The Application Of Radiology In Assessing And Managing Pulmonary Diseases

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Abstract

With a variety of clinical and pathologic characteristics, chronic obstructive pulmonary disease (COPD) is a complicated, diverse disorder. Quantitative CT imaging has garnered significant attention in recent years due to its ability to offer a more accurate and unbiased evaluation of COPD. Quantitative imaging characteristics may be used to quantify emphysema, small-airway disease, and additional illnesses such as pulmonary artery changes, cardiovascular disease, cachexia, as well as osteoporosis, which are the main components of COPD. A growing body of research suggests that these metrics are linked to clinical indicators of illness extent, breathing-related symptoms, exacerbations of COPD, and death. Although the findings are promising, there are still several challenges when employing this quantitative method in routine clinical practice for the management of COPD patients. This article provides an overview of the present technological state of quantitative CT evaluation, with a focus on its health effects and limits. In addition, we explore current obstacles and the prospective future use of quantitative CT scans in evaluating COPD.

Keywords: Chronic Obstructive Lung Disease (COPD), Emphysema, Quantitative Evaluation, CT scans, Airway Remodeling.

Introduction

Chronic obstructive pulmonary disease (COPD) is a prevalent condition that may be prevented and treated. It is characterized by a persistent restriction of airflow, which often worsens over time. This condition is linked to increased chronic inflammation in the airways and lungs (1). Chronic Obstructive Pulmonary Disease (COPD) is a significant contributor to illness and death in the general population. According to the World Health Organization (WHO), it is projected to become the third most common cause of death globally. It is a diverse and intricate disorder, exhibiting a broad range of clinical and pathologic features. While pulmonary function test (PFT) measurements are routinely used for the diagnosis and categorization of COPD severity, they are unable to adequately include the many pathophysiologic abnormalities that exist in COPD. In addition, the Pulmonary Function Test (PFT) is often not very sensitive to detecting early stages and subtle changes in Chronic Obstructive Pulmonary Disease (COPD), prior to observable alterations in functional parameters (2,3). In addition, individuals who have identical pulmonary function test (PFT) scores may have entirely distinct clinical and radiological characteristics.

In the era of precision medicine, a more detailed comprehension of how clinical diseases present and their connection with the internal development of diseases will have important consequences for disease treatment and our knowledge of the disease process. The most often used imaging technique for examining the chest is CT scan, which is less invasive and offers valuable insights into the structural and underlying pathophysiological alterations in patients with COPD. CT scans enable the direct examination of the physical features and spatial distribution of emphysema and small airway disease, which are the primary components of COPD, inside a living organism. Nevertheless, the conventional approach of qualitative visual CT evaluation, which has been widely used to extract information from CT scans, is susceptible to inconsistencies across different readers and sometimes even within the same reader. This hampers its use in many clinical and experimental contexts (4). Consequently, there has been a substantial increase in the need for more unbiased CT-based measurements in the last ten years.

The recent advancements in quantitative CT imaging technologies have generated significant attention in this context. These approaches have the capability to provide more accurate and consistent assessments of the severity and distribution of emphysema and airway illness (5). In the first stages, the focus of research on the measurement of CT in COPD was mostly on quantifying emphysema. Recently, there has been a rise in papers focusing on the airway aspect of COPD. These articles may be categorized into two groups: direct measurements of airway parameters and quantification of air trapping, which is the functional expression of small airway illness. This review provides a concise overview of past research on the measurement of Chronic Obstructive Pulmonary Disease (COPD), emphasizes the present principles, and explores the future trajectory of quantified CT imaging.

