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Original article

Quantitative Assessment of COPD Patients Using Computed Tomography

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Abstract

Background: Worldwide, COPD is a substantial cause of both morbidity and mortality. **This study objective is to** evaluate how computed tomography (CT) can be utilized in quantitative assessment of COPD patients in terms of parenchyma and airways lumina. **Methods:** This prospective observational analytical study compromised 80 participants who were categorized into 3 groups: Group I: 40 patients having COPD (FEV1/FVC < 70 in PFTS). Group II: 25 apparently healthy smokers. Group III: 15 apparently healthy (non-smokers). **Results**: LAA - 950 HU insp demonstrated a significant positive correlation with the smoking index (r = 0.686, P < 0.0001. It revealed a significant negative correlation with FEV1 (r = -0.368, P = 0.019). %LAA - 856 HU expiration was significantly lower in Group II and Group III in comparison with Group I, with Group III also significantly lower than Group II. Wall area (%) was significantly higher in group I than in groups II and III. Bronchial wall thickness revealed significant positive correlations with the smoking index (r = 0.695, P < 0.0001). **Conclusion:** The study successfully demonstrated the strong predictive value of spirometric measures such as FEV1, FEV1 ratio, and FEV1/FVC in identifying structural changes within the lungs of COPD patients, as measured through CT imaging. These findings underscore the interplay between functional impairments and anatomical alterations in the progression of COPD, including increased bronchial wall thickness, wall area, and the presence of low attenuation areas, which are indicative of emphysematous damage.

Keywords: Quantitative Assessment; COPD; Computed Tomography; Airways Lumina.

Introduction

Worldwide, COPD is a substantial cause of both morbidity and mortality. By 2030, COPD is expected to rank as the fourth leading cause of death (1), COPD is a multifaceted condition with diverse clinical and pathological features, all characterized by the spirometric indication of airflow obstruction. Whereas airway narrowing and parenchymal destruction are known to cause airflow obstruction in COPD, but these cannot be differentiated using standard spirometry. Nonetheless, standard spirometry is widely utilized for enrolling patients and evaluating outcomes in clinical and pharmacologic research (2).

Irreversible hyperinflation of the lung parenchyma, characteristic of pulmonary emphysema, plays a crucial role in the compromised lung function seen in chronic obstructive lung disease.

Individuals suffering from emphysema exhibit a greater lung volume compared to normal individuals, yet the change of volume between inspiration and expiration is less than that of nonsmokers who are healthy (3).

For diagnosing COPD, the pulmonary function test (PFT) is considered the gold standard, often revealing a decreased FEV1, an elevated TLC, and a lowered FEV1/forced vital capacity (FVC) ratio (4).

Spirometry is a cost-effective, easily reproducible, and widely accessible test. Nonetheless, it has drawbacks, including its inapplicability to patients presenting with their first exacerbation. Moreover, spirometry is effort-dependent, which means it is not feasible for elderly patients, those with neurological or psychiatric issues, or individuals with oro-facial trauma or tumors to complete the test (5).

COPD's intricate pathophysiology is not entirely revealed by tests related to the lung function alone. Therefore, there is a significant clinical need for diagnostic methods and biomarkers that, alongside lung function tests, can accurately define COPD and evaluate specific subtypes, or phenotypes, with distinct prognostic and therapeutic implications (6, 7).

Chest computed tomography (CT) is considered as an imaging technique that is non-invasive and it offers deeper insights into the pathophysiological aspects of the lungs, enhancing our understanding of disease variability and aiding in the detailed characterization of COPD phenotypes (7).

By quantifying attenuation values of CT, the emphysema extent can be assessed. Low attenuation volumes (LAVs) are thought to represent emphysematous lung parenchyma and have been shown to correlate with the degree of lung function loss (8).

The objective of our study was to examine how CT can be utilized for the quantitative assessment of both lung parenchyma and airway lumina in individuals with COPD.

Patients and methods

Eighty patients were allocated into three groups in this prospective observational

analytical study. **Group I**: 40 patients having COPD (FEV1/FVC < 70 in PFTS). **Group II:** 25 apparently healthy smokers. **Group III**: 15 control samples (non-smokers).

Between March 1, 2023, and March 30, 2024, they were picked from the Chest Disease Department of Benha University Hospital.

Every single participant gave their written, informed consent. Benha Faculty of Medicine's Research Ethics Committee gave its approval. **(MS 31-11-2020)**

Inclusion criteria were Patients diagnosed with (COPD) according to GOLD guidelines 2023 and age over 18 years.

