

Quantitative CT parameters correlate with lung function in chronic obstructive pulmonary disease: a systematic review and meta-analysis

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Abstract

Abstract purpose: The aim of the study was to analyze the correlation between quantitative computed tomography (CT) parameters and airflow obstruction in patients with chronic obstruction pulmonary disease (COPD). **Methods:** PubMed, Embase, Cochrane and Web of Knowledge were searched by two investigators from inception to 2018, using a combination of pertinent items to discover articles that investigated the relationship between CT measurements and lung function parameters in patients with COPD. Five reviewers independently evaluated the quality, extracted data and evaluated bias. The correlation coefficient was calculated and heterogeneity was explored. The following CT measurements were extracted: percentage of lung attenuation area < -950 Hounsfield Units (HU), mean lung density, percentage of airway wall area, air trapping index, airway wall thickness. Two airflow obstruction parameters were extracted: forced expiratory volume in the first second as a percentage of prediction (FEV₁ % pred) and FEV₁ divided by forced expiratory volume lung capacity. **Results:** A total of 117 studies (19,942 participants) were identified, 36 of which (4,762 participants) were suitable for meta-analysis. Results from our analysis demonstrated that there was a significant correlation between quantitative CT parameters and lung function. The absolute pooled correlation coefficients ranged from 0.44 (95% CI, 0.36 to 0.53) to 0.71 (95% CI, 0.65 to 0.77) for inspiratory CT and 0.59 (95% CI, 0.53 to 0.65) to 0.66 (95% CI, 0.61 to 0.72) for expiratory CT. **Conclusions:** Results from this analysis demonstrated that quantitative CT parameters are significantly correlated with lung function in patients with COPD. With recent advances in chest CT, we can evaluate morphological features in the lungs that cannot be obtained by other clinical indices, such as pulmonary function tests. Therefore, CT can provide a quantitative method to advance the development and testing of new interventions and therapies for patients with COPD. **Keywords:** Airway obstruction, Systematic review, Meta-analysis.

Background

Chronic obstructive pulmonary disease (COPD) is a common inflammatory lung disease characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities[1,2]. There is a high incidence of COPD worldwide and it is currently the fourth leading cause of death in the world. However, it is expected to become the third leading cause of death by 2020[3]. In addition, COPD has a long course and progressive development. The treatment effect of advanced COPD is poor and the disability rate is high, which seriously affects the quality of life. Therefore, accurate evaluations of the conditions of patients with COPD are necessary in order to select the correct treatment plans and improve the conditions of patients. Although the majority of patients followed a path of disease progression in which the severity of COPD tracked the severity of airflow limitation, the conventional method (such as pulmonary function tests, PFTs) fail to provide – information about regional pulmonary dysfunction[4]. Studies have shown that the use of the fixed forced expiratory volume in the first second/ forced vital capacity (FEV₁/FVC) ratio to define airflow limitation may result in more frequent diagnoses of COPD in the elderly, and less frequent diagnoses in adults < 45 years of age (especially in patients with mild COPD), as compared with the use of the low limit of normal (LLN) values for FEV₁/FVC[5,6]. However,

from a scientific or clinical perspective, it is difficult to determine if the criteria of LLN will result in optimal diagnostic accuracy for COPD. Additionally, studies have shown that FEV₁ is only weakly correlated with the severity of symptoms and health status of patients with COPD[7,8]. Further, the predictive value of FEV₁ for the risk of future acute exacerbation is very low. That is, it is controversial to use pulmonary function to diagnose and evaluate the severity of COPD. However, from the point of scientific research, an objective index should be developed to prevent missed diagnoses, excessive medical treatment, and underestimation of the disease.

With the rapid development of CT imaging technology, there has been a dramatic reduction in the radiation burden associated with CT in recent years, and a diagnostic improvement compared with classical chest X-ray[9]. Through objective quantitative evaluation of pulmonary emphysema and airways disease, CT may help achieve clinically meaningful phenotyping. Furthermore, quantitative CT is a new computational radiomics method that allows the extraction and processing of multiple features from imaging data in order to objectively and reproducibly characterize the main pathological changes during COPD[10]. Quantitative CT can help physicians to quantify and localize the relative volumes of emphysema and gas trapping in patients with COPD by using low attenuation areas[11]. In addition, the COPDGene® Study evaluating the accuracy of the GOLD stages in diagnosing airflow obstruction demonstrated that PFTs do not reflect the severity of quantitative CT parameters accurately[12]. Thus, accurate quantitative CT parameters of emphysema and airway wall changes could help characterize lung dysfunction in patients with COPD.

In recent years, many studies that have investigated the correlation between lung function and quantitative CT have been conducted, but there is still a lack of convincing multi-center studies[13-16]. Therefore, we conducted a systematic review and meta-analysis to analyze the correlation between quantitative computed tomography(CT) parameters and airflow obstruction in patients with chronic obstruction pulmonary disease (COPD).

Materials And Methods

The study was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement[17]. Since this meta-analysis only used data from published studies, no ethical approval was provided.

