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Clinical evaluation of pulmonary quantitative computed tomography parameters for diagnosing eosinophilic chronic obstructive pulmonary disease: Characteristics and diagnostic performance

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Abstract

Aims: To investigate the characteristics and diagnostic performance of quantitative computed tomography (QCT) parameters in eosinophilic chronic obstructive pulmonary disease (COPD) patients.

Methods: High-resolution CT scans of COPD patients were retrospectively analyzed, and various emphysematous parenchyma measurements, including lung volume (LC), lung mean density (LMD), lung standard deviation (LSD), full-width half maximum (FWHM), and lung relative voxel number (LRVN) were performed. The QCT parameters were compared between eosinophilic and noneosinophilic COPD patients, using a definition of eosinophilic COPD as blood eosinophil values ≥ 300 cells·μL^{-1} on at least three times. Receiver operating characteristic curves and area under the curve (ROC-AUC) and python were used to evaluate discriminative efficacy of QCT.

Results: Noneosinophilic COPD patients had a significantly lower TLMD (−846.3 ± 47.9 Hounsfield Unit [HU]) and TFWHM(162.5 ± 30.6 HU) compared to eosinophilic COPD patients (−817.8 ± 54.4, 177.3 ± 33.1 HU, respectively) (p = 0.018, 0.03, respectively). Moreover, the total LC (TLC) and TLSD were significantly lower in eosinophilic COPD group (3234.4 ± 1145.8, 183.8 ± 33.9 HU, respectively) than the noneosinophilic COPD group (5600.2 ± 1248.4, 203.5 ± 20.4 HU, respectively) (p = 0.009, 0.002, respectively). The ROC-AUC values for TLC, TLMD, TLSD, and TFWHM were 0.91 (95% confidence interval [CI], 0.828–0.936), 0.66 (95% CI, 0.546–0.761), 0.64 (95% CI, 0.524–0.742), and 0.63 (95% CI, 0.511–0.731), respectively. When the TLC value was 4110 mL, the sensitivity was 90.7% (95% CI, 79.7–96.9), specificity was 77.8% (95% CI,

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57.7–91.4) and accuracy was 86.4%. Notably, TLC demonstrated the highest discriminative efficiency with an F1 Score of 0.79, diagnostic Odds Ratio of 34.3 and Matthews Correlation Coefficient of 0.69, surpassing TLMD (0.55, 3.66, 0.25), TLSD (0.56, 3.95, 0.26), and TFWHM (0.56, 4.16, 0.33).

Conclusion: Eosinophilic COPD patients exhibit lower levels of emphysema and a more uniform density distribution throughout the lungs compared to noneosinophilic COPD patients. Furthermore, TLC demonstrated the highest diagnostic efficiency and may serve as a valuable diagnostic marker for distinguishing between the two groups.

KEYWORDS

COPD, emphysema, eosinophilic, pulmonary function test, quantitative CT

1 | INTRODUCTION

Chronic obstructive pulmonary disease (COPD) is characterized by airway inflammation, lung parenchymal destruction,[1] remodeling of small airways, and irreversible airway obstruction.[1] The severity of COPD is classified into stages I-IV according to the Global Initiative for Chronic Obstructive Lung Disease (GOLD) criteria.[2] The 2019 GOLD report introduced blood eosinophil counting as a biomarker to guide the initiation or de-escalation of inhaled corticosteroids.[3] Previous studies have assessed various thresholds for eosinophilia, including a relative eosinophil count of 2% and absolute eosinophil counts of 150, 300, and 340 cells·μL^{-1}.[4] It has been observed that using a cut-off of 300 cells·μL^{-1}, approximately 20% of COPD patients exhibit an eosinophilic phenotype.[4] The roles of eosinophils in COPD development have been demonstrated in a limited number of animal and human studies.[5]

Traditionally, the diagnosis of COPD has relied on spirometric measurements of forced expiratory volume in 1 s (FEV1) and forced vital capacity (FVC).[6] However, recent studies have identified several limitations with this approach. Hardie et al.[7] demonstrated a risk of over-diagnosis of COPD among the elderly population. Cerveri et al.[8] highlighted an underestimation of airflow obstruction among young adults. The therapeutic decisions in COPD management have largely been based on spirometry.[6] However, the 2017 GOLD report acknowledged that spirometry alone does not adequately address the complex pathophysiology of the disease and is no longer sufficient for guiding treatment decisions.[6]

