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Original Article

# Is There a Correlation Between the Location of the Clot in the Pulmonary Arterial Tree with the Location of the Mucus Plug in the Pulmonary Bronchial Tree in Patients with chronic obstructive pulmonary disease Experiencing Pulmonary Embolism? Novel Findings

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Abstract

**OBJECTIVE:** The study aimed to investigate the impact of mucus plugs on the localization of clots in pulmonary embolisms among chronic obstructive pulmonary disease (COPD) patients.

**MATERIAL AND METHODS:** The retrospective study examined 200 participants diagnosed with both COPD and pulmonary embolism. Of these, 100 patients exhibited mucus plugs in the segmental and subsegmental branches of the pulmonary bronchial tree, while the remaining 100 did not, using computed tomography images for diagnosis. Data collection encompassed a comprehensive review of patient records, including medical history and imaging reports, to determine the presence of mucus plugs and the localization of clots in pulmonary embolism cases.

**RESULTS:** Patients with mucus plugs exhibited a notably longer duration of COPD ($P$ = .021) and a higher mean pulmonary arterial occlusion index (23 vs. 12, $P$ = .001). Moreover, the prevalence of clots in major pulmonary arteries was significantly elevated in the mucus plug group compared to the non-mucus plug group ($P$ < .05). Conversely, patients without mucus plugs displayed a higher incidence of clots in segmental and subsegmental arteries ($P$ < .001). Strong positive correlations existed between mucus plugs in segmental branches and clots in major pulmonary arteries, with moderate to strong correlation coefficients (0.51 to 0.62, $P$ < .05). Additionally, strong negative correlations were observed between mucus plugs in segmental branches and clots in segmental and subsegmental arteries, with correlation coefficients (CC) ranging from −0.74 to −0.76 ($P$ < .05). Similarly, a significant negative correlation was noted between mucus plugs in subsegmental branches and clots in subsegmental arteries (CC: −0.68 and −0.71, $P$ < .05).

**CONCLUSION:** The results suggest that mucus plugs may be associated with increased severity of COPD, higher pulmonary arterial occlusion index, and altered clot distribution within the pulmonary artery tree. These findings emphasize the importance of recognizing mucus plugs as a key consideration in COPD assessment and management, potentially influencing disease severity, vascular remodeling, and thrombotic risk management.

**KEYWORDS:** Embolism, pulmonary CT angiography, mucus plug
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## INTRODUCTION

Pulmonary embolism (PE) is a life-threatening event characterized by obstructing pulmonary arteries due to blood clots originating from other body parts.[1-7] Among the diverse population of individuals affected by PE, those with chronic obstructive pulmonary disease (COPD) present a unique challenge to physicians and researchers. COPD is a chronic respiratory disease often caused by long-term exposure to irritants such as cigarette smoke, impairing lung function.[8-11] Individuals diagnosed with COPD may undergo excessive mucus production and an increase in the number of goblet cells. The presence of mucus plugging, as observed on CT scans, has been linked to reduced lung function, poorer health-related quality of life, and increased levels of emphysema in patients with Chronic Obstructive Pulmonary Disease (COPD).[12-15] The CT scan and fiberoptic bronchoscopy (FOB) can be used for the assessment of mucus plugs in the airways. Detecting mucus plugs in the bronchial tree with computed tomography (CT) scans is often considered superior to fiberoptic bronchoscopy (FOB) for several reasons. Firstly, CT scans provide a comprehensive view of the entire bronchial tree, including the larger airways and smaller bronchioles. At the same time, FOB may struggle to visualize certain areas,

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particularly the peripheral airways, adequately. Additionally, CT scans are non-invasive and can be performed quickly and easily, unlike FOB, which requires the invasive insertion of a flexible bronchoscope. Furthermore, CT scans are highly reproducible and can be reviewed by multiple radiologists, reducing the potential for bias compared to FOB, where interpretation may vary among different bronchoscopists. No information is available regarding the potential impact of mucus plugs in the bronchial tree on the localization of blood clots within the pulmonary arterial tree. Unlike the traditional pattern observed in PE cases, where clots tend to lodge in the lower lobes of the lungs, COPD-related factors might cause deviations from this norm. Factors such as impaired blood flow, altered ventilation-perfusion ratios, and lung structural changes may lead to unique clot distribution patterns and clinical manifestations.[16-19]

To the best of our knowledge, our study is the first attempt to investigate clot localization in pulmonary embolism among patients with COPD. With the prevalence of COPD increasing worldwide and the potentially fatal consequences of pulmonary embolism, it is crucial to identify and address the specific challenges faced by individuals with COPD when it comes to clot localization. By comprehending the underlying mechanisms and exploring novel diagnostic tools, clinicians can effectively manage this dual burden, improve patient outcomes, and develop tailored strategies to prevent and treat pulmonary embolism in COPD.