Data sources and searches

PubMed, Embase, Cochrane and Web of Knowledge were searched for articles published from their inception to December 2018, using a combination of pertinent items to discover articles that investigated the relationship between CT measurements and lung function parameters in patients with COPD. Language restrictions were not implemented. Meanwhile, manual retrieval was also carried out. Generally, the literature search was conducted using three keywords, such as 'chronic obstructive pulmonary disease', 'pulmonary function test', and 'CT'. Besides, the Boolean operator 'AND' was used in these three

sets of keywords, and 'OR' was used within each group. The detailed search process is shown in Supplementary Table 1. To obtain a comprehensive retrieval of the literature, we also scanned all the bibliographies of the relevant publications, as well as related comments. When the required data were ambiguous or missing, we contacted the authors.

Study selection

Each study was evaluated independently and systematically by five investigators with more than 6 years of thoracic radiology related working experiences. Articles were included in the systematic review if they met the following criteria: (1) all patients with stable COPD were ≥ 18 years old, human beings, without a history of dementia and have no changes in medication or acute exacerbation within the past 6 weeks; (2) interventions included participants who had clearly described PFT, according to the guidelines of the American Thoracic Society (ATS), the European Respiratory Society (ERS), or other similar methods; (3) the relationship between quantitative CT and PFT was analyzed; (4) and the methods of the study included randomized control trial (RCTs), observational (prospective and retrospective cohort) studies, and cross-sectional studies. In addition, the exclusion criteria were as follows: (1) case reports, letters, and conference abstracts; (2) studies with outcomes from only PFT or quantitative CT; (3) interventions included participants who were included in other studies within the past 6 weeks; (4) interventions included participants with other confounding diseases (such as interstitial lung disease, chronic bronchitis, α -1 anti-trypsin, asthma, lung cancer, other lung surgery, active pulmonary tuberculosis, ect.); (5) interventions included participants with diseases that affected adequate breathing (such as pericardial effusion, pleural effusion, and arterial oxygen saturation $< 90\%$ at rest).

Articles were included in the meta-analysis if (1) the study included a comparable proportion of GOLD 1-4 grades patients; (2) had a sample size ≥ 20 (20 subjects would provide a power of 0.90 when detecting a typical effect correlation coefficient (CC) of 0.60); (3) provided the percentage of lung attenuation area under -950 HU ($\%LAA \leq 950$), mean lung density (MLD), wall area percentage (WA%) in airways \geq fifth airway generation, air trapping index (ATI) (airway wall thickness (WT), and airway lumen area (AI) by volumetric multi-detector CT (MDCT); (4) CCs of lung function and quantitative CT; (5) and parameters of lung function included the predicted forced expiratory volume in the first second as percentage ($FEV_1\%pred$) and FEV_1 divided by the forced volume vital capacity (FEV_1/FVC). Articles were excluded in the meta-analysis if: (1) the relevant data were ambiguous or missing, and we could not contact the authors and; (2) the CT examination only provided selected pulmonary levels or the slice increment was larger than the thickness. If duplicate data was used, the study with the largest sample was included in the analysis.

Data extraction and quality assessment

Two reviewers independently screened articles for fulfillment of inclusion and exclusion criteria. Any disagreements or discrepancies were resolved through a consensus. Data tables were made to extract all relevant data from texts, tables, and figures of each study, including study characteristics, participant

characteristics, methodology, and CCs. %LAA-950, MLD, 15 percentile point of lung density (Perc 15), lung volume (LV), WA%, WT, AI, and ATI were recorded in the systematic review. Six CT measurements including %LAA-950, MLD, WA%, WT, AI, and ATI, were pooled in the meta-analysis, and two PFT parameters including FEV₁ %pred and FEV₁/FVC were extracted.

Furthermore, the Quality Assessment of Diagnostic Accuracy Studies (QUADAS) tool[18] was used for study methodological quality and potential bias. A study with a QUADAS score ≥ 11 points was deemed as high quality, while a study with a score ≤ 11 was considered to be of low quality.

Data synthesis and analysis

The overall measure was the correlation coefficient (CC) between CT and PFT parameters. The Hedges-
Vevea random effects model and normality Z-test were used to calculate the pooled 95% confidence intervals (95% CIs). We calculated the correlation between %LAA-950 and FEV₁%pred, %LAA-950 and FEV₁/FVC, %LAA-950 and FEV₁%pred, %LAA-950 and FEV₁/FVC, WA% and FEV₁%pred in inspiratory, MLD and FEV₁% pred, MLD and FEV₁/FVC, ATI and FEV₁/FVC, WT and FEV₁%pred, WT and FEV₁/FVC, AI and FEV₁%pred, AI and FEV₁/FVC, %LAA-950 and FEV₁%pred(GE), and %LAA-950 and FEV₁%pred (Siemens, Toshiba, and Philips). If evaluating multiple layers of bronchi, we chose the smallest bronchi. Heterogeneity was evaluated using the I² index. Additionally, we used a random effects model rather than a fixed effect model because the former was better equipped to explain the heterogeneity between the studies. Subgroup analyses were used to determine the impact of individual variables and the potential sources of heterogeneity. Also, the potential publication bias was assessed using the Begg's test.

