The Added Value of Artificial Intelligence to Chest Computed Tomography in Early Detection of Chronic Obstructive Pulmonary Disease.

Maha M. Saad[1]*, Ahmed A. Bayoumy[2], Magdy M. EL-Nisr[1], Noha M. Zaki[3], Tarek H. Khalil[1], Ahmed F. ELserafi[1].

[1]Department of Diagnostic Radiology, Faculty of Medicine, Suez Canal University, Ismailia, Egypt
[2]Chest unit, Department of Internal Medicine, Faculty of Medicine, Suez Canal University Ismailia, Egypt.
[3]Department of Diagnostic Radiology, Faculty of Medicine, Ain Shams University, Cairo, Egypt

Abstract

Background: **Recent developments in Artificial Intelligence (AI) applications allow for the automatic identification and measurement of Chronic Obstructive Pulmonary Disease (COPD) on chest computed tomography (CT). The forced expiratory volume in the first second (FEV1) levels on pulmonary function test (PFT), while useful as the main technique of staging and measuring COPD severity, do not provide an accurate status on both the type of COPD and the degree of lung involvement detected on chest CT.** ***Aim:*****The purpose of this study is to clarify the function of AI in estimating COPD severity.** ***Methods:*** **We employed an 80-case cross-sectional investigation with a non-contrast CT chest and a computer-aided detection (CAD) system (Coreline Soft's AVIEW). Expiratory Low Attenuation Area% -856 (%LAA -856 HU_{EXP}) and Air Trapping Index (ATI) are used to diagnose small airway disease. The severity of COPD was determined using spirometry, which was computed as the ratio of forced expiratory volume in the first second (FEV1) to forced vital capacity (FVC).** ***Results:*** **The patients were split into four groups based on the spirometry results: mild (n=23), moderate (n=39), severe (n=17), and extremely severe (n=1). Group 3 of the Global Initiative for Obstructive Lung Disease (GOLD) staging scheme had Exp. LAA-856 (%) that was significantly higher than groups 2 and 1. Additionally, ATI in group 3 was considerably higher compared to groups 2 and 1 .*****Conclusions:*** **Exp.LAA-856% and ATI were found to be significantly related to COPD severity as measured by dyspnea scale and spirometry.**

Keywords: Artificial intelligence, Small airway disease, Expiratory Low Attenuation Area, Air Trapping Index

Background

The fourth most common cause of death and 3rd leading cause of disability according to the United States Centers for Disease Control and Prevention (CDC) is Chronic Obstructive Pulmonary Disease (COPD) which involves two main conditions: chronic bronchitis & emphysema [(1)].

The combined evaluation of emphysema and bronchial wall thickening on CT can help characterize heterogeneous pattern of COPD.[(2)]

Pulmonary emphysema, defined as irreversible destruction of airway

*Corresponding author: mahamamdoh888@yahoo.com

walls and dilatation of air spaces distal to the terminal bronchioles, so emphysema appears as a region of relatively lower Housenfield Units (HU) (lower CT attenuation) [(3)].

Emphysema index or %LAA-950, which defines the area of the lung less than -950HU, is widely used to estimate the emphysema component in COPD patients [(4)].

Small airway remodeling is the other component of COPD and is known to be the most powerful determinant of airflow limitation. Various airway parameters can be obtained from CT, including wall area (WA), lumen area (LA), airway wall thickness (AWT), lumen diameter, Wall Area percentage (WA%), and Internal Perimeter (Pi). Recently, another effective CT airway parameter called Internal Perimeter 10 mm (Pi10) was introduced to avoid the potential bias that may happen due to the different distribution of airway sizes.[(5)]

Air trapping measurement is another indirect method for assessing small airway disease. It can be simply assessed by using CT to evaluate the percentage of low attenuation area at the threshold of -856 HU, which is the threshold of normal lung tissue in inspiration.