Chest computed tomography (CT) allows for the classification of COPD into different phenotypes, including emphysema predominant, airway predominant, or mixed types, based on morphological changes.[9] Compared to spirometry, chest CT provides additional information by detecting features such as emphysema, bronchial wall thickening, and air trapping in COPD,[10] which are associated with increased mortality.[11,12] Specifically, CT-diagnosed emphysema is strongly correlated with a more rapid decline in FEV1.[13] Furthermore, CT is crucial for differentiating pulmonary fibrosis from COPD.[13] Previous studies have primarily focused on examining the relationship between pulmonary function tests (PFT) and quantified chest CT measurements.[14,15] However, a detailed and systematic analysis of quantitative computed tomography (QCT) parameters in eosinophilic COPD patients has not been conducted. Therefore, the primary objective of this study is to employ SyngoPulmo3D software (Siemens Healthcare) to acquire the following QCT parameters for the entire lungs and each lung lobe (upper and lower lobes of the left lung [UL, LL], upper, middle, and lower lobes of the right lung [UR, MR, and LR]): lung volume (LC), lung mean density (LMD), lung standard deviation (LSD), full-width half maximum (FWHM), and lung relative voxel number (LRVN). The study aims to compare and analyze the differences in these QCT parameters between patients with eosinophilic and noneosinophilic COPD. The secondary objectives involve the construction of receiver operating characteristic (ROC) curves to assess the diagnostic efficiency of the QCT parameters, specifically TLC, TLMD, TLSD, and TFWHM, in distinguishing between eosinophilic and noneosinophilic COPD. Additionally, this study utilizes Python for comparative analysis of the discriminative efficacy of these QCT parameters.

2 | METHODS

2.1 | Patients characteristics

The sample size for this study was meticulously calculated to ensure the robustness of our statistical analysis. A predefined alpha level of 0.05 was selected, reflecting our commitment to maintaining the Type I error rate at a conventional level. Concurrently, a beta level of 0.1 was established, guaranteeing substantial statistical power, signifying our capacity to accurately detect true effects when present. The area under the ROC curve (AUC) was chosen as the primary indicator for estimating the required sample size. Previous research reported the prevalence of eosinophilic COPD within a range of 18.84%–66.88%, with an average prevalence of 54.95% across multiple studies.[16] To initially estimate the sample size, QCT

parameters were collected from 26 COPD patients, including 10 with eosinophilic COPD and 16 with noneosinophilic COPD. The calculated AUC values for TLC, TLMD, and TLSD were found to range from 0.71 to 0.91. The null hypothesis, set at a specific value of 0.05, was used for this calculation, resulting in a sample size estimate ranging from 18 to 58. Taking into account the exclusion criteria, a total of 91 COPD patients were initially screened. Ten patients were excluded from the original recruitment, resulting in a final cohort of 81 patients included in our study.

We employed a consecutive sampling method to screen a total of 91 COPD patients who underwent chest CT, PFT, and other examinations between June 2020 and October 2022. The interval between each assessment did not exceed 2 months. Written informed consent was obtained from all patients before any study-related procedures. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. The inclusion criteria for the COPD group were as follows: (1) According to the GOLD criteria, patients had a chronic cough lasting for at least 2 years and expectoration for at least 3 consecutive months per year. After inhaling bronchodilators, the FEV1 to FVC ratio was <0.70. (2) Patients were aged over 40. (3) COPD patients had no exacerbations requiring antibiotics or oral corticosteroids in the preceding 6 weeks. The exclusion criteria were as follows: a diagnosis of any other lung disease such as interstitial pneumonia, fibrosis, bronchiectasis, tuberculosis, or lung cancer. Finally, a total of 10 patients were excluded from the original recruitment, including two patients with interstitial pneumonia, five patients with bronchiectasis, one patient with fibrosis, and two patients with lung cancer.

2.2 | Eosinophilic COPD

Peripheral blood samples were collected from the patients via veins. Following previous studies that assessed the thresholds for eosinophilia,[4] a diagnosis of eosinophilic COPD was established when the peripheral blood eosinophil count was ≥300 cells/μL on at least three separate occasions.

2.3 | PFT

PFT was performed using the Jaeger MasterScope device in accordance with the guidelines set forth by the American Thoracic Society and Global Initiative for Asthma[17] The following parameters were measured: total lung volume (TLC), FVC, FEV1, FEV1/FVC ratio, and diffusing capacity of the lung for carbon monoxide corrected for hemoglobin (DLCOHb).