In addition, we divided the radiation doses into 950HU and < 950HU (such as 910HU, 900HU) and divided breath-holding procedures into inspiratory and expiratory. We also divided CT machines into GE and Siemens, Toshiba, and Philips. All statistical analyses were performed using Stata 15.0 and SPSS 18.0. Further, sensitivity analyses were conducted to assess the impact of each study on the results of the pooled study by eliminating each study. Finally, analysis trimming and filling were carried out if necessary.

Results

Study selection

From the electronic databases (PubMed, Embase, Cochrane and Web of Knowledge), a total of 2208 studies were included (Supplementary Figure 1), and 1961 citations were excluded based on their titles or abstracts. After screening the text of 247 articles, 130 studies were excluded from the systematic review. The reasons for exclusion were that the studies did not include: a large enough COPD sample or there was not association between quantitative CT and PFTs. According to the exclusion criteria of the meta-analysis, 81 studies were excluded. The reasons for exclusion were as follows: (1) selection bias, (2) small sample size, (3) MDCT volume scans were not available, (4) quantitative CT parameters were not

included, and (5) PFT parameters were not included. Finally, 117 articles were used for systematic review and 36 articles were included in the meta-analysis.

Systematic review

The systematic review included a total of 19,942 participants. The age of patients range from 40-80, and there were 12,252 (61.4%) men, 5676 (28.5%) women, 2014 (10%) of the participants did not specify their gender (Supplementary Table 2). This study included RCTs and cohort studies. Of these, articles 51.6% (61 articles) were from Europe, 29.9% (35 articles) were from Asia, 14.5% (17 articles) were from North America, 3.4% (4 articles) from Oceania. Further, 106 (90.6 %) were written in English, 5 (4.2 %) in Italian, 4 (3.4 %) in Chinese, 1 (0.9 %) in French, and 1 (0.9 %) in Polish.

The sample sizes of the recent publications were significantly larger than before, and the CT equipment was more advanced (Supplementary Figure 2). Articles included a variety of breath-holding procedures, such as only inspiratory, expiratory, or both inspiratory and expiratory.

The selected articles included 75 quantitative CT parameters and 27 pulmonary function parameters (Supplementary Figure 4 and Figure 5), and the final parameters for the systemic review included %LAA-950, MLD, WA%, ATI, WT, AI, FEV₁%pred, and FEV₁/FVC. The common threshold defining the lung parenchyma in emphysema was -900 to -960HU, and the most commonly used threshold was -950 HU[19]. In some study, different thresholds in the same sample had different correlations with airflow obstruction parameters in PFTs[13,15,30,35]. The broad range of published CCs between CT and PFTs parameters were as follow: %LAA-950 and FEV₁%pred, -0.66 to -0.09[13,14]; %LAA-950 and FEV₁/FVC, -0.75 to -0.09[13,65]; %LAA-950 and FEV₁%pred, -0.63 to -0.28[14,55]; %LAA-950 and FEV₁/FVC, -0.66 to -0.54[14,30]; WA% and FEV₁%pred, -0.713 to -0.044[25,66]; MLD and FEV₁%pred, 0.18 to 0.85 [13,64]; MLD and FEV₁/FVC, 0.21 to 0.89[13,14]; ATI and FEV₁%pred, -0.725 to -0.29[36,43]; WT and FEV₁%pred, -0.68 to -0.13[28,30]; WT and FEV₁/FVC, -0.62 to -0.05[28,30]; AI and FEV₁%pred, 0.73 to 0.14[23,28]; AI and FEV₁/FVC, 0.32 to 0.07[28,41]; %LAA-950 and FEV₁%pred by GE, -0.67 to -0.43[21,56]; %LAA-950 and FEV₁%pred by non-GE (such as Siemens, Toshiba, and Philips), -0.67 to -0.43 [34,42](Supplementary Table 3).

Risk of bias in the meta-analysis

All articles included in the meta-analysis were high quality; QUADAS scores ranged from 12.5 to 13.5(Supplementary Table 4 and Supplementary Figure 6). Generally, the risk of bias was assessed by reviewers using a recognized bias tool. QUADAS 2 where CT density was being considered as a diagnostic tool. Funnel plots and Begg-Mazumdar/Egger tests were selected to assess publication bias and reduce bias by excluding date or language limits during our search. No publication bias was found (Supplementary Table 5).