Air Trapping Index (ATI) is another method that depends on the HU difference of image voxels detected on co-registered inspiratory and expiratory CT scans [(6, 7)]. Spirometry is the used tool for COPD diagnosis, by the existence of a post-bronchodilator (Forced Expiratory Volume in 1st second\ Forced Vital Capacity) FEV1/FVC ratio less than 0.70. For classification of COPD severity, the GOLD staging system is commonly used but cannot determine its subtypes [(8)].

Artificial Intelligence (AI) is a combination of computer science, mathematics, physiology, and other disciplines. The main aim of AI is to produce intelligent machines. The intelligence involves thinking, making decisions and solving problems by learning [(9)]. AI surpass recognizing complex patterns in images and provide a quantitative assessment in automated mode. More reproducible and accurate radiology assessments can be made when AI is implemented into the clinical workflow to assist clinicians [(9)].

In our study we aim to evaluate the efficacy of AI based COPD diagnosis by CT, in COPD severity assessment in comparison with the utilized clinical & spirometric measures to set cut off values for each parameter. Which will help classify the severity of the disease in the future by using CT, identify the efficient and valuable role of each parameter in the early detection, diagnosis, determine severity of disease by correlating with clinical diagnosis and spirometric results, and provide quantitative information and structural assessment to facilitate early diagnosis with less time consumption and accurate precise end results.

Methods

A written informed consent from all patients provided for the current study, licensed by the regional institutional ethics committee with ethical approval ID number of 4229 before doing any investigations or taking any data or doing any imaging techniques.

The research was executed in the CT unit – in radiology department and all cases were referred from chest department at Suez Canal University hospital in Ismailia, Egypt, with remote online access to a "Coreline Soft's AVIEW " which is a Computer Aided Detection (CAD) System. Coreline Soft develops medical 3D imaging software. Its product offerings include AVIEW, a suit of quantitative analysis software for lung disease powered by a fully automated AI algorithm. The company was founded in 2012 and is based in Seoul, South Korea.

We included 80 patients in our investigation (with no restrictions on gender or age, however most of them were old age males), which was carried out as a descriptive cross-sectional study across two years, from the June of 2020 to the June of 2022. Inclusion criteria included (a) Referred COPD patients for a chest-CT scan to evaluate the morphological disease pattern, and its severity, or referred COPD patients to exclude coexisting malignancy; (b) patients referred for a CT chest scan to identify the cause of recent or prior history of dyspnea, chronic productive cough and wheezy chest, for more than three consecutive months were involved in our study because they were clinically suspected to have COPD [10].

Exclusion criteria included (a) Refusal to participate in the study, (b) Coexisting lung carcinoma, (c) Patients have pneumonia in time of study, (d) Coexisting suspected pulmonary nodule, and (e) CT-Chest with IV contrast & (f) pregnant women [11].

All patients underwent a CT chest scan without IV contrast after having their medical histories (age, smoking status, symptoms including dyspnea and a productive cough, etc.) reviewed.

CT Technique:

CT imaging process was performed using 16 slice scanner, Activion 16 model TSX-031A-2012 with standard accessories (Toshiba Medical Systems) In Ismailia city, Egypt.

- **CT Protocol:**

CT scan was performed as follows:

- In cranio-caudal direction (Head first, Supine position).
- Both Inspiratory& Expiratory CT was obtained.
- Beginning from the apices of the lung to costophrenic angles.
- The Slice thickness is 1mm.
- kVp =120, and mAs =80–100.
- Reconstruction algorithms were smooth & sharp (Gantry Rotation time= 0.75, Detector width= 0.5mm & Kernel= FC51).
- Pitch less than one
- Contrast did not used.

Patients with breathing problems were trained and the scan was done after breath hold practice.

- **Post-Processing:**

The Deep Learning Convolutional Neural Networks algorithm (CNN)-based AView platform from Coreline Soft, which is a multiplatform software programme for medical imaging computing, was used to carry out the post-processing. A chest CT image is used to plan the AVIEW Metric Chest Imaging Platform, an artificial intelligence-based precision medical system that can test for COPD and associated co-morbidities automatically.

CNN algorithm was used for airway segmentation and deep lobe segmentation; the time per case was saved from 60 minutes to 3 minutes, from 40 minutes to 2 minutes respectively **(Figure.1)**.