Exclusion criteria were patients suffering from lung cancer, history of thoracic surgery, for instance, heart valve replacement and lung volume reduction surgery (LVRS), thoracic deformity caused by pulmonary tuberculosis, massive pleural effusion, congenital thoracic deformity, kidney insufficiency diseases, active pulmonary tuberculosis, bronchial asthma, interstitial fibrosis of the lung, pleural thickening, consolidation of the lung, heart, liver, and individuals with an ongoing AECOPD.

The study involved detailed history taking for all cases, encompassing [Age, sex, history of smoking, symptoms and duration of illness.], clinical examination. **Pulmonary Function Tests (PFTs). CT examination. CT quantification.**

Spirometry was done utilizing Jaeger *Master Screen PFT CareFusion* UK Ltd, Basingstoke, UK.

A few practices attempt of forced expiratory maneuvers were done first. At least three acceptable maneuvers were conducted. Acceptable maneuvers include a good start, no hesitation, and a smooth continuous exhalation. The most favorable values for FVC and FEV1 were documented.

CT examination: CT examination was done (CT scanner gantry manufactured by TOSHIBA was utilized, model: CXXG-010A), and volumetric CT scans were done for all participants at maximum inspiration and at the conclusion of a normal expiration. For the CT scans, a tube potential peak of 120 kVp was used, with a mAs of 200 for inspiratory images and 50 for expiratory images, alongside a gantry rotation time of 0.5 seconds.

CT quantification: The following quantitative parameters were determined, including:

(1) LAA% refers to the proportion of the lung parenchyma that exhibits low attenuation on CT images, indicative of emphysematous changes. These areas are typically defined by a threshold, such as pixels with attenuation values below -950 Hounsfield Units (HU) on inspiratory scans and below -856HU at expiration (%LAA -856exp). This provides a precise assessment of the severity of emphysematous damage in COPD patients. It links to airflow obstruction severity and can provide insight into disease heterogeneity.

(2) Bronchial wall thickness, measured with mm,

(3) The WA% of the bronchial wall area is derived from the formula (bronchial area - luminal area) / bronchial area.

(4) Phenotypic patterns of (COPD).

Statistical analysis

Utilizing SPSS version 28, the data management and statistical analyses were done (IBM, Armonk, New York, USA). For estimating the quantitative data normality, the Shapiro-Wilk test was employed, alongside methods like direct data visualization. Based on their distribution, quantitative data were presented either as means with standard deviations or as medians with ranges. For categorical data, results were expressed as frequencies and percentages. Group comparisons for quantitative variables were performed with one-way ANOVA for data that was normally distributed and the Kruskal-Wallis test for non-normally distributed data.

The Chi-square test or Fisher's exact test was used to compare categorical variables. Correlations were analyzed utilizing Pearson's or Spearman's methods, depending on data type. To predict CT measures from physiological indices, multivariate linear regression analysis was done, with regression coefficients and 95% confidence intervals calculated. Statistical tests were conducted as two-tailed, with a significance level set at a p-value below 0.05.

Results

In accordance with the results, no significant differences were observed in terms of age and gender. The smoking index in group II was significantly lower in comparison with that in group I. The FEV1 and FEV1 ratio showed significant differences across the groups. Specifically, significant variations were observed between groups I and II, I and III, as well as between II and III. The FVC and FVC ratio also displayed significant differences among the groups, with group I have significantly lower values compared to both groups II and III. Additionally, group II had significantly lower values than group III. The FEV1/FVC ratio also varied significantly between the groups. **Table 1**

Bronchial wall thickness (mm) was significantly different between the studied groups as the mean values of bronchial wall thickness (mm) increased in group I than healthy smokers (group II) and healthy non-smokers (group III). Wall area% significantly differed between the studied groups Group I had a significantly higher value than both groups II and III. %LAA - 950 HU insp., %LAA - 856 HU exp significantly differed across the studied groups. Group I had a significantly higher value than both groups II and III. Additionally, it was significantly greater in group II in comparison with group III. **Table 2**

Bronchial wall thickness revealed significant positive correlations with the smoking index.