Several of the meta-analyses showed slight heterogeneity. The I^2 index was > 50 % for correlations between WA% and FEV₁ %pred in inspiration (P = 0.017, I^2 index = 61.1%), WT and FEV₁/FVC in inspiration (P = 0.000, I^2 index = 96.1%), AI and FEV₁ %pred in inspiration (P = 0.000, I^2 index = 90.7%), and AI and FEV₁/FVC in inspiration (P = 0.031, I^2 index = 71.1%). Because heterogeneity was high, a sensitivity analysis were conducted to explore the sources of the heterogeneity. Finally, we found that Washko's[28] study was the main source of heterogeneity mainly because subjects with GOLD 3 and 4 diseases were pooled into one group (GOLD 3&4) due to limited numbers of subjects with GOLD stage 4 disease which may cause selection bias.

Synthesis of results in the meta-analysis

A total of 4762 participants were included in the meta-analysis (Supplementary Figure 3). The CC between %LAA-950 and FEV₁%pred in inspiration was reported in 24 articles [14,21-23,25-27,29-32,34,36,40-42,46,48-50,53-56]. Two [22,28] National Lung Screening Test (NLST) cohorts and three [25,26,47] Korean Obstruction Lung Disease (KOLD) cohorts were performed. The pooled CC between %LAA-950 and FEV₁%pred was -0.51 (-0.56, -0.47), -0.59 (-0.65, -0.53) in inspiration and expiration, respectively. The pooled CC between %LAA-950 and FEV₁/FVC was -0.64 (-0.68, -0.59), -0.66 (-0.72, -0.61) in inspiration and expiration, respectively.

Ten articles [21,23-25,28,31,42,51,53,58] reported CCs between WA% and FEV₁%pred in inspiration. Two articles [21,25] were excluded because airway measurements only involved airway above the fifth generation. Another article 33 was excluded because it did not report which airway were measured, making data extraction difficult. Therefore, a total of 7 articles were included [23,24,31,42,51,53,58]. In the included literature, the average lumen diameter of the peripheral airway was about 2 - 3 mm. The pooled CC value between WA% and FEV₁%pred was -0.46 (95% CI: -0.55, -0.38) in inspiration. Expiratory CT was not used for airway measurements.

No duplicate reports were found when extracting data related to MLD. The CC between MLD and FEV₁%pred was reported in five articles [25,30,31,43,63]. Two [43,63] KOLD cohorts were excluded because the article quality scores were not high and the post-CT processing method was different than that used in the other studies. Three articles [25,30,31] were included. The pooled CC between MLD and FEV₁%pred was 0.44 (95% CI: 0.36, 0.53) and MLD and FEV₁/FVC was 0.54 (95% CI: 0.39, 0.68) in inspiration.

Only three studies [36,43,47] were analyzed according to strict criteria for inclusion. From these studies, we determined that the pooled CC between ATI and FEV₁/FVC was -0.71 (95% CI: -0.77, -0.65) in inspiration. This study did not analyze ATI and FEV₁%pred because few articles included this information.

Three articles [28,33,52] reported CCs between WT and FEV₁%pred in inspiration. The pooled CC between WT and FEV₁%pred was -0.15 (95% CI: -0.25, -0.05) in inspiration, and the pooled CC of WT and FEV₁/FVC

was -0.33 (95% CI: -0.69, 0.02) in inspiration.

Five articles [24,28,31,52,58] reported CCs between AI and FEV₁%pred in inspiration. However, AI and FEV₁/FVC only had three groups of data, and the heterogeneity of this data was relatively large, it was necessary to study further. The pooled CC between AI and FEV₁%pred was 0.40 (95% CI: 0.20, 0.59) in inspiration, and the pooled CC of AI and FEV₁/FVC was 0.21 (95% CI: 0.07, 0.35) in inspiration.

Eight articles [21,23-25,28,31,42,51,53,58] reported CCs between LAA-950 and FEV₁%pred using GE in inspiration. Five articles [26,34,42,46,50] reported CCs between LAA-950 and FEV₁%pred using other brands of CT machines (such as Siemens, Toshiba, and Philips) in inspiration. The pooled CC between LAA-950 and FEV₁%pred using GE was -0.50 (95% CI: -0.56, -0.45) and -0.59 (95% CI: -0.65, -0.53) between LAA-950 and FEV₁%pred using other brands of CT machines.

Subgroup analysis

We performed a subgroup analysis, depending on the radiation dose. At ≥950 doses (such as ≥910HU, ≥900HU), the pooled CC was -0.48 (95% CI: -0.56, -0.39). At doses of <950HU, the pooled CC was -0.51 (95% CI: -0.56, -0.47). There was no significant difference between %LAA-950 and FEV₁%pred (P > 0.05). Subgroup analysis was performed for inspiratory and expiratory CT. Compared with inspiratory CT, expiratory CT %LAA-950 showed a stronger negative correlation with FEV₁%pred (P < 0.05), MLD and FEV₁%pred showed a stronger positive correlation (P < 0.001), but there were no significant correlations between %LAA-950 and FEV₁/FVC, or MLD and FEV₁/FVC (P > 0.05). Subgroup analyses were also performed based on the brands of CT machines. The pooled CC was -0.50 (95% CI: -0.56, -0.45) in the first group (GE) and -0.59 (95% CI: -0.65, -0.53) in the second group (Siemens, Toshiba, and Philips). That is, there was no significant difference between %LAA-950 and FEV₁%pred according to CT machine (P > 0.05) (Supplementary table 5 and 6).

