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# Artificial Intelligence–based CT Assessment of Bronchiectasis: The COPDGene Study

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# Abstract

**Background:** CT is the standard method used to assess bronchiectasis. A higher airway-to-artery diameter ratio (AAR) is typically used to identify enlarged bronchi and bronchiectasis; however, current imaging methods are limited in assessing the extent of this metric in CT scans.

**Purpose:** To determine the extent of AARs using an artificial intelligence–based chest CT and assess the association of AARs with exacerbations over time.

**Materials and Methods:** In a secondary analysis of ever-smokers from the prospective, observational, multicenter COPDGene study, AARs were quantified using an artificial intelligence tool. The percentage of airways with AAR greater than 1 (a measure of airway dilatation) in each participant on chest CT scans was determined. Pulmonary exacerbations were prospectively

determined through biannual follow-up (from July 2009 to September 2021). Multivariable zero-

inflated regression models were used to assess the association between the percentage of airways with AAR greater than 1 and the total number of pulmonary exacerbations over follow-up. Covariates included demographics, lung function, and conventional CT parameters.

**Results:** Among 4192 participants (median age, 59 years; IQR, 52–67 years; 1878 men [45%]), 1834 had chronic obstructive pulmonary disease (COPD). During a 10-year follow-up and in adjusted models, the percentage of airways with AARs greater than 1 (quartile 4 vs 1) was associated with a higher total number of exacerbations (risk ratio [RR], 1.08; 95% CI: 1.02, 1.15; P= .01). In participants meeting clinical and imaging criteria of bronchiectasis (ie, clinical manifestations with 3% of AARs >1) versus those who did not, the RR was 1.37 (95% CI: 1.31, 1.43; P< .001). Among participants with COPD, the corresponding RRs were 1.10 (95% CI: 1.02, 1.18; P= .02) and 1.32 (95% CI: 1.26, 1.39; P< .001), respectively.

**Conclusion:** In ever-smokers with chronic obstructive pulmonary disease, artificial intelligencebased CT measures of bronchiectasis were associated with more exacerbations over time.

Clinical trial registration no. NCT00608764

#### Summary

Among ever-smokers from the COPDGene cohort, an increased percentage of artificial intelligence–based airway-to-artery diameter ratios at chest CT were associated with a higher total number of exacerbations during follow-up.

Bronchiectasis is a condition marked by irreversible airway widening that is associated with an increase in the susceptibility to recurrent inflammation and infections, thus causing progressive structural damage (1). Bronchiectasis is recognized as a clinically relevant manifestation in ever-smokers with chronic obstructive pulmonary disease (COPD), affecting 4%–72% of these individuals (2–7). CT is the standard modality used in assessing bronchiectasis, and a meta-analysis (8) showed that in 89% of evaluated studies a high airway-to-artery diameter ratio (AAR) was considered a criterion for bronchiectasis. Although the measurements of the airway and the pulmonary arteries on single-section (SS) CT images have an excellent ability to determine whether the AAR is high, the approach is time-consuming and generally includes a restricted number of airway sections (9), making it challenging to determine the extent of increased AARs throughout the lungs. These limitations hamper the application of quantitative approaches in large studies. Furthermore, although prior automated approaches for bronchiectasis have been used in smaller studies (10,11,12), we are not aware of studies in which researchers have reported the application of an artificial intelligence (AI)-based tool in a large cohort and then reported its clinical implications. A high proportion of AARs greater than 1 indicates a higher risk of respiratory morbidity.

AI approaches, such as convolutional neural networks, can improve the process of measuring and classifying airways and vessels to produce accurate measurements for diagnosing bronchiectasis (10,13,14). Thus, we have developed an AI-based imaging tool to quantify AARs, and we determined the percentage of AAR greater than 1 and applied this tool in a large cohort of ever-smokers (15). We compared the AI- and SS-based AAR

measurements and visual bronchiectasis CT scores and aimed to test the hypothesis that in ever-smokers, a higher proportion of AARs greater than 1 is associated with more exacerbations over time. In prior investigations, researchers demonstrated that exacerbation episodes are a cause of morbidity and health care use in individuals with bronchiectasis and COPD, are considered a key end point in recent clinical trials for both diseases, and are associated with structural damage such as emphysema and small airway disease (16–19).