In contrast, it revealed significant negative correlations with FEV1, FEV1 ratio. The strongest negative correlation was seen between bronchial wall thickness and FEV1/FVC ratio. Bronchial wall thickness did not reveal significant correlations with age, FVC and FVC ratio. Wall Area% demonstrated a significant positive correlation with the smoking index. In contrast, it revealed a significant negative correlation with FEV1 FEV1 ratio and the strongest significant negative correlation appeared with FEV1/FVC Wall area did not reveal significant correlations with age and FVC and FVC ratio. **Table 3**

LAA - 950 HU insp. demonstrated a significant positive correlation with the smoking index. In contrast, it revealed a significance negative correlation with FEV1, FEV1 ratio and the strongest significant negative correlation appeared with FEV1/FVC. %LAA - 950 HU insp. did not reveal significant correlations with age and FVC, and FVC ratio.

%LAA - 856 HU exp demonstrated a significant positive correlation with the smoking index. In contrast, it revealed a significant negative correlation with FEV1, FEV1 ratio and the strongest significant negative correlation appeared with FEV1/FVC while, %LAA - 856 HU exp. did not reveal significant correlations with age, FVC and FVC ratio. **Table 4**

The regression analyses revealed that FEV1, FEV-1 ratio and FEV1/FVC were significant predictors of bronchial wall thickness, controlling for age and gender while, FVC and FVC ratio were not significant predictors of bronchial wall thickness, controlling for age and gender. **Table 5**

The regression analyses revealed that FEV1, FEV-1 ratio and FEV1/FVC were significant predictors of Wall Area (%), controlling for age and gender while, FVC and FVC ratio were not significant predictors of Wall Area (%), controlling for age and gender. The regression analyses revealed that FEV1, FEV-1 ratio and FEV1/FVC were significant predictors of %LAA - 950 HU insp. and %LAA - 856 HU exp controlling for age and gender while, FVC and FVC ratio were not significant predictors of %LAA - 950 HU insp., controlling for age and gender. **Table 6**

Table 1: General characteristics, and spirometry results of the studied groups

Demographic characteristics	Group I (COPD) (n = 40)	Group II (Healthy smokers) (n = 25)	Group III (Healthy nonsmokers (n = 15)	P-value
Age (years)	57 ± 6.59[a]	55 ± 7.04[a]	59 ± 6.41[c]	0.220
Sex Males	24 (60)[a]	17 (68)[a]	10 (66.7) [a]	0.795
Females	16 (40)[a]	8 (32)[a]	5 (33.3) [a]	
Smoking index	425 (0 – 668)[a]	176 (103 – 276)[b]	0 (0)[c]	<0.00۱*
Spirometry results				
FEV1	1.14 ± 0.43[a]	3.5 ± 0.19[b]	3.9 ± 0.40[c]	<0.00۱*
FEV1 ratio (%)	28 ± ۱۱[a]	87 ± 4[b]	97 ± 10[c]	<0.00۱*
FVC	1.84 ± 0.62[a]	4.41 ±0.19[b]	4.87 ± 0.62[c]	<0.00۱*
FVC ratio (%)	37 ± 12[a]	88 ± 3[b]	97 ± 12[c]	<0.00۱*
FEV1/FVC (%)	61 ±7 [a]	79 ± 2 [b]	80 ± 2 [b]	<0.00۱*

Table 2: Chest computed tomography findings in the studied groups

	Group I (n = 40)	Group II (n = 25)	Group III (n = 15)	P
Br. wall thickness (mm)	1.6 ± 0.2	1.2 ± 0.1	0.8 ± 0.1	<0.0001*
Wall Area (%)	52 ± 3.5	40 ± 2.8	32 ± 1.9	<0.0001*
%LAA - 950 HU insp	31.6 ± 5.1	12.3 ± 0.4	2.5 ± 0.6	<0.0001*
%LAA - 856 HU exp	49.1 ± 7.2	18.8 ± 6.1	8.1 ± 0.2	<0.0001*

* Different superscripted small letters in the same row are considered significantly different (P < 0.05); LAA: Low Attenuation Area

Table 3: Correlation between bronchial wall thickness and other parameters and between wall area and other parameters in group **I**

	Bronchial wall thickness (mm)	
	r	**P**
Age (years)	**-0.033**	**0.836**
Smoking index	**0.695**	**<0.0001***
FEV1	**-0.361**	**0.021***
FEV1 Ratio (%)	**-0.359**	**0.022***
FVC	**-0.110**	**0.498**
FVC Ratio (%)	**-0.101**	**0.535**
FEV1/FVC (%)	**-0.854**	**<0.0001***
	Wall Area (%)	
	r	**P**
Age (years)	**-0.074**	**0.649**
Smoking index	**0.682**	**<0.0001***
FEV1	**-0.346**	**0.028***
FEV1 Ratio (%)	**-0.344**	**0.029***
FVC	**-0.079**	**0.548**
FVC Ratio (%)	**-0.088**	**0.586**
FEV1/FVC (%)	**-0.898**	**<0.0001***

* Different superscripted small letters in the same row are considered significantly different (P<0.05); r: correlation coefficient; FEV: Forced Expiratory Volume; FVC: Forced Vital Capacity.