Discussion

In the current study, we conducted a systematical review and meta-analysis to determine the relationship between quantitative CT parameters and airflow obstruction in patients with COPD. The result of this meta-analysis suggested that there were correlations between CT measurements of emphysema or peripheral airway and airflow obstruction parameters in PFTs in patients with COPD, both in inspiratory and expiratory CT. In the included studies, the absolute CCs of CT measurements and airflow limitation were as follows: inspiratory CT, 0.44 to 0.71 and expiratory CT, 0.59 to 0.66. These results were consistent with other studies that have revealed that expiratory CT can be used as an auxiliary examination for inspiratory CT. This reconfirmed our hypothesis that there was a significant correlation between the proportion of emphysema, MLD, AI, ATI, WT, and lung function in patients with COPD. Therefore, this approach generates reproducible and sensitive measurements of COPD that are related to pulmonary

ventilation and perfusion as well as the anatomical and morphological features of the airway wall and parenchyma.

Pulmonary function is the main objective test for determining airflow limitation. FEV₁/FVC can detect mild airflow obstruction, which is beneficial for early detection and treatment of patients with COPD. However, lung function does not provide information on regional dysfunction. With the widespread use of quantitative CT and the continuous improvement of corresponding software, lung structure and function abnormalities can be regionally identified and measured. %LAA-950 and MLD can reflect the extent of damage to the lung parenchyma. Meanwhile, it can be used to measure the thickness of the bronchial wall to assess the degree of airflow obstruction. Thus, quantitative CT is a comparatively superior method for identifying morphological information regarding the degree of airway stenosis and the proportion of emphysema, which are complementary to lung function.

This systematic review included ≥ 10 different CT measurements. However, because of the insufficient number of studies, only 6 items (%LAA-950, %LAA-950 MLD, WA%, AI, ATI, and WT) were used in the meta-analysis. We also evaluated FEV₁/FVC and FEV₁%pred from PFTs because these are important factors associated with the diagnosis of COPD and the classification of airflow limitation. Furthermore, the above two parameters were relatively comprehensive and easy to extract.

We performed a subgroup analysis based on different respiratory processes (including inspiratory and expiratory processes). Our results demonstrated that CT measurements in expiratory were more strongly correlated with FEV₁%pred than inspiratory, but less correlated with FEV₁/FVC in expiratory than in inspiratory [13,14,29]. This was consistent with other findings have suggested that CT measurements in expiratory are more strongly correlated with airflow limitation than in inspiratory [59-61]. However, the significance of expiratory CT data for the assessment of COPD still requires additional data for further study. Further, we also performed a subgroup analysis according to the brand of CT machines, and the results indicated that %LAA-950 was correlated with lung function regardless of the brand of CT machine, which was consistent with previous studies by imaging experts [19]. Meanwhile, studies have shown that low radiation doses (which provides protection for patients) do not alter the correlation between CT emphysema quantification and airflow limitation compared to normal doses. While the prolonged examination time also reminded us to perform adequate breathing training for patients before CT examination.

Some researchers have studied the third to fifth or sixth generation airways and found that the correlation between airway wall measurements and PFTs was stronger in the smallest airways [19,23,31]. In order to reduce the deviation caused by different airway generations, we unified ≥ 5 th generation airways and included them in the meta-analysis. From our results, the correlation between WA% and FEV₁%pred was -0.47. Based on the above results, the airway WT measurement from CT was more reliable in the smallest airway.

Although some previous meta-analyses [15,16,20,59] have evaluated the relationship between quantitative CT and lung function in patients with COPD, the current meta-analyses reconfirmed these findings and had multiple advantages. First of all, this meta-analysis had a large sample size, which made our results more reliable. Second, all included studies had more quantitative CT parameters, such as WT and AI. Subgroup analyses were also performed according to the radiation dose (%LAA-950HU, 910HU, and 900HU) and the brands of CT machines. These comparisons have often been overlooked in previous studies and we found that there are many brands of CT machines (such as GE, Siemens, Toshiba and Philips). Therefore, it is necessary to conduct subgroup analyses to determine if brands of CT machines impact the results. Third, the results of most studies were highly consistent. After sensitivity analysis and publication bias analysis, the source of heterogeneity has been found, which provides ideas for future experimental designs. Fourth, our results enriched and validated the previous conclusions.