2.4 | CT scanning

Chest CT scans were conducted with the patients in the supine position, during full inspiration and breath-holds, using a third-generation dual-source CT system (Somatom FORCE, Siemens Healthineers). The scan parameters were set as follows: 120 kVp tube voltage, 96 mAs automated tube current, and a slice thickness of 5.0 mm. All images were reconstructed with a pulmonary window setting of −500 Hounsfield Units (HU) for the window level and 1300 HU for the window width. The reconstructed images had a slice thickness of 1.0 mm and were processed using the third-generation iterative reconstruction technique known as Adaptive Model-based Iterative Reconstruction (Siemens Healthineers).

2.5 | Pulmonary quantitative CT analysis

The SyngoPulmo3D software (Siemens Healthcare) was utilized to obtain the quantitative parameters. The lungs were automatically segmented and manually reviewed, if necessary, into five regions: UL, LL and UR, MR, and LR. The following quantitative parameters were measured: LC, FWHM, LSD, LRVN, and mean lung density (MLD). The MLD was reported in HU,[18] and a threshold of −950 HU was used to identify lung emphysema on the inspiratory CT scans.[18] The FWHM represents the width at the half maximum of the voxel count to a specific HU value curve, indicating the density distribution of the lung parenchyma.[18]

2.6 | Statistical analysis

Statistical analysis was performed using IBM SPSS Statistics software (version 24.0) and python (version 3.11.4). The Kolmogorov–Smirnov test was used to test the normality of distribution. Normally distributed continuous variables were expressed as mean ± SD, and nonnormally distributed parameters were presented as the median (interquartile range). Categorical data were presented as counts and percentages. continuous variables differences of PFT data and QCT parameters were compared between the two groups with the independent sample *t* test, while the chi-square test was used for categorical data. Furthermore, to evaluate the diagnostic accuracy of TLC, TLMD, TLSD, and TFWHM in distinguishing between eosinophilic and noneosinophilic COPD, ROC curves were constructed. The Area Under the Curve (AUC) was calculated as a measure of overall discriminative performance, with values closer to 1 indicating a higher diagnostic accuracy. In addition, python was used to calculate pretest probability such as the positive and negative likelihood ratios, the precision, F1 score, diagnostic Odds ratio, and Matthews correlation coefficient of TLC, TLMD, TLSD, and TFWHM. All statistical analyses were two-sided, and a $p < 0.05$ was considered statistically significant.

3 | RESULTS

3.1 | Baseline demographics and clinical characteristics

A total of 81 patients diagnosed with COPD were included in the study, with 27 (33.3%) meeting the criteria for eosinophilic COPD.

TABLE 1 Demographics and clinical characteristics of eosinophilic COPD and noneosinophilic COPD.

Patients, *n*	Eosinophilic COPD (27)	Noneosinophilic COPD (54)	*p* Value
Demographics			
Age (years)	71.5 ± 10.6	68.2 ± 9.3	0.161
Female *n*(%)	2 (7.4%)	9 (16.7%)	0.252
Clinical characteristics			
BMI (kg/m^2)	22.7 ± 3.9	22.3 ± 3.3	0.629
HR (min^{-1})	81.2 ± 13.7	87.1 ± 16.6	0.112
Hypertension *n*(%)	15 (55.6%)	18 (33.8%)	0.045
Diabetes mellitus *n*(%)	9 (33.3%)	12 (22.2%)	0.282
Current smoker *n*(%)	17 (63%)	31 (57.4%)	0.631
Laboratory findings			
WBC × 10^9 cells (L^{-1})	10.3 ± 2.7	12.4 ± 4	0.820
Eosinophils cells (μL^{-1})	609.6 ± 281.5	172.1 ± 81.5	<0.001
BNP (pg/mL)	1369.2 ± 3126.4	586.4 ± 1965.5	0.172
Long-term oxygen use *n*(%)	2 (7.4%)	3 (5.6%)	0.744
Inhaled corticosteroids use *n*(%)	14 (51.9%)	25 (46.3%)	0.637
Chronic oral steroids use *n*(%)	12 (44.4%)	23 (42.6%)	0.543
Heart failure *n*(%)	5 (18.5%)	13 (24.1%)	0.571
Exacerbation *N*(%)	12 (40.7%)	15 (55.6%)	0.597[a]

Abbreviations: BMI, body mass index; BNP, brain natriuretic peptide; COPD, chronic obstructive pulmonary disease; HR, heart rate beats; WBC, white blood cells.

