Study linking mucus plugs and COPD mortality could help save lives

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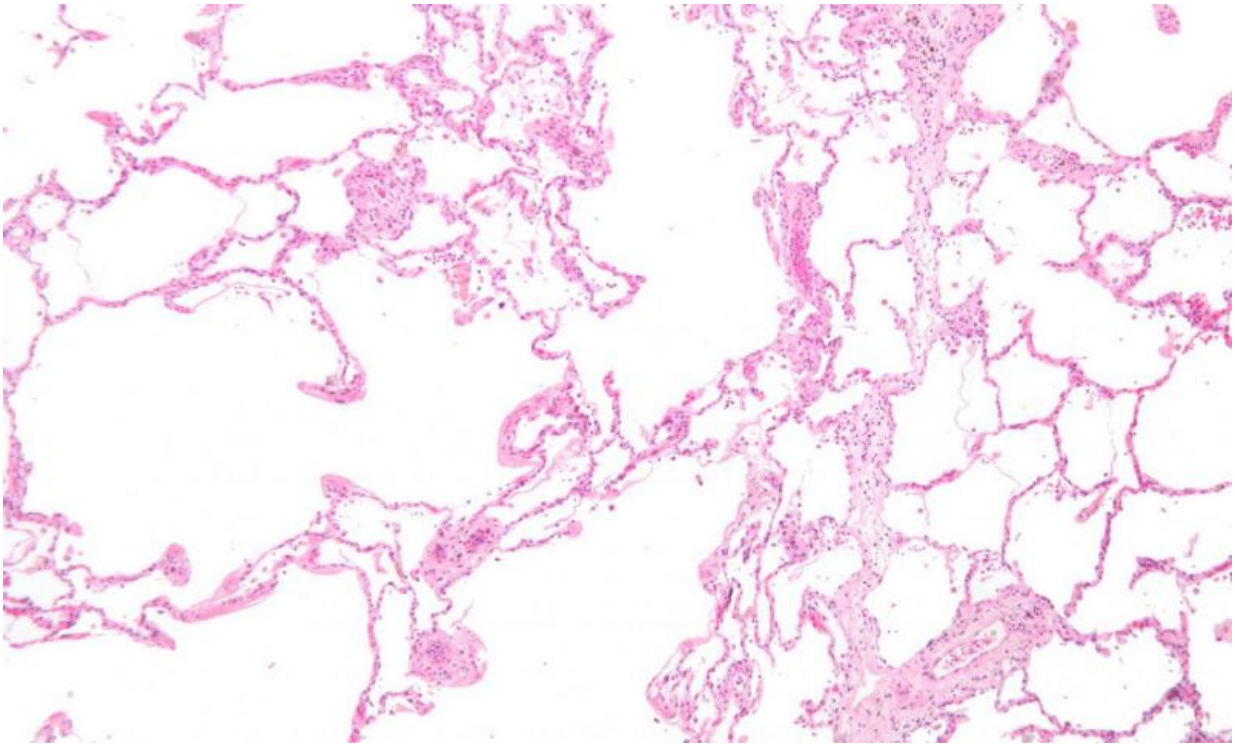

Micrograph showing emphysema (left – large empty spaces) and lung tissue with relative preservation of the alveoli (right). Credit: Wikipedia, CC-BY-SA 3.0

A retrospective analysis of patient data from the COPDGene study suggests that targeting mucus plugs could help prevent deaths from chronic obstructive pulmonary disease—the fourth leading cause of death in the United States

Many patients with chronic obstructive pulmonary disease (COPD) experience airway-clogging mucus plugs, an accumulation of mucus in the lungs that can affect quality of life and lung functioning. A new study led by researchers from Brigham and Women's Hospital, a founding member of the Mass General Brigham healthcare system, has found that mucus plugs were also associated with greater mortality. The findings, published in *JAMA* and presented simultaneously at the American Thoracic Society 2023 International Conference, could help doctors reduce the death toll of COPD, which is one of the most common and deadly respiratory diseases.

"As a chronic disease, COPD can't be cured, but our findings suggest that using therapies to break up these mucus plugs could help improve outcomes for COPD patients, which is the next best thing," said corresponding author Alejandro A. Diaz, MD MPH, an associate scientist in the Division of Pulmonary and Critical Care Medicine at the Brigham. "Mucus is something that we already know a lot about from a basic science standpoint, and there are also a lot of mucus-targeting therapies that either already exist or are in development for other diseases, so it's an extremely promising target."

COPD affects 15.9 million people in the United States and is the fourth leading cause of death. It most often occurs as a result of cigarette smoking or long-term exposure to air pollutants. The progression of COPD can be slowed by eliminating the exposure to these pollutants, but there is no way to cure the disease. And the standard therapeutic approach for COPD has gone largely unchanged for many years.

"For the last four decades we've had only two targets for COPD therapies –either promoting bronchial dilation, which means making the airways themselves wider, or reducing bronchial inflammation," said Diaz. "This is telling us that there may be more we can do about this disease than we realized before."

The current study was an observational retrospective analysis of data from the Genetic Epidemiology of COPD (COPDGene) study, a large-scale clinical study that aimed to investigating the underlying genetic risk factors of COPD. The study included over 10,000 participants, recruited between 2007 and 2011, and included people with COPD at different stages, from the mildest to the most severe.

For this new observational study, the researchers looked at data from over 4,000 of these patients. To determine which patients had mucus plugs, the researchers analyzed chest CT scans from the patients, taken at their first visit to the clinic. Performing CT scans on all patients regardless of their self-reported symptoms allowed the researchers to find mucus plugs even in patients who did not feel sick.

"Creating mucus is a normal part of the body's immune response, but usually we cough it up as we're getting better," said Diaz. "COPD causes the body to produce too much mucus and makes it harder to clear out, so you end up with these mucus plugs that aren't strongly correlated with any specific symptoms and can go undetected."

The researchers found that over the course of the study, the mortality rate for COPD patients with no detectable mucus plugs was 34 percent. For patients with mucus plugs in up to two lung segments, the mortality rate jumped to 46.7 percent. For patients with plugs in three or more lung segments, the mortality rate was 54.1 percent.

"The data show a compelling association between the accumulation of these mucus plugs and overall mortality, but we don't know anything about what's driving it yet," adds Diaz.

Because mucus is a known therapeutic target for other diseases, the researchers are next planning to test existing mucus-targeting therapies in people with COPD to determine if treating the mucus plugs could

have a positive impact on patient outcomes.

In the meantime, the research demonstrates that there are factors affecting COPD mortality that we still know little about, and that not all these factors will necessarily appear as symptoms for the patient.

"The fact that these mucus plugs were associated with mortality across different disease phases tells us that there are aspects of COPD progression that can be picked up by a CT scan even if they're not felt by the patient," said Diaz. "It's not so simple as to say every person with COPD needs to run out and get a CT scan tomorrow, but it's something for clinicians to consider when they're working with their patients."

More information: Airway-occluding mucus plugs and mortality in patients with chronic obstructive pulmonary disease, *JAMA* (2023). DOI: 10.1001/jama.2023.2065

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