Meanwhile, this meta-analysis inevitably had some limitations. First, the results of this study may be influenced by the age, race, and the male-female ratio. Additionally, the severity of the disease varied among participants in the included studies. Second, some of the research data were obviously wrong or lost, therefore we did not extract them, and this led to a further reduction in sample size. Third, a variety of quantitative CT parameters and PFTs parameters were extracted for systematic evaluation but only representative parameters with complete data were selected for the meta-analysis. Measurements that were not included may be valuable for the evaluation of COPD, and these measurements require further research. Above all, the interval time between lung function and quantitative CT was inconsistent, and this may have impacted the measurements of quantitative CT parameters. In addition, we used different brands of CT machines, post-processing software, work stations that we did not examine in more details because their impact was considered less relevant [19]. This study also conducted a subgroup analysis according to the brands of CT machines, and the results showed that quantitative CT parameters were correlated with lung function regardless of the brands of CT machines. Thus, this systematic review was based on studies of high methodological quality, and there was no publication bias, therefore the results have a certain strength of argumentation.

Conclusions

Results from this study provided evidence that quantitative CT parameters are significantly correlated with lung function in patients with COPD. These results also showed the proportion of emphysema and air trapping in expiratory. CT parameters were used as a complementary diagnostic tool for PFTs. Quantitative CT may provide a morphological approach for accurate and early diagnosis of COPD and testing new interventions and therapies for patients with COPD.

Abbreviations

%LAA \leq 950: Percentage of lung attenuation area under -950 HU; AI: Airway lumen area; ATI: Air trapping index; ATS: American Thoracic Society; CC: Correlation coefficient; CI: Confidence interval; COPD: Chronic obstructive pulmonary disease; CT: Computed tomography; ERS: European Respiratory Society;

FEV₁%pred: Forced expiratory volume in the first second as percentage from predicted; FEV₁/FVC: FEV₁ divided by the forced volume vital capacity; GOLD: Global initiative for chronic Obstructive Lung Disease; HU: Hounsfield unit; LV: Lung volume; MLD: Mean lung density; PFT: Pulmonary function test; PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-analyses; QUADAS: Quality Assessment of Diagnostic Accuracy Studies; WA%: Wall area percentage; WT: Airway wall thickness.

Declarations

Ethics approval and consent to participate

Not applicable. There is no ethical approval, because we only use published studies data for Meta-analysis.

Consent for publication

Not applicable, because we only use published studies data for Meta-analysis.

Availability of data and material

Not applicable. There is no relevant raw data, because we only use published studies data for Meta-analysis. For the data we extracted, please refer to the supplementary table 2 and table 3.

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Competing interests

The authors declare that they have no competing interests.

Authors' contribution

Yan Wang, Shan Lin and Wei Guan conceived and designed the paper. Yan Wang, Shan Lin were responsible for all data gathering, extraction, and analysis. Dong Han was the primary independent reviewer, with bias and quality of data extraction reviewed by Shan Lin, Wei Guan and Jing Wu. All authors contributed toward data analysis, drafting and revising this paper and agree to be accountable for all aspects of the work.

