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CT Quantification of Parenchymal and Airway Parameters on 64 Slice MDCT in Patients of Chronic Obstructive Pulmonary Disease

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Abstract

Background: Chronic Obstructive Pulmonary Disease (COPD) represents an important public health challenge and is a major cause of chronic morbidity and mortality throughout the world. Aim: To quantify CT parenchymal and airway parameters in cases of COPD and to correlate CT parameters with the functional parameters of airway obstruction [FEV1, FVC, FEV1/ FVC]. **Methods:** An observational prospective study was performed in 100 patients diagnosed of chronic obstructive disease on spirometry. These patients underwent chest X ray in PA and lateral view and NCCT/CECT scan of chest in expiratory and inspiratory phases. 50 controls were selected retrospectively with normal inspiratory NCCT scan. **Results:** Quantitative CT parameters were found to be significantly different in the COPD cases compared to the controls. Among the quantitative parenchymal parameters, mean lung density, Percentage of Low Attenuation Area <-950HU, Percentage of Low Attenuation Area <-850HU showed significant correlation with FEV1, FVC and FEV1/FVC. Wall area of segmental bronchi demonstrated significant negative correlation with FEV1, FVC and FEV1/ FVC ratio. Wall area % showed significant negative correlation with FEV1 and FVC. **Conclusions:** In this study, we concluded that the quantitative CT parameters can be used to assess the severity of the COPD, as significant change in these values was noted with change in severity of COPD. Quantitative CT parameters also showed significant correlation with pulmonary function tests and can be used as complementary diagnostic tool.

Keywords: Chronic Obstructive Pulmonary Disease, Mean Lung Density, Wall Area, Luminal Area (Ai).

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INTRODUCTION

Chronic Obstructive Pulmonary Disease (COPD) is a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases. Chronic obstructive pulmonary disease (COPD) is defined by the Global Initiative for Chronic Obstructive Lung Disease as "a disease state characterized by airflow limitation that is not fully reversible".[1]

The airflow limitation in COPD is produced by a combination of small

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airway remodeling and emphysema with varying distribution and varying severity. On the basis of standard pulmonary function tests relative contribution of these two pathologic processes is difficult to determine but it is clinically important because of its implications on the patient's response to therapeutic procedures.2 Morphologic changes that include bronchial wall thickening, emphysema, hyperinflation of the lung, expiratory air trapping, and vascular pruning may be seen and assessed quantitatively at computed tomography (CT). Thus, CT has been used to differentiate between airway-predominant and emphysema-predominant COPD.[2,3]

Substantial heterogeneity exists among patients with COPD with respect to physiological characteristics, clinical presentation, imaging characteristics, disease progression, response to therapy and, ultimately, survival.[4] COPD typically is diagnosed on demonstration of airflow limitation with the use of pulmonary function tests (PFTs). PFTs are also useful tools to assess COPD severity.[5] However PFTs have several limitations in the diagnosis of COPD and assessment of COPD progression. First, the rate of decline of lung function varies with COPD severity, subjects of more advanced COPD often have slower rates of absolute change in spirometric measures.[6,7] Second, PFTs do not differentiate between the various pathophysiological contributors of COPD, including emphysema, airway inflammation, and small airway destruction.[8] Visual CT imaging evaluation shows that subjects with COPD have a heterogeneous group of abnormalities, composed of a variety of patterns of emphysema, large airway inflammation, and non-emphysematous obstruction due to small airway disease. Although visual CT imaging evaluation can provide information about emphysema distribution, it does not quantify the severity of emphysema. Quantitative CT imaging can help in assessing the severity of emphysema and also evaluates the lobar distribution of emphysema. However, quantitative CT imaging also has few limitations, including overestimation of emphysema in subjects of severe airflow obstruction.[9]

Emphysematous lung destruction leads to replacement of normal lung parenchyma (which has a typical attenuation about -850 HU on inspiratory CT) by air-filled spaces, with CT attenuation close to -1000 HU. From the early days of CT, it was apparent that measurement of CT attenuation values could help in assessing the extent of emphysema. Müller et al.[10] were the first to describe and confirm pathologically the density mask technique, in which CT pixels having attenuation below a certain threshold value (initially -910 HU) were considered emphysematous.