## **Materials and Methods**

#### **Participant Cohort**

In this secondary analysis, we used data collected by the COPDGene study (ClinicalTrials.gov number, NCT00608764) (15). Current and former heavy ever-smokers (10 pack-years) who were aged 45–80 years were recruited from 2008 to 2011. Participants with an active pulmonary disease other than COPD or asthma and those who had an exacerbation 4 weeks before the start of the study were excluded. All participants completed questionnaires and underwent spirometry and standardized volumetric chest CT scanning. We used a convenience sample of 4192 participants in whom AAR measurements were performed (Fig 1), including those from three spirometric groups: preserved ratio impaired spirometry, Global Initiative for Obstructive Lung Disease stage 0 (ie, at risk), and Global Initiative for Obstructive Lung Disease stages 1–4 (ie, COPD). All participants provided written informed consent to participate. The institutional review board at each participating clinical center approved the protocol. Additional details are provided in Appendix E1 (online).

#### **CT Algorithm to Quantify AARs**

The COPDGene CT protocols were described in a prior study (15). The assessment of the AARs involved five steps with two steps involving deep learning techniques, which are detailed in Appendix E1 (online). The steps are as follows: first, segmentation of the lungs (20); second, three-dimensional reconstruction of the airway and vessel trees (Fig 2) (21–23); third, separation of pulmonary arteries from pulmonary veins (13,14); fourth, sizing of the airways and vessels (13); and fifth, pairing of the airways and pulmonary arteries. Airway-and-artery pairs were selected to compute AARs (Fig 3). We report the percentage of airways with AARs greater than 1 obtained from all airway-and-artery pairs with an artery cross-sectional area of 5 mm<sup>2</sup> or greater; higher values indicated a greater extent of airway enlargement at CT. If an examination yielded 3000 AARs and 150 were greater than 1, then the percentage of AAR greater than 1 was 5%. A cutoff point of AAR greater than 1 is typically used to assess bronchiectasis in research and clinical settings (8). Reproducibility of the percentage of AAR greater than 1 was assessed on 20 CT scans, as detailed in Appendix E1 (online).

#### CT Single-section Measurements of Airways and Pulmonary Arteries

To assess the correlation of AARs with SS AARs, we used standardized airway sampling in 409 of 4192 participants in the COPDGene study (Fig 1; Appendix E1 [online]). Airway lumen and artery diameters were computed in six bronchial paths, and the SS AARs were averaged to obtain the mean SS AAR per CT. The percentage of SS AARs greater than 1 was calculated as the ratio of the number of SS AARs greater than 1 to the total number of SS AARs multiplied by 100 (9).

#### Visual Assessment of Bronchiectasis at CT

To compare the percentage of AAR greater than 1 and visual ascertainment of bronchiectasis, we used the bronchiectasis severity CT score data in 724 of 4192 participants (Fig 1). These data in 724 participants were used in a prior study (19) reporting on emphysema and small airway disease in bronchiectasis. Details of the visual assessment are provided (Appendix E1 [online]). The CT score was based on the degree of bronchial dilation, the type of bronchiectasis, the number of bronchopulmonary segments affected, and the presence of wall thickness and mucus plugging in affected bronchi. CT scores were categorized as 0, 1–2, 3–5, and greater than 5 and compared with quartiles of percentage of AAR greater than 1.

#### **Additional Baseline CT Measurements**

Additional CT measurements of emphysema, airways, and small pulmonary arteries were obtained and are described in Appendix E1 (online). These measurements included low attenuation areas less than –950 HU and the square root of the wall area of a hypothetical 10-mm inner-perimeter airway.

#### Outcomes

More details on the outcomes are provided in Appendix E1 (online). The main outcome was exacerbation over time, which was assessed during the longitudinal follow-up program of the COPDGene study. An exacerbation was defined as an increase or onset of respiratory symptoms (cough, phlegm, dyspnea) treated with antibiotics and/or corticosteroids. Secondary outcomes included phlegm, cough, and dyspnea at baseline. Dyspnea was assessed with the modified Medical Research Council score (15). Cough and phlegm were dichotomized as yes or no, and the dyspnea score was dichotomized as high (2) or low (<2).

#### Spirometry

Spirometric measurements of lung function were performed before and after the administration of albuterol according to American Thoracic Society recommendations. Postbronchodilator forced expiratory volume in 1 second (FEV<sub>1</sub>) and forced vital capacity are expressed as percentages of predicted values (24). We used FEV<sub>1</sub> percent predicted as a secondary outcome in the cross-sectional analysis. COPD was defined as FEV<sub>1</sub> less than 0.7, preserved ratio-impaired spirometry as FEV<sub>1</sub>-to–forced vital capacity ratio of 0.7 or greater and FEV<sub>1</sub> predicted less than 80%, and at-risk as FEV<sub>1</sub>-to–forced vital capacity ratio of 0.7 or greater and FEV<sub>1</sub> predicted of 80% or greater.

#### **Other Covariates**

Data regarding demographics, medical history, and oxygen saturation were collected with standardized questionnaires and procedures (Appendix E1 [online]).

