Original Research Article

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

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Abstract

Aim: To assess the relationship between quantitative computed tomography parameters and spirometric measurements of disease severity in cases with COPD. **Materials and Methods**: The present study was conducted in the Department of Radiology, Katihar Medical College and Hospital, Katihar, Bihar, India and Arc Hospital, Bhagalpur fromDecember 2018 to November 2019. A total of 200 cases between age group 30 to 70 years, who were proved to have COPD by pulmonary function test were included. 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 were measured manually and their average value was considered. Correlations analysis was conducted between spirometric measurements and QCT measures. **Results:** A total of 200 cases between age group 30 to 70 years, who were proved to have COPD by pulmonary function test were recruited. Majority cases were in between age group 50-55 years(27.5%).17.5% cases with GOLD stage 1, 33.5% cases with GOLD stage 2, 25.5% cases with GOLD stage 3 and 23.5% cases were having disease of GOLD stage 4.The mean values of low attenuation areas in inspiration <-950HU was gradually increased from GOLD stage-I to GOLD stage-IV. **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] is a very common disease in developing as well as developed countries. This is due to several factors like smoking, air pollution, and occupational exposure. However, it is a heterogeneous disease, and pulmonary function tests alone could not explain the disease heterogeneity.[1]

Chronic obstructive pulmonary disease (COPD) exhibits significant variations in its clinical presentation and rate of disease progression among affected individuals.[2]

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After the diagnosis, various methods are used to assess the severity and monitor the progress and response to treatment. The diagnostic modalities include diffusing capacity, spirometry, arterial blood gas analysis and radiological techniques like CT and X-ray.[3]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) 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.[4]The chronic obstructive pulmonary disease (COPD) includes two phenotypically related

diseases: emphysema and chronic bronchitis.[5] The main pathological changes in COPD patients include inflammation and deficient gas exchange. Emphysema is considered parenchymal-predominant pathology, which is characterized by abnormal over-distension of the alveoli and irreversible destruction of the supporting structures. These changes lead to almost permanent damage to gaseous exchange.[6]Chronic bronchitis is an airwaypredominant disease.[7]The emphysematous phenotype is mainly associated with severe form of the disease.[8] It is important to define whether the pathological changes are airway-predominant or parenchymalpredominant pathology. This will affect the management plane by applying specific therapies to prevent airway remodeling or parenchymal destruction.[9] Pulmonary function tests can be used to assess the severity of COPD. COPD cases with FEV1/FVC less than 70% revealed respiratory dysfunction.[10] However, PFTs have several limitations including inability of some patients to do such tests due to their poor clinical condition, weakness, or associated disorders affects tests results.[11,12]

Material and Methods

The present study was conducted in the Department of Radiology, Katihar Medical College and Hospital, Katihar, Bihar, India and Arc Hospital, Bhagalpur from December 2018 to November 2019 after taking the approval of the protocol review committee and institutional ethics committee.

Inclusion and exclusion criteria

A total of 200 cases between age group 30 to 70 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.

Methodology

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 CT scan. 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 chestwas 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

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2010) and then exported to data editor page of SPSS version 19 (SPSS Inc., Chicago, Illinois, USA). Descriptive statistics included computation of percentages and means. Test applied for the analysis was Pearson correlation coefficient test. The confidence interval and p-value were set at 95% and 5%.

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)		
Below 45	39	19.5%
45-50	49	24.5%
50-55	55	27.5%
55-60	36	18%
Above 60	21	10.5%
Gender		
Male	140	70%
Female	60	30%
Details of GOLD stage		
Stage-I	35	17.5%
Stage-II	67	33.5%
Stage-III	51	25.5%
Stage-IV	47	23.5%

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

Parameter	GOLD Stage			
	Stage1(n=35)	Stage2 (n=67)	Stage3 (n=51)	Stage 4(n=47)
Age (In years)	52.19±3.10	52.49±4.44	52.87±2.78	53.19±4.75
FEV1	1.419±0.16	1.371±0.080	1.21±0.061	0.062±0.498
FVC	2.377±0.280	1.70±0.184	1.33±0.362	0.891±0.289
FEV1/FVC	0.532±0.0224	0.687±0.0474	0.577±0.0405	0.564±0.0491
% lung ATT <-950HU	6.381±0.664	9.612±1.742	14.799±1.687	27.89±2.687
% lung ATT<-856HU	21.471±5.271	28.844±5.364	47.902±6.236	58.623±6.211
MLAI	-833.26±7.54	-856.74±6.07	-881.45±7.42	-897.19±7.65
MLAE	-712.52±8.45	-731.28±10.88	-827.50±12.33	-882.20±22.75
TLC (L)	6.112±2.354	6.254±3.547	6.587±4.128	6.904±5.857
FRC (L)	3.120±0.356	3.354±0.562	3.448±0.521	3.695±0.539
Inner diameter (mm)	4.434±0.214	4.211±0.582	4.147±0.987	3.678±0.875
AWWT	1.164±0.112	1.378±0.477	1.486±0.317	1.579±0.149
Inner area (mm2)	10.889±2.741	9.678±1.452	9.107±0.784	8.174±0.527
Outer area (mm2)	31.431±2.897	30.741±2.287	29.876±2.651	28.182±2.697
Wall area (mm2)	25.11±1.989	23.241±2.102	22.478±2.362	21.835±2.546

Table 3: Mean values of pulmonary function and QCT parameters in COPD

Parameter	FEV1		FEV1/FVC	
	Pearson correlation	Significance (2 tailed)	Pearson correlation	Significance (2 tailed)
FEV1/FVC	0.778	0.002	-	-
% lung ATT <-950HU	-0.814	0.005	-0.769	0.004
% lung ATT<-856HU	-0.937	0.004	-0.772	0.003
MLAI	0.803	0.004	0.765	0.005
MLAE	0.815	0.004	0.710	0.005
Inner diameter (mm)	0.877	0.005	0.774	0.005
AWWT	-0.631	0.005	-0.504	0.003
Inner area (mm2)	0.724	0.005	0.732	0.001
Outer area (mm2)	0.607	0.005	0.562	0.005
Wall area (mm2)	-0.034	0.231	-0.321	0.374

Discussion

Pulmonary function tests are important in the diagnosis and monitoring of COPD[13]. 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[14,15]. 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 200 cases between age group 30 to 70 years, who were proved to have COPD by pulmonary function test were recruited. Majority cases were in between age group 50-55 years (27.5%). 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. In this study, 17.5% cases with GOLD stage 1, 33.5% cases with GOLD

stage 2, 25.5% cases with GOLD stage 3 and 23.5% cases were having disease of GOLD stage 4 .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[16]. A study by Silvia 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[17].

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 (-0.769) and FEV1 (-0.814) (p<0.005). Forair trapping, low attenuation areas in expiration <-856HU showed correlation for both FEV1/FVC (-0.772) and FEV1 (-0.937) (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 [18-22]. 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[23]. 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[24-26]. 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 inadults.

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[27]. 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 ableto predict GOLD class 3 or 4 severity in COPD with a sensitivity of 83% and specificity of 89%[28]. According to Kumar *et al*., 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[29].

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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