## MATERIAL AND METHODS

### Study Design and Participants

This article presents a retrospective study on 200 patients diagnosed with chronic obstructive pulmonary disease (COPD) and pulmonary embolism (PE). The study included 100 patients with mucous plugs in the segmental and subsegmental branches of the pulmonary bronchial tree and 100 without any mucous plugs. The participants were selected from a diverse population of COPD patients admitted to the pulmonary department of a tertiary care hospital between February 2011 and December 2022. The study design aimed to analyze the impact of mucous plugs on the localization of clots in pulmonary embolisms among COPD patients.

**Main Points**

- Patients with mucus plugs exhibited a significantly longer duration of COPD compared to those without mucus plugs.
- The pulmonary arterial occlusion index (PAOI) was markedly higher in the group with mucus plugs, compared to the group without mucus plugs.
- In patients with mucus plugs, there was a higher prevalence of clots in the main pulmonary artery (MPA), right pulmonary artery (RPA), left pulmonary artery (LPA), and lobar arteries compared to patients without mucus plugs.
- Strong positive correlations were found between the presence of a clot in the main pulmonary artery (MPA) and right pulmonary artery (RPA) with the presence of a mucus plug in segmental branches.

### Data Collection

Patient records were thoroughly reviewed and extracted for analysis, including medical history and imaging reports (such as computed tomography angiography). The data collection process focused on identifying relevant information regarding the presence or absence of mucous plugs in the pulmonary bronchial tree and the corresponding clot localization in pulmonary embolism.

### Categorization of Patients

Based on the presence or absence of mucous plugs, the study cohort was divided into two groups: Group A (n = 100) included COPD patients with mucous plugs, and Group B (n = 100) consisted of those without mucous plugs.

### Localization of Clots

The location of clots in the pulmonary vasculature was determined for each patient by analyzing imaging reports. The pulmonary artery obstruction index (PAOI) was calculated for each patient by a radiologist with 15 years of experience in this field blinded to the mucus plug's location in the bronchial tree (Figures 1A and 2A).

### Localization of Mucus Plugs

The patients' lung CT scans were thoroughly examined by another radiologist, unaware of the clot's location in the pulmonary artery. The purpose was to identify mucus plugs in the segmental and subsegmental branches. To identify mucus plugs, Lung CT images were reviewed to find areas of high density or opacity in the bronchial tree with rounded or tubular shapes within the airways, following the contours of the airway and obstructing the passage of air (Figures 1B and 2B).

### Statistical Analysis

Descriptive data were expressed as mean ± SD for continuous variables and number (percentage) for categorical variables. Means of continuous variables were compared using an independent group *t*-test or Mann–Whitney *U*-test. Proportions for categorical variables were compared using the chi-square test. Pearson's or Spearman's correlation tests tested the association between quantitative variables. All statistical analyses were performed using SPSS version 22.0 software (IBM, Armonk, NY, USA), and $P < .05$ was considered statistically significant.

### Ethical Considerations

The local Ethics Committee approved our retrospective cohort study IAU (Approval number: 9916, Date: March 24, 2023). Informed consent was waived. This study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki.

