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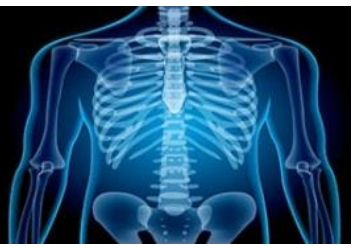

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The relationship between quantitative computed tomography parameters and spirometric measurements of disease severity in chronic obstructive pulmonary disease (COPD)

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Abstract
Background: Chronic obstructive pulmonary disease (COPD) is characterized by emphysematous destruction of lung parenchyma and airway remodeling which lead to limitation of airflow. Computed tomography is of considerable value in quantifying the severity of the disease in COPD either by visual or by quantitative CT techniques (QCT). This study was designed to assess the relationship between quantitative computed tomography parameters and spirometric measurements of disease severity in cases with COPD.
Materials and Methods: A total of 100 cases between age group 41 to 65 years, who were proved to have COPD by pulmonary function test were recruited. Inspiratory CT was designed to take a deep breath and plain CT chest was taken at full inspiration to obtain total lung capacity. Expiratory CT was asked to hold breath in normal expiration and CT chest was taken to obtain functional residual capacity. Inner and outer diameters and wall thick ness were measured manually and their average value was considered. Correlations analysis was conducted between spirometric measurements and QCT measures.
Results: The mean values of low attenuation areas in inspiration <-950HU was gradually increased from GOLD stage-I to GOLD stage-IV. Mean values of low attenuation areas in expiration <-856HU was gradually decreased from GOLD stage-I to GOLD stage-IV. Low attenuation areas in inspiration <-950HU showed correlation for both FEV1/FVC (-0.752) and FEV1 (-0.806) (p<0.005). Low attenuation areas in expiration <-856HU showed correlation for both FEV1/FVC (-0.786) and FEV1 (-0.928) (p<0.005).
Conclusion: In COPD cases, there is a strong association between spirometric measurements and QCT measurements of inspiratory and expiratory low attenuation areas.

Keywords: Chronic obstructive pulmonary disease (COPD), quantitative CT (QCT), Global Initiative for Chronic Obstructive Lung Disease (GOLD)

Introduction
Chronic obstructive pulmonary disease (COPD) exhibits significant variations in its clinical presentation and rate of disease progression among affected individuals [1]. After the diagnosis, various methods are used to assess the severity and monitor the progress and treatment response. The diagnostic modalities include diffusing capacity, spirometry, arterial blood gas analysis and radiological techniques like CT and X-ray [2]. The detection of relevant COPD phenotypes is a challenging and exciting research priority. Since quantification techniques have been improved during the past decades, CT can now measure the well-known disease components in COPD, such as emphysema, small airways disease, and large airways disease; this makes quantitative computed tomography (CT) may be a highly interesting modality to detect these pathologies *in vivo*, because its separate analysis of disease components may allow morphologic phenotyping and visual evaluation of CT images for pathology is time-consuming and prone to considerable observer variability [3]. Literature suggest that emphysema-dominant and airway wall thickening-dominant groups of COPD patients can be separated by quantitative CT [4]. This study was designed to assess the quantitative computed tomography parameters and clinical measures of disease severity in cases with COPD.

Materials and Methods

The present prospective study was conducted in the Department of Radio diagnosis, Apollo institute of medical sciences from April 2018 to December 2019. A total of 100 cases between age group 41 to 65 years, who were proved to have COPD by pulmonary function test and cases willing to participate in the study were included. Cases with systemic disorders, other respiratory complication and not willing to participate in the study were excluded. Study procedure and methodology was explained and informed consent was obtained from all the cases. Study protocol was approved by the institutional ethics committee.

The quantitative CT analysis was performed by using GE evolution 128 CT scanner. The obtained values were evaluated by lung volumetry software. CT scan of the thoracic region from apex of lung till the level of the suprarenal glands has been taken. Emphysema defined as the percentage of low attenuation areas ≤-950 HU on inspiratory CT, air trapping defined as the percentage of low attenuation areas ≤-856 HU on expiratory. Inspiratory CT was designed to take a deep breath and plain CT chest was taken at full inspiration to obtain total lung capacity. Expiratory CT was asked to hold breath in normal expiration and CT chest was taken to obtain functional residual capacity. Inner and outer diameters and wall thickness of segmental bronchus were measured manually and their average value was considered. Statistical analysis was done by using SPSS version 20.0.

Results

Table 1: Distribution of cases as per Global Initiative for Chronic Obstructive Lung Disease (GOLD).

