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Impact of emphysema and airway wall thickness on quality of life in smoking-related COPD

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Summary
Background: Limited data are available as to the relationship between computed tomography (CT) derived data on emphysema and airway wall thickness, and quality of life in subjects with chronic obstructive pulmonary disease (COPD). Such data may work to clarify the clinical correlate of the CT findings.
Methods: We included 1778 COPD subjects aged 40–75 years with a smoking history of at least 10 pack-years. They were examined with St George's Respiratory Questionnaire (SGRQ-C) and high-resolution chest CT. Level of emphysema was assessed as percent low-attenuation areas less than −950 Hounsfield units (%LAA). Airway wall thickness was estimated by calculating the square root of wall area of an imaginary airway with an internal perimeter of 10 mm (Pi10).
Results: In both men and women, the mean total score and most of the subscores of SGRQ-C increased with increasing level of emphysema and increasing level of airway wall thickness, after adjusting for age, smoking status, pack years, body mass index and FEV_1. The highest gradient was seen in the relationship between the activity score and the emphysema level. The activity score increased by 35% from the lowest to the highest emphysema tertile. The relationship between level of emphysema and the total SGRQ-C score became weaker with

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increasing GOLD (Global initiative for Chronic Obstructive Lung Disease) stages ($p < 0.001$), while the impact of gender was limited.
Conclusion: In subjects with COPD, increasing levels of emphysema and airway wall thickness are independently related to impaired quality of life.

Introduction

Chronic Obstructive Pulmonary Disease (COPD) is among the leading causes of death worldwide and associated with a substantial morbidity.[1] COPD is characterized by airflow limitation, which forms the basis for the diagnosis and staging of the disease.[2] However, it is widely acknowledged that airflow limitation in terms of forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) does not explain the whole picture of COPD.[3]

The functional abnormalities are known to be caused by changes to the lung anatomy, and it is thought that small airway remodeling and emphysematous destruction contribute independently to the functional abnormalities. Computed tomography (CT) of the chest offers the opportunity to divide the disease into anatomically based phenotypes of disease, commonly referred to as emphysematous or airway phenotypes.[4] It is thought that a more complete anatomic description of the lung will allow for the possibility to study more specific COPD related genes and biomarkers than when using spirometry alone.[5,6]

From a patient perspective the concept of airway wall thickening and level of emphysema as measured by CT remains abstract. A major concern to the patient is the level of respiratory symptoms, particularly dyspnea, as well as quality of life (QoL). While the relationship of respiratory symptoms to CT findings has recently been examined,[7,8] limited data are available as to how CT derived emphysema level and airway wall thickness relate to QoL. In a selective group of advanced COPD patients examined prior to lung volume reduction surgery, lung transplantation or resection for potential bronchogenic malignancy, Han et al. found increased level of emphysema and airway wall thickness related to impaired quality of life.[9] In two other studies comprising primarily men, increased level of emphysema was also found to be associated to a worse quality of life.[10,11] A recent report from the COPDGene trial found both level of emphysema and airway wall thickness related to impaired QoL in terms of St George Respiratory Questionnaire (SGRQ), with airway wall thickening being more strongly related to QoL than extent of emphysema.[12]

To our knowledge, no data are available as to whether the relationship between CT derived emphysema and airway thickness and QoL differ by gender or whether the CT-QoL relationships vary with severity of disease. Such data may work to clarify the clinical correlate of the CT findings and enhance the interpretation of chest CT in the clinical setting.

We hypothesized that emphysema and airway wall thickness are independently associated to impaired level of QoL. To test this hypothesis, we used the "Evaluation Of COPD Longitudinally To Identify Predictive Surrogate Endpoints (ECLIPSE) Study (Clinicaltrials.gov identifier NCT00292552; GSK Study Code SCO104960). ECLIPSE includes questionnaires, spirometry, exercise testing and computed tomography (CT) scans from smokers suffering from COPD, non-smoker controls and smoker controls with no evidence of COPD which offers the opportunity to examine to what extent CT findings explain QoL status beyond that offered by spirometry. Finally, we aimed to examine to what degree the CT-QoL relationship varies by gender and disease status.

Methods

Participants

The population under study was the Evaluation of COPD Longitudinally to Identify Predictive Surrogate Endpoints (ECLIPSE) cohort. The trial has been approved by the relevant ethics and review boards at participating centers and written informed consent was obtained from all participants. A list of all participating centres can be found in Appendix 2. The aims and operational aspects of the ECLIPSE cohort have been described elsewhere.[13] Individuals aged 40–75 years were recruited to the study if they had a smoking history of $\geq$10 pack-years, a post-bronchodilator ratio between forced expiratory volume in 1 s (FEV_1) and forced vital capacity (FVC) $\leq$0.7. In the current analysis only COPD subjects were included, because the SGRQ-c was developed to assess quality of life in COPD subjects. Individuals recruited to the study were genotyped for α_1-antitrypsin deficiency and six PiZZ and 11 PiSZ individuals were identified and also excluded from the analysis.[5]

Pulmonary function testing

Pulmonary function testing (PFT) included post-bronchodilator forced expiratory volume in one second as percentage of predicted (FEV_1%) and forced vital capacity (FVC) with a pneumotachograph, performed following American Thoracic Society (ATS) guidelines. Subjects were asked to withhold bronchodilator medication for at least 6 h prior to testing. COPD subjects were staged according to the GOLD guidelines.[14]

Computed tomography

Computed tomography scans were acquired using multidetector-row CT scanners (GE Healthcare or Siemens Healthcare) with a minimum of 4 rows and obtained in supine position, at suspended full inspiration without administration of intravenous contrast. Exposure settings were 120 kVp and 40 mAs and images were reconstructed at