## RESULTS

In the present study, a total of 200 patients with COPD and acute pulmonary embolisms were studied. Among them, 100 patients had mucus plugs in segmental and subsegmental branches, while the remaining 100 patients did not have mucus plugs in their pulmonary bronchial tree. The mean age of patients in the group with mucus plugs was 63 years (range: 41-73), whereas in the group without mucus plugs, it was 58 years (range: 46-68), and the difference was not statistically

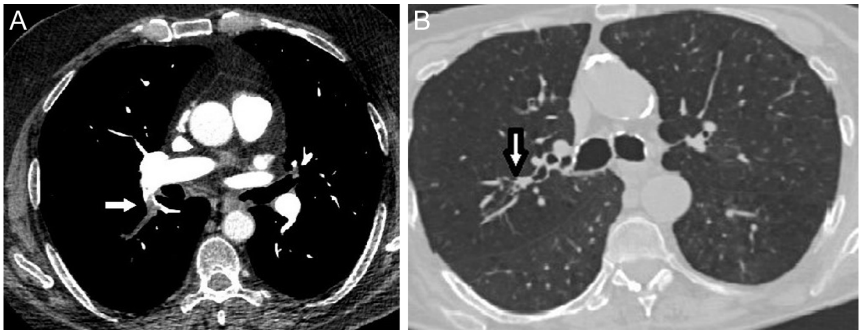


**Figure 1.** Pulmonary embolism in a patient with COPD. (A) The axial image from the pulmonary CTA shows the presence of clot in the superior segment of the right lower lobe artery (white arrow). (B) The axial image from the chest CT exhibits the mucus plug in the posterior segment of the right upper lobe artery (white arrow).

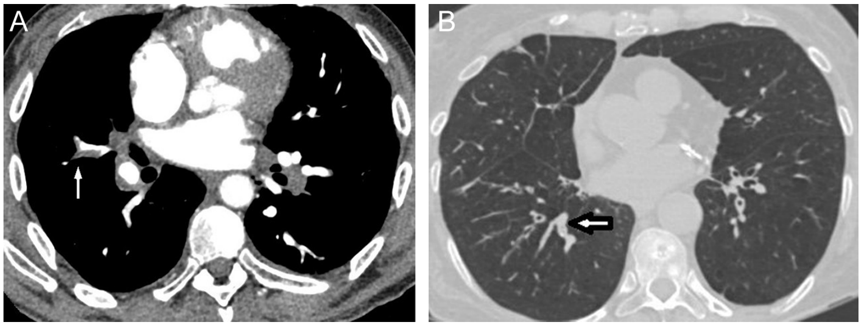


**Figure 2.** Pulmonary embolism in a patient with COPD. (A) The axial image from the pulmonary CTA shows the presence of clot in the right middle lobe segmental arterial branches (white arrow). (B) The axial image from the chest CT exhibits the mucus plug in the posterior segment of the right lower lobe artery (white arrow).

significant. Patients with mucus plugs had a significantly higher duration of COPD than those without (*P*-value: .021).

The Pulmonary Arterial Occlusion Index (PAOI) was 23 in the group with mucus plugs, which is higher than the PAOI of 12 in the group without mucus plugs, and this difference was statistically significant (*P*-value: .001). Furthermore, the number of patients with clots in the main pulmonary artery (MPA), right pulmonary artery (RPA), left pulmonary artery (LPA), and lobar arteries were higher in the group with mucus plugs compared to the group without mucus plugs (11, 10, 9, and 15 vs. 6, 4, 3, and 8, respectively), and this difference was statistically significant (*P*-value < .05).

In the group without mucus plugs, the number of patients with clots in segmental and subsegmental arteries was higher than in the group with mucus plugs (64 and 59 vs. 41 and 38, respectively), and this difference was statistically significant (*P*-value < .001). These findings are summarized in Table 1.

There was a moderately strong correlation between the presence of a clot in the main pulmonary artery (MPA) and right pulmonary artery (RPA) with the presence of a mucus plug in segmental branches (correlation coefficient: 0.54 and 0.51, respectively), and this correlation was statistically significant (*P*-value < .05). Additionally, a strong correlation was observed between the clot in the left pulmonary artery (LPA) and the mucus plug in the segmental branches, with a correlation coefficient of 0.62, which was statistically significant (*P*-value = .002).

Furthermore, a strong negative correlation was found between the presence of a clot in the segmental and subsegmental arteries and the presence of a mucus plug in the segmental branch, with correlation coefficients of −0.74 and −0.76, respectively. These correlations were statistically significant (*P*-value < .05).

Regarding the mucus plug in the subsegmental branches, a significantly meaningful strong negative correlation was observed only between the presence of a clot in the segmental and subsegmental branches and the presence of a mucus plug in the subsegmental branch, with correlation coefficients of −0.68 and −0.71, respectively (*P*-value < .05) (Table 2).

