Title: Pulmonary arterial enlargement and acute exacerbations of COPD

Dr. James 1910 Wells jmwells@uab.edu MD 1, Dr. George 1922 Washko gwashko@partners.org MD 2, Dr. MeiLan 1923 Han mrking@med.umich.edu MD 3, Dr. Naseer 1924 Abbas nasr77@yahoo.com MD 1, Dr. Hrudyay 1925 Nath hnath@uabmc.edu MD 4, Dr. Albert 1926 Mamary albert.mamary@tuhs.temple.edu MD 5, Dr. Elizabeth 1929 Regan regane@njhealth.org MD 6, Prof. Dr William 1930 Bailey wcbailey@uab.edu MD 1, Prof. Dr Fernando 1935 Martinez fmartine@umich.edu MD 3, Ms. Elizabeth 1938 Westfall elizabeth.westfall@ccc.uab.edu 1, Dr. Russell 1941 Bowler bowlerr@njc.org MD 6 and Dr. Mark 1942 Dransfield mdransfield99@msn.com MD 1. 1 Lung Health Center, Division of Pulmonary and Critical Care, University of Alabama at Birmingham (UAB), AL, United States, 35294 ; 2 Pulmonary Division, Brigham & Women's Hospital, Boston, MA, United States, 02115 ; 3 Division of Pulmonary and Critical Care, University of Michigan, Ann Arbor, MI, United States, 48109 ; 4 Department of Radiology, University of Alabama at Birmingham (UAB), AL, United States, 35294 ; 5 Section of Pulmonary and Critical Care, Temple University, Philadelphia, PA, United States, 19122 and 6 Pulmonary Division, National Jewish Hospital, Denver, CO, United States, 80206.

Body: Background: Exacerbations of COPD (AECOPD) are associated with accelerated loss of lung function and mortality. Identification of patients at risk for these events, particularly those requiring hospitalization, is of major importance. Severe pulmonary hypertension is an important complication of advanced COPD and predicts AECOPD though pulmonary vascular abnormalities also occur early in the disease. We hypothesized that a computed tomography (CT) metric of pulmonary vascular disease (pulmonary artery (PA) enlargement as determined by a PA/Aorta (A) ratio > 1) would predict severe AECOPD. Methods: The COPDGene study is a multicenter, observational trial that enrolled current and former smokers with COPD. We determined the association between PA/A>1 and severe AECOPD through pulmonary vascular abnormalities also occur early in the disease. We hypothesized that a computed tomography (CT) metric of pulmonary vascular disease (pulmonary artery (PA) enlargement as determined by a PA/Aorta (A) ratio > 1) would predict severe AECOPD. Methods: The COPDGene study is a multicenter, observational trial that enrolled current and former smokers with COPD. We determined the association between PA/A>1 and severe AECOPD requiring hospitalization as reported at enrolment and then examined its utility as a predictor of these events in longitudinal follow-up as well as in an external validation cohort [Evaluation of COPD Longitudinally to Identify Predictive SurrogateEndpoints (ECLIPSE)] using logistic and zero-inflated negative binomial regression and adjusting for known risk factors for AECOPD. Results: Multivariate logistic regression demonstrated a significant association between PA/A>1 and severe AECOPD [OR 3.60 (95% CI, 2.49-5.22, p<0.001)] at enrolment in COPDGene. PA/A>1 also independently predicted the occurrence [OR 2.03 (95% CI, 1.17-3.49, p=0.01) in COPDGene and OR 2.80 (95% CI, 2.11-3.71, p<0.001) in ECLIPSE] and frequency of future severe AECOPD in both cohorts. In ECLIPSE, PA/A>1 was the strongest predictor of severe AECOPD over both 1 and 3 years of follow-up. Conclusions: CT detected pulmonary artery enlargement (PA/A>1) predicts severe COPD exacerbations.