Significant lung airway feature extraction via composite bridge regression: how lung airway remodeling impairs asthma quality of life

Kung-Sik Chan1,2, Kun Chen6, Eric A. Hoffman4,5, Sally E. Wenzel7, Mario Castro8 and Ching-Long Lin2,3

1Department of Statistics & Actuarial Science, 2IIHR-Hydroscience & Engineering, 3Department of Mechanical & Industrial Engineering, 4Department of Biomedical Engineering, 5Department of Radiology, The University of Iowa, Iowa City, Iowa, U.S.A.
6Department of Statistics, University of Connecticut, Storrs, CT, U.S.A.
7Division of Pulmonary, Allergy, and Critical Care Medicine,
The University of Pittsburgh, Pennsylvania, U.S.A.
8Department of Internal Medicine and Pediatrics, Washington University,
St. Louis, Missouri, U.S.A.

Abstract

Rationale: An important health outcome for asthmatic patients is quality of life (QoL), for instance, as measured by the Juniper Asthma Quality of Life Questionnaire (AQLQ). It is pivotal to elucidate how lung remodeling affects QoL. To our knowledge, the problem of identifying which set of human lung airway features assessed via quanatitative computed tomography (QCT) for best predicting the AQLQ score has not been studied, the solution of which facilitates exploring how lung remodeling affects QoL.

Methods: The AQLQ scores, several demographic variables, plus CT images of 41 healthy, 23 non-severe asthmatic and 71 severe asthmatic subjects at TLC collected from two centers of NIH-sponsored severe asthma research program (SARP) were employed. Quantitative image analysis was performed via the Apollo Workstation (VIDA Diagnostics). A new composite bridge penalized regression scheme for feature selection was applied to jointly select which airway segment features, including generational average wall thickness, lumen area, diameter, etc. and the corresponding (within- and between-segment) variances, are significant predictors of the AQLQ score, across generations, and for each significant feature, simultaneously identify in which generations it is significant, after adjusting for age and BMI.

Results: QoL generally decreases with age ($p=0.005$) and BMI ($p=0.002$). Moreover, greater impairment of asthma quality of life is predicted by lung remodeling in terms of thicker wall of airway segments, increased within-segment variation and reduced between-segment variation in wall thickness ($p=0.01$; everything else being equal, these wall-thickness variables explained 10% of the variation in AQLQ score), reduced within-segment variation and increased between-segment variation in diameter ($p<0.0001$; 24%), increased within-segment variation in lumen area ($p<0.0001$; 16%), reduced mean perimeter and increased within-segment variation in perimeter ($p<0.0001$; 26%), more circular segment cross sectional geometry and increased shape differences between segments ($p=0.02$; 7%), plus the presence of lung hyperinflation as indicated by increased airway angle and reduced between-segment variation in angle ($p<0.0001$; 10%), in certain generations from the 1st to 6th generations.
Conclusions: Using the new penalized regression scheme allows us to find significant lung airway features that are associated with the global AQLQ score and domain AQLQ scores. The selected feature sets provide tools for further investigation (such as through the use of computational fluid dynamics to assess effects on breathing mechanics) as to how such feature combinations serve to effect QoL.
Acknowledgments: This work was supported in part by NIH grants U01 HL114494, R01 HL094315, R01 HL064368, R01 HL112986, R01 HL091762, U10 HL109257, UL1 TR000448 and S10 RR022421.