MATERIALS & METHODS

A Prospective, observational study was performed in 100 patients diagnosed of COPD on spirometry. Chest X rays

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alongwith inspiratory and expiratory chest CT scans were done in the patients to determine the quantitative CT parameters.

Inclusion criteria

1. Patients aged 35 years and above.
2. Patients diagnosed to be that of COPD based on history, clinical symptoms and spirometry.
3. Patients who are relatively stable, ambulatory and cooperative.

Exclusion Criteria

1. Any concurrent pulmonary disorder other than COPD.
2. Serious, unstable cardiovascular or neurological disease or poor general condition of patient.
3. Recent exacerbation of COPD requiring ICU/Hospital admission within last 4 weeks.
4. Patients with destroyed lungs as a sequelae of past infection.
5. Patients <35 years.
6. Patients who refuse to give consent.
7. Patients with past TB with deranged PFT.
8. Patients with GOLD stage IV.

Study design

After obtaining a written informed consent from the patient, the study was carried out in the Department of Radio-Diagnosis, Guru Nanak Dev Hospital, Amritsar with permission from Institutional Ethical Committee, Government Medical College, Amritsar.

100 patients of COPD who satisfied the selection criteria underwent pulmonary function tests [PFT] on a spirometer. Subsequently plain radiograph (PA and lateral views) and Non-contrast computed tomography of the chest on a 64 slice MDCT scanner was done within seven days of the doing PFT. Both the end inspiratory and the end expiratory chest CT's were done for each patient. These images were used for data analysis.

The pre-decided imaging parameters (for the CT chest and plain radiographs) were be determined and their findings were recorded on a predesigned proforma.
During scanning the morphological CT parameters [parenchymal and airway parameters] that were considered were:

CT parameters: Lung parenchyma parameters-

A. To look for emphysema: in End inspiratoy CT:

1) Mean lung density [MLD].
2) % of low attenuation areas less than-950HU [%LAA (-950HU)].

B. Air trapping indices: in end expiratory CT:

1) % of low attenuation areas less than -850HU [%LAA (-850HU)].
2) Ratio of inspiratory / expiratory (I/E) lung volume.
3) Ratio of inspiratory / expiratory (I/E) lung attenuation.
4) Small airway disease: areas of trapping due to functional small airway disease ratio of expiratory (<-850 HU) / inspiratory (<-950 HU) lung density.

Airway Parameters:

Airway parameters were obtained from the segmental airways of both lungs:

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right (Upper lobe, middle lobe and lower lobe) and left (Upper, lingular and lower lobe).

The parameters determined were:

1) **Bronchial wall morphometry:** Inner luminal area(Ai), bronchial wall thickness(WT), wall area(WA) wall area percentage(WA %).
2) **Bronchial wall attenuation.**
Additional findings in the main bronchi, trachea and the lung parenchyma were noted and recorded.

The plain radiographic parameters considered were:

- PA view – Right Diaphragmatic Height (DMHT) and Right Lung Length (LL).
- Lateral view – Retrosternal Space (RSP).

Functional PFT parameters included:
Forced expiratory volume in first second, forced vital capacity, ratio of forced expiratory volume in first second to forced vital capacity [FEV1, FVC, FEV1/FVC].

RESULTS

A total of 100 COPD cases, were included into the study conducted from November 2018- November 2020. Spirometry, chest radiography and non-contrast CT examination both in inspiratory and expiratory phase was performed in all of these patients. 50 controls were selected retrospectively, who had normal CT chest done in the inspiratory phase. These CT chest images were post processed to get QCT parameters (MLD, %LAA $_{(-950HU)}$ inner luminal area, wall thickness, wall area, wall area percentage and wall attenuation).