Table 4: Correlation between %LAA - 950 HU insp. and other parameters and between %LAA 856 HU exp. and other parameters in group I

	%LAA - 950 HU insp	
	r	**P**
Age (years)	**-0.071**	**0.659**
Smoking index	**0.686**	**<0.0001***
FEV1	**-0.368**	**0.019***
FEV1 Ratio (%)	**-0.364**	**0.020***
FVC	**-0.106**	**0.513**
FVC Ratio (%)	**-0.095**	**0.556**
FEV1/FVC (%)	**-0.913**	**<0.0001***
	%LAA - 856 HU exp.	
	r	**P**
Age (years)	**-0.074**	**0.647**
Smoking index	**0.678**	**<0.0001***
FEV1	**-0.446**	**0.003***
FEV1 Ratio (%)	**-0.441**	**0.004***
FVC	**-0.191**	**0.236**
FVC Ratio (%)	**-0.179**	**0.268**
FEV1/FVC (%)	**-0.896**	**<0.0001***

* Different superscripted small letters in the same row are considered significantly different (P<0.05); r: correlation coefficient; FEV: Forced Expiratory Volume; FVC: Forced Vital Capacity.

Table 5: Multivariate linear regression analysis to predict bronchial wall thickness and wall area (%)

	Bronchial wall thickness	
	B (95% CI) †	**P-value**
FEV1	-0.127 (-0.235 to -0.020)	0.021*
FEV1 Ratio	-0.005 (-0.009 to -0.001)	0.022*
FVC	-0.026 (-0.106 to -0.05)	0.498
FVC Ratio	-0.001 (-0.005 to -0.002)	0.535
FEV1/FVC	-0.018 (-0.021 to `- 0.014)	< 0.0001*
	Wall Area (%)	
	B (95% CI) †	**P-value**
FEV1	-6.259 (-11.82 to - 0.692)	0.028*
FEV1 Ratio	-0.248 (-0.471 to - 0.0259)	0.029*
FVC	-1.227 (-5.326 to 2.872)	0.548
FVC Ratio	-0.055 (-0.257 to 0.147)	0.586
FEV1/FVC	-0.982 (-1.141 to - 0.8247)	< 0.0001*

* Different superscripted small letters in the same row are considered significantly different (P<0.05); †Adjusted for age and gender; B: Regression coefficient; 95% CI: 95% Confidence interval; FEV: Forced Expiratory Volume; FVC: Forced Vital Capacity.

Table 6: Multivariate linear regression analysis to predict %LAA - 950 HU insp and %LAA - 856 HU exp.

	%LAA - 950 HU insp.	
	B (95% CI) †	**P-value**
FEV1	-5.637 (-10.31 to -0.964)	0.019*
FEV1 Ratio	-0.223 (-0.409 to - 0.035)	0.020*
FVC	-1.130 (-4.599 to 2.339)	0.513
FVC Ratio	-0.050 (-0.222 to 0.121)	0.556
FEV1/FVC	-0.846 (-0.970 - 0.723)	<0.0001*
	%LAA - 856 HU exp.	
	B (95% CI) †	**P-value**
FEV1	-8.174 (-13.550 to - 2.797)	0.003*
FEV1 Ratio	-0.323 (-0.538 to - 0.107)	0.004*
FVC	-2.432 (-6.527 to 1.663)	0.236
FVC Ratio	-0.112 (-0.315 to 0.090)	0.268
FEV1/FVC	-0.993 (-1.155 to - 0.831)	<0.0001*

* Different superscripted small letters in the same row are considered significantly different (P < 0.05); †Adjusted for age and gender; B: Regression coefficient; 95% CI: 95% Confidence interval; FEV: Forced Expiratory Volume; FVC: Forced Vital Capacity.

