Toward Population-based Analysis: Improved CT-based Measures of Air-trapping and Airway Dimension in a Multi-Center Asthmatic Study

Ching-Long Lin1,2, Sanghun Choi1,2,3, Sally E. Wenzel5 and Mario Castro6
and Eric A. Hoffman3,4

1Department of Mechanical and Industrial Engineering, 2IIHR-Hydroscience & Engineering,
3Department of Biomedical Engineering, 4Department of Radiology,
The University of Iowa, Iowa City, Iowa, U.S.A.
5Division of Pulmonary, Allergy, and Critical Care Medicine,
The University of Pittsburgh, Pennsylvania, U.S.A.
6Department of Internal Medicine and Pediatrics, Washington University,
St. Louis, Missouri, U.S.A.

Abstract

Rationale: Quantitative computed tomography (CT)-based images of total lung capacity (TLC) and functional residual capacity (FRC) have been used to analyze airway dimension and air-trapping (residual air), respectively. However, existing studies of luminal area (LA) and wall thickness (WT) were inconclusive among different studies, and the existing density-threshold air-trapping method was problematic due to differences in multi-center scanners and breath-hold coaching methods. This study introduces a fraction-threshold air-trapping method that adjusts for inter-site and inter-subject variations, and further investigates the alterations of LA and WT in asthmatic populations along with the improved normalization. This is a critical step toward population-based analysis that allows utilization of CT data collected by multiple centers.

Methods: CT images of 50 healthy, 42 non-severe asthmatic and 52 severe asthmatic subjects at TLC and FRC were employed. The data were acquired via two centers of NIH-sponsored severe asthma research program (SARP) at the University of Pittsburgh and the Washington University in Saint Louis, and a NIH bioengineering research partnership at the University of Iowa. A new fraction-based approach with the Hounsfield Unit of air corrected by tracheal density was applied to quantify air-trapping percentage (AirT%), and a new slope-based clustering method was employed to control lung volume variation at FRC. Besides, pulmonary function test (PFT)-based TLC lung volume was used to improve normalization of dimensional variables, such as LA and WT, and subsequently control inter-subject variability.

Results: The fraction-based measure of air-trapping collapses data of healthy subjects into a single regression line regardless of scanner variation, and differentiates the regression of severe asthmatics from that of healthy subjects and non-severe asthmatics. Consequently, as compared with traditional constant-value-based clustering, the new slope-based clustering method reduces misclassification rate of healthy subjects to air-trapped severe asthmatics from 50% to 22%. The bulk WT increases in both non-severe and severe asthmatics. The LA and luminal circularity are significantly reduced in severe asthmatics, being different from non-severe asthmatics. Furthermore, the air-trapped regions detected in asthmatics are significantly correlated with the reduced hydraulic diameter caused by airway constriction and non-circularity.

Conclusions: The fraction-based measure of air-trapping enables differentiation of severe asthma from non-severe asthma and healthy population. We speculate that regional alterations of airways shall be associated with abnormal lung function, i.e. air-trapping.

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