Table 1: Sex Distribution of Cases [N=100] and Controls [N=50]

Sex	Group	
	Group A (Cases)	**Group B (Controls)**
Male	93 93.0%	26 52.0%
Female	7 7.0%	24 48.0%
Age(Years)	59.03±7.702	52.90±10.983
Pack Years*	25.51±10.958	0[a]

* Pack years - not determined in controls

This table shows that the cases were predominantly seen in males, constituting 93% of total cases. However, the controls comprised 52% males and 48% females. The mean age of cases was reported to be 59.03 years. The mean of pack years in cases was seen to be 25.51.

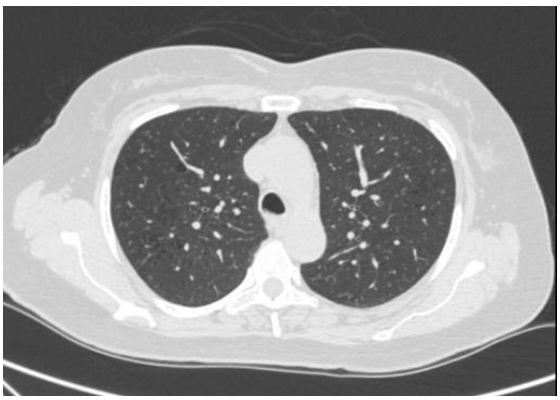

Figure 1: Axial CT section of a 59 year old female, with complaints of dyspnoea, showingcentrilobular pattern of emphysema.

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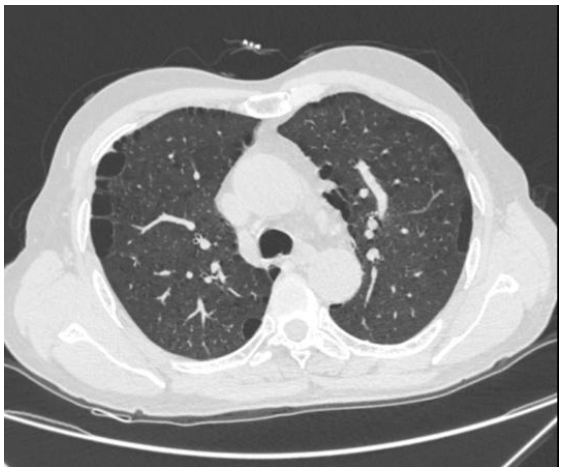

Figure 2: Axial CT section of a 57 year male COPD patient showing both centrilobular and paraseptal pattern of emphysema

Table 2: Descriptive Values of the Quantitative Parenchymal Parameters

		N	Mean±S.D.	P value
Mean Lung Density	Cases	100	-883.2±12.21	0.000
	Controls	50	-837.1±27.2	
Percentage of Low Attenuation Area &<-950HU	Cases	100	29.79±4.16	0.000
	Controls	50	4.163±5.20	
Percentage of Low Attenuation Area [-850 to -950HU]	Cases	100	33.93±2.88	.
	Controls	0*	0.00±0.00	
Percentage of Low Attenuation Area <-850HU	Cases	100	63.69±4.97	.
	Controls	0*	0.00±0.00	
I/E Lung Volume	Cases	100	1.19±0.10	.
	Controls	0*	0.00±0.00	
I/E Lung Attenuation	Cases	100	1.02±0.017	.
	Controls	0*	0.00±0.00	
E[-850HU]/I[-950HU]	Cases	100	0.94±0.006	.
	Controls	0*	0.00±0.00	

P value could not be determined as one group is empty.