#### **Definition of Bronchiectasis**

We used the clinical features of a bronchiectasis definition for COPD proposed by international experts and added to the percentage of AAR greater than 1 (25). Bronchiectasis was defined using the following criteria: high percentage of AAR greater than 1 (ie, 3%) based on the median value; and two or more of manifestations of cough, phlegm, Modified Medical Research Council dyspnea score of 1 or greater, and two or more exacerbations in the year before enrollment.

#### **Statistical Analysis**

Additional details on the statistical analysis are provided in Appendix E1 (online). The association between percentage of AAR greater than 1 and the total number of exacerbations over time was assessed using longitudinal Poisson regression analysis with a zero-inflated model, log link, and time of follow-up as an offset. The estimates represent RRs of total exacerbations during follow-up. The percentage of AAR greater than 1 was categorized into quartiles (ie, percentile cutoff points 25th, 50th, and 75th), with quartile 1 used as a reference and quartile 4 as the main predictor. The models for exacerbations included age, sex, ethnicity, body mass index, smoking status (current vs former), pack-years smoked, FEV<sub>1</sub>, oxygen saturation, low attenuation areas less than -950 HU, square root of the wall area of a hypothetical 10-mm inner-perimeter airway, and CT scanner make and model as covariates. Separate analyses for exacerbations were performed across subgroups, including preserved ratio impaired spirometry, at-risk ever-smokers, COPD, emphysema, and chronic bronchitis. A statistician (W.W.) performed the analyses using software (SAS 9.4; SAS Institute). A *P* value less than .05 was considered to indicate statistical significance.

#### Results

#### **Participant Characteristics**

Among 10 198 participants in the COPDGene study, after excluding 66 because of missing spirometry data, we included 4192 participants in whom AI-based measurements were performed (Fig 1). Tables in Appendix E1 (online) show the characteristics of participants included and not included in our study (Table E1 [online]) and in those who had available SS-based measurements (Table E2 [online]) and visual scores (Table E3 [online]). Table 1 shows the characteristics of the study participants per quartile of percentage of AAR greater than 1. The percentage of AAR greater than 1 was not related to small pulmonary arteries, measured as the volume of arteries smaller than 5 mm<sup>2</sup> in cross section on contrast-unenhanced CT images ( $\beta = -0.045 \pm 0.065$  [standard error]; P = .49). Table 2 shows the characteristics of the participants by bronchiectasis definition status.

#### Comparison of the Percentage of AAR Greater than 1 and SS AAR Measurements

The percentage of AAR greater than 1 was directly correlated with the mean SS airway lumen diameter ( $\beta = 0.019 \pm 0.002$ ; *P*<.001) and the percentage of SS AAR greater than 1 ( $\beta = 0.752 \pm 0.067$ ; *P*<.001) but not with the mean SS artery diameter ( $\beta = 0.004 \pm 0.008$ ; *P*=.21).

#### Comparison of AAR Greater than 1 and Visual Bronchiectasis CT Scores

Table 3 shows the comparison of the quartiles of percentage of AAR greater than 1 and visual bronchiectasis CT scores. The visual scores and quartiles of percentage of AAR greater than 1 were classified in the same category in 34.9% (253 of 724) of the scans. The percentage of AAR greater than 1 classified 50.7% (367 of 724) of scans as one category more severe and 14.4% (104 of 724) of scans as one category less severe than the visual scores. The most substantial discrepancy was in participants without visual evidence of bronchiectasis (ie, score 0) but classified as having quartile 2 to quartile 4 of percentage of AAR greater than 1 (293 of 724; 40.5%). Compared with participants without visual bronchiectasis and in quartile 1 of percentage of AAR greater than 1 (n = 293) were older (median age, 59 vs 60 years; P = .04), more likely to be men (118 of 293 [40%] vs 43 of 199 [22%]; P < .001), had a greater emphysema percentage on CT scans (median, 3.1% vs 0.98%; P < .001), and tended to have more exacerbations per year (mean, 0.28 vs 0.38; P = .08).

#### Percentage of AAR Greater than 1, Lung Function, and Respiratory Symptoms

In models adjusted for age, sex, ethnicity, height, smoking status (current vs former), packyears smoked, oxygen saturation, emphysema percentage at CT, square root of the wall area of a hypothetical 10-mm inner-perimeter airway, and CT scanner make and model, compared with participants in quartile 1 of percentage of AAR greater than 1, those in quartile 4 had a lower FEV<sub>1</sub> percent predicted (least square mean,  $80\% \pm 21$  [SD] vs 76%  $\pm$  30; *P* < .001). In models adjusted for all covariates except height, which was replaced by body mass index and FEV<sub>1</sub> was added, participants in quartile 1 versus quartile 4 of percentage of AAR greater than 1 had higher odds of phlegm (odds ratio, 1.39; 95% CI: 1.13, 1.69; *P* = .003) and a modified Medical Research Council dyspnea score of 2 or greater (odds ratio, 1.50; 95% CI: 1.19, 1.88; *P* < .001). A percentage of AAR greater than 1 was not associated with cough (odds ratio, 1.06; 95% CI: 0.86, 1.30; *P* = .19).

