Title: Computed Tomography Airway Count in Asthma: Relationships with Asthma Severity and Airway Structure-function

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Structured Abstract:

Introduction: In patients with asthma, airway abnormalities may affect the entire airway tree. The large airways have been extensively evaluating using x-ray CT, which has provided strong evidence of thickened airway walls and airway occlusions [1, 2]. Recently, in patients with mild chronic obstructive pulmonary disease (COPD), the total number of airways visible on CT, or total airway count (TAC), revealed missing distal airways that were associated with thinning airway walls [3]. We wondered if these airway observations in COPD have implications for airways disease in asthma and accordingly, our objective was to evaluate CT TAC in patients with asthma across a range of asthma severities and explore potential relationships of TAC with asthma severity, airway morphology, pulmonary function and pulmonary functional magnetic resonance imaging (MRI).

Methods: Participants underwent pulmonary function tests, CT and hyperpolarized 3He MRI. Airways were segmented from CT using commercial software (VIDA Diagnostics Inc., Coralville, USA). CT TAC was quantified as the sum of airways in the segmented airway tree [3] and airway wall area percent (WA%) and lumen area (LA) were measured. MRI ventilation abnormalities were quantified as the ventilation defect percent (VDP) [4]. Asthma severity was defined according to Global Initiative for Asthma (GINA) treatment steps [5] and TAC was compared between asthma severity groups using an analysis of covariance (ANCOVA) adjusted by age, sex and body mass index (BMI) as potential covariates, with post-hoc Holm-Bonferroni correction for multiple comparisons. Multivariable models were generated to determine the relative contributions of CT airway measurements and MRI VDP to pulmonary function.

Results: We evaluated 70 participants including 15 mild, 19 moderate and 36 severe asthmatics. As compared with mild, TAC was significantly diminished in moderate (p=0.03) and severe asthma (p=0.045). Fifth generation airways were CT-invisible or missing in 69/70 participants; the most common number missing was 10. Participants with ≥10 missing airways (n=34) had worse WA% (p<0.0001), LA (p<0.0001) and VDP (p=0.03) than those with <10 missing airways (n=36). In a multivariable model, CT TAC (β=0.27, p=0.03) and MRI VDP (β=0.53, p<0.0001) combined to predict the forced expiratory volume in 1s (FEV1; R=0.70, p<0.0001).

Discussion: Participants with a greater number of missing airways had worse MRI ventilation. Thicker airway walls and narrower lumens in airways with missing daughter branches suggest that it is obstruction, and not airway destruction that is responsible for our findings. MRI in combination with CT provides a structure-function personalized imaging approach to evaluate patients with asthma.