Mean lung density was found to be lower in the cases (-883.2 HU) as compared to the controls (-837.1HU) and this difference was found to be statistically significant.The Percentage of Low Attenuation Area <-950HU, indicating combined air trapping and emphysematous changes, was more in the cases with mean of 27.79 in cases and 4.16 in the controls. The percentage of Low Attenuation Area <-950HU and tracheal dimensions was found to be highly significant statistically. Percentage of Low Attenuation Area [-850 to -950HU], Percentage of Low Attenuation Area <-850HU, I/E Lung Volume, I/E Lung Attenuation and E[-850HU]/I[-950HU] were obtained only in cases, as expiratory scan was not done in controls.

Table 3: Descriptive values of quantitative airway parameters.

	Group	N	Mean Std. Deviation	P value
Inner Luminal Area[mm²]	Cases	100	9.78±2.47	0.000
	Contr	50	6.98±2.5	

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	ols		9	
Wall Thickness (cm)	Cases	100	0.125±0.017	0.180
	Controls	50	0.091±0.030	
Wall Area[mm²]	Cases	100	17.99±3.62	0.000
	Controls	50	9.70±3.56	
Wall Area %age	Cases	100	64.59±7.90	0.000
	Controls	50	58.20±7.81	
Wall Attenuation (HU)	Cases	100	-313.7±172.4	0.000
	Controls	50	63.46±281.7	

Among the airway parameters, inner luminal area, wall area, wall area % and wall attenuation was found to be statistically highly significant. Wall thickness was not found to be significant statistically.

Inner luminal area was more in the cases compared to controls with mean value of 9.78mm2 in the cases and 6.98mm2 in the controls.

Wall thickness, wall area and wall area percentage was also higher in the cases than controls with mean value of 0.125cm, 17.99 mm2, 64.59% in the cases and 0.09cm, 9.7 mm2, 58.20% in the controls respectively.

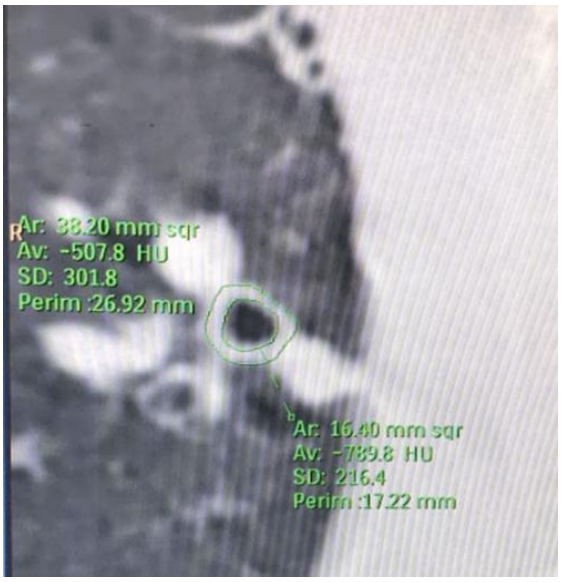

Figure 3: Inner luminal (16.4mm²) and outer luminal area (38mm²) taken at the level of segmental bronchus in a patient of COPD using free hand technique

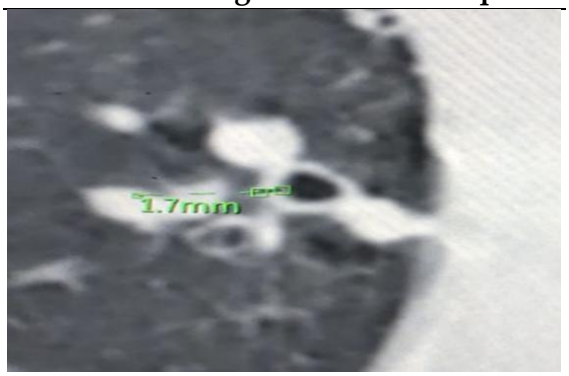

Figure 4: Wall thickness measured with the help of two dimensional calipers in a 60 year old patient of paraseptal emphysema showing increased wall thickness maximum upto 1.7mm.