#### Percentage of AAR Greater than 1 and Exacerbations

Among the 3715 participants (89%) with longitudinal data regarding exacerbations, 48% experienced one or more episodes during a median follow-up of 10.3 years, and their mean number of exacerbations per year per quartile of percentage of AAR greater than 1 was as follows: quartile 1, 0.7; quartile 2, 0.9; quartile 3, 0.9; quartile 4, 1.0 (P<.001). The corresponding values in participants who met and did not meet the bronchiectasis definition criteria were 1.2 and 0.7 (P<.001), respectively. Overall, after adjusting for age, sex, ethnicity, body mass index, smoking status (current vs former), pack-years smoked, FEV<sub>1</sub>, oxygen saturation, CT measures of emphysema and square root of the wall area of a hypothetical 10-mm inner-perimeter airway, and CT scanner make and model, those in quartile 4 versus quartile 1 of percentage of AAR greater than 1 had a higher total number of exacerbations during follow-up (RR, 1.08; 95% CI: 1.02, 1.15; P= .01) (Fig 4). The estimates when using high (<3%) versus low percentage of AAR greater than 1 (<3%) based on the median were as follows: RR, 1.09 (95% CI: 1.04, 1.14; P<.001; Table E4 [online]).

The RR among participants who met the bronchiectasis definition (vs those who did not) was 1.37 (95% CI: 1.31, 1.43; P < .001; Fig 4).

# Percentage of AAR Greater than 1 and Exacerbations in Spirometric and Phenotypic Groups

Table E5 (online) shows the participants' characteristics per spirometric group. Those in quartile 4 versus quartile 1 of percentage of AAR greater than 1 had a higher total number of exacerbations over time: preserved ratio impaired spirometry (RR, 1.15; 95% CI: 0.88, 1.50; P = .30); at-risk ever-smokers (RR, 1.09; 95% CI: 0.94, 1.26; P = .26); and COPD (RR, 1.10; 95% CI: 1.02, 1.18; P = .02; Fig 4). The RRs per COPD phenotype were as follows: emphysema, 1.13 (95% CI: 1.04, 1.24; P = .006); and chronic bronchitis, 1.22 (95% CI: 1.08, 1.38; P = .002; Fig 4). The results for each group using a high (3%) versus a low (<3%) percentage of AAR greater than 1 are shown in Table E4 (online). Among participants who met the bronchiectasis definition (vs those who did not), the RRs were as follows: preserved ratio impaired spirometry, 1.15 (95% CI: 0.95, 1.39; P = .16); at-risk ever-smokers, 1.61 (95% CI: 1.45, 1.79; P < .001); COPD, 1.32 (95% CI: 1.26, 1.39; P < .001); emphysema, 1.38 (95% CI: 1.30, 1.46; P < .001); and chronic bronchitis, 1.46 (95% CI: 1.34, 1.59; P < .001; Fig 4).

# Discussion

To examine the association of airway-to-artery diameter ratios with exacerbations over time, we studied 4192 ever-smokers from the COPDGene cohort. During a 10-year follow-up, after adjustment for age, sex, ethnicity, body mass index, pack-years, current smoking, oxygen saturation, forced expiratory volume in 1 second, CT measures of emphysema and wall thickness, and scanner make and model, a percentage of airway-to-artery diameter ratio (AAR) greater than 1 (quartile 4 vs 1) was associated with a higher total number of exacerbations (risk ratio [RR], 1.08; 95% CI: 1.02, 1.15; P = .01). When clinical manifestations (ie, cough, phlegm, dyspnea, and exacerbation history) were combined with the percentage of AAR greater than 1 to define bronchiectasis, the RR was 1.37 (95% CI: 1.31, 1.43; P < .001). Among participants with chronic obstructive pulmonary disease, the RRs for AAR greater than 1 and those meeting the clinical and imaging criteria of bronchiectasis were 1.10 (95% CI: 1.02, 1.18; P = .02) and 1.32 (95% CI: 1.26, 1.39; P < .001), respectively.

