

# Validation of the use of Cromolyn Sodium as a Marker of Aspiration in Patients with Bronchiectasis and Other Respiratory Diseases

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## Background

- ❖ Micro-aspiration may contribute to the pathogenesis of many respiratory conditions. Yet, reliable methods to confirm micro-aspiration are lacking.
- ❖ Cromolyn sodium may be a useful marker of aspiration owing to its pharmacokinetics.
- ❖ When ingested, 0.5% cromolyn sodium is systemically absorbed. Conversely, when instilled into the lungs, 30-50% is absorbed, of which >50% is then renally excreted unmetabolized.

## Aims

- ❖ To detect cromolyn sodium in the urine of patients with respiratory conditions, and to confirm aspiration following oral ingestion via bronchoscopy.

## Methods

- ❖ Respiratory patients requiring bronchoscopy, and healthy controls were included.
- ❖ All participants ingested 200mg of cromolyn sodium after their evening meal, and 200mg before retiring to bed.
- ❖ Patients undergoing morning bronchoscopy additionally consumed 50ml blue food colouring with the cromolyn sodium.
- ❖ Participants collected all urine overnight following cromolyn ingestion.

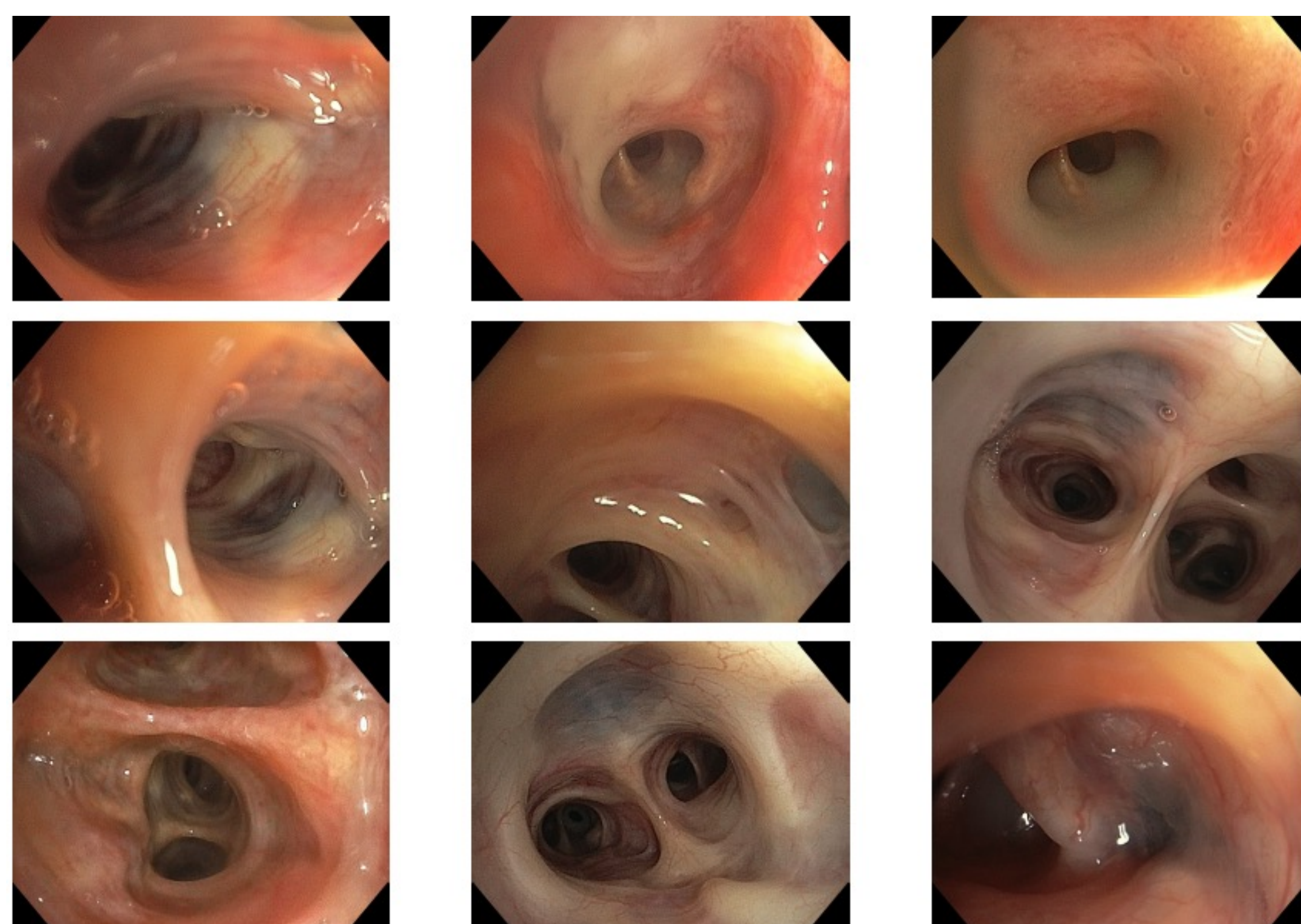


Figure 1: Endobronchial examination with evidence of blue-dye staining

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## Results



Figure 2: BAL with blue-dye stained mucous plug

- ❖ 46 patients and 21 controls were enrolled.
- ❖ Blue-staining was visualised at bronchoscopy in 80% (35/44) of patients.
- ❖ Eighty-seven percent of NTM patients (27/31;  $p = 0.098$ ) and 75% of bronchiectasis patients (15/20;  $p = 0.538$ ) had blue-stain visualised.
- ❖ A significant difference in urinary cromolyn/creatinine (mg/mmol) was detected between patients and controls ( $p = 0.004$ ); particularly in those with a history of GORD ( $p=0.021$ ), Hull score >13 ( $p=0.01$ ) and acid suppression use ( $p=0.029$ ).
- ❖ Within the patient cohort, there was no significant association between urinary cromolyn and other markers of aspiration.
- ❖ Urinary cromolyn was detected in some patients not previously diagnosed with GORD or aspiration.