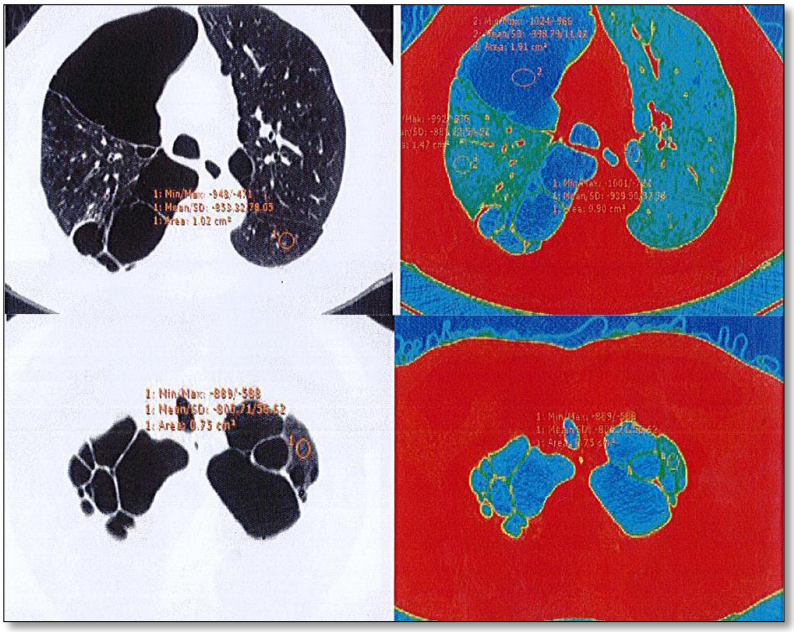

Figure 1: CT done showing mild to moderate bilateral emphysematous changes.

A male patient, ٧٠ years old, heavy smoker, presented with severe progressive dyspnea. PFT done showing: FEV1/FVC%= 38%, FEV1%=14%, FVC%= 28%. QCT done showing: WA%= 83.3%, WT= 1.8 mm, %LAA-950 Hu insp.= 35.4%, %LAA-856 Hu exp.= 63.3%.

Discussion

This study reported no significance regarding the difference between age (P= 0.220) and sex (P = 0.795) among studied groups. While a significantly higher smoking index was noted in group I in comparison with group II. (P < 0.0001).

Near to our results, Chauhan et al. revealed that most of the patients were elderly, and their age was in between 61 and 70 years, and their mean age is 64 years. Male patients had a mean smoking index of 562.89 ± 369.66. Predictably, those with elevated SI values also had lower BMI, especially in the emphysema-predominant group, with a significant correlation between these variables. (1)

In the present study, significant differences were noted across all lung function metrics among the three groups. Group I had markedly lower FEV1, FEV1 ratio, FVC, and FVC ratio in comparison with Groups II and III (all P < 0.0001), with FEV1 also differing significantly between Groups II and III (P = 0.004). FEV1/FVC ratios were lowest in Group I in comparison with the other groups (P<0.0001), and the variation between groups II and III was not significant. (P = 0.82).

Also, Chae et al., reported that COPD patients exhibited significantly decreased FEV1 (% predicted) and FEV1/FVC ratios relative to normal individuals (p value= 0.001). (9)

As regard CT quantitative measurements, in the current study, significant differences were observed in bronchial wall thickness, wall area percentage, and %LAA across the studied groups. Group I exhibited the highest bronchial wall thickness in comparison with Group II and Group III, wall area in comparison with Group II and Group III and %LAA -950 HU insp. in comparison with Group II and Group III all $P < 0.0001$. Additionally, %LAA -856 HU exp. was significantly higher in Group I in comparison with Group II and Group III, with Group II also significantly higher than Group III.

Parallel to these results, Zhu et al. included 284 patients with symptoms related to the respiratory system who used to smoke or currently smoke. The study reported that when COPD severity increases, the LAA-950 value starts to increase gradually. However, there was no difference observed across OLD grade I with non-COPD patients ($p = 0.56 > 0.05$), there was a significant difference between patients classified as GOLD grades II to IV and those not suffering from COPD. (all $p < 0.0001$). (10)

In this study, wall area% increased with increasing severity of COPD which showed a significant positive correlation with the smoking index but negatively correlated with FEV1, FEV1 ratio, and most strongly with FEV1/FVC .No significant correlations were found between wall area and age, FVC, or FVC ratio .Similarly, bronchial wall thickness increased with elevation in COPD severity was positively correlated with the smoking index and negatively correlated with FEV1, FEV1 ratio, and FEV1/FVC. It showed no significant correlation with age, FVC, or FVC ratio.

Inflammation plays a crucial role in COPD development, driven by the release of inflammatory mediators and destructive enzymes from immune cells, especially those that infiltrate tissues.