Parameters	Total cases (n=100)	
	Number	Percentage
Age (In years)		
41-45	21	21%
46-50	23	23%
51-55	25	25%
56-60	20	20%
61-65	11	11%
Sex		
Male	78	68%
Female	22	22%
Details of GOLD stage		
Stage-I	08	08%
Stage-II	31	31%
Stage-III	24	24%
Stage-IV	22	22%

Table 2: Mean values of pulmonary function and QCT parameters in COPD.

Parameter	GOLD Stage			
	Stage 1 (n=8)	Stage 2 (n=31)	Stage 3 (n=24)	Stage 4 (n=22)
Age (In years)	51.28±3.17	51.74±4.38	51.98±2.28	52.45±4.63
FEV1	1.521±0.17	1.281±0.085	1.11±0.045	0.052±0.525
FVC	2.560±0.281	1.62±0.194	1.45±0.374	0.986±0.297
FEV1/FVC	0.581±0.0237	0.628±0.0453	0.594±0.0424	0.570±0.0482
% lung ATT <-950HU	5.471±0.671	9.237±1.655	15.522±1.592	28.98±2.564
% lung ATT<-856HU	19.363±5.182	27.564±5.681	46.852±6.545	59.872±6.318
MLAI	-851.27±7.84	-866.23±6.79	-874.45±7.68	-891.18±7.34
MLAE	-751.54±7.29	-789.27±10.35	-818.20±11.92	-838.19±11.02
TLC (L)	5.282±1.326	5.312±4.104	5.437±4.571	5.794±5.328
FRC (L)	3.120±0.356	3.354±0.562	3.448±0.521	3.695±0.539
Inner diameter (mm)	3.572±0.212	3.314±0.387	3.151±0.650	2.896±0.619
AWWT	1.388±0.222	1.513±0.366	1.578±0.214	1.650±0.158
Inner area (mm2)	9.985±2.183	8.562±1.320	8.016±0.652	7.159±0.473
Outer area (mm2)	30.582±2.657	29.331±2.129	28.766±2.548	28.182±2.651
Wall area (mm2)	24.01±1.947	22.314±2.027	22.146±2.282	21.542±2.443

Figure 1: CT images of the lungs of COPD patient with GOLD stage 3 disease.

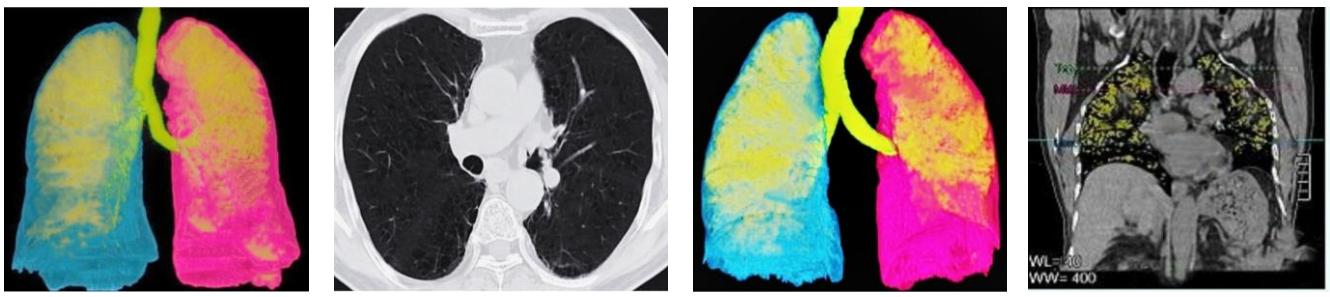

Table 3: Pearson correlation of pulmonary function parameters in COPD.

Parameter	FEV1		FEV1/FVC	
	Pearson correlation	Significance (2 tailed)	Pearson correlation	Significance (2 tailed)
FEV1/FVC	0.786	0.003	-	-
% lung ATT <-950HU	-0.806	0.005	-0.752	0.004
% lung ATT<-856HU	-0.928	0.002	-0.786	0.003
MLAI	0.823	0.003	0.734	0.005

MLAE	0.802	0.003	0.722	0.005
Inner diameter (mm)	0.857	0.005	0.748	0.005
AWWT	-0.621	0.005	-0.529	0.002
Inner area (mm2)	0.763	0.005	0.726	0.001
Outer area (mm2)	0.629	0.005	0.554	0.005
Wall area (mm2)	-0.024	0.227	-0.331	0.389