## DISCUSSION

The role of lung CT in various diseases is well-known.[20,21] The results of the present study provide important insights into the relationship between mucus plugs and clot formation in patients with COPD and acute pulmonary embolisms. The study population comprised 200 patients, half with mucus plugs in segmental and subsegmental branches. In contrast, the other half did not exhibit mucus plugs in their pulmonary bronchial tree.

Interestingly, patients with mucus plugs had a significantly longer duration of COPD than those without. This suggests a potential association between the presence of mucus plugs and the progression or severity of COPD. Additionally, the pulmonary arterial occlusion index (PAOI) was significantly higher in patients with mucus plugs, indicating a greater degree of arterial obstruction in this group. Furthermore, the analysis revealed a notable difference in the distribution of clots among the study groups. Patients with mucus plugs had a higher incidence of clots in the main pulmonary artery, right

**Table 1.** Comparison of Patient Characteristics and the Level of Thrombosis in the Pulmonary Artery Tree Between Two Groups of COPD Patients: Those with Mucus Plugs and Those Without.

| Variables | COPD Patients With Mucus Plugs and Pulmonary Embolism N = 100 | COPD Patients Without Mucus Plugs and With Pulmonary Embolism N = 100 | *P* |
|---|---|---|---|
| Age, years, median (25-75th percentiles) | 63 (41-73) | 58 (46-68) | .061 |
| Male gender | 68 (68%) | 64 (64%) | .064 |
| Years diagnosed with COPD (95% Confidence Interval) | 15 (11-19) | 12 (9-15) | .021 |
| PAOI (95% Confidence Interval) | 23 (18-31) | 12 (8-17) | .001 |
| **Level of thrombosis** | | | |
| MPA | 11 (11%) | 6 (6%) | .012 |
| RPA | 10 (10%) | 4 (4%) | .041 |
| LPA | 9 (9%) | 3 (3%) | .047 |
| Lobar artery | 15 (15%) | 8 (8%) | .003 |
| Segmental artery | 41 (41%) | 64 (64%) | .002 |
| Subsegmental artery | 38 (38%) | 59 (59%) | .001 |

pulmonary artery, left pulmonary artery, and lobar arteries than those without mucus plugs. These findings were consistent with the results of the meta-analysis conducted by Aleva et al., in which they found that in patients with COPD, sixty-eight percent of the emboli discovered were located in the main pulmonary arteries, lobar arteries, or interlobar arteries.[22] Conversely, patients without mucus plugs had a higher prevalence of clots in the segmental and subsegmental arteries. These findings highlight the importance of considering mucus plugs and clot formation when evaluating patients with acute pulmonary embolisms.

A moderately strong positive correlation was observed between clots in the main pulmonary artery and the right pulmonary artery with mucus plugs in segmental branches. Similarly, a strong positive correlation was found between the clot in the left pulmonary artery and mucus plugs in segmental branches.

In contrast, a strong negative correlation was observed between clots in the segmental and subsegmental arteries and mucus plugs in the segmental branch. These findings suggest that mucus plugs may be associated with a reduced likelihood of clot formation in the segmental and subsegmental arteries. Furthermore, when considering mucus plugs in the subsegmental branches, a significant negative correlation was noted between clots in the segmental and subsegmental arteries and mucus plugs in the subsegmental branch. This indicates that mucus plugs in subsegmental branches may be associated with a reduced risk of receiving clots in these specific regions. Factors such as impaired blood flow resulting from altered ventilation-perfusion ratios following the obstruction caused by mucus plugs and lung structural changes may lead to distinct clot distribution patterns and clinical manifestations.[23-25] This implies that the vasoconstriction caused in the segmental and subsegmental branches, due to the bronchial tree obstruction caused by mucus plugs

