ($n=5$)	PSE ($n=3$)	
Exacerbations, mean ± SD						
Total number	1.90 ± 0.81	2.13 ± 0.35	2.40 ± 0.58	2.00 ± 1.0	2.00 ± 1.0	0.771¥
Moderate	1.90 ± 0.82	2.13 ± 0.83	2.40 ± 0.54	2.20 ± .83	1.33 ± 0.57	0.370
Severe	1.41 ± 0.56	1.38 ± 0.52	1.40 ± 0.55	1.67 ± 0.58	1.40 ± 0.89	**0.022**
GOLD grading, *N* (%)						0.555*
Gold 1	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	1 (33.3)	
Gold 2	28 (59.6)	7 (14.9)	5 (10.6)	5 (10.6)	2 (4.3)	
Refined ABCD assessment tool, *N* (%)						
B	7 (58.3)	2 (16.7)	0 (0.0)	2 (16.7)	1 (8.3)	0.657*
D	22 (57.9)	6 (15.8)	5 (13.2)	3 (7.9)	2 (5.3)	
BODE index, mean ± SD	2.03 ± 0.98	2.13 ± 1.12	2.80 ± 1.30	2.60 ± 1.14	1.00 ± 0.10	0.156¥
6 min walking test, mean ± SD						
- 6 min walking test, distance, meters	456.34 ± 26.27	444.63 ± 47.86	467.40 ± 28.95	414.80 ± 36.80	412.67 ± 47.05	**0.026**¥
- Initial SpO2, %	95.10 ± 1.72	94.13 ± 2.35	95.40 ± 1.34	93.00 ± 1.00	94.67 ± 2.08	0.123
- Final SpO2, %	92.10 ± 6.11	91.38 ± 3.54	94.80 ± 2.28	90.60 ± 1.34	92.67 ± 2.88	0.733
Modified Medical Research Council Scale, mean ± SD	2.07 ± 0.75	1.88 ± 0.83	2.40 ± 0.55	3.20 ± 0.84	1.00 ± 0.10	**0.003**
CAT Questionnaire Total score, mean ± SD ¥	21.69 ± 5.47	25.63 ± 4.27	35.40 ± 2.60	24.00 ± 3.16	18.00 ± 3.46	**< 0.001**¥
- Cough (CAT 1)	3.45 ± 0.68	3.88 ± 0.64	4.20 ± 0.44	3.60 ± 0.89	3.33 ± 0.58	0.149
- Mucus (CAT 2)	3.59 ± 0.73	3.88 ± 0.62	4.20 ± 0.45	3.80 ± 0.44	3.33 ± 0.57	0.286
- Chest tightness (CAT 3)	2.66 ± 0.93	2.88 ± 0.83	3.80 ± 0.44	2.60 ± 1.140	2.00 ± .0.10	**0.040**
- Walk Uphill (CAT 4)	2.52 ± 0.94	2.88 ± 0.85	3.62 ± 0.58	2.40 ± 0.548	1.33 ± 0.57	**0.011**
- Home activity (CAT 5)	2.31 ± 0.89	2.63 ± 0.91	3.60 ± 0.54	2.40 ± 1.140	1.33 ± 0.58	**0.013**
- Leaving home (CAT 6)	2.00 ± 0.80	2.38 ± 1.06	3.00 ± 0.70	1.80 ± 0.837	1.33 ± 0.57	**0.041**
- Sleep (CAT 7)	3.41 ± 0.90	3.75 ± 0.70	4.20 ± 0.83	3.60 ± 0.548	3.33 ± 0.55	0.357
- Energy (CAT 8)	1.93 ± 0.70	2.50 ± 0.92	3.40 ± 0.54	1.80 ± 0.837	2.00 ± .0.10	**0.002**
SGRQ-c Questionnaire Total score (%), mean ± SD	53.73 ± 7.70	55.00 ± 8.09	53.15 ± 9.86	50.52 ± 7.86	42.92 ± 4.10	0.206¥
- Symptoms score (%)	60.97 ± 8.92	62.09 ± 8.37	60.70 ± 15.30	53.72 ± 11.52	48.60 ± 6.25	0.166
- Activity score (%)	58.28 ± 10.39	50.11 ± 9.23	61.91 ± 10.64	56.71 ± 13.03	53.20 ± 9.67	0.269
- Impact score (%)	48.49 ± 8.71	47.96 ± 5.82	51.05 ± 10.50	45.74 ± 9.32	39.49 ± 5.03	0.399

GOLD Global Initiative on Obstructive Lung Disease, *BODE* body mass index, airflow Obstruction, Dyspnea and Exercise capacity, *CAT* COPD assessment test, *SGRQ* St. George's Respiratory Questionnaire, *CLE* centrilobular emphysema, *ADE* advanced destructive emphysema, *CON* confluent emphysema, *PSE* paraseptal emphysema

Row percent was used * Pearson Monte Carlo test; ¥ ANOVA test

an unfortunate association between exacerbation and emphysema [16].

