Risk Factors for Polycythemia and Increased Hematocrit in Smokers with and Without Chronic Obstructive Pulmonary Disease

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Introduction/Rationale: Cigarette smoking and chronic obstructive pulmonary disease (COPD) are both frequently associated with secondary polycythemia. However, risk factors for polycythemia and increased hematocrit have not been studied in a large cohort of extensively phenotyped smokers with and without COPD. Methods: Current and former smokers from the COPDGene study were analyzed. Polycythemia was defined with the 2016 WHO diagnostic criteria: hemoglobin >16.5 g/dL and/or hematocrit >49% in men; hemoglobin >16.0 g/dL and/or hematocrit >48% in women. Age, sex, race (non-Hispanic White and African American), smoking status, spirometry (forced expiratory volume in 1s [FEV₁] % predicted, forced vital capacity [FVC] % predicted, and FEV₁/FVC % predicted), oxygen saturation (SpO₂, four tiers with 88, 92, and 96% as cutoffs), long-term oxygen therapy (LTOT), obstructive sleep apnea, chronic kidney disease (CKD), congestive heart failure (CHF), and quantitative chest computed tomography (CT) measurements of emphysema and expiratory gas trapping were evaluated for association with polycythemia and hematocrit. Logistic and linear regression analyses were conducted in R v3.6. Results: In a total of 5529 subjects from the COPDGene, polycythemia was found in 224 (8.0%) of male and 63 (2.3%) of female participants. The mean hematocrit levels were 43.2% (standard deviation 4.3%) in males and 40.7% (3.7%) in females. In multivariable logistic model, worse FEV₁ % predicted (OR 1.10 per decrease by 10-point, 95% CI 1.04-1.18) and SpO₂ (OR 1.54 per one-tier worsening, CI 1.27-1.88), male sex (OR 3.92, CI 2.92-5.25), current smoking (OR 2.35, CI 1.80-3.06), and Denver location (OR 4.16, CI 3.05-5.67) were associated with higher risk for polycythemia. In addition, subjects with LTOT at rest (OR 0.16, CI 0.08-0.33) and during sleep (OR 0.52, CI 0.29-0.92), CKD (OR 0.10, CI 0.01-0.69), and African American race (OR 0.63, CI 0.46-0.86) had lower prevalence of polycythemia. In multivariable linear model, male sex, current smoking, Denver location, and worse SpO₂ were associated with significantly higher hematocrit level, and percent emphysema on CT was positively associated with hematocrit level (β=0.05, CI=0.03-0.06). Additionally, age, African American race, use of LTOT, and comorbidities of CKD and CHF were negatively associated with hematocrit level. Conclusion: In a large cohort of smokers, lower FEV₁ and oxygen saturation, male sex, and current smoking were associated with increased risk while use of LTOT at rest and during sleep and African American race were associated with decreased risk for polycythemia. In addition, percent emphysema on CT was positively associated with hematocrit level.

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