Measurement of Emphysema

Pulmonary emphysema is a significant characteristic of chronic obstructive pulmonary disease (COPD), characterized by abnormal and permanent enlargement of air gaps and damage to the walls of the airways beyond the terminal bronchioles. Emphysema is characterized by a higher amount of air in the lungs compared to normal lung tissue, resulting in an area with reduced CT attenuation, indicated by lower Hounsfield units (HU). The density mask approach, first published in 1988, measures emphysema by computing the voxels that have a lower value than a certain Hounsfield Unit (HU) threshold. These voxel regions are referred to as low attenuation areas (LAA) (6). The Hounsfield Unit (HU) threshold of -910 was first suggested in 1988, and subsequent studies have examined alternative threshold values. In 2006, Madani et al. (7) shown that the best Hounsfield Unit (HU) threshold for macroscopic and microscopic pathologic correlations is either -960 HU or -970 HU. However, the use of higher threshold values increases the sensitivity to image noise. Therefore, the threshold value of -950 HU is widely accepted as it provides a balance between sensitivity and noise. The percentage area of lung with a density less than -950 HU, known as the emphysema index or %LAA-950, is commonly used to estimate the emphysema component in patients with chronic obstructive pulmonary disease (COPD).

A different method, using the frequency histogram of lung attenuation, computes the lung parenchymal Hounsfield Units (HU) at a certain percentile on the histogram. The number referred to as the "percentile index" has been validated using pathologic specimens, and it has been determined that the ideal threshold is the first percentile (7). However, due to concerns about the occurrence of more visual distortions and noise at the first percentile level, the 15th percentile threshold is often used (8, 10). The percentile index is considered to be more resilient in assessing longitudinal fluctuations in emphysema and is less affected by changes in lung volume (8, 11).

A fundamental constraint of CT histogram measuring methods is their failure to include the diverse patterns of distribution, size, or clusters of emphysema, which may significantly impact the assessment of a patient with COPD. Given that emphysema is a disease that affects specific regions, it is crucial to identify the anatomical zones where emphysema is present, rather than just measuring the overall extent of emphysematous involvement. Presently, the majority of quantitative CT techniques have the capability to partition each lung into distinct anatomical regions, enabling the computation of ratios that measure the degree of emphysema in various lung zones. Additionally, newer techniques allow for the division of lobes to accurately measure the volumes of each lobe and objectively assess the amount of emphysema. In order to measure the extent of emphysematous changes in the lung tissue, researchers have employed a method called low attenuation cluster analysis. This involves determining the power-law exponents of emphysema holes, which indicates how emphysema areas are grouped together to form clusters of varying sizes. The power-law exponents provide information about the distribution of emphysema and the degree of clustering. Previous studies have utilized this approach to assess the local size of lung parenchyma affected by emphysema (12, 13, 14).

The quantification of emphysema is a very straightforward process. Studies have shown that quantitative CT measurements are more closely related to macroscopic measurements of emphysema than visual CT assessments (15). Density-based emphysema assessment has shown higher accuracy in detecting the deterioration of emphysema in patients with α1-antitrypsin deficiency. As a result, it has been widely acknowledged as an effective diagnostic tool for identifying the course of the illness (16). The CT density mask approach was determined to be correlated with COPD mortality and is considered a more powerful prediction factor for cardiac and respiratory mortality compared to the global initiative for chronic obstructive lung disease (GOLD) staging (17, 18). Patients who had higher quantitative markers of emphysema had a faster deterioration in pulmonary function test (PFT) characteristics (19). In addition, quantitative measures of emphysema have been shown to be associated with frequent exacerbation and more severe clinical outcomes resulting from exacerbation episodes (20, 21, 22).

After considering the heterogeneity of emphysema measured using quantitative CT, it was found that emphysema in the basal region of the lung is linked to a more significant decrease in forced expiratory volume in 1 second (FEV1). Emphysema in central areas of the lung has a stronger association with airflow limitation compared to emphysema in the outer regions of the lung (23, 24). According to a study, there was a correlation between the assessed heterogeneity of emphysema distribution and a reduction in FEV1 and FEV1/forced vital capacity (FVC) (25). When comparing the %LAA-950 value derived from the whole lung, measurements based on histograms of distinct emphysema patterns were shown to be more accurate in predicting PFT findings, severity of dyspnea, and quality of life (26). Furthermore, the therapeutic significance of the geographical distribution of emphysema has been shown in the selection of ideal candidates for lung volume reduction surgery (27).