In accordance with this study, Chen et al. reported that the 6MWT walking distance was inversely correlated with the HRCT emphysema score, indicating that morphological and airflow limitations affect walking performance [25].

We found that there was considerable variance between the frequency of COPD clinical phenotypes among the diverse radiological phenotypes. However, Miravitlles et al. reported that AE were highly observed in mild-to-moderate CLE patients, ADE, and PSE; however, ACO and NON-AE were less common among patients, consequently; clinical phenotypes were highly allied with radiological results] [26].

In harmony with this study, Bafadhel et al. disclosed that patients with EM on CT scan had worsened lung function, airflow obstruction, and larger increases in residual lung volume, compared with patients with radiologic evidence of BE [bronchiectasis phenotype] or BWT [bronchial wall thickening phenotype], although the clinical features of airway inflammation, health status, and microbiologic inflammation are vague between these radiologic phenotypes [27]. Correspondingly, in a prior

Table 4 The CT intra-luminal diameters at selected levels of all the included cases ($N=50$)

CT inter-lumen diameter (mm)	Patients with COPD with CT scan data ($n=50$), (mean ± SD)					*P* value¥
	Mild CLE ($n=29$	Moderate CLE ($n=8$)	CON ($n=5$)	ADE ($n=5$)	PSE ($n=3$)	
Insp-RB1	7.87 ± 1.21	8.33 ± 1.15	6.29 ± 1.21	7.60 ± 1.57	7.66 ± 0.61	0.044
Insp-RB10	4.42 ± 0.86	4.64 ± 1.00	4.12 ± 0.69	3.86 ± 0.58	4.07 ± 0.65	0.484
Insp-LB3	3.41 ± 0.61	3.35 ± 0.69	3.33 ± 0.48	3.02 ± 0.90	3.26 ± 0.48	0.784
Exp-RB1	6.60 ± 1.43	6.87 ± 1.27	6.96 ± 1.73	7.11 ± 1.06	7.32 ± 1.69	0.046
Exp-RB10	3.28 ± 0.90	3.11 ± 0.86	3.54 ± 1.34	3.22 ± 0.68	3.46 ± 1.19	0.944
EXP-LB3	2.22 ± 0.52	1.91 ± 0.45	2.09 ± 0.77	1.93 ± 0.66	2.93 ± 0.25	0.043

Row percent was used ¥ ANOVA test. Continues data represented as mean, SD; *SD* standard deviation, *RB1* apical bronchus of the right upper lobe, *RB10* the posterior basal bronchus of the right lower lobe, *LB3* the anterior bronchus of the left upper lobe, *CLE* centrilobular emphysema; *ADE* advanced destructive emphysema, *CON* confluent emphysema, *PSE* paraseptal emphysema

Table 5 Pulmonary function test parameters of the study population stratified according to CT diverse phenotype groups ($n=50$)

	Patients with COPD with CT scan data ($n=50$), mean ± SD					*P* value¥
	Mild CLE ($n=29$)	Moderate CLE ($n=8$)	CON ($n=5$)	ADE ($n=5$)	PSE ($n=3$)	
Pre-bronchodilator (%)						
FEV1	58.00 ± 5.02	61.25 ± 2.05	51.40 ± 5.89	50.80 ± 3.63	57.33 ± 2.88	< 0.001
FVC	94.07 ± 3.55	92.25 ± 3.95	93.60 ± 2.07	91.00 ± 5.14	95.00 ± 1.73	0.351
FEV1/FVC	54.14 ± 3.94	53.25 ± 4.49	55.00 ± 3.31	54.20 ± 3.83	54.67 ± 3.05	0.950
Post-bronchodilator (%)						
FEV1	59.62 ± 4.36	60.38 ± 5.06	58.00 ± 5.70	65.00 ± 1.22	63.33 ± 3.21	0.043
FVC	94.97 ± 3.09	93.75 ± 3.32	94.40 ± 1.67	92.20 ± 4.55	95.00 ± 1.73	0.442
FEV1/FVC	57.17 ± 4.08	55.88 ± 4.48	57.60 ± 3.36	56.60 ± 4.72	57.00 ± 2.64	0.938

Row percent was used ¥ ANOVA test

FEV1 forced expiratory volume in one second, *FVC* forced vital capacity, *CLE* centrilobular emphysema, *ADE* advanced destructive emphysema, *CON* Confluent emphysema, *PSE* Paraseptal emphysema

Table 6 Correlation between FEV1% and inter-luminal diameter during the inspiratory phase

CT inter-luminal diameter	FEV1%	
	r	*P**
RB1	+0.58	< 0.001
RB10	+0.38	0.007
LB3	+0.46	0.001

* Pearson correlation coefficient, the sign before "*r*" denotes the direction of relation, $P<0.05$ considered significant

Table 7 Correlation between FEV1% and inter-luminal diameter during the expiratory phase

CT inter-luminal diameter	FEV1%	
	r	*P**
RB1	+0.62	< 0.001
RB10	+0.72	< 0.001
LB3	+0.51	< 0.001

RB1 apical bronchus of the right upper lobe, *RB10* the posterior basal bronchus of the right lower lobe, *LB3* the anterior bronchus of the left upper lobe

* Pearson correlation coefficient, the sign before "*r*" denotes the direction of relation, $P<0.05$ considered significant

study, the patients were categorized into emphysema-predominant and airway-predominant sub-groups and displayed that emphysema cases had lower FEV1 and were more functionally restricted, with higher BODE scores and minor BMI [22]. However, Shaikh et al. did not find any statistically considerable alliance between FEV1 and emphysema percent in any particular lung lobe [28].