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Figures

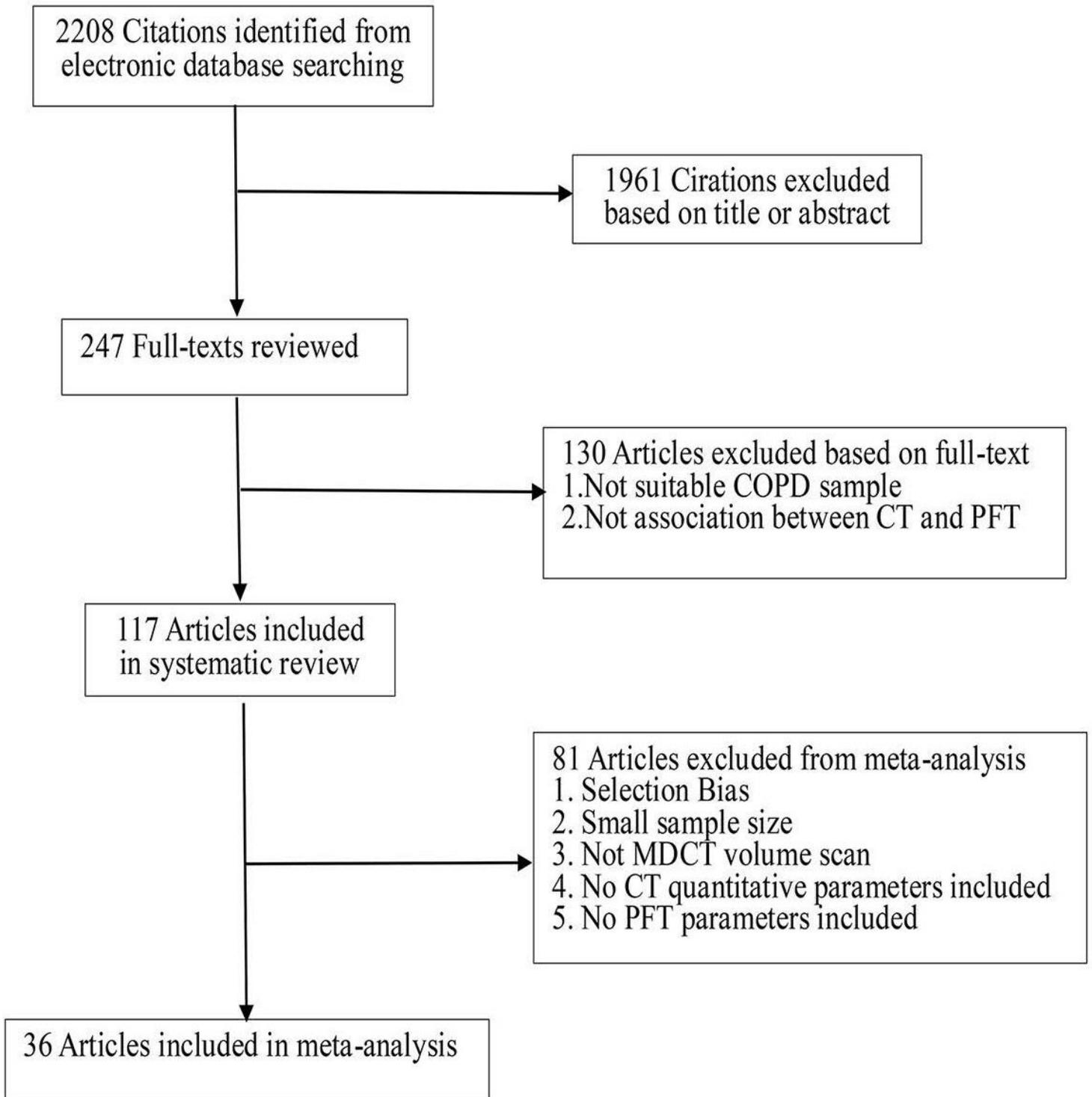


Figure 1

Flowchart of literature review and selection. COPD =Chronic obstructive pulmonary disease; PFT =Pulmonary function test; MDCT = Multi-detector computed tomography.

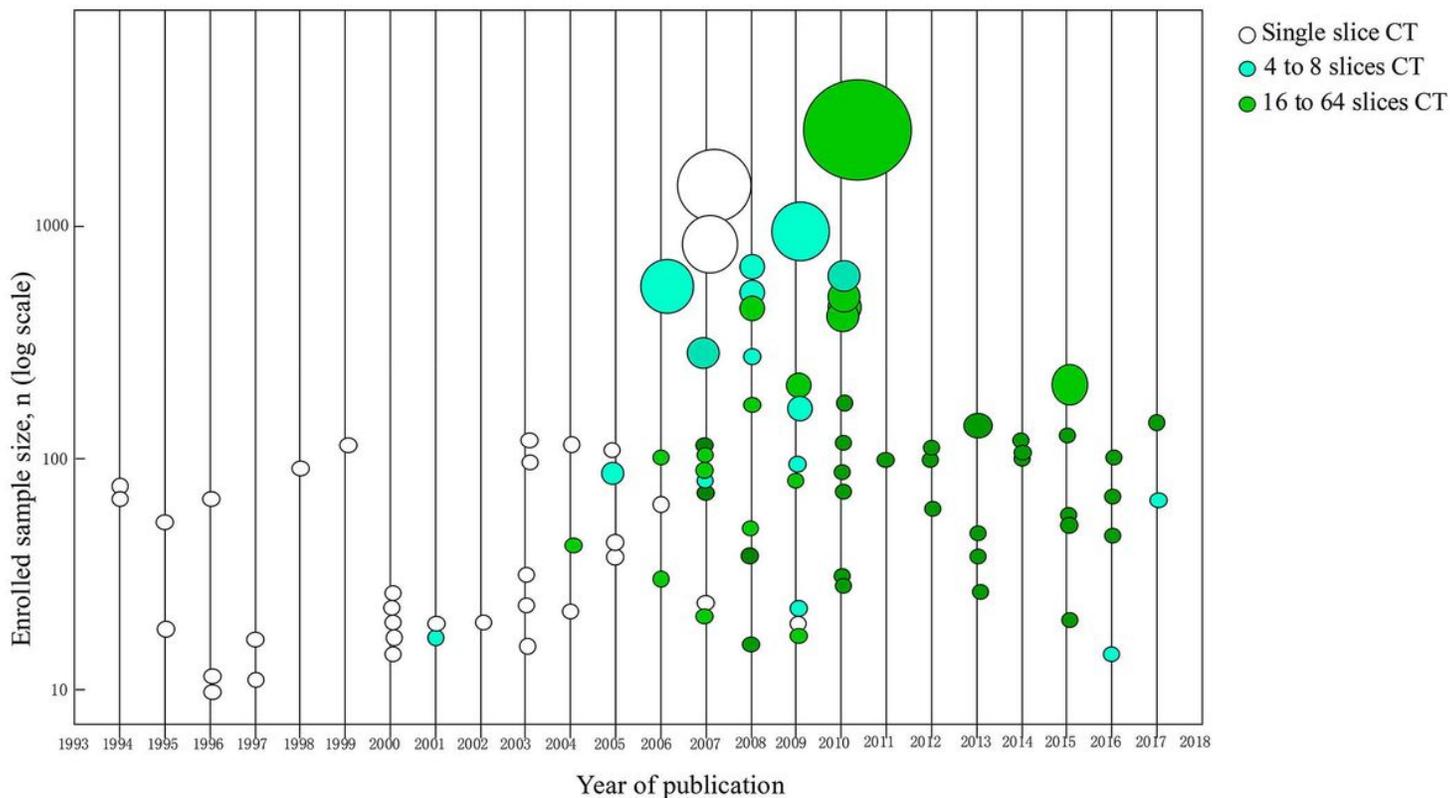


Figure 2

Sample size of the articles included in the systematic review by year of publication and MDCT. MDCT = Multi-detector computed tomography