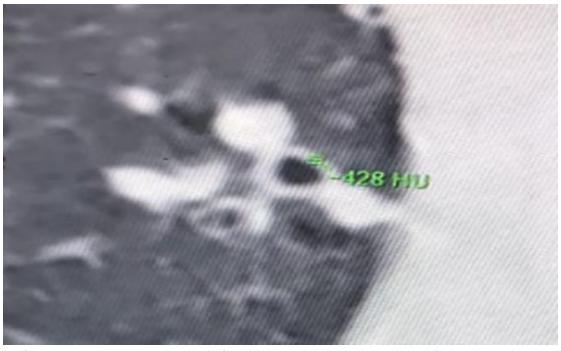

Figure 5: Bronchial wall attenuation taken with pixel at the level of segmental

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bronchus and at the point of peak attenuation.

Table 4: Correlation of Parenchymal Parameters with Spirometry Parameters

		Mean Lung Density	Percentage of Low Attenuation Area <-950HU	Percentage of Low Attenuation Area [-850 to -950HU]	Percentage of Low Attenuation Area <-850HU	I/E Lung Volume	I/E Lung Attenuation	E[-850HU]/I[-950HU]
FEV1	Pearson Correlation	.302**	-.403**	-.104	-.393**	.363**	.119	.011
FVC	Pearson Correlation	.255*	-.364**	-.108	-.364**	.375**	.171	.052
FEV1/FVC	Pearson Correlation	.511**	-.354**	-.098	-.343**	.150	.225*	-.008

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

Table 5: Correlation of Airway Parameters with Spirometry Parameters

		Inner Luminal Area[Ai]	Wall Thickness	Wall Area	Wall Area %age	Wall Attenuation
FEV1	Pearson Correlation	-.088	-.155	-.446**	-.250*	.011
FVC	Pearson Correlation	-.094	-.085	-.438**	-.244*	.013
FEV1/FVC	Pearson Correlation	-.179	-.229*	-.198*	.001	.038

Among the quantitative parenchymal parameters, mean lung density, Percentage of Low Attenuation Area <-950HU, Percentage of Low Attenuation Area <-850HU and I/E Lung Volume showed significant correlation with FEV1 and FVC.

Mean lung density, Percentage of Low Attenuation Area <-950HU, Percentage of Low Attenuation Area <-850HU and I/E Lung Attenuation demonstrated significant correlation with FEV1/FVC. Percentage of Low Attenuation Area [-850 to -950HU] showed negative correlation with FEV1, FVC and FEV1/FVC but were found not to be statistically significant. I/E Lung Attenuation showed positive correlation with FEV1 and FVC but were found not to be statistically significant. E[-850HU]/I[-950HU] showed positive correlation with FEV1,

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FVC and negative correlation with FEV1/FVC, but these were not found to be statistically significant. [Table 4]

- Wall area demonstrated significant negative correlation with FEV1, FVC and FEV1/FVC. With decrease in FEV1 (increase in COPD severity), FVC and FEV1/FVC there was increase in the value of wall area.
- Wall area % demonstrated significant negative correlation with FEV1 and FVC.
- Inner Luminal Area [Ai] and Wall Thickness showed negative correlation with FEV1, FVC and FEV1/FVC, but were found not be significant statistically. Wall Attenuation showed positive correlation with FEV1, FVC and FEV1/FVC, but were not significant statistically. [Table 5]

DISCUSSION

An observational prospective study was performed out in 100 patients diagnosed of chronic obstructive pulmonary disease on spirometry and 50 controls were selected retrospectively with normal inspiratory NCCT scan.