[a]Data are presented as *n*(%), mean ± SD. Eosinophilic COPD was defined as having at least three separate absolute blood eosinophil counts ≥300 cells·μL^{-1}. Exacerbation: exacerbation history in the 12 months prior.

The average age of eosinophilic COPD patients (71.5 ± 10.6 years) was slightly higher than that of noneosinophilic COPD patients (68.2 ± 9.3 years), but the difference was not statistically significant ($p > 0.05$). Eosinophilic COPD patients had a significantly higher prevalence of hypertension compared to noneosinophilic COPD patients ($p = 0.045$). There were no significant differences between the two groups in terms of age, sex, ratio, body mass index, heart rate, and diabetes mellitus ($p > 0.05$) (Table 1).

3.2 | PFT data

The TLC%pred of eosinophilic COPD patients was significantly lower than that of noneosinophilic COPD patients (83.7 ± 7.5 vs. 107.7 ± 13.8, respectively; $p < 0.001$). In addition, the DLCOHb was significantly higher in the eosinophilic COPD group (36.7 ± 7.6) compared to the noneosinophilic COPD group (29.5 ± 7.1) ($p < 0.001$). The values of FEV1%pred, FVC%pred, and FEV1/FVC% were slightly higher in eosinophilic COPD patients compared to the controls, but the differences were not statistically significant ($p > 0.05$) (Table 2).

TABLE 2 Pulmonary function test data of eosinophilic COPD and noneosinophilic COPD.

Patients, *n*	Eosinophilic COPD (27)	Noneosinophilic COPD (54)	*p* Value
FEV1% pred	45.9 ± 14.8	41.5 ± 22.8	0.362
FVC % pred	65.1 ± 13.6	63.7 ± 16.9	0.735
FEV1/FVC %	53.1 ± 11.7	47.4 ± 15.8	0.102
TLC % pred	83.7 ± 7.5	107.7 ± 13.8	< 0.001
DLCOHb % pred	36.7 ± 7.6	29.5 ± 7.1	< 0.001
GOLD airflow limitation severity			
GOLD 1 (FEV1 ≥ 80% pred)	1 (1.2%)	0	0.155
GOLD 2 (50% ≤ FEV1 < 80% pred)	15 (18.5%)	23 (28.4%)	0.165
GOLD 3 (30% ≤ FEV1 < 50% pred)	10 (12.2%)	22 (27.2%)	0.748
GOLD 4 (FEV1 < 30% pred)	3 (3.7%)	6 (7.4%)	0.524

Abbreviations: COPD, chronic obstructive pulmonary disease; DLCOHb, diffusing capacity of the lung for carbon monoxide corrected for hemoglobin; FEV1, forced expiratory volume in 1s; FVC, forced vital capacity; GOLD, Global Initiative for Chronic Obstructive Lung Disease; TLC, total lung capacity.

3.3 | The pulmonary quantitative CT parameters

When analyzing the quantitative CT parameters of the entire lungs, significant statistical differences were observed in LC, LSD, LMD, and FWHM between the two groups. Specifically, compared to noneosinophilic patients (−846.3 ± 47.9 HU), eosinophilic patients had a higher LMD (−817.8 ± 54.4 HU)($p = 0.018$). The FWHM was significantly higher in the eosinophilic COPD group (177.3 ± 33.1 HU) compared to the noneosinophilic COPD group (162.5 ± 30.6 HU) ($p = 0.03$) (Figure 1). Moreover, the LC and LSD of the entire lungs were significantly lower in the eosinophilic COPD group (3234.4 ± 1145.8, 183.8 ± 33.9 HU, respectively) compared to the noneosinophilic COPD group (5600.2 ± 1248.4, 203.5 ± 20.4 HU, respectively) ($p = 0.009$, $p = 0.002$, respectively).

When examining the quantitative CT parameters of each lung lobe (UL, LL; UR, MR, and LR), inconsistent results were observed.