A limitation of the current visual and quantitative approaches for bronchiectasis is that they do not provide a comprehensive assessment of the complex morphologic changes throughout the bronchial and pulmonary artery trees observed in ever-smokers (8,9,11,12). In our study, we used an AI-based method to assess these structures and provide a continuous metric of the extent of airway dilation on CT scans, building on prior studies (10,11,12,26,27) that demonstrated the use of AI in the detection of bronchiectasis and COPD. The percentage of AAR greater than 1 was correlated with other quantitative measures, SS AARs and the percentage of SS AAR greater than 1, substantiating the AI-based metric. However, the AI-based metric did not align well with the visual CT scores. The percentage of AAR greater than 1 seemed to capture airway dilation relative to artery size in participants who were not

identified as having bronchiectasis at visual inspection. An interpretation of these findings is that subtle detection of a larger airway size relative to artery size is a difficult and likely variable visual task, compounded by the presence of smoking-related pathologic features at CT, such as emphysema. Additionally, it may represent mismatching of the airways and nearby arteries in some lung zones because of anatomic variability and technical failure (eg, failure to properly match corresponding generations of airways and arteries). The quartiles of percentage of AAR greater than 1 are only one feature, versus the several features of the visual scores. However, a strength of an AI-based imaging metric is that it will likely provide the same result for a given CT scan on different instances, as demonstrated by a perfect intrascan reproducibility for the percentage of AAR greater than 1 (Appendix E1 [online]). However, it is likely that human readers' measurements and visual inspections present more variation across instances. A potential use of an AI-based tool would be as an aid in quickly identifying CT scans with features of bronchiectasis for an in-depth human inspection.

In patients with coexisting COPD and bronchiectasis, the prevalence of exacerbations can reach up to 72% (18,28,29). During a 4-year follow-up, COPD increased the risk of exacerbation by 43% in patients with bronchiectasis (16). Our study showed that an increased percentage of AAR greater than 1 was associated with a higher total number of exacerbations over time in the entire cohort of ever-smokers and in those with COPD and its main phenotypes: emphysema and chronic bronchitis. The findings support a contribution of structural factors to exacerbation and may help explain why these episodes are frequent in individuals with coexisting COPD and bronchiectasis, supporting previous observations that demonstrated that an increased burden of small airway disease on CT scans is linked to a higher exacerbation risk in ever-smokers with COPD-and-bronchiectasis overlap (19). Note that the airway wall area was the smallest in participants in quartile 4 of the percentage of AAR greater than 1 (Table 1), suggesting that in the smoking population, a percentage of AAR greater than 1 may reflect the effect of airway dilation on wall thickening, a distinct type of bronchiectatic airway, or a bronchovascular process that deserves further investigation. The results also suggest that percentage of AAR greater than 1 seems to provide complementary information about the exacerbations over time to that of airway wall thickening and emphysema, which were included in the models. Additionally, the association of the combined percentage of AAR greater than 1 and clinical manifestations with exacerbations over time was stronger than that of the percentage of AAR greater than 1 alone, supporting recommendations by experts regarding the use of both imaging and clinical features to define bronchiectasis for clinical trials (30). These findings agree with bronchiectasis and COPD studies showing the effects of clinical manifestations on future exacerbations, such as chronic cough, chronic phlegm, and a history of exacerbations (16,31). We also observed effects of percentage of AAR greater than 1 on the total number of exacerbations in participants with two main phenotypes of COPD: emphysema and chronic bronchitis. The findings were consistent with those of smaller studies in patients with coexisting bronchiectasis-chronic bronchitis and bronchiectasis-emphysema (19,32). Collectively, these findings suggest a complex interplay between bronchiectasis at CT and smoking-related pathologic findings that modifies susceptibility to exacerbations.

We observed that in preserved ratio impaired spirometry and at-risk individuals, a higher percentage of AAR greater than 1 tended to be associated with a higher total number of exacerbations over time, although the difference was not statistically significant. The associations were stronger and statistically significant in at-risk participants meeting the definition of bronchiectasis. These findings highlight the relevance of respiratory symptoms and structural lung damage in ever-smokers who do not meet the spirometric criteria for COPD.

Additionally, a higher percentage of AAR greater than 1 was cross-sectionally associated with lung function impairment and respiratory symptoms. Prior studies (33,34) yielded different results for the association of quantitative and subjective measures of bronchiectasis with lung function and symptoms. The association of an increased percentage of AAR greater than 1 with lung function impairment, phlegm, and dyspnea is particularly relevant because bronchiectasis at CT in the COPDGene cohort was mostly mild to moderate, suggesting that the metric seemed sensitive to the clinical manifestations of diseases (19).