Figure.1 (a) Automatic airway segmentation (b) Automatic lobe segmentation

- **Image Analysis:**

The Picture Archiving and Communication System (PACS) (Synapse (Fujifilm), Version 4.4.200, in Ismailia city, Egypt) was used to automatically generate a report and record the CT parameters for the diagnosis of the COPD.

Indirect evaluation methods for small airway disease (air trapping by obstruction):

(i) %LAA -856 HU$_{EXP}$

LAA -856 HU$_{EXP}$ was calculated automatically using a threshold of -856 HU to assess the percentage of low attenuation area on a chest CT scan. The assumption was that a healthy expiratory lung should exhibit higher attenuation than this number, and the threshold was chosen since it is known to represent the attenuation of normally inflated inspiratory lung.[12] **(figure.2).**

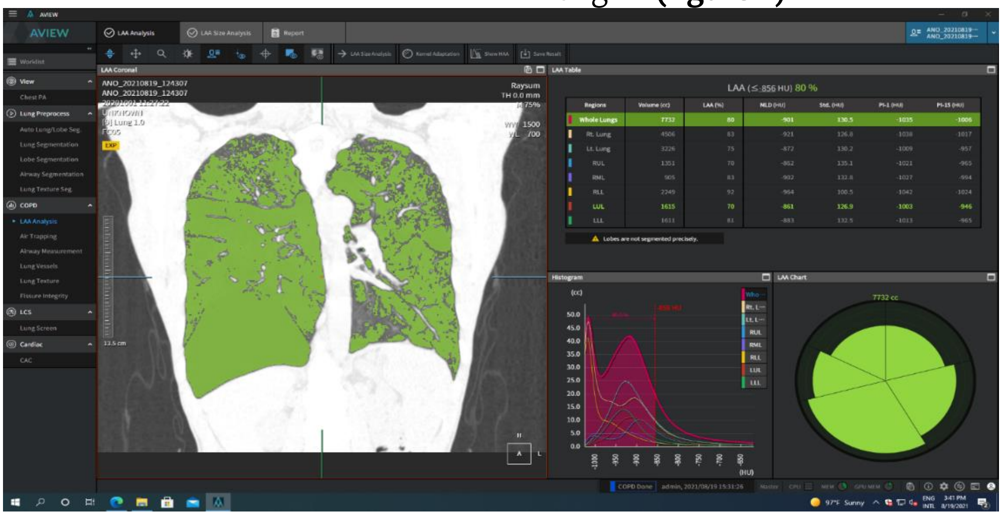

Figure.2 Exp-856 HU $_{EXP}$ analysis of the whole lung, Right & Left lobes separately and segments of each lobe in illustrated table, chart and histogram as above. The green coded areas in the coronal image and chart show the lung areas with attenuation less than -856 during expiration indicating the air trapping and its distribution throughout the lung with total percent of 80% in this patient.

(ii) Air trapping Index (INS\EXP registration).

By defining air trapping as regions with less attenuation change than the predetermined threshold (60 HU), the air trapping index permitted voxel-by-voxel analyses of attenuation changes during inspiration and expiration. (12) **(figure.3).**