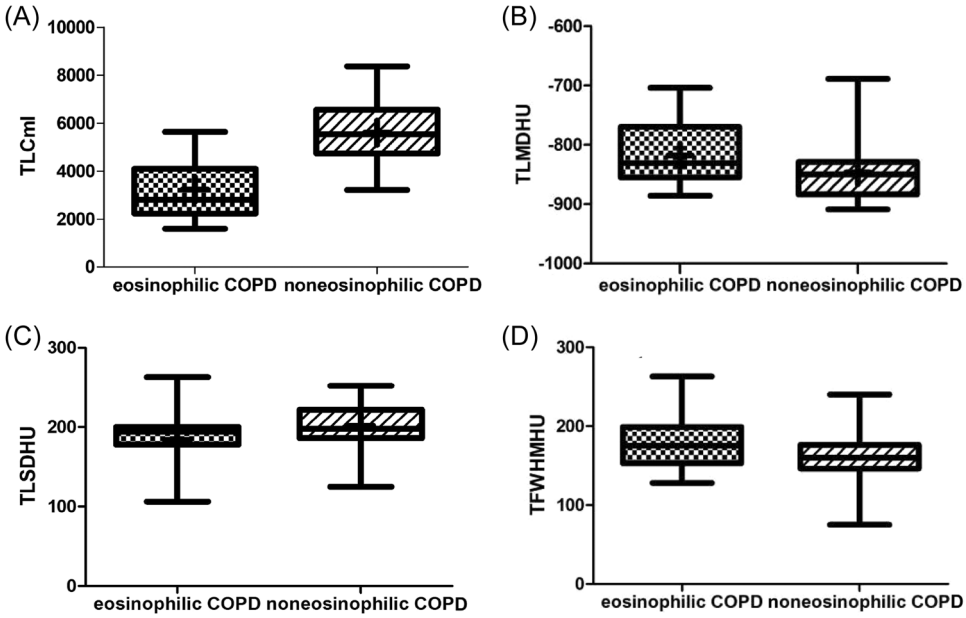

FIGURE 1 (Red) TLC, total lung volume ($p < 0.01$). (Green) TLMD, total lung mean density ($p < 0.05$). (Blue) TLSD, total lung standard deviation ($p < 0.01$). (Purple) TFWHM, total lung full-width half maximum ($p < 0.05$).

Specifically, the LC of each lung lobe (UL, LL; UR, MR, and LR) in the eosinophilic COPD group was significantly lower than the control group. LMD, LSD (UL, LL, UR, MR), and RVN (UL, LL) exhibited statistically significant differences between the two groups. However, there were no statistically significant differences observed in the parameters of LR-LMD, LR-LSD, UR-RVN, MR-RVN, and LR-RVN between the two groups ($p > 0.05$) (Table 3).

3.4 | The diagnostic efficiency of pulmonary quantitative CT parameters

The area under curve values the ROC for TLC, TLMD, TLSD, and TFWHM were 0.91 (95% confidence interval [CI], 0.828–0.936), 0.66 (95% CI, 0.546–0.761), 0.64 (95% CI, 0.524–0.742), and 0.63 (95% CI, 0.511–0.731), respectively (Figure 2). These four pulmonary quantitative parameters exhibited significant differences between eosinophilic COPD and noneosinophilic COPD. Among these parameters, TLC demonstrated the highest diagnostic efficiency with a sensitivity of 90.7% (95% CI, 79.7–96.9), specificity of 77.8% (95% CI, 57.7–91.4), and accuracy of 86.4% when the TLC value was 4110 mL, meanwhile, the sensitivity and specificity of TLMD, TLSD, and TFWHM were respectively 85.19% (95% CI, 66.6–95.8), 38.89% (95% CI, 25.9–53.1), 85.9% (95% CI, 66.3–95.8), 40.74% (95% CI, 27.6–55.0), and 59.26% (95% CI, 38.8–77.6), 74.07% (95% CI, 60.2–85.0).

3.5 | Diagnostic test comparisons

When comparing the diagnostic efficacy of TLC, TLMD, TLSD, and TFWHM, TLC demonstrated the highest efficiency. The F1 Score, indicative of a test's accuracy, was 0.79 for TLC, while it was 0.55 for TLMD, 0.56 for TLSD, and 0.56 for TFWHM. Additionally, the Diagnostic Odds Ratio, a measure combining sensitivity and specificity, was 34.3 for TLC, 3.66 for TLMD, 3.95 for TLSD, and 4.16 for TFWHM. The Matthews Correlation Coefficient, reflecting the quality of binary classifications, was 0.69 for TLC, 0.25 for TLMD, 0.26 for TLSD, and 0.33 for TFWHM. TLC exhibited the highest precision at 81% (95% CI, 0.71–0.91) compared to TLMD (41%, 95% CI, 0.31–0.51), TLSD (42%, 95% CI, 0.32–0.52), and TFWHM (53%, 95% CI, 0.43–0.64). Moreover, the positive and negative likelihood ratios for TLC were 8.40 and 0.24, respectively. For TLMD, these ratios were 1.39 and 0.38; for TLSD, 1.43 and 0.36; and for TFWHM, 2.28 and 0.55, respectively.