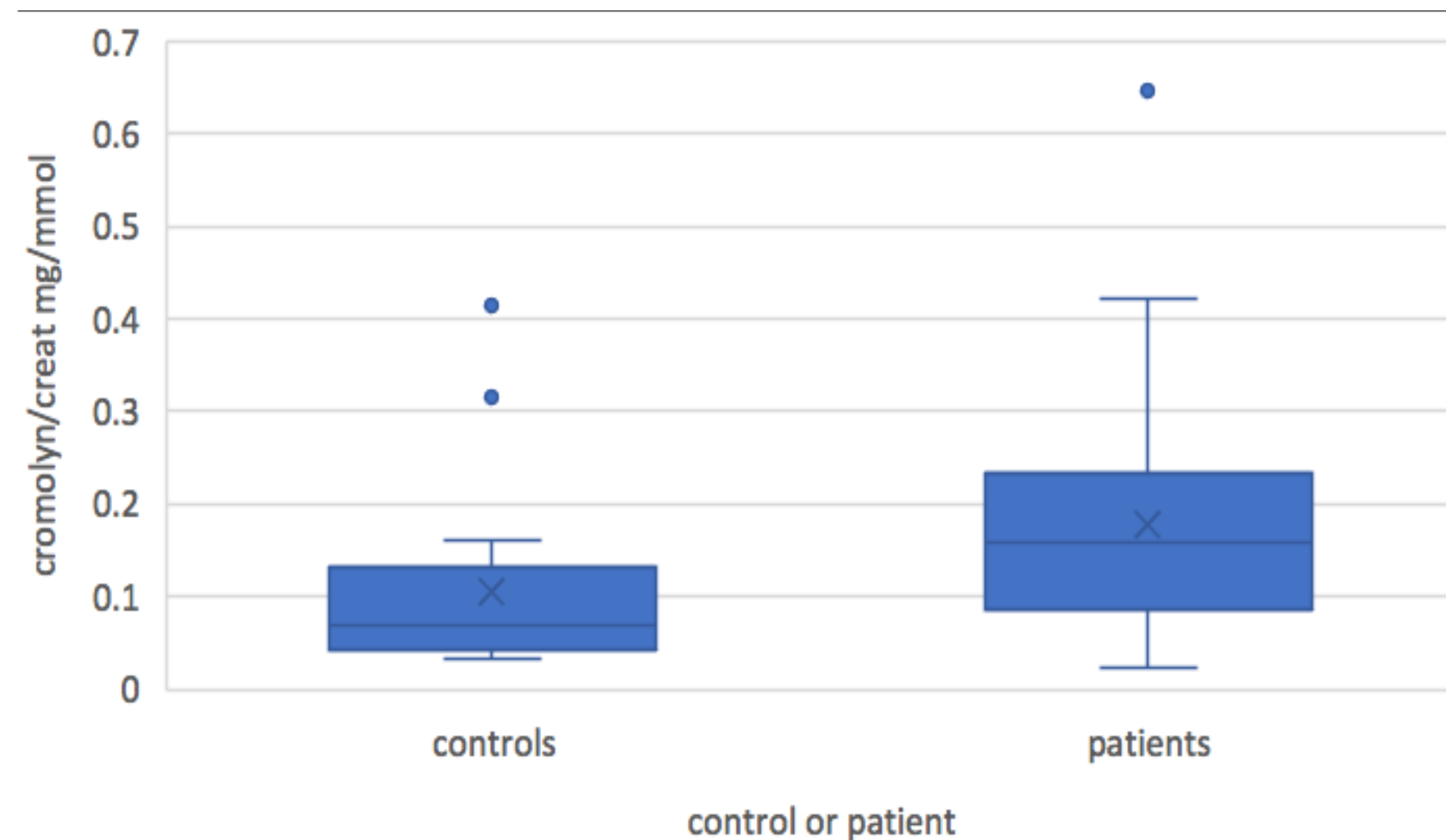


Figure 3: Distribution of urinary cromolyn/creatinine in patients and controls

- ❖ 67 separate broncho-alveolar lavage (BAL) samples were sent from 32/46 patients and assessed for presence of blue dye pigment.
- ❖ Blue dye pigment was detected in 59/67 BAL samples.
- ❖ However, a significant correlation was not observed between the amount of urinary cromolyn and the amount of blue dye pigment in the BAL sample.
- ❖ A significant association was observed with the macroscopic visualisation of blue-dye endobronchially, with the lab detection of blue-dye pigment in BAL samples ( $p = 0.042$ ).