**Table 2.** Correlation Between the Location of the Clot in the Pulmonary Artery Tree and the Location of the Mucus Plug in the Pulmonary Bronchial Tree

| | Level of Mucus Plug | Segmental Branch | *P* | Subsegmental Branch | *P* |
|---|---|---|---|---|---|
| Level of thrombose | | | | | |
| MPA<br>Correlation coefficient | – | 0.54 | .001 | 0.51 | .66 |
| RPA<br>Correlation coefficient | – | 0.51 | .045 | 0.42 | .071 |
| LPA<br>Correlation coefficient | – | 0.62 | .002 | 0.12 | .18 |
| Lobar arteries<br>Correlation coefficient | – | 0.3 | .064 | 0.56 | .29 |
| Segmental arteries<br>Correlation coefficient | – | -0.74 | .001 | -0.68 | .002 |
| Sub-segmental arteries<br>Correlation coefficient | – | −0.76 | .003 | −0.71 | .014 |

in these regions, might render these arterial branches less susceptible to thrombosis in COPD patients with mucus plugs. Consequently, the clots are more likely to migrate to other branches with better aeration. As we know, the presence of clots in the proximal parts of the pulmonary arterial tree is associated with a higher pulmonary arterial occlusion index (PAOI) and an increased likelihood of right ventricular dysfunction and mortality. Therefore, the findings of this study can assist clinicians in predicting the location of clots in the pulmonary arterial system of patients with COPD and PE, even before performing CT pulmonary angiography (CTPA) in patients with a previous history of mucus plugs. This foresight can contribute to better management plans for these patients. Additionally, clinicians can comprehend that if patients with COPD and mucus plugs develop pulmonary embolism, they may experience a higher obstruction index and mortality rate. Consequently, clinicians may adopt a different approach for treatment planning and management of patients with COPD and deep vein thrombosis (DVT) as a prophylaxis of PE. These findings can aid clinicians in providing more informed and tailored care to their patients. Since no study has been conducted on this topic thus far, we could not compare our findings with previous studies.

The findings of this study suggest several potential clinical impacts. Firstly, the association between mucus plugs and increased severity of COPD underscores the importance of identifying and addressing mucus plug formation in COPD management. Clinicians may need to consider mucus plugs as a potential marker of disease progression and adjust treatment strategies accordingly. Secondly, the higher pulmonary arterial occlusion index (PAOI) in patients with mucus plugs highlights the potential for mucus plugs to contribute to pulmonary vascular remodeling and vascular resistance, which could have implications for pulmonary hypertension management. Additionally, the altered clot distribution within the pulmonary artery tree in patients with mucus plugs may influence treatment decisions regarding anticoagulation therapy and risk stratification for pulmonary embolism recurrence. Overall, these findings underscore the importance of considering mucus plugs as a potential factor in the assessment and management of COPD patients, with potential implications for disease severity, vascular remodeling, and thrombotic risk.

This study has several limitations. Firstly, its retrospective design and lack of randomization hinder the establishment of causal relationships between mucus plugs and clot localization, potentially introducing bias. Moreover, the sample size of 200 patients may limit the generalizability of the findings. Additionally, important factors influencing clot localization in pulmonary embolism among COPD patients, such as the severity of COPD, comorbidities, and treatment regimens, were not extensively evaluated. Furthermore, the interpretation of images was conducted by a single radiologist, which, despite efforts to ensure consistency and accuracy, raises concerns about the subjective nature of radiological interpretation and the potential for bias.

## CONCLUSION

This study provides valuable insights into the relationship between mucus plugs and clot formation in patients with COPD and acute pulmonary embolisms. The results suggest that mucus plugs may be associated with increased severity of COPD, higher pulmonary arterial occlusion index, and altered clot distribution within the pulmonary artery tree. These findings underscore the need for further research to better understand these associations' underlying mechanisms and clinical implications.

**Availability of Data and Materials:** The data that support the findings of this study are available on request from the corresponding author.

**Ethics Committee Approval:** This study was approved by Ethics Committee of IAU University (approval number: 9916; date: March 24, 2023).

**Informed Consent:** Informed consent was waived due to the retrospective course of study.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – N.A., Z.N.; Design – Z.N., M.A.; Supervision – M.A., A.S.; Resources – M.A., Z.N.; Materials – M.A., A.S.; Data Collection and or Processing – M.A.; Analysis and/or Interpretation – A.S.; Literature Search – M.A., A.S.; Writing – N.A., Z.N.; Critical Review – M.A., Z.N.

**Declaration of Interests:** The authors have no conflicts of interest to declare.

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