4 | DISCUSSION

Many studies have established eosinophilic COPD as a distinct phenotype,[4] and peripheral eosinophilia has been identified as a predictor of steroid responsiveness in COPD patients.[19,20] However, there is a paucity of research focusing on imaging biomarkers in eosinophilic COPD phenotype. In our study, we utilized modern imaging techniques and advanced postprocessing methods to comprehensively evaluate the QCT parameters of eosinophilic COPD patients. Our findings revealed that the prevalence of eosinophilic COPD, based on a threshold of eosinophils ≥300 cells·μL^{-1}, was 33.3%, which is consistent with previously reported rates.[16] This study contributes to filling the existing gap in the literature regarding imaging biomarkers in eosinophilic COPD phenotype.

Emphysema is a major pathological change observed in COPD, characterized by abnormal and permanent enlargement of distal

TABLE 3 Pulmonary QCT parameters of eosinophilic COPD and noneosinophilic COPD.

Patients *n*	Eosinophilic COPD (27)	Noneosinophilic COPD (54)	*p* Value
T-LC (mL)	3234.4 ± 1145.8	5600.2 ± 1248.4	0.009
UL-LC (mL)	866.7 ± 341.6	1437.4 ± 336.5	0.004
LL-LC (mL)	575.7 ± 234.3	1116.3 ± 396.3	0.001
UR-LC (mL)	807.5 ± 279.9	1330.8 ± 337.2	0.005
MR-LC (mL)	304.8 ± 129.9	523.8 ± 224.3	0.007
LR-LC (mL)	665.8 ± 289.9	1157.5 ± 332.1	0.002
T-LMD (HU)	−817.8 ± 54.4	−846.3 ± 47.9	0.018
UL-LMD (HU)	−825.9 ± 46.0	−860.1 ± 40.5	0.001
LL-LMD (HU)	−804.4 ± 72.6	−839.7 ± 60.2	0.023
UR-LMD (HU)	−829.4 ± 53.3	−857.5 ± 45.4	0.015
MR-LMD (HU)	−798.7 ± 172.4	−885.8 ± 235.2	0.033
T-LSD (HU)	183.8 ± 33.9	203.5 ± 20.4	0.002
UL-LSD (HU)	174.9 ± 42.8	190.7 ± 15.8	0.019
LL-LSD (HU)	181.6 ± 36.5	205.9 ± 26.5	0.001
UR-LSD (HU)	173.9 ± 31.7	191.7 ± 18.5	0.002
MR-LSD (HU)	176.0 ± 37.5	200.7 ± 29.5	0.002
T-FWHM (HU)	177.3 ± 33.1	162.5 ± 30.6	0.03
UL-FWHM (HU)	163.8 ± 24.7	150.9 ± 25.3	0.03
LL-FWHM (HU)	182.4 ± 33.2	164.2 ± 35.5	0.04
UR-FWHM (HU)	163.9 ± 28.5	149.7 ± 29.8	0.02
MR-FWHM (HU)	157.7 ± 32.4	134.6 ± 43.0	0.02
LR-FWHM (HU)	185.1 ± 46.8	162.1 ± 37.9	0.05
UL-RVN	0.47 ± 0.07	0.53 ± 0.14	0.04
LL-RVN	0.41 ± 0.10	0.47 ± 0.16	0.04

Abbreviations: COPD, chronic obstructive pulmonary disease; FWHM, full-width half maximum; LMD, lung mean density; LRVN, relative voxel number; LSD, lung standard deviation; QCT, quantitative computed tomography; TLC, total lung volume; TLMD, total lung mean density; TLSD, total lung standard deviation; UL,LL, upper, lower lobe of left lung; UR, MR,LR, upper, middle, lower lobe of right lung.

