European Respiratory Society
Annual Congress 2013

Abstract Number: 753

Publication Number: P4221

Abstract Group: 6.1. Epidemiology

Keyword 1: Biomarkers **Keyword 2:** Epidemiology **Keyword 3:** Spirometry

Title: Elevated serum iron as a marker for spirometric resistance to cigarette smoke: The Takahata study

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Body: Background: Many cigarette smokers develop COPD. However, pulmonary function is preserved in some elderly individuals despite smoking, and their characteristics have not been investigated. We aimed to identify a biomarker in individuals in whom lung health is maintained despite smoking. Methods: Blood sampling and spirometry were performed on 3,257 subjects who participated in a community-based annual health check in Takahata, Japan, from 2004 to 2006. We selected 119 elderly smokers (age ≥ 70, Brinkman index ≥ 600, smoking years ≥ 30). The ‘smoking resistant’ group met the following criteria: $FEV_1/FVC \geq 0.7$, and FEV_1 %predicted ≥ 80. Spirometry was re-evaluated in 147 male, current smokers in 2009. Results: Increased serum iron (sFe) levels were demonstrated in the smoke resistant group compared with the non-resistant group. In those with low sFe levels, FEV_1/FVC was reduced in males, and FEV_1 %predicted was reduced in females. These spirometric measures were positively associated with sFe levels in men, but not in women. Multiple linear regression analysis revealed that sFe levels were predictive for spirometric values, independent of other clinical factors. In addition, sFe levels were predictive for a decline in FEV_1. Conclusion: Serum iron levels may be a biomarker for the spirometric susceptibility of individuals to cigarette smoke.