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Title: Airway wall thickness and COPD: Analysis of spatially comparable airways. The MESA COPD study

Dr. Benjamin 25067 Smith benjamin.m.smith@mcgill.ca MD ^{1,2}, Dr. Eric 25068 Hoffman eric-hoffman@uiowa.edu ³, Dr. Kathleen 25069 Donohue kd2128@columbia.edu MD ¹, Dr. Dan 25070 Rabinowitz dan@stat.columbia.edu ⁴ and Dr. R. Graham 25071 Barr rgb9@columbia.edu MD ¹. ¹ Medicine, Columbia University, New York, NY, United States, 10032 ; ² Medicine, McGill University, Montreal, QC, Canada, H3G1A4 ; ³ Radiology, University of Iowa, Iowa City, IA, United States, 52242 and ⁴ Statistics, Columbia University, New York, NY, United States, 10027 .

Body: The relationship of airway remodelling to COPD is poorly understood. COPD is associated with loss of peripheral airways and reduced airway lumen dimensions, which may introduce bias when sampling airways to evaluate wall thickness. We assessed the relationship between airway wall thickness and COPD using spatially comparable bronchi. The MESA COPD Study recruited smokers aged 50–79 yrs. Spatially comparable airways were defined by 3 approaches: anatomic name, generation number and distance from trachea. Airway dimensions were quantified by CT using APOLLO software (Vida). Analyses were adjusted for age, sex, body size, race and lung volume. Among 314 participants, 47% had COPD. Comparing anatomically matched airways, there were greater odds of COPD with decreasing wall thickness (Table). Similar associations were obtained matching on generation or distance from the trachea. In contrast, airways sampled by lumen diameter were more proximal in COPD compared to controls ($p < 0.001$), and the association with wall thickness was reversed (Table).

Table: Odds of COPD per standard deviation DECREMENT in airway wall thickness (95%CI)

Anatomically matched bronchi	Trachea: 1.1 (0.7to1.6)	Mainstems: 1.3 (1.0to1.5)	Lobar: 1.2 (1.0to1.4)	Segmental: 1.3 (1.2to1.5)	Subsegmental: 1.4 (1.2to1.6)
Lumen diameter matched bronchi	>11mm: 1.0 (0.9to1.2)	11to9mm: 0.9 (0.8to1.2)	9to7mm: 0.8 (0.7to0.9)	7to5mm: 0.7 (0.6to0.8)	5to3mm: 0.8 (0.8to0.9)

Analysis of spatially comparable airways demonstrated increased odds of COPD with decreasing wall thickness. In contrast, sampling airways by lumen diameter resulted in selection of more proximal airways in COPD compared to controls and introduced bias in the assessment of airway wall dimensions.