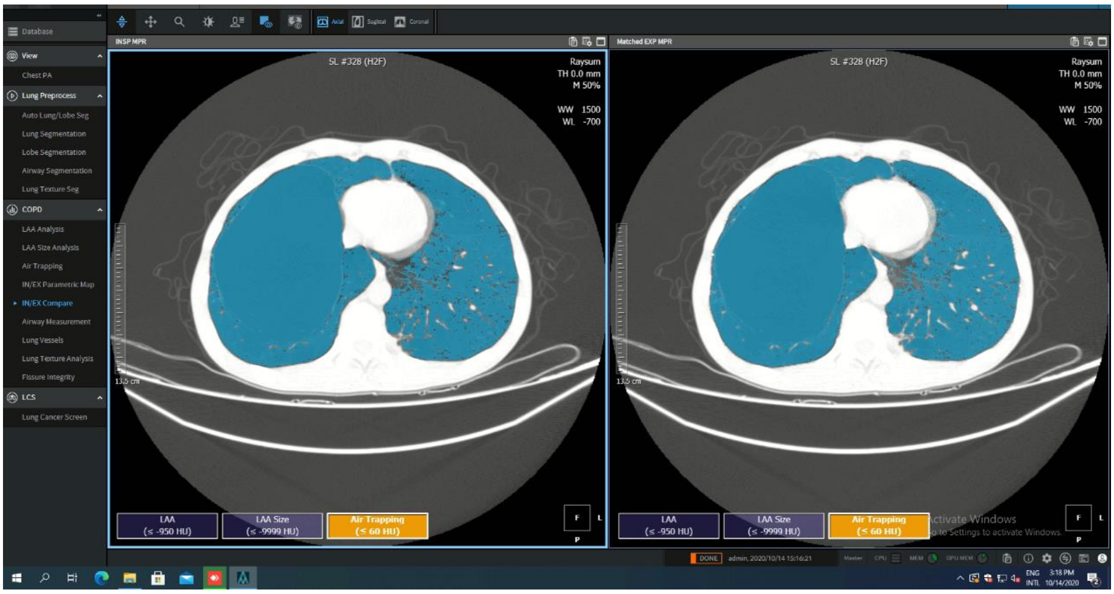

Figure.3 Air Trapping Index automation through voxel-by-voxel comparisons of attenuation changes between inspiration and expiration, with air trapping index defined as areas with less change in attenuation than the preset threshold (60 HU).

Spirometry and clinical parameters:

The American Thoracic Society (ATS) recommended a pulmonary function test to measure the patient's forced expiratory volume in one second (FEV1) and predicted percentage FEV1 (so referred to as FEV1%). [13].

The modified medical research council (mMRC) dyspnea scale was used to assess each patient's dyspnea , which is a five-point scale ranging from grade 0 – 4 [14].

Statistical analysis

SPSS version 22.0 (IBM, Armonk, New York, U.S) was used for all analyses. Significance was observed with p-value <0.05.

The Kolmogorov-Smirnov test and histogram analysis were used to examine the distributional pattern of the variables. The mean and standard deviation were used to express data having a normal distribution. The Pearson correlation coefficient for normally distributed variables was used to calculate the correlation between CT-based AI parameters, spirometry, and dyspnea. To distinguish between COPD severity classes, the receiver operator characteristic (ROC) curve was employed.

Results

The demographic information of the included population (n=80) showed that the mean age of the patients was 60. Only two (2%) females were present, making up nearly all of the population (97.5%). The patients were categorized as GOLD 1: mild (n=23), GOLD 2: moderate (n=39), GOLD 3: severe (n=17), and GOLD 4: very severe (n=1) based on the results of the spirometry. In comparison to the mild and moderate categories, the severe group's mean age was considerably higher (73.2 against 52.6 and 58.7 years, respectively, p0.0001). To characterize significant differences between radiological parameters in relation to the severity of COPD stages ANOVA test was used. Exp. LAA -856 (%) in GOLD groups 2& 1 were substantially lesser than in GOLD group 3. Additionally, when compared to group 3, ATI in the GOLD 1&2 groups were significantly lower.

Both Exp. LAA -856 (%) & ATI had a significant positive relationship with dyspnea score and negative relationship with FEV1% **(table 1)**

Table (1) Correlations between CT values and FEV1 & dysponea scale:

Variables	Correlation coefficient (r)	p-value
	FEV1	
Exp. LAA -856 (%)	-0.722	<0.0001**
ATI	-0.653	<0.0001**
	Dysponea scale	
Exp. LAA -856 (%)	0.662	<0.0001**
ATI	0.631	<0.0001**

**Significant p<0.05, **Highly significant p<0.01.*
***ATI** Air Trapping Index* ***Exp.LAA** Expiratory Low Attenuation Area*

A threshold of 13.3 was a significant cutoff with a sensitivity of 90.0% and a specificity of 78.3% (AUC=0.861, p0.0001) for the differentiation of moderate from mild COPD, according to the receiver operator characteristic (ROC) curve assessment of Exp. LAA -856 (%). To get the best values of Exp. LAA -856 (%), the threshold was 20.7 with a specificity of 90% but a sensitivity of 80% **(table 2)**.