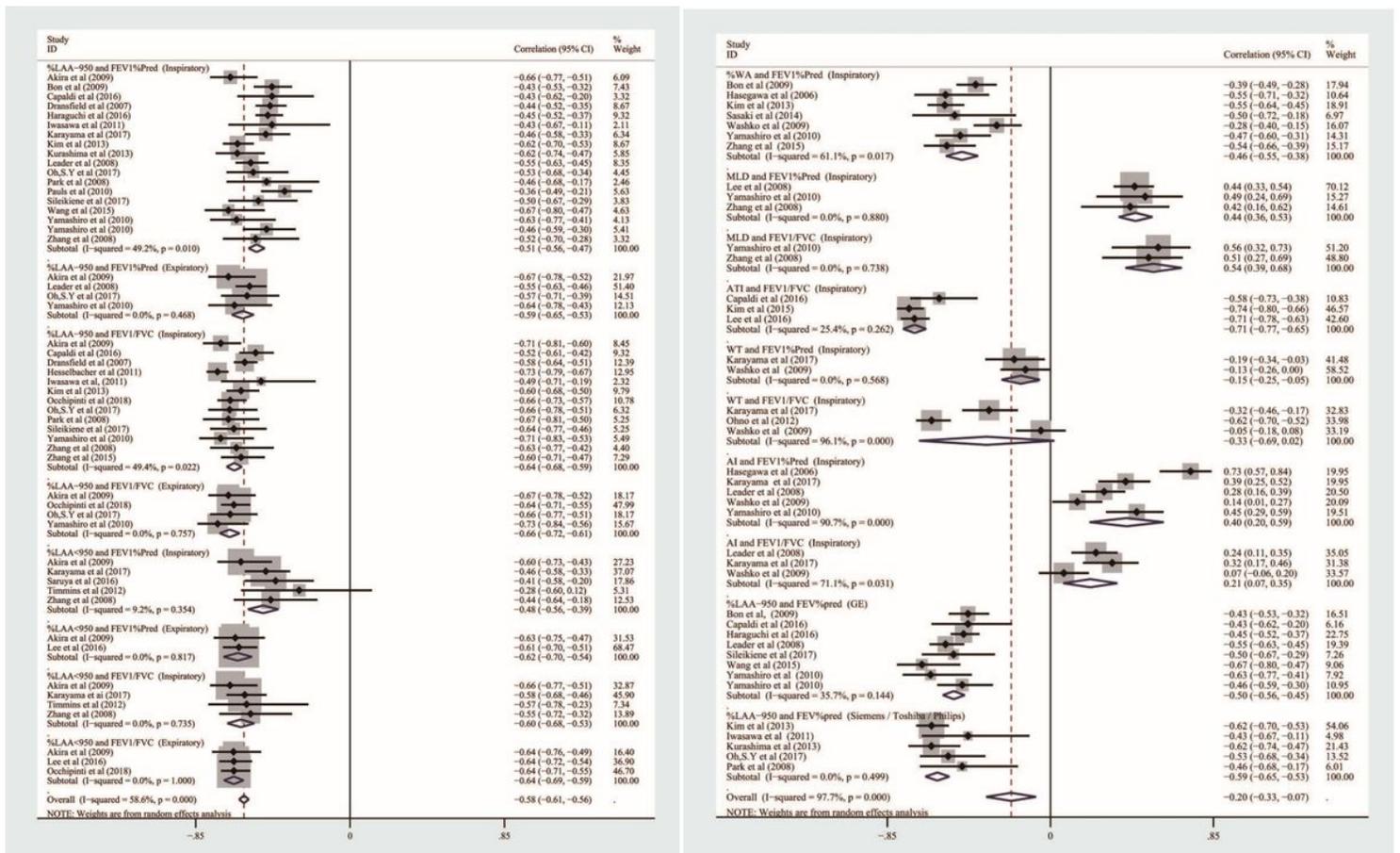


Figure 3

Forest plots for correlations between CT measurements and airflow obstruction. CCI = Confidence interval; P(Z) = P value of Z test; FEV1 %pred = percentage of the predicted forced expiratory volume in the first second; FEV1/FVC = FEV1 divided by forced vital capacity; %LAA-950 = percentage lower attenuation area than -950 HU; MLD = mean lung density; Perc15 = 15 percentile point of lung density; WA% = wall area percentage

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