Mucus plugging, disease severity and sputum myeloperoxidase concentration in bronchiectasis

Sun-Hyung Kim[1,8], Ki Man Lee[1,8], Jin Young Yoo[2], Kum Ju Chae[3], Geun-Hyeong Kim[4], Jun Yeun Cho[1], Nguyen Minh The[5], Eung-Gook Kim[6], Joong-Kook Choi[6], Kang Hyeon Choe[1], Hyun Lee[7,9] and Bumhee Yang[1,9]

[1]Division of Pulmonary and Critical Care Medicine, Department of Internal Medicine, Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, Republic of Korea. [2]Department of Radiology, Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, Republic of Korea. [3]Department of Radiology, Research Institute of Clinical Medicine of Jeonbuk National University-Biomedical Research Institute of Jeonbuk National University Hospital, Jeonju, Republic of Korea. [4]The Medical Artificial Intelligence Center, Chungbuk National University Hospital, Chungbuk National University College of Medicine, Cheongju, Republic of Korea. [5]Department of Tuberculosis and Lung Disease, Military Hospital 175, Ho Chi Minh City, Vietnam. [6]Department of Biochemistry, Chungbuk National University College of Medicine, Cheongju, Republic of Korea. [7]Division of Pulmonary Medicine and Allergy, Department of Internal Medicine, Hanyang University College of Medicine, Seoul, Republic of Korea. [8]S-H. Kim and K.M. Lee contributed equally. [9]H. Lee and B. Yang contributed equally.

Corresponding author: Bumhee Yang (ybhworld0415@gmail.com)

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Sputum myeloperoxidase concentration is independently associated with an increased extent of mucus plugging (MP), suggesting that it could serve as a potential biomarker for evaluating MP in bronchiectasis https://bit.ly/4f212WG

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Abstract

Background Bronchiectasis is characterised by impaired mucociliary clearance, leading to persistent mucus accumulation, known as mucus plugging (MP). Myeloperoxidase (MPO) is a key molecule that activates neutrophilic inflammation during bronchiectasis, leading to disease progression. However, whether sputum MPO concentration is an independent factor associated with MP remains unclear.

Methods We retrospectively evaluated 78 patients with bronchiectasis at Chungbuk National University Hospital (Cheongju, Republic of Korea) between June 2022 and April 2023. According to the extent of MP on chest computed tomography, participants were divided into high MP (MP in >9 bronchopulmonary segments) and low MP (MP in ⩽9 bronchopulmonary segments) groups. We evaluated whether sputum MPO concentration is independently associated with MP using multivariable adjusted logistic regression analyses.

Results There were 59 (75.6%) and 19 (24.4%) participants in the low and high MP groups, respectively. Compared with the low MP group, the high MP group had significantly higher disease severity, as measured by the modified Reiff score ($p<0.001$) and FACED score ($p=0.003$). Sputum MPO concentration was significantly correlated with the extent of MP ($\rho=0.313$, $p=0.009$). In addition, sputum MPO concentration was independently associated with a high extent of MP even after adjusting for potential confounders (adjusted OR 1.60 (95% CI 1.06–2.42)).

Conclusions Sputum MPO concentration was associated with a high degree of MP, suggesting a potential role of MPO in the pathogenesis of mucus plugging.

Introduction

Bronchiectasis is a chronic lung disease in which the bronchi are permanently dilated, causing chronic respiratory symptoms and repeated infections [1]. A key pathological feature of bronchiectasis is impaired mucociliary clearance, which leads to persistent mucus accumulation in the bronchial tree [2]. This accumulation, known as mucus plugging (MP), may play a pivotal role in the pathophysiology of the disease and has significant clinical implications. In cystic fibrosis bronchiectasis, MP is a prognostic factor

for the development of bronchial enlargement and is associated with exacerbation and decreased lung function [3, 4].

Myeloperoxidase (MPO) is the most abundant protein in neutrophils and is important for neutrophil activation [5]. The release of MPO following neutrophil activation catalyses the conversion of hydrogen peroxide and chloride ions to hypochlorous acid [6]. Thus, it is critically involved in host defence against bacteria, viruses and fungi [7]. MP is considered an important predisposing factor for bacterial infection and inflammation, and can lead to hypoxic damage and necrosis of airway epithelial cells by increasing epithelial oxygen consumption in cystic fibrosis [8–10]. Notably, sputum MPO levels were recently shown to reflect disease activity in bronchiectasis [11]. In addition, even when bacterial infection was eliminated in an animal model, MP persisted, showing a correlation between airway neutrophilia, airway damage and inflammatory response activity [12]. As such, if the bronchus is filled with mucus, an increase in disease severity and neutrophil-activating substances, such as MPO, is expected; however, the relationship between MP and MPO is unclear.

Therefore, this study aimed to investigate the association of MP with disease severity and sputum MPO concentration in patients with bronchiectasis.

Methods

Study population

We conducted a retrospective analysis of data prospectively collected from 78 patients with bronchiectasis who underwent measurement of sputum MPO concentration at Chungbuk National University Hospital (Cheongju, Republic of Korea) between June 2022 and April 2023. All patients in this study were registered in the Korean Multicenter Bronchiectasis Audit and Research Collaboration (KMBARC) registry, a prospective, non-interventional, observational cohort study of bronchiectasis in Korea [13–15].

Study objectives

The primary objective of this study was to evaluate whether sputum MPO concentration is an independent factor associated with the extent of MP. The secondary objective of this study was to compare the disease severity of bronchiectasis according to the extent of MP. The disease severity of bronchiectasis was estimated by Bronchiectasis Severity Index (BSI) [16], FACED (percentage predicted Forced expiratory volume in 1 s (FEV_1), Age, Chronic colonisation of *Pseudomonas aeruginosa*, Extension and Dyspnoea) score [17] and modified Reiff score [18].

Clinical data

Data on demographics (age, sex and body mass index (BMI)), smoking status and comorbidities were prospectively collected when the patients were registered in the KMBARC registry. Dyspnoea was evaluated using the modified Medical Research Council (mMRC) scale [19]. Symptoms were evaluated using a validated Korean version of the Bronchiectasis Health Questionnaire (BHQ) for quality of life [20, 21]. The BSI and FACED score were used to assess the severity of bronchiectasis, as previously described [16, 17]. Acute exacerbation of bronchiectasis was defined as the worsening of three or more major symptoms lasting ⩾48 h, resulting in a change in treatment. The major symptoms include cough, sputum volume/viscosity, sputum suppuration, dyspnoea, exercise ability, fatigue, malaise and haemoptysis [22]. Moreover, severe acute exacerbation was defined as visiting the emergency room or being hospitalised because of worsening symptoms.

Laboratory tests

Blood biomarkers

White blood cell counts, neutrophil counts and high-sensitivity C-reactive protein (hs-CRP) levels were measured during stable state for all patients.

Pulmonary function tests

Pre- and post-bronchodilator spirometry was performed based on American Thoracic Society/European Respiratory Society criteria [23]. The absolute values of FEV_1 and forced vital capacity (FVC) were recorded, and the percentages of the predicted values for FEV_1 and FVC were calculated using an automatic calculator, with a reference equation obtained from a representative Korean sample [24].

Modified Reiff score and MP

Chest computed tomography (CT) was performed when the bronchiectasis was in stable state.

The presence and severity of bronchiectasis were evaluated in 18 bronchopulmonary segments of the lung using the modified Reiff score [25]. MP was defined when the airway was obstructed completely by mucus in the cross-section of the chest CT. Based on the extent of MP, high MP was defined when MP was observed in >9 bronchopulmonary segments. Otherwise, it was classified as low MP [25]. To validate this cut-off value using our own dataset, we analysed the area under the curve (AUC) of bronchopulmonary segments for the prediction of acute exacerbation. The AUC was highest at 10 bronchopulmonary segments (supplementary table S1).

Two pulmonologists (S-H. Kim and B. Yang) and one radiologist (J.Y. Yoo) reviewed all CT images in a blinded manner. We utilised Fleiss' κ coefficient to evaluate the inter-observer variability among the three independent observers who scored each CT for mucus. In instances where there was a discrepancy in the extent of MP among the interpreters (a difference of ⩾2 points between any two of the three observers), we reached a consensus through discussion. When the difference was <2 points between any two of the three observers, we calculated the mean of the three observer scores as the final mucus score. In this study, the calculated Fleiss' κ coefficient was 0.89, which signifies an "almost perfect" agreement as per the strength of agreement scale [26].

Microbiology

Spontaneous sputum samples were obtained from all patients. The specimens were subjected to microbiological analysis, according to standard methods [27]. Conventional semiquantitative bacterial cultures were also used. All samples underwent initial Gram staining before sputum culture if the Murray–Washington criteria were met [28]. Non-tuberculous mycobacterial pulmonary disease was diagnosed using the clinical and microbiological criteria provided by the American Thoracic Society/Infectious Diseases Society of America [29].

Sputum MPO concentration

Sputum MPO concentration was recommended to be measured within 3 days of CT scan acquisition. The sputum MPO function profile was determined using AnyLab F Myeloperoxidase (Z-Biotech, Cheongju, Republic of Korea), a point-of-care test method based on immunofluorescence. Subsequently, the cartridge was removed from the product pouch and placed on a flat surface. Using a pipette, we added 3–5 µL of phlegm from the patient to the tube containing the detection buffer. The lid of the detection buffer was closed, and the sample was mixed thoroughly with the detection buffer by shaking the tube ∼10 times. Next, 100 µL of sample mixture was pipetted out and dispensed into