Table (2) Discriminating thresholds and diagnostic performance off or distinguishing Exp. LAA 856 (%) moderate from mild COPD using forced expiratory volume in the first second (FEV1) spirometric parameter as a reference (gold) standard:

Coordinates of ROC curve	Threshold for achieving optimal sensitivity and specificity	Threshold for achieving near-90% sensitivity	Threshold for achieving near-90% specificity
AUC	0.861		
Standard error	0.049		
95%CI	0.765-0.957		
P-value	<0.0001**		
Cut-off	≥13.3	≥13.3	≥20.7
Sensitivity			
TP/(TP+FN)	90.0%	90.0%	80.0%
Specificity			
TN/(TN+FP)	78.3%	78.3%	82.5%

ROC curve=receiver operating characteristics curve, AUC=area under ROC curve, CI=confidence interval, TP=true positive, FN=false negative, TN=true negative, FP=false positive.

Receiver operator characteristic (ROC) analysis of the Exp. LAA -856 (%) dataset revealed that a threshold of 57.5 was a significant cutoff with a

sensitivity of 78.0% and specificity of 74.4% (AUC=0.744, p=0.003). This cutoff was used to distinguish between severe and mild COPD. To get the best values of Exp.LAA-856 **(table 3)**, the threshold was set at 65.0 when the specificity was set at close to 90% (with 56.0% sensitivity).
On the one hand, the (ROC) curve analysis of the ATI for identifying moderate and mild COPD indicated a sensitivity of 80% and a specificity of 70% (AUC=0.814, p0.0001). **(Table 4)** shows that, in contrast, the threshold was 19.3 when setting near 90% sensitivity (with 61% specificity) and 39.5 when setting near 90% specificity (with 62% sensitivity).

Table (3) Discriminating thresholds and diagnostic performance of Exp. LAA 856 (%) for distinguishing severe from moderate COPD using forced expiratory volume in the first second (FEV1) spirometric parameter as a reference (gold) standard:

Coordinates of ROC curve	Threshold for achieving optimal sensitivity and specificity	Threshold for achieving near-90% sensitivity	Threshold for achieving near-90% specificity
AUC	0.744		
Standard error	0.069		
95%CI	0.609-0.878		
P-value	0.003**		
Cut-off	≥57.5	≥43.7	≥65.0
Sensitivity			
TP/(TP+FN)	78.0%	89.0%	56.0%
Specificity			
TN/(TN+FP)	74.4%	41.0%	85.0%

ROC curve=receiver operating characteristics curve, AUC=area under ROC curve, CI=confidence interval, TP=true positive, FN=false negative, TN=true negative, FP=false positive

Table (4) Discriminating thresholds and diagnostic performance of ATI (≤60HU) (%) for distinguishing moderate from mild COPD using forced expiratory volume in the first second (FEV1) spirometric parameter as a reference (gold) standard:

Coordinates of ROC curve	Threshold for achieving optimal sensitivity and specificity	Threshold for achieving near-90% sensitivity	Threshold for achieving near-90% specificity
AUC	0.814		
Standard error	0.058		
95%CI	0.700-0.929		
P-value	<0.0001**		
Cut-off	≥27.95	≥19.3	≥39.5
Sensitivity			
TP/(TP+FN)	80.0%	85.0%	62.0%
Specificity			
TN/(TN+FP)	70.0%	61.0%	83.0%

ROC curve=receiver operating characteristics curve, AUC=area under ROC curve, CI=confidence interval, TP=true positive, FN=false negative, TN=true negative, FP=false positive.

The ROC curve of ATI, however, revealed that a threshold of 61.0 was a significant cutoff with a sensitivity of 78.0% and a specificity of 67.0% (AUC=0.748, p=0.003) for the differentiation of severe from mild COPD. (**Table 5)** shows that the threshold was 69.0 when setting near-90% specificity (with 61.1% sensitivity) and 56.0 when setting near-90% sensitivity (with 60.0% specificity).