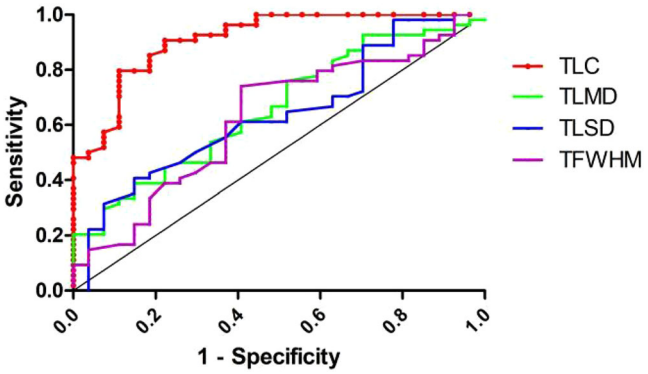

FIGURE 2 The receiver operating characteristic curves of these four parameters. (Red) TLC, total lung volume ($p < 0.01$). (Green) TLMD, total lung mean density ($p < 0.05$). (Blue) TLSD, total lung standard deviation ($p < 0.01$). (Purple) TFWHM, total lung full-width half maximum ($p < 0.05$).

airspaces.[21] Emphysema is associated with lower MLD on CT scans,[22] which aligns with histological evidence of emphysema. In our study, we observed that eosinophilic COPD patients exhibited lower LC and higher MLD compared to noneosinophilic COPD patients. There are several potential explanations for these findings. First, previous research has shown that COPD exacerbations are more frequent and severe in patients with blood eosinophil counts of <50 cells/μL. These exacerbations are often associated with infections and are linked to a higher risk of adverse outcomes, including increased airway wall and/or alveolar destruction, compared to patients with eosinophil counts above 150 cells/μL.[23] Second, eosinophilic exacerbations are typically characterized by rapid symptomatic recovery and fewer treatment failures compared to noneosinophilic exacerbations.[15,24,25] Finally, noneosinophilic COPD patients with more recurrent infective exacerbations may be prone to small-airway inflammation, airway remodeling,[15] increased resistance in small airways with an internal diameter of <2 mm, and enlargement of distal airspaces. LC and LMD serve as indicators of emphysema severity, which is associated with hyperinflation and structural damage. With increased LC, the mean lung density further decreases. Therefore, the observed differences in LC and LMD between eosinophilic and noneosinophilic COPD patients may be attributed to variations in exacerbation characteristics, disease progression, and the underlying pathophysiology of the two phenotypes.

The SyngoPulmo3D software enabled precise segmentation of the lung into five parts and calculation of pulmonary QCT parameters for the whole lung and each lobe. Our study revealed that eosinophilic COPD patients exhibited lower LSD and higher FWHM, which are closely associated with the density distribution of lung parenchyma[26] and functional parameters of emphysema (RV%TLC) and obstruction (FEV1%VC).[26] These findings suggest that the density distribution of lung parenchyma in eosinophilic COPD patients was more homogeneous than noneosinophilic COPD patients (Figure 3). This indicates mild destruction of distal airspaces and alveolar walls, resulting in less air trapping in the alveoli of eosinophilic COPD patients. These results further support previous studies that have shown a correlation between PFT and quantitative CT findings.[27] Furthermore, our study revealed that other COPD-related parameters, such as FEV1%pred, FVC%pred, and FEV1/FVC %, indicated better lung function in the eosinophilic COPD group compared to the noneosinophilic COPD group. This finding is consistent with previous studies that have demonstrated a positive association between high eosinophil counts and higher FEV1 values.[28] Finally, we compared the AUC values of TLC, TLMD, TLSD, and TFWHM, which reflect the accuracy of these parameters in distinguishing between eosinophilic COPD and noneosinophilic COPD. Among these parameters, TLC showed the highest diagnostic