Calverley et al. reported that both FEV_1 and FVC increased considerably after inhaling salbutamol in COPD patients [29] and we confirmed similar results.

In our study, we disclosed there was a moderate positive correlation between the predicted FEV1% and the corresponding inter-luminal diameter at the selected

levels (RB1 and LB3) in the inspiratory phase of respiration and there was a positive correlation in the expiratory phase of respiration between the predicted FEV1% and the equivalent inter-luminal diameter at the selected levels (RB1, LB3, and RB10).

Recently, Mahros et al. demonstrated that there was a considerable positive relation between CT noticed airway inter-luminal area at the expiratory stage of respiration and the FEV1%, while the equivalent correlation at the inspiratory stage was not ominous. Later, the thickness of the airway wall provides further restriction force during expiration. moreover, the narrowing in the expiratory phase was more pronounced than in the inspiratory one owing to the thickness of the airway wall and the collapsibility of the bronchi. Furthermore, with diminishing the size of the airway luminal area as sloping from the third generation level to the fifth one, the link was improved which confirms the present theory that the sub-segmental bronchus affects the obstruction level of COPD rather than the segmental bronchus [30]. Moreover, a recent study disclosed that quantitative CT parameters are ominously allied with lung function among COPD cases [31]. However, previous studies disclosed opposite results [32, 33].

Several factors may help to explain these differences between studies: Individual differences come first, followed by airway heterogeneity in COPD patients, and last, patients' diversity. Traditional pulmonary functions are unable to provide the same level of regional information that a quantitative CT scan does [34, 35]. Finally, despite the fact that the FEV1 parameter was a crucial factor in determining airflow restriction in COPD research, its function became flawed since it had little ability to distinguish between regional variations in lung diseases in addition to airway anomalies. Several airway troubles, comprising loss of bronchiolar tethering with alveolar obliteration, fibrosis, mucous metaplasia, inflammation, and smooth muscle hypertrophy, need more quantitative analysis utilizing MDCT, which helps in differentiating diverse COPD phenotypes [21].

Finally, we argue that additional studies are necessary to prove quantitative CT analysis as an imaging biomarker of illness that may be applied practically to COPD patients and considered a useful research tool to give insights into the disease. The results of CT analysis must be compared to outcome indicators and disease activity indicators. Few long-term studies have been conducted thus far, and those that have produced inconsistent findings.

Our research faced a number of limitations; The first is the small sample size, the second is the inter-observer variability in CT interpretation, and the third is that we only use visual scoring for COPD and don't use any additional automated techniques like [CT densitometry: it is a computerized identification of the lung attenuation area (LAA)] that were developed to segment the lung parenchyma and quantify emphysema. Fourth, there were only three bronchial levels that we could find: B1, B3, and B10. Fifth: the frightening radiation exposure levels were noticed while examining the relation between the inspiratory and expiratory phases. In addition to the severity of COPD and its distribution, the pathogenicity of the condition meant that the level of obstruction may be at a diverse bronchial lobe rather than what we defined in our study.

Conclusion

We confirmed that COPD is a highly heterogeneous illness, with multiple variable clinical, physiological, and radiological phenotypes. Phenotyping COPD patients is crucial to accomplishing a more tailored management. Furthermore, HRCT can well be allied with the PFT parameters.

Abbreviations

ADE	Advanced destructive emphysema
CT	Computed tomography
COPD	Chronic obstructive pulmonary disease
CLE	Centrilobular emphysema
CON	Confluent emphysema
HRQoL	Health-related quality of life
PSE	Paraseptal emphysema.
RB1	Apical bronchus of the right upper lobe
RB10	The posterior basal bronchus of the right lower lobe
LB3	The anterior bronchus of the left upper lobe
FEV1	Forced expiratory volume in the first second
FVC	Forced vital capacity
GesEPOC	The Spanish COPD Guidelines

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None.

Authors' contributions

IG was the principal investigator, formulated the idea, and wrote the first draft of the discussion. ZR collected the data, formulated the results, and edited the final draft and revision. SKM was responsible for methodology writing the manuscript and statistical analysis. SA supervised and reviewed data collection, statistical analysis, and writing. AHM was a major contributor to interpreting the radiological data. The manuscript has been read and approved by all the authors.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

The Research Ethics Committee at the Faculty of Medicine, Aswan University, has approved the study (IRB number: 425/12/19) and all patients provided written informed consent before participation.

Consent for publication
The manuscript has been read and approved by all the authors.

Competing interests
The authors declare that they have no competing interests.

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