Table (5) Discriminating thresholds and diagnostic performance of ATI (≤60HU) (%) for distinguishing severe from moderate COPD using forced expiratory volume in the first second (FEV1) spirometric parameter as a reference (gold) standard:

Coordinates of ROC curve	Threshold for achieving optimal sensitivity and specificity	Threshold for achieving near-90% sensitivity	Threshold for achieving near-90% specificity
AUC	0.748		
Standard error	0.064		
95%CI	0.623-0.873		
P-value	0.003**		
Cut-off	≥61.0	≥56.0	≥69.0
Sensitivity			
TP/(TP+FN)	78.0%	89.0%	61.1%
Specificity			
TN/(TN+FP)	67.0%	60.0%	82.1%

ROC curve=receiver operating characteristics curve, AUC=area under ROC curve, CI=confidence interval, TP=true positive, FN=false negative, TN=true negative, FP=false positive.

Discussion:

The severity of COPD and the structural alterations due to inflammation in the airways are both generally exacerbated by frequent smoking [15]. This discovery was reinforced by our finding that all patients (100%) in the severe group, 64.1% in the moderate group, and 21.7% in the mild group were heavy smokers (p0.0001). Of our COPD patients, just one (4.3%) did not smoke.

When airway obstruction causes lung lobules to remain inflated and exhibit a less-than-normal increase in attenuation during expiration, this condition is known as "air trapping," an indirect HRCT measurement of minor airway dysfunction that results in a mosaic pattern of attenuation. But to some extent, this phenomena is seen even in healthy, non-smoking people with no airway obstruction [16, 17].

We measured air trapping in our study, and it was quantified as the proportion of LAA 856 HU on expiratory CT, or "Exp LAA -856 (%)".

FEV1 and Exp. LAA -856 (%) had a negative correlation (r=-0.72, p0.0001).

Similar to this, Schroeder et.al discovered a significant (p0.0001) correlation between quantitative CT measures of LAA and spirometry (FEV1). With increasing disease severity (GOLD staging), there was a decrease in both the inspiratory and expiratory volume changes (p 0.0001) [18].

Numerous investigations have demonstrated a substantial correlation between spirometry abnormalities and quantitative CT evidence of expiratory air trapping. Like in our analysis, the majority of these investigations employed a threshold-based density mask approach with threshold values of 856 HU. Because the mean attenuation of a regularly inflated lung (6 mL air per gram of lung) is 856 HU on inspiration, this value was chosen as the threshold for air trapping on expiratory CT [19].

Therefore, the attenuation should be greater than 856 HU during expiration in a typical lung. The connection between expiratory CT and airflow limitaion in cigarette smokers with or without COPD has been examined in some studies [4, 20].

The findings of our study support the concept that the FEV1 measure offers a reliable independent measure of airflow obstruction because they show a substantial correlation between air trapping detected on expiratory CT and expiratory airflow obstruction assessed by FEV1.

Furthermore, premature airway closure and destabilization during expiration are linked to both loss of alveolar attachments and occlusion of the tiny conductive airways. As a result, it could be challenging to tell apart air trapping on CT scans, which can be seen in both conditions, from emphysema, which is typically not observed in asthma. To try and differentiate between these two illness situations, Matsuoka et.al have reported a quantitative technique. They removed voxels below -950 HU as a validated representative of emphysema areas on CT images in COPD patients exhibiting emphysema. Using a threshold determined at -860 HU, they demonstrated that the relative change in lung density between an inspiratory and an expiratory CT scan had a significant link with FEV1, FEF25%-75%, and RV/TLC. They came to the conclusion that their approach can help COPD patients distinguish between air trapping and emphysema [20].

As an indirect tool for assessing small airway disease, the Air trapping Index (INS-EXP registration) was also evaluated in our investigation.

By defining air trapping as regions with less attenuation change than the predetermined threshold (60 HU), the air trapping index permitted voxel-by-voxel comparisons of attenuation changes between inspiration and expiration [12].