Measurement of Airway Disease

Airway remodeling, namely in the small airways, is a crucial element in chronic obstructive pulmonary disease (COPD) and is recognized as the primary cause of restricted airflow. A tiny airway is characterized by an interior diameter less than 2 mm. However, due to the poor spatial resolution of modern CT scanners, accurately measuring the size of small airways has proved to be very difficult. Present quantitative CT methods enable the creation of three-dimensional models of the airways and accurate non-invasive assessment of segmental and sub-segmental airways, which are considered "large airways". Nevertheless, a prior study shown that alterations in the larger airways are indicative of changes in the smaller airways upon pathological analysis, and the quantified computed tomography (CT) characteristics of the larger airways were found to be associated with pulmonary function test (PFT) outcomes (28). Furthermore, the CT characteristics assessed in the more distant airways had more robust relationships with spirometry, as shown by a study (29). Hence, it might be beneficial to get quantified airway parameters from detectable big airways on CT scans of individuals with COPD.

Challenges and Prospects for the Future

While the quantitative analysis of CT scans has shown promising outcomes, further research is necessary to include quantitative CT characteristics as imaging biomarkers that may be effectively used in the management of COPD patients. Initially, it is necessary to standardize, optimize, and simplify the procedures used to quantify the different components of COPD. While some approaches have shown strong associations with physiological or clinical characteristics, there is still no agreement or universally accepted method for accurately measuring each component of COPD. Moreover, quantitative metrics obtained from CT scans might be affected by several circumstances, such as patient weight, sufficiency of inspiration, CT manufacturer, and calibration. Efficiently optimizing CT methods and implementing quality control in image capture are crucial for conducting large-scale multicenter/multinational studies and facilitating comparisons of outcomes across diverse participants. Furthermore, it is crucial to decrease the time and effort needed for quantitative evaluation, including post-processing operations, by automating the procedures. This would enhance their clinical accessibility and usefulness.

The current GOLD approach does not endorse the regular use of CT scanning in COPD. It merely suggests that CT scanning may be beneficial in ruling out other potential diagnoses or when contemplating surgical interventions such lung volume reduction surgery. The primary reason for this is the limited amount of data indicating that information obtained from CT scans may effectively improve treatment regimens, predict treatment response or prognosis, and ultimately impact the death rate of patients with COPD. Many previous researches have compared quantitative CT parameters with basic PFT findings. However, more analyses are required to evaluate their correlation with disease outcome measures, treatment effects, and other clinically important indicators of disease severity.

Studying the connection between genetic information and quantitative imaging measures in COPD might provide important insights into the causes of the illness. This is because the specific symptoms of COPD can differ based on genetic differences. Furthermore, it is necessary to conduct further longitudinal cohort studies in order to monitor changes in computed tomography (CT) over time and get a precise understanding of illness development and how it may be accurately measured using quantitative CT imaging. Additional research should be conducted to examine the clinically significant phenotypes of chronic obstructive pulmonary disease (COPD) using quantitative computed tomography (CT) methods. This knowledge might have a significant impact on COPD trials and the development of drugs, which are currently in high demand in the medical field.

Finally, it is important to enhance quantitative CT analysis by using the growing array of modern and current technology. Reducing the dosage of radiation in CT scans is crucial for long-term research and the increased use of CT in clinical settings. This may be achieved by the implementation of low dose protocols, noise reduction techniques, and advanced image reconstruction algorithms. Dual-energy CT technology enables the assessment of lung function and has the potential for further use in quantitatively evaluating patients with chronic obstructive pulmonary disease (COPD). In the age of big data analysis, radiomics is a burgeoning area of research that involves extracting high throughput data and analyzing a vast array of sophisticated quantitative imaging properties, frequently using automated or semi-automated methods. While the majority of radiomics studies have mostly focused on cancer research, the utilization of radiomics in COPD might provide more valuable information. Artificial intelligence, including deep learning and machine learning, has garnered significant global interest in recent years. Despite being a relatively unexplored domain, it has immense promise and can be further enhanced by quantitative CT technology.