COPD involves a series of structural changes, such as increased airway epithelial cell proliferation, thickening of the RBM, collagen buildup, peribranchial fibrosis, airway epithelial-to-mesenchymal transition, and smooth muscle cell hyperplasia. Small airway remodeling is a major factor in causing airway obstruction and airflow restriction in patients with COPD. (11)

The findings from current study are well-aligned with the research carried out by de Boer et al., It highlights the significant utility of advanced imaging techniques in enhancing the diagnostic precision of COPD assessments. Specifically, de Boer's findings on the correlation of emphysema quantification with pulmonary function tests (PFTs) particularly the inverse correlations with FEV1 and FVC which are critical in staging COPD. (12)

In this study, %LAA - 856 HU exp. demonstrated a significant positive correlation with the smoking index. In contrast, it revealed a significant negative correlation with FEV1, FEV1 ratio and the strongest significant negative correlation appeared with FEV1/FVC. %LAA - 856 HU exp. did not reveal significant correlations with age and FVC, and FVC ratio.

Chae et al.'s results provided strong backing and additional validation for these findings, demonstrating the most substantial correlations with FEV1/FVC, FEV1 % LAA insp, and % LAA exp in emphysema patients as well as in healthy individuals. This correlation mirrors our own results, which indicate significant associations between various CT quantification metrics such as %LAA at specific Hounsfield Units and spirometric indices (9).

Multivariate linear regression analyses predicting bronchial wall thickness revealed that FEV1, FEV1 ratio, and FEV1/FVC significantly predicted bronchial wall thickness (p-values: FEV1 = 0.021, FEV1 ratio = 0.022, FEV1/FVC < 0.0001), indicating that lower spirometric values are associated with thicker bronchial walls, a hallmark of COPD progression. FVC and FVC ratio were not significant predictors. the bronchial wall thickness increases, it aligns with the anticipated COPD progression where inflammation and structural changes lead to thicker airway walls. This suggests that as airflow obstruction worsens, measurable changes in the bronchial anatomy become more pronounced, which can be quantitatively assessed through CT imaging. In contrast, FVC and FVC ratio did not show significant predictive value, which may indicate that these measures are less directly related to airway remodeling seen in COPD.

Multivariate linear regression analyses regarding wall area percentage found that FEV1, FEV1 ratio, and FEV1/FVC were significant predictors of increased wall area percentage (P-values: FEV1 = 0.028, FEV1 ratio = 0.029, FEV1/FVC < 0.0001), reflecting the inflammatory and fibrotic changes within the airways.

The significant predictive ability of FEV1, FEV1 ratio, and FEV1/FVC for %LAA at 950 HU and 856 HU on inspiration and expiration respectively highlights the relationship between decreased lung function and increased presence of emphysematous tissue (low attenuation areas). This underscores the utility of these CT-based measures in identifying and quantifying the extent of emphysematous destruction in the lung parenchyma. These low attenuation areas are indicative of regions where air is trapped distal to the terminal bronchiole. The hallmark of emphysema is the abnormal, permanent expansion of lung air spaces with wall destruction, devoid of fibrosis. This results in the destruction of lung parenchyma, reduced elasticity, breakdown of alveolar walls, loss of support, and early collapse of alveoli. (13)

Nearly similar results were obtained by Schroeder et al., who found that the regression between FEV_1/FVC and % LAA-950 at 95% was −0.77 to −0.74, while it was −0.68 to −0.65 for FEV1. The authors also revealed that the regression between FEV_1/FVC and % LAA- 856 at 95% was −0.85 to −0.83, while it was −0.78 to −0.75 for FEV1. (14)

Furthermore, Paoletti et al., single multivariate linear regression models were employed to predict CT lung attenuation, with %LAA-950 as the dependent variable and FEV1/VC as the

independent variable. The analysis revealed a coefficient of -0.19. (15)

Conclusion

This study successfully demonstrated the strong predictive value of spirometric measures such as FEV1, FEV1 ratio, and FEV1/FVC in identifying structural changes within the lungs of COPD patients, as measured through CT imaging. These findings underscore the interplay between functional impairments and anatomical alterations in the progression of COPD, including increased bronchial wall thickness, wall area, and the presence of low attenuation areas, which are indicative of emphysematous damage. The significant correlations between these spirometric measures and CT-derived metrics highlight their combined utility in a more comprehensive clinical assessment of COPD, facilitating early diagnosis and the monitoring of disease progression.

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