In our research, we discovered a negative correlation between ATI (60HU) and FEV1 (p 0.01). Additionally, we discovered that the severe group had substantially higher ATI (60HU) (%) values than the mild and moderate groups (F=32.6; p0.0001).

The identical programme (Aview, Coreline Soft) that we used to develop the EATC (Emphysema air trapping composite) mapping was employed by Hwang et.al to produce the following results, three lung regions make up the lung parenchyma: Normal lung parenchyma, emphysema, and Functional air trapping (ATI's equivalent in our study) .

Hwang et.al found that with an increase in GOLD stage, fAT and Emph increased, while normal significantly decreased [21].

They discovered that fAT and Emph had substantial and moderate negative associations with measures of airflow limitation, forced expiratory volume in one second (FEV1) and forced vital capacity (FVC)/FEV1 ($r = -0.567$ and -0.659, respectively, all $p < 0.001$). fAT showed the highest correlation with mean forced expiratory flow between 25% and 75% of FVC (FEF25-75%), residual volume (RV), and RV/total lung capacity (TLC) ($r = -0.502$-0.491, $p < 0.001$), which are measures of pulmonary air trapping or small-airway dysfunction, while Emph showed the highest correlation with the carbon monoxide diffusing capacity corrected for hemoglobin concentration (DLCO) ($r = -0.516$, $p < 0.001$), which is a measure of parenchymal destruction [21].

To distinguish between three patient categories based on the gold stage, we added cut off values for ATI to our study:

A threshold of 27.95 was a significant cutoff for the discrimination of moderate from mild COPD in ATI, with a sensitivity of 80.0% and a specificity of 70.0% (AUC=0.814, p0.0001), and for the discrimination of moderate from mild COPD in ATI, with a threshold of 27.95 (AUC=0.814, p0.0001).

One of the benefits of our study is that it is homogeneous because only one CT scanner was used.

Our ability to establish cutoff values for quantitative CT parameters with excellent diagnostic accuracy, which can offer radiologists important information, is another noteworthy strength of our research. The reference standard spirometry parameter (FEV1), which provides valid results for the investigated variables, was used to determine the all-diagnostic values of the CT parameters.

Last but not least, we made an effort to remove confounding variables by removing instances with lesions that might be cancerous, which can impact overall lung density and skew our results.

The relatively small sample size (n=80) of patients, though with an adequate representative sample in each subgroup of COPD severity (mild=23, moderate=39, and severe=18), limits the generalizability of our study results to the COPD population.

It is necessary to standardize, optimize, and simplify the techniques used to measure the many aspects of COPD.

Quantitative CT also has a number of drawbacks. Different scanner models, reconstruction techniques, and CT protocol factors including voxel size, tube voltage, and tube current-exposure time product all have a substantial impact on the determination of CT attenuation of the lung. Additionally, differences in lung volumes during inspiration and expiration as well as acquisition methods affect CT attenuation values. The study's significant correlations, however, imply that the variation brought on by these technical aspects may be rather slight.

Conclusions:

The severity of COPD as determined by the dyspnea scale and spirometry was found to be substantially correlated with the Expiratory LAA -856% and ATI. That may aid in directing care plans and enhancing the course of COPD. Due to the structural assessment and quantitative data, it offers, early and accurate diagnoses are made possible.

List of Abbreviations.

AI Artificial Intelligence
ATI Air Trapping Index
AWT Airway Wall Thickness
CNN Convolutional Neural Networks
COPD Chronic Obstructive Pulmonary Disease
EATC Emphysema air trapping composite
Exp.LAA Expiratory Low Attenuation Area
fAT Functional Air Trapping
FEV1 Forced Expiratory Volume in first second
FVC Forced Vital Capacity
GOLD Global Initiative for Obstructive Lung Disease
HRCT High Resolution Computed Tomography
HU Housenfield Units
LAA Low Attenuation Area
LA Lumen area
PACS Picture archiving and communication system
Pi Internal Perimeter
TLC Total Lung Capacity
WA wall area

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