Summary

Quantitative CT imaging is a very promising method for accurately evaluating the manifestation of diseases. It has already shown correlations with conventional clinical and physiological indicators of COPD. Quantitative CT analysis offers accurate measurements of two primary characteristics of COPD, namely emphysema and airway disease, as well as many additional aspects such as changes in pulmonary vessels, atherosclerosis, cachexia, and osteoporosis. These measured criteria serve as valuable research tools for comprehending the inherent diversity of COPD and aiding in the identification of its core etiology. The use of these methods to clinical practice has the potential to generate personalized treatment plans and enhance disease outcomes in individuals with COPD.

References

1. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med 2013;187:347–365.
2. Lopez AD, Shibuya K, Rao C, Mathers CD, Hansell AL, Held LS, et al. Chronic obstructive pulmonary disease: current burden and future projections. Eur Respir J 2006;27:397–412.
3. Schroeder JD, McKenzie AS, Zach JA, Wilson CG, Curran-Everett D, Stinson DS, et al. Relationships between airflow obstruction and quantitative CT measurements of emphysema, air trapping, and airways in subjects with and without chronic obstructive pulmonary disease. AJR Am J Roentgenol 2013;201:W460–W470.
4. Cavigli E, Camiciottoli G, Diciotti S, Orlandi I, Spinelli C, Meoni E, et al. Whole-lung densitometry versus visual assessment of emphysema. Eur Radiol 2009;19:1686–1692.
5. Galbán CJ, Han MK, Boes JL, Chughtai KA, Meyer CR, Johnson TD, et al. Computed tomography-based biomarker provides unique signature for diagnosis of COPD phenotypes and disease progression. Nat Med 2012;18:1711–1715.
6. Müller NL, Staples CA, Miller RR, Abboud RT. "Density mask". An objective method to quantitate emphysema using computed tomography. Chest 1988;94:782–787.
7. Madani A, Zanen J, de Maertelaer V, Gevenois PA. Pulmonary emphysema: objective quantification at multi-detector row CT--comparison with macroscopic and microscopic morphometry. Radiology 2006;238:1036–1043.
8. Heussel CP, Herth FJ, Kappes J, Hantusch R, Hartlieb S, Weinheimer O, et al. Fully automatic quantitative assessment of emphysema in computed tomography: comparison with pulmonary function testing and normal values. Eur Radiol 2009;19:2391–2402.
9. Lee YK, Oh YM, Lee JH, Kim EK, Lee JH, Kim N, et al. Quantitative assessment of emphysema, air trapping, and airway thickening on computed tomography. Lung 2008;186:157–165.
10. Stolk J, Dirksen A, van der Lugt AA, Hutsebaut J, Mathieu J, de Ree J, et al. Repeatability of lung density measurements with low-dose computed tomography in subjects with alpha-1-antitrypsin deficiency-associated emphysema. Invest Radiol 2001;36:648–651.
11. Dirksen A. Monitoring the progress of emphysema by repeat computed tomography scans with focus on noise reduction. Proc Am Thorac Soc 2008;5:925–928.