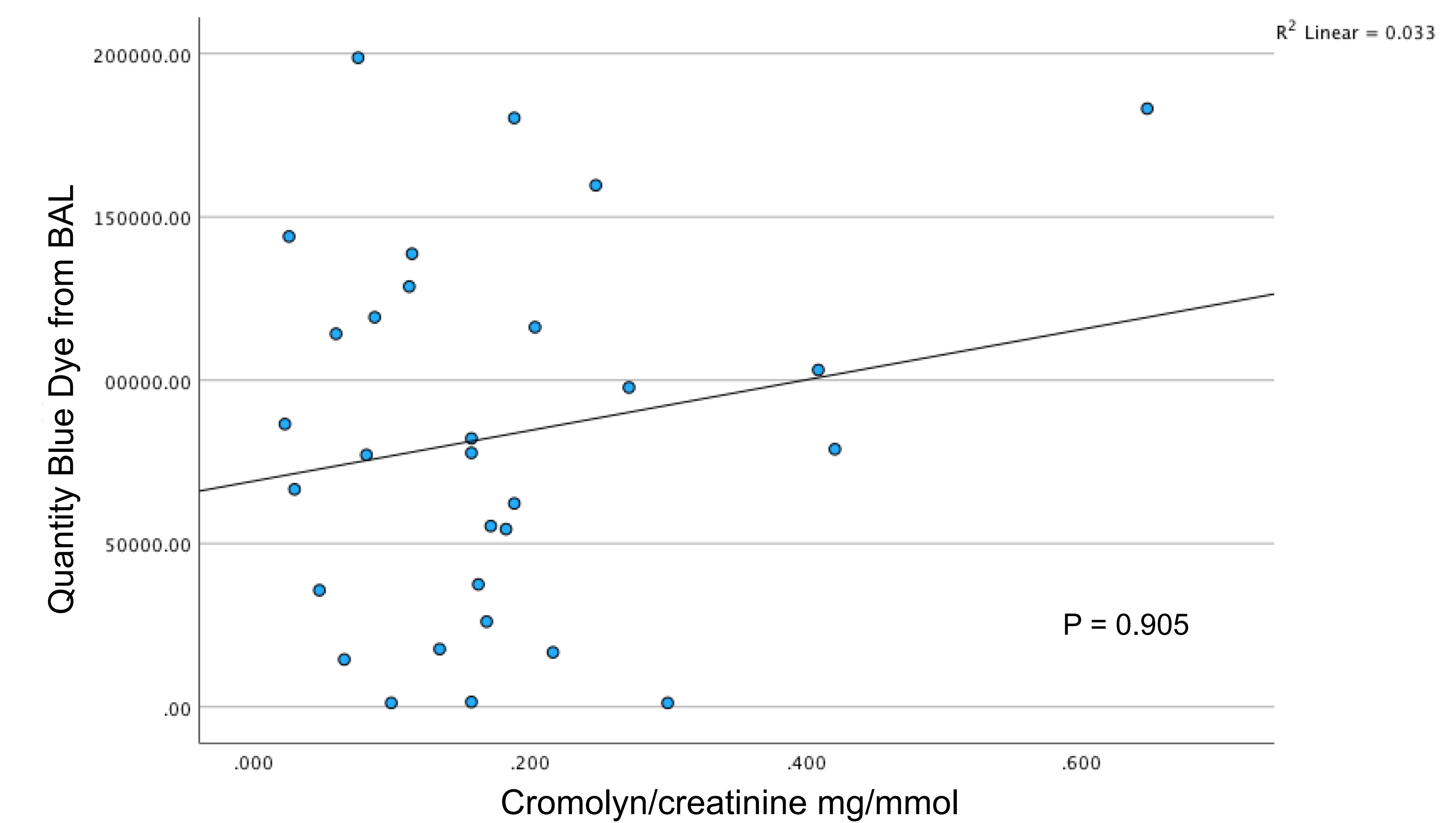


Figure 4: The association of urine cromolyn/creatinine is not significantly associated with the quantity of blue dye in bronchoalveolar lavage.

## Discussion

- ❖ A significant difference between the amount of urinary cromolyn detected in respiratory patients, and the amount of urinary cromolyn detected in controls was shown. This suggests urinary cromolyn may be a sensitive marker of micro-aspiration in patients with respiratory disease.
- ❖ Analysis of BAL samples demonstrated presence of blue-dye pigment in suspected cases of micro-aspiration.
- ❖ There were limitations in testing blue-dye pigment from BAL sample to reliably ascertain if this truly correlated with amount of urinary cromolyn.

## Conclusion

- ❖ The prevalence of aspiration was high among our patient cohort, determined by an elevated urinary cromolyn.
- ❖ Urinary cromolyn identified patients with aspiration not previously confirmed with traditional diagnostics.
- ❖ Future validation studies on larger cohorts will evaluate different cromolyn dosages and a urinary concentration that determines a positive result.