A concern about the AARs is that functional and pathologic changes in the intraparenchymal pulmonary vasculature, such as hypoxemia-induced vasoconstriction, increased vessel size, and vessel remodeling, can increase or decrease the AARs. This could potentially lead to overdiagnosis and underdiagnosis of bronchiectasis at CT (7). The high SS AARs evaluated in a few airway sections were from smaller arteries, which was likely related to hypoxemia-induced vasoconstriction (9). The percentage of the AAR greater than 1 metric did not show this pattern because it was directly related to airway lumen diameter and was not related to the mean artery diameter or a small pulmonary artery volume, supporting its association with airway size. Additionally, the association between oxygen saturation and the percentage of AAR greater than 1 was statistically significant but weak (Pearson correlation coefficient r = -0.036; P = .02), and this factor was accounted for in our models. Thus, the results suggest that AI-based techniques might be considered along with other features to assess bronchiectasis at CT (25). If this metric is validated in other cohorts, it may provide a quantitative imaging marker for clinical and epidemiologic investigation.

Several study limitations are noted. First, the COPDGene cohort included heavy eversmokers, so caution should be exercised when extrapolating these findings. Second, although the COPDGene study excluded participants who reported clinically diagnosed bronchiectasis, high-quality volumetric CT scans made testing an imaging algorithm for AARs possible. Third, the imaging algorithm was not validated at histologic analysis. However, in a previous study (35), presurgical CT and resected lung tissue assessments of AARs were related. Fourth, we used only one AAR cutoff point; therefore, comparisons with other cutoff points are lacking.

In summary, in a smoking cohort, an increased percentage of airway-to-artery diameter ratio (AAR) greater than 1 was associated with a higher total number of exacerbations over time. The associations were stronger when the percentage of AAR greater than 1 was combined with clinical features of bronchiectasis and in those with chronic obstructive pulmonary disease, emphysema, and chronic bronchitis. Further studies determining the optimal cutoff

points of automated airway-to-artery diameter ratios for the diagnosis and prognosis of bronchiectasis are desirable.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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## Data sharing:

Data generated or analyzed during the study are available from the corresponding author by request.

# Abbreviations

AAR	airway-to-artery diameter ratio		
AI	artificial intelligence		
COPD	chronic obstructive pulmonary disease		
FEV <sub>1</sub>	forced expiratory volume in 1 second		
RR	risk ratio		
SS	single section		

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### Key Results

- Using the COPDGene cohort, an artificial intelligence–based tool was developed to measure the airway-to-artery diameter ratios (AAR), a measure of bronchiectasis, at chest CT.
- Overall, a higher percentage of AAR greater than 1 was associated with a higher number of exacerbations (adjusted risk ratio [RR], 1.08; P=.01, quartile 4 vs quartile 1).
- Similar results were observed in participants with chronic obstructive pulmonary disease (adjusted RR, 1.10; *P*=.02), emphysema (adjusted RR, 1.13; *P*=.006), and chronic bronchitis (adjusted RR, 1.22; *P*=.002).



#### Figure 1:

Flowchart of COPDGene participant selection. A percentage of airway-to-artery diameter ratio (AAR) greater than 1 is the percentage of artificial intelligence (AI)–based AARs greater than 1.



#### Figure 2:

Three-dimensional CT reconstructions of the pulmonary arterial and bronchial trees. (**A**, **C**) The pulmonary arterial tree is color-coded, with cyan and blue indicating large and small branches, respectively, and the bronchial tree is color-coded, with red and orange indicating large and small branches, respectively. (**A**, **B**) Images in a 66-year-old woman with chronic obstructive pulmonary disease (COPD) without bronchiectasis. (**C**, **D**) Images in a 80-year-old woman with COPD with bronchiectasis (arrowheads in **D**). (**B**, **D**) Images show the percentage of artificial intelligence–based airway-to-artery diameter ratios (AARs) greater than 1.



#### Figure 3:

Matching process to compute artificial intelligence-based CT measurements of the airwayto-artery diameter ratios (AARs). (A) An airway with an accompanying pulmonary artery selected (green rectangle) to illustrate the process. (B) Particles in the airway lumen and accompanying artery. Dashed lines indicate airway and artery particles that match each other (ie, matching candidate pairs). The green ellipse depicts the airway-to-artery particle pair used to compute an AAR. The technique calculates thousands of AARs per CT image.

