

Title: Pulmonary Imaging to Understand Asthma Progression to Chronic Obstructive Pulmonary Disease

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Structured Abstract:

In patients with asthma, chronic airways disease typically results in variable airflow obstruction that may be partially or completely reversed with bronchodilators. Many asthmatics maintain stable lung function and bronchodilator reversibility over time, while a subset of patients may experience accelerated lung function decline and eventually lose post-bronchodilator reversibility. Recent epidemiological studies (To et al, 2016; To et al, 2017) have revealed that in up to 10% of asthmatics, airways disease may lead to chronic, persistent airflow obstruction and chronic obstructive pulmonary disease (COPD), but the mechanisms underlying these changes are not fully understood.

Airway remodeling caused by chronic inflammation has been suggested to mediate changes that result in irreversible airflow obstruction. Hyperpolarized noble gas magnetic resonance imaging (MRI) provides a way to probe airway function and has revealed the presence of non-random ventilation defects in asthma that are the functional consequences of airway remodeling, inflammation and/or mucus plugging (Svenningsen et al, 2018). We postulated that MRI ventilation defects could be a sensitive predictor of diminished post-bronchodilator reversibility in patients with asthma. In 11 patients with mild-moderate asthma in whom there were no changes in mean lung function, medication or exacerbations, MRI ventilation defects were spatially persistent and uniquely predicted post-bronchodilator reversibility approximately 6.5 years later.

Remodeled and inflamed airways can also be segmented and directly measured using thoracic x-ray computed tomography (CT) from the trachea to the smaller airways at the resolution limit of the CT system (~2mm). The total number of CT-segmented airways was previously shown to reflect early airway-related disease changes and play a role in bronchodilator response and accelerated disease progression in patients with early/mild COPD (Kirby et al, 2018). We wondered about CT total airway count (TAC) as a biomarker of asthma pathogenesis to COPD and hypothesized that TAC would also be related to bronchodilator reversibility in asthma. In a total of 58 patients with asthma, TAC was significantly related to bronchodilator reversibility and fixed airflow obstruction; participants meeting the criteria for fixed airflow obstruction for COPD had significantly less airways than those that did not have fixed airflow obstruction.

Although epidemiological studies have suggested that asthma progression to COPD may be relatively common, it remains difficult to identify patients that are at risk for disease worsening including loss of bronchodilator reversibility using current clinical tools. Our results suggest pulmonary MRI and CT biomarkers may help understand the transition from asthma to fixed airflow obstruction and COPD and identify patients at-risk.