The cases were predominantly seen in males, constituting 93% of total cases. The mean age of cases was 59.03 ± 7.7years. The mean age of controls was calculated to be 52.90 years, 26% being males and 24% females. A cross sectional study performed in 10,187 subjects, by bhatt et al,[11] found the mean age of 59.6 ± 9years in COPD patients and smoking pack years was 44.2 ± 25.0 years. The mean pack years calculated in our study was 25.51 years. Smoking history was seen to be highly prevalent in the cases (94% of total cases). In a previous Indian study, Gupta et al,[12] discovered the mean pack years to be 33.25 and mean age of COPD to be 58.55 years in 40 patients.

Table 6: QCT Parenchymal Parameters in Cases in Our Study Compared to Previous Studies

Study Number of cases	MLD	%LAA (-950HU)	%LAA (-850HU)	%LAA (-850 to 950HU)	I/E vol	I/E att	$E_{(-850HU)}/I_{(-950HU)}$
Our study (n=100)	-883±12.2	29.7±4.16	63.6±4.9	33.93±2.8	1.19±0.1	1.02±0.1	0.94
Nambu et al,[13] (n=188)	NA	17.1±13.1	42.76±21.1	NA	NA	NA	NA
Lee et al,[14](n=34)	-880±33	21.0±17.0	NA	NA	NA	NA	NA
Occhipinti et al,[15](n=194)	NA	14.0±12.0	45.0±20.0	NA	NA	NA	NA
Chen et al,[16] (n=69)	901.96±28.5	43.8±12.6	51.9±14.5	NA	NA	NA	NA

Table 7: QCT airway parameters in cases in our study compared to previous studies.

StudyNumber of controls [N]	Ai [seg]mm2	WT [seg] Cm	WA [seg] mm^2	WA% [seg]	WAT [seg] HU
Our studyN=50	9.78±2.4	0.12±0.01	17.99±3.6	64.59±7.9	-313±172
Hartley,[17] et alN= 81	11.3±3.0	NA	18.1±3.3	62.7±2.2	NA
Nakano,[18] et alN=114	17.3±7.6	0.15±0.02	NA	64.5±7.9	NA

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Chen et al,[16]N=69	13.15±3.9	NA	21.19±4.5	62.42±2.6	NA
Mair et al,[19] N=56	NA	0.2±0.4	NA	74±4	NA

Mean lung density was found to be lower in the cases (-883.2 HU) as compared to the controls (-837.1HU) and this difference was found to be statistically significant. The Percentage of Low Attenuation Area <-950HU, indicating combined air trapping and emphysematous changes, was significantly more in the cases with mean of 27.79 in cases and 4.16 in the controls.

The mean of percentage of low attenuation area <850HU, percentage of low attenuation area [-850 to -950 HU], I/E lung volume, I/E lung attenuation and E[-850HU]/I[-950HU] was found to be 63.69, 33.93, 1.19, 1.02 and 0.94 in the cases respectively. [Table 6]

Among the airway parameters, inner luminal area, wall area, wall area % and wall attenuation was found to be statistically highly significant. Wall thickness was not found to be significant statistically. Inner luminal area was more in the cases compared to controls with mean value of 9.78mm2 in cases and 6.98mm^2 in controls.

Wall thickness, wall area and wall area percentage were also higher in the cases than controls with mean value of 0.125cm, 17.99 mm2, 64.59% in the cases and 0.09cm, 9.7 mm2, 58.20% in the controls respectively.

Greater variability in the airway parameters compared to parenchymal parameters has been assumed due to post processing softwares provided by different vendors and manual tracing methods used. Acquisition factors [slice thickness,image noise] also play a role in variability. Variations in mean values can also be due to difference in the number of subjects taken, gender, age, ethnicity, built, smoking status and the severity of COPD in the selected individuals.

CONCLUSION

In this study, we concluded that the quantitative CT parameters which are easily available can be effectively used to diagnose the cases of COPD and to assess severity of the COPD. These CT parameters showed significant correlation with pulmonary function tests. Thus, they can be used by clinicians as a diagnostic tool for early diagnosis of the disease and early & effective treatment of the patients.

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