Percentage of AAR>	1 Effect (Quartile 4 vs 1)	High Percentage of AA	R>1 + Clinical Manifestation Effect
	RR [95% CI]		RR [95% CI]
Overall A	<b>—</b>	В	
PRISm	1.08 [1.02 - 1.15] P= .01		1.37 [1.31 - 1.43] P<.001
	1.15 [0.88 - 1.50] P= .30	-	1 15 [0.95 - 1.39] P = 16
-At-Risk			
CORD	1.09 [0.94 - 1.26] P= .26		1.61 [1.45 - 1.79] P<.001
-COPD	1.10 [1.02 - 1.18] P= .02		1.32 [1.26 - 1.39] P<.001
Emphysema	<b>—</b>		
1 9	1.13 [1.04 - 1.24] P= .006		1.38 [1.30 - 1.46] P<.001
Chronic	1.22 [1.08 - 1.38] P= .002		1.46 [1.34 - 1.59] P<.001
Bronchitis			
0.5 0.6 0.7 0.8 0.9	1.0 1.1 1.2 1.3 1.4 1.5	1.6 0.5 0.6 0.7 0.8 0.9 1	.0 1.1 1.2 1.3 1.4 1.5 1.6 1.7 1.8 1.9

Risk ratio [RR] of total number of exacerbations during follow up

#### Figure 4:

(A, B) Forest plots of the association of the percentage of airway-to-artery diameter ratios (AAR) greater than 1 at CT (quartile 4 vs 1) alone (A) and a high percentage of AAR greater than 1 (3%) and clinical manifestations (B) with exacerbations over time, according to spirometric and phenotypic groups. The estimates represent the risk ratio (RRs) of the total number of exacerbations during the follow-up time and 95% CIs from multivariable Poisson zero-inflated models. The model included all quartiles, and the figure reported estimates for quartile 4 only, using quartile 1 as a reference. COPD = chronic obstructive pulmonary disease, PRISm = preserved ratio impaired spirometry.

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Characteristic	Quartile 1 ( $n = 1567$ )	Quartile 2 ( $n = 648$ )	Quartile 3 $(n = 1089)$	Quartile 4 ( $n = 888$ )
Age (y)	57.1 (50.9–64.3)	59.6 (52.2–66.6)	60.7 (52.6–67.8)	61.1 (53.3–68.9)
Men*	464 (29.6)	300 (46.3)	615 (56.5)	499 (56.2)
Non-Hispanic White *	1022 (65.2)	420 (64.8)	755 (69.3)	549 (61.8)
Height (cm)	165.1 (160.0–171.0)	168.0 (162.0–175.0)	170.2 (164.0–177.0)	170.5 (163.8–178.3)
BMI (kg/m <sup>2</sup> )	28.6 (25.0–32.8)	28.1 (24.4–32.3)	28.8 (24.9–33.1)	27.8 (24.3–32.5)
Pack-years smoked	37.7 (25.4–51.2)	39.6 (26.9–54.0)	39.0 (26.5–54.0)	39.0 (26.0–58.6)
Current smoking status *	944 (60.2)	359 (55.4)	490 (45.0)	374 (42.1)
$\operatorname{Cough}^*$	610 (38.9)	221 (34.1)	395 (36.3)	328 (36.9)
Phlegm*	534 (34.1)	239 (36.9)	393 (36.1)	372 (41.9)
mMRC dyspnea score 2*	619 (39.6)	276 (42.7)	495 (45.6)	468 (52.8)
Two or more exacerbations in the year before enrollment $^{st}$	109 (28.8)	60 (15.9)	98 (25.9)	111 (29.4)
Resting oxygen saturation (%)	97 (96–98)	97 (95–98)	96 (95–98)	96 (95–98)
FEV <sub>1</sub> (L)	2.13 (1.68–2.60)	2.12 (1.50–2.76)	2.20 (1.46–2.84)	2.14 (1.22–2.92)
FEV <sub>1</sub> percent predicted	82.3 (68.3–94.6)	77.8 (57.2–92.9)	78.0 (53.9–93.0)	77.6 (48.2–99.0)
FVC (L)	2.95 (2.44–3.51)	3.05 (2.47–3.80)	3.23 (2.52–3.91)	3.18 (2.43-4.04)
FVC percent predicted	87.5 (76.3–98.3)	86.9 (74.9–98.5)	86.7 (74.1–97.1)	88.5 (72.5–100.8)
FEV <sub>1</sub> -to-FVC ratio	0.74 (0.65–0.80)	0.71 (0.56–0.78)	0.70 (0.53–0.78)	0.69(0.49-0.78)
LAA-950 (%)	0.86 (0.27–2.99)	1.70 (0.51–6.31)	2.83 (0.79–10.62)	$3.70\ (1.00{-}10.85)$
Pi10 (mm)	2.31 (2.04–2.68)	2.35 (1.96–2.82)	2.23 (1.87–2.78)	2.13 (1.69–2.95)
AAR > 1 (%)	0 (0–1)	2 (2,3)	5 (4–6)	11 (9–15)

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mMRC dyspnea score, nine participants; LAA-950 and square root of the wall area of a hypothetical 10-mm inner-perimeter airway (Pi10) at CT, 233 participants. Percentage of airway-to-artery diameter Note ----Unless otherwise indicated, data are medians; data in parentheses are IQRs. Number of participants with missing values: pack-years, three participants; resting oxygen saturation, two participants; ratio (AAR) greater than 1 is the percentage of artificial intelligence-based AARs greater than 1. BMI = body mass index, FEV1 = forced expiratory volume in 1 second, FVC = forced vital capacity, LAA-950 = low attenuation areas less than -950 HU, mMRC = modified Medical Research Council, Pi10 = the square root of the wall area of a hypothetical 10-mm inner-perimeter airway.