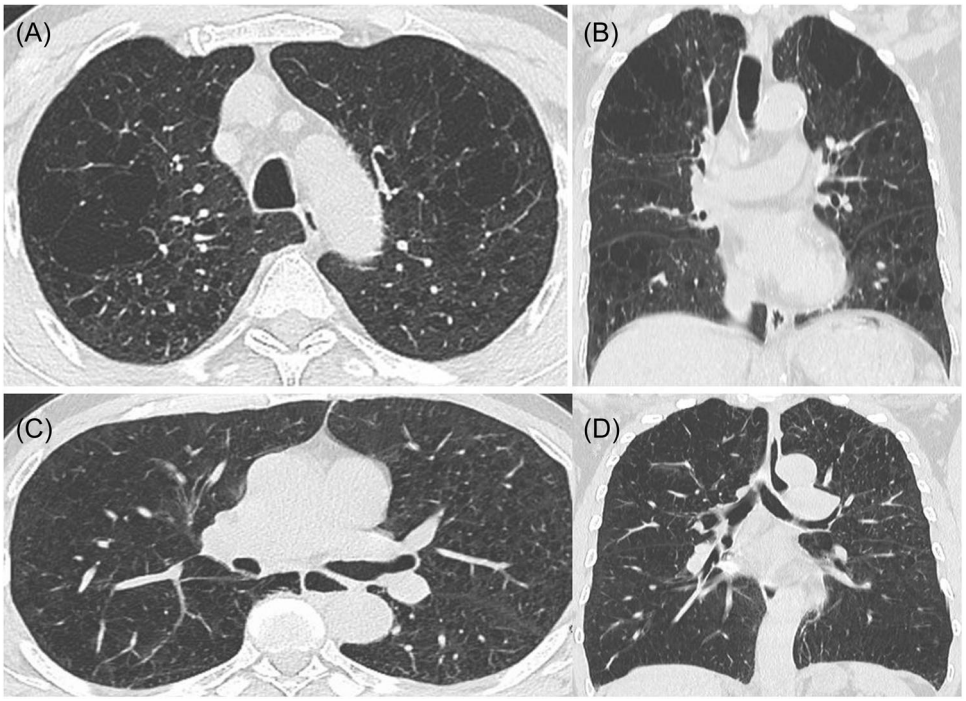

FIGURE 3 The axial and coronal computed tomography (CT) images. CT images of noneosinophilic chronic obstructive pulmonary disease (COPD) patient (A and B) demonstrates more severe emphysema and more uneven density distribution in the whole lung and each lobe compared to the eosinophilic COPD patient (C and D).

efficiency, with a sensitivity of 90.7% and a specificity of 77.8% when the TLC value was 4110 mL. Furthermore, we employed Python to calculate the pretest probability of TLC, TLMD, TLSD, and TFWHM. Our results demonstrated that TLC outperformed the other parameters in terms of discriminative efficacy. It yielded a higher F1 Score of 0.79, a more substantial Diagnostic Odds Ratio of 34.3, and a superior Matthews Correlation Coefficient of 0.69 when compared to the other three parameters. Additionally, TLC displayed the highest precision among all parameters. These findings emphasize the diagnostic potential of TLC in distinguishing between eosinophilic and noneosinophilic COPD cases, making it a promising candidate for clinical application. The high sensitivity, specificity, and precision of TLC contribute to its superior diagnostic performance and its potential to aid in the accurate identification and management of different COPD phenotypes. Further research and validation studies may reinforce the utility of TLC as a valuable diagnostic marker in clinical practice.

We conducted a comprehensive assessment of the differences between eosinophilic COPD and noneosinophilic COPD based on pulmonary QCT parameters. However, there were several limitations to this study. First, the retrospective study was carried out at only one center and the number of COPD patients in this study was relatively small. Second, we did not analyze expiratory lung CT in COPD, which could provide further quantification of air trapping extension. The decision was forced by the choice of scanning protocol and safety reasons. Finally, we were unable to analyze long-term follow-up outcomes such as hospitalization rates or mortality. Therefore, further studies involving a larger number of COPD patients with both inspiratory and expiratory lung CT scans are needed to address these limitations.

5 | CONCLUSIONS

QCT parameters, including LSD, FWHM, LC, LMD, and LRVN, provide objective results for assessing the distribution and severity of emphysema. In our study, the eosinophilic COPD group demonstrated a lower degree of emphysema and a more uniform density distribution in the whole lung and each lobe compared to the noneosinophilic COPD group. Among the QCT parameters evaluated, TLC demonstrated the highest diagnostic efficiency and may be considered as a valuable diagnostic marker for distinguishing between eosinophilic and noneosinophilic COPD. These results contribute to the understanding of the distinct phenotypes of COPD and highlight the potential utility of QCT parameters in the assessment and diagnosis of eosinophilic COPD.

AUTHOR CONTRIBUTIONS

Yumeng Liu: Conceptualization; data curation; writing—original draft. **Chao Lu**: Methodology; project administration; software. **Wenfang Chen**: Data curation; formal analysis; funding acquisition; project administration; validation. **Zhenyu Liu**: Data curation; formal analysis; resources; writing—review and editing. **Songxiong Wu**: Methodology; resources; software. **Hai Ye**: Conceptualization; data curation; formal

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The authors declare that the data are available.

ETHICS STATEMENT

The Review Board of Scientific Research of General Hospital of Shenzhen University provided approval for this work, and the approval number: KYLL-2022K-0106. Written informed consent were obtained from all patients before any study-related procedures. This study was performed according to the principles outlined in the Declaration of Helsinki.

TRANSPARENCY STATEMENT

The lead author Guangyao Wu affirms that this manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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