12. Gietema HA, Müller NL, Fauerbach PV, Sharma S, Edwards LD, Camp PG, et al. Quantifying the extent of emphysema: factors associated with radiologists' estimations and quantitative indices of emphysema severity using the ECLIPSE cohort. Acad Radiol 2011;18:661–671.
13. Hwang J, Lee M, Lee SM, Oh SY, Oh YM, Kim N, et al. A size-based emphysema severity index: robust to the breath-hold-level variations and correlated with clinical parameters. Int J Chron Obstruct Pulmon Dis 2016;11:1835–1841.
14. Mishima M, Hirai T, Itoh H, Nakano Y, Sakai H, Muro S, et al. Complexity of terminal airspace geometry assessed by lung computed tomography in normal subjects and patients with chronic obstructive pulmonary disease. Proc Natl Acad Sci U S A 1999;96:8829–8834.
15. Bankier AA, De Maertelaer V, Keyzer C, Gevenois PA. Pulmonary emphysema: subjective visual grading versus objective quantification with macroscopic morphometry and thin-section CT densitometry. Radiology 1999;211:851–858.
16. Dirksen A, Dijkman JH, Madsen F, Stoel B, Hutchison DC, Ulrik CS, et al. A randomized clinical trial of alpha(1)-antitrypsin augmentation therapy. Am J Respir Crit Care Med 1999;160(5 Pt 1):1468–1472.
17. Haruna A, Muro S, Nakano Y, Ohara T, Hoshino Y, Ogawa E, et al. CT scan findings of emphysema predict mortality in COPD. Chest 2010;138:635–640.
18. Johannessen A, Skorge TD, Bottai M, Grydeland TB, Nilsen RM, Coxson H, et al. Mortality by level of emphysema and airway wall thickness. Am J Respir Crit Care Med 2013;187:602–608.
19. Mohamed Hoesein FA, de Hoop B, Zanen P, Gietema H, Kruitwagen CL, van Ginneken B, et al. CT-quantified emphysema in male heavy smokers: association with lung function decline. Thorax 2011;66:782–787.
20. Han MK, Kazerooni EA, Lynch DA, Liu LX, Murray S, Curtis JL, et al. Chronic obstructive pulmonary disease exacerbations in the COPDGene study: associated radiologic phenotypes. Radiology 2011;261:274–282.
21. Jairam PM, van der Graaf Y, Lammers JW, Mali WP, de Jong PA. PROVIDI Study group. Incidental findings on chest CT imaging are associated with increased COPD exacerbations and mortality. Thorax 2015;70:725–731.
22. Oh YM, Sheen SS, Park JH, Jin UR, Yoo JW, Seo JB, et al. Emphysematous phenotype is an independent predictor for frequent exacerbation of COPD. Int J Tuberc Lung Dis 2014;18:1407–1414.
23. Nakano Y, Sakai H, Muro S, Hirai T, Oku Y, Nishimura K, et al. Comparison of low attenuation areas on computed tomographic scans between inner and outer segments of the lung in patients with chronic obstructive pulmonary disease: incidence and contribution to lung function. Thorax 1999;54:384–389.
24. Parr DG, Stoel BC, Stolk J, Stockley RA. Pattern of emphysema distribution in alpha1-antitrypsin deficiency influences lung function impairment. Am J Respir Crit Care Med 2004;170:1172–1178.
25. Chae EJ, Seo JB, Song JW, Kim N, Park BW, Lee YK, et al. Slope of emphysema index: an objective descriptor of regional heterogeneity of emphysema and an independent determinant

of pulmonary function. AJR Am J Roentgenol 2010;194:W248–W255.
26. Castaldi PJ, San José R, Mendoza CS, Hersh CP, Laird N, Crapo JD, et al. Distinct quantitative computed tomography emphysema patterns are associated with physiology and function in smokers. Am J Respir Crit Care Med 2013;188:1083–1090.
27. Nakano Y, Coxson HO, Bosan S, Rogers RM, Sciurba FC, Keenan RJ, et al. Core to rind distribution of severe emphysema predicts outcome of lung volume reduction surgery. Am J Respir Crit Care Med 2001;164:2195–2199.
28. Nakano Y, Wong JC, de Jong PA, Buzatu L, Nagao T, Coxson HO, et al. The prediction of small airway dimensions using computed tomography. Am J Respir Crit Care Med 2005;171:142–146.
29. Hasegawa M, Nasuhara Y, Onodera Y, Makita H, Nagai K, Fuke S, et al. Airflow limitation and airway dimensions in chronic obstructive pulmonary disease. Am J Respir Crit Care Med 2006;173:1309–1315.