Discussion

Pulmonary function tests are important in the diagnosis and monitoring of COPD [5]. Changes like bronchial wall thickening, expiratory air trapping, hyperinflation of the lung and vascular pruning may be seen and characterized quantitatively at CT. Thus, CT has been used to differentiate between airway predominant and emphysema predominant COPD [6, 7]. Several lung attenuation parameters have been developed based on results of histogram analysis of the frequency distribution of the attenuation values of the lung, to objectively quantify pulmonary emphysema with CT. This study was designed to determine whether measurements of lung attenuation obtained from 3D lung reconstructions at inspiration and expiration reflect the severity of chronic obstructive pulmonary disease (COPD). The lung function measurements at inspiration and expiration with measurements of lung attenuation on 3D lung reconstructions were correlated and evaluated the relationship between severity of COPD, reflected by GOLD staging and measurements of lung attenuation on 3D lung reconstructions. A total of 100 cases between age group 41 to 65 years, who were proved to have COPD by pulmonary function test were recruited. Majority cases were in between age group 46-55 years (48%). The severity of the disease is commonly classified as per the GOLD staging system, where GOLD -I is defined by FEV1≥80% predicted, GOLD-II is FEV1 50-80% of predicted, GOLD-III is FEV1 30-50% of predicted and GOLD -IV is FEV1<30% of predicted [4]. In this study, 8% cases with GOLD stage 1, 31% cases with GOLD stage 2, 24% cases with GOLD stage 3 and 22% cases were having disease of GOLD stage 4 (Table 1). A study by Virginija Sileikiene *et al*., included mild and moderate COPD cases as GOLD stage I-II and severe COPD cases under GOLD stage III-IV [8]. A study by **S**ilvia Maria Doria da Silva *et al*., to investigate cases with severe COPD and its association of CT findings and functional variables included 21 cases under GOLD stage 3 and 44 cases under GOLD stage 4 [9].

In this study, the mean values of low attenuation areas in inspiration <-950HU was gradually increased from GOLD stage-I to GOLD stage-IV. Mean values of low attenuation areas in expiration <-856HU was gradually decreased from GOLD stage-I to GOLD stage-IV. The mean values of TLC and FRC were gradually increased from GOLD stage–I to GOLD stage-IV. The mean values of inner area, outer area and wall area were gradually decreased from GOLD stage-I to GOLD stage-IV. For emphysema, low attenuation areas in inspiration <-950HU showed correlation for both FEV1/FVC (-0.752) and FEV1 (-0.806) (p<0.005). For air trapping, low attenuation areas in expiration <-856HU showed correlation for both FEV1/FVC (-0.786) and FEV1 (-0.928) (p<0.005).

Study by Bergin *et al*., Hruban *et al*., Miller *et al*. and Kuwano *et al*., found a good correlation between radiological visual assessment and pathological report at the comparable or same lung fragment (10-14). Miller *et al*. stated that it is difficult to determine the early forms of pulmonary emphysema on CT scans due to lesion size (<5mm) and also reported that quantitative evaluation of CT scans frequently underrate the disease extent [15]. According to Mascalchi M. COPD pulmonary function measurements are not linearly related to CT lung attenuation and the complexity of COPD cannot be expressed with a simple measurement of expiratory airflow obstruction [16-18]. In this study, QCT assessments of inspiratory and expiratory low-attenuation areas correlate with airflow obstruction assessed by measures of FEV1 and FEV1/FVC and that these parameters increase in severity with increasing GOLD stage. CT-determined LAA-856E is strongly associated with decline in airflow in patients with COPD. CT is uniquely able to detect, classify, and quantify LAA-950I in adults.

According to METS OM *et al*., quantitative CT might gain an important role in both phenotyping and (early) diagnosis of COPD patients, which might lead to the detection of treatable COPD subgroups and prevention of morbidity and mortality due to this disease [19]. Sasaki *et al*. studied 32 patients and concluded that a cut- off value of 1.51 for WA% ratio of 5th to 1st generation airway was able to predict GOLD class 3 or 4 severity in COPD with a sensitivity of 83% and specificity of 89% [20]. According to Kumar *et al*., that the QCT parameters showed an inverse relationship with the FEV1. Of the three, LAA% showed the best correlation with FEV1 (r = -0.58) for the whole sample [21].

Conclusion

The quantitative measurement of emphysema using CT is not routinely used in the clinical approach, due to its high costs, sophisticated image data processing, and radiation exposure. QCT of the lung parenchyma uses accurate measures of lung density to generate histogram statistics of the lung to detect lower-density areas of the lung that correspond to emphysema on total lung capacity (TLC) scans. Univariate correlation between airway measures and spirometric impairment is less strong; inclusion of these measures in the multiple regression models strengthens the correlation. QCT measurements of inspiratory and expiratory low-attenuation areas are strongly associated with spirometric impairment in COPD patients. Air trapping on expiratory imaging measured as LAA-856E strongly correlates with physiologic measurements of airway obstruction.

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