

Mucus Plugs Occluding COPD Airways: A Review of Their Clinical Impact

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COPD is a heterogenous, complex disease. Changes to the mucociliary system are central airway pathology of COPD. The airway pathology is characterized by excess mucus production, hypersecretion, and reduced clearance, leading to accumulation in the airways as plugs.¹ Mucus plugs completely occluding the medium-to-large-sized airways (i.e., ~2-10 mm-lumen diameter) are observed on computed tomography (CT) scans in up to 67% of individuals with COPD and are associated with airflow obstruction, lower oxygen saturation, and reduced exercise capacity.^{2,3} Further, up to 30% of individuals with COPD who do not report cough or phlegm, typical symptoms of mucus pathology, present with mucus plugs occluding airway lumen.² As mucus plugs provide a potential target for therapeutical intervention, further preliminary studies have investigated whether this airway pathology is associated with clinically relevant outcomes, such as exacerbations, mortality, and changes in lung function.

In participants with COPD from the COPDGene cohort, during a median follow-up of over 9 years, the incidence of exacerbations per 100 person-years was 43.7, 62.4, and 74.6 for participants with 0, 1-2, and ≥ 3 lung segments with mucus plugs, respectively. In adjusted models, airway mucus plugs were associated with increased frequency of total exacerbations during follow-up (rate ratio [RR] [95% confidence interval], 1.07 [1.03 – 1.11] and RR 1.14 [1.10 – 1.19] for those with 1-2 vs 0 and ≥ 3 vs 0 lung segments with mucus plugs). The all-cause mortality rate in participants with COPD without mucus plugs and 1-2 and ≥ 3 lung segments with mucus plugs was 34%, 47%, and 54%, respectively. In adjusted models, the presence of mucus plugs was associated increased risk of all-cause mortality (adjusted hazard ratio of death of 1.15 [95% CI, 1.02 – 1.29] and 1.24 [95% CI, 1.10 – 1.41] for those with 1-2 vs. 0 and ≥ 3 vs. 0 lung segments with mucus plugs, respectively). Finally, in participants with both baseline and 5-yr CT scans evaluated, persistently positive vs. persistently negative mucus plug status was associated with a greater decline in FEV₁ (-65.5 mL [SE 20.7], p=0.002; -2.66 % predicted [SE 0.74], p<0.001) and higher odds of rapid decline in FEV₁, i.e., drop in FEV₁>40 mL per year (OR [95% CI] 1.59 [1.19 – 2.12]). When compared to persistently positive, resolved mucus plugs status was associated with improvement in FEV₁ (97.6 mL [SE 23.2], p<0.001; 4.07% predicted [SE 0.83], p<0.001). The results suggest that mucus pathology is associated with important COPD outcomes and support further investigation of therapeutic interventions targeting mucus plugs.

References

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