CHEST

Quantitative CT Measures of Bronchiectasis in Smokers

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BACKGROUND: Bronchiectasis is frequent in smokers with COPD; however, there are only limited data on objective assessments of this process. The objective was to assess broncho-vascular morphology, calculate the ratio of the diameters of bronchial lumen and adjacent artery (BA ratio), and identify those measurements able to discriminate bronchiectasis.

METHODS: We collected quantitative CT (QCT) measures of BA ratios, peak wall attenuation, wall thickness (WT), wall area, and wall area percent (WA%) at matched fourth through sixth airway generations in 21 ever smokers with bronchiectasis (cases) and 21 never-smoking control patients (*control* airways). In cases, measurements were collected at both *bronchiectatic* and *nonbronchiectatic* airways. Logistic analysis and the area under receiver operating characteristic curve (AUC) were used to assess the predictive ability of QCT measurements for bronchiectasis.

RESULTS: The whole-lung and fourth through sixth airway generation BA ratio, WT, and WA% were significantly greater in bronchiectasis cases than control patients. The AUCs for the BA ratio to predict bronchiectasis ranged from 0.90 (whole lung) to 0.79 (fourth-generation). AUCs for WT and WA% ranged from 0.72 to 0.75 and from 0.71 to 0.75. The artery diameters but not bronchial diameters were smaller in *bronchiectatic* than both *nonbronchiectatic* and *control* airways ($P < .01$ for both).

CONCLUSIONS: Smoking-related increases in the BA ratio appear to be driven by reductions in vascular caliber. QCT measures of BA ratio, WT, and WA% may be useful to objectively identify and quantify bronchiectasis in smokers.

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FOR EDITORIAL COMMENT SEE PAGE 1204

ABBREVIATIONS: AATD = alpha-1 antitrypsin deficiency; AUC = area under the receiver operating characteristic curve; BA ratio = ratio of the diameters of bronchial lumen and adjacent artery; CCC = concordance correlation coefficients; %LAA-950 = attenuation areas below -950 Hounsfield units; PWA = peak wall attenuation; QCT = quantitative CT; WA = wall area; WA% = wall area percent; WT = wall thickness

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Bronchiectasis is a pathological enlargement of the airways.[1] Several studies suggest that bronchiectasis in subjects with COPD is frequent and associated with longer hospital stays and higher risk for death.[2-5] The diagnosis of this condition is made on the basis of visual identification of an airway whose diameter is greater than of the adjacent artery (the BA ratio) and a lack of airway tapering on CT scans or lung tissue.[6-8]

There is an extensive body of literature focused on the clinical associations and prognostic value of visual detection of bronchiectasis on CT scans,[2,3,6,9] but only a small number of CT studies in children have reported quantitative CT (QCT) measures of the disease.[10,11] Despite the high prevalence of bronchiectasis in patients with COPD (up to 56% in some series),[2,3,5] we are not aware of published investigations focused on QCT measures of BA ratio and airway morphology to detect bronchiectasis in smokers. Unlike more severe forms of bronchiectasis found in cystic fibrosis and alpha-1 antitrypsin deficiency (AATD),[12] bronchiectasis in non-AATD COPD is typically more subtle,[2,5,13] which limits adoption of universal visual standards for disease detection. Our goal was to determine objective metrics of bronchovascular morphology for the detection of bronchiectasis. Using data from the COPDGene Study,[14] we examined measures of airway morphology such as the peak wall attenuation (PWA, a measure of wall attenuation),[15,16] wall thickness (WT), wall area (WA), the WA percent ([WA%] = total bronchial area – WA/total bronchial area $\times 100$),[17] bronchial and artery calibers, and the BA ratio. We included metrics of the vasculature since an increased bronchial lumen or a decreased arterial caliber could both result in a BA ratio >1, which is a commonly used threshold to define bronchiectatic dilation of the airway.[11,18] Finally, we explored the relationship between oxygen saturation and artery diameters made on the basis of a prior study demonstrating increased BA ratios in people living in altitude.[18]

Methods

Study Cohort

The COPDGene Study was designed to assess the genetic and epidemiological determinants of COPD.[14] Smokers (10 or more pack-years) who were 45 to 80 years old were recruited to this study. Subjects with active pulmonary disease other than COPD and asthma were excluded and subjects who had an acute respiratory disease episode (ie, new or increase in respiratory symptoms) within a month before enrollment were also excluded. A subset of never-smoking control patients (N = 108) with normal pulmonary function tests and no history of pulmonary diseases were also included. All subjects provided written informed consent to participate in the study. The institutional review board at each participating clinical center approved the COPDGene study, and the Partners HealthCare Research Committee (2007P-000554) approved the current study.

Study Design

A convenience sample of bronchiectasis cases was identified by visually reviewing approximately 300 serially acquired CT scans from the COPDGene cohort. A pulmonologist with experience in lung imaging identified 25 subjects with bronchiectasis using the criteria described in e-Appendix 1. The presence or absence of bronchiectasis in this cohort was adjudicated by a second pulmonologist. Concordant diagnoses of bronchiectasis were made in 21 subjects, which then became the final cohort of cases. Control subjects (N = 21) were randomly chosen from non-smoking control patients.

CT Analysis

Lung Volume and Emphysema: COPDGene imaging protocols are provided in e-Appendix 1.[14] Total lung volume at full inspiration was used as a radiologic measure of total lung capacity and was expressed as % of predicted values.[19] Emphysema was measured as percent of low attenuation areas below -950 Hounsfield units (%LAA-950).[20]

Bronchiectasis Scoring: Inspiratory CT scans were visually scored (restricted to bronchiectasis subjects) by a third pulmonologist who agreed with the other 2 readers on the presence of bronchiectasis in all selected CT scans. The bronchiectasis score sheet is shown in e-Table 1. The mean bronchiectasis CT score was used for analysis.

Bronchovascular Bundle Measurements: A trained analyst with 3 years of experience in lung imaging performed the CT measures of the bronchovascular bundle.[18,21] Note that airway types are here named (and *italicized*) as *control* (from nonsmoking subjects), *nonbronchiectatic,* and *bronchiectatic* (the 2 latter are from bronchiectasis subjects). BA ratios and airway morphology measurements were collected and matched on the basis of generations. In control patients, we used anatomically matched sites in the right upper lobe apical bronchus and the right lower lobe basal posterior bronchus.[22] In bronchiectasis subjects, we measured 1 of the affected bronchial paths per lobe (range, 1-4). *Nonbronchiectatic* airways were also measured in an unaffected lobe remote from the visually determined pathologic airways. All measurements were manually at the midpoint of one airway branch of the fourth, fifth, and sixth generations and adjacent pulmonary artery.[22] The bronchial lumen and artery diameters were measured at both the longest and shortest axes using a Slicer digital ruler. Measures of PWA, WA, WT, and WA % were performed as described previously.[23] Bronchial lumen and artery diameters as well as the BA ratios were computed using an average of the long and short cross sectional axes for each generation and whole lung. Intra- and inter-analysts reproducibility assessment is described in the e-Appendix 1.[21,23]

Clinical and Physiologic Assessments: Demographic and clinical data with standardized questionnaires including a modified adult respiratory questionnaire were collected (questionnaires are available at www.COPDGene.org).[14] We used the question, "Do you usually bring up phlegm from your chest on getting up, or first thing in the morning?" to evaluate sputum production. Spirometric measures of lung function were performed before and after the administration of albuterol according to