\* Data are numerators, with percentages in parentheses.

	Participants Meeting the Broncl	niectasis Definition Criteria	
Characteristic	Did Not Meet $(n = 3180)$	Met $(n = 1012)$	P Value
Age (y)	58.9 (52.0–66.2)	59.2 (52.0–66.6)	.04
Men*	1317 (41.4)	561 (55.4)	<.001
Non-Hispanic White *	2124 (66.8)	622 (61.5)	.002
Height (cm)	167.6 (161.3–175.0)	170.2 (163.5–177.0)	<.001
BMI (kg/m <sup>2</sup> )	28.3 (24.8–32.5)	28.8 (24.7–33.8)	.03
Pack-years smoked	37.5 (25.0–51.0)	42.3 (30.5–62.5)	<.001
Current smoking status *	1641 (51.6)	526 (52.0)	.84
Cough*	807 (25.4)	747 (73.81)	<.001
Phiegm*	755 (23.7)	783 (77.4)	<.001
mMRC dyspnea score $2^*$	1092 (34.4)	855 (75.7)	<.001
Two or more exacerbations in the year before enrollment $^{\ast}$	140 (4.4)	238 (23.5)	<.001
Resting oxygen saturation (%)	97 (95–98)	96 (94–98)	<.001
FEV <sub>1</sub> (L)	2.24 (1.69–2.80)	1.71 (1.10–2.51)	<.001
FEV <sub>1</sub> percent predicted	83.8 (67.0–96.7)	62.3 (40.5–83.4)	<.001
FVC (L)	3.10 (2.51–3.79)	2.89 (2.26–3.66)	<.001
FVC percent predicted	89.0 (67.0–96.6)	79.8 (66.8–93.6)	<.001
FEV <sub>1</sub> -to-FVC ratio	0.74~(0.63-0.80)	0.61 (0.44–0.75)	<.001
LAA_950 (%)	1.42 (0.41–4.87)	4.13(0.88 - 15.90)	<.001
Pi10 (mm)	2.23 (1.90–2.66)	2.57 (2.04–3.16)	<.001
AAR >1(%)	2 (0–5)	7 (4–10)	<.001

Characteristics of the Participants by Bronchiectasis Definition Status

Note.—Unless otherwise indicated, data are medians and data in parentheses are IQRs. Percentage of airway-to-artery diameter ratio (AAR) greater than 1 is the percentage of artificial intelligence-based AARs greater than 1. BMI = body mass index, FEV I = forced expiratory volume in 1 second, FVC = forced vital capacity, LAA-950 = low attenuation areas less than -950 HU, mMRC = modified Medical Research Council, Pi10 = the square root of the wall area of a hypothetical 10-mm inner-perimeter airway.

\* Data are numerators, with percentages in parentheses.

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Table 2:

#### Table 3:

Comparison of the Quartiles of Percentage of Airway-to-Artery Diameter Ratio Greater than 1 and Visual Bronchiectasis CT Severity Scores

	Median Values of Percentage of AAR >1 for Each Quartile			
Visual C Score	T Quartile 1, 0%	Quartile 2, 2%	Quartile 3, 5%	Quartile 4, 11%
0	199*	80 <sup>†</sup>	128 <sup>†</sup>	85 <sup>†</sup>
1–2	39	12*	24	22
3–5	24	8	22*	28
>5	7	6	20	20*

Note.—The data from 724 COPDGene study participants were used. The percentage of airway-to-artery diameter ratio (AAR) greater than 1 classified 50.7% (367 of 724) of CT scans as one category above and 14.4% (104 of 724) of CT scans as one category below the visual score. Percentage of AAR greater than 1 is the percentage of artificial intelligence–based AARs greater than 1 on CT scans.

\* Visual bronchiectasis CT severity scores and quartiles of percentage of AAR greater than 1 agreed in 253 of 724 (34.9%) of CT scans.

 $^{\dagger}$ The highest discrepancy was in participants without bronchiectasis at visual assessment (score of 0) but classified as having quartile 2–4 of percentage of AAR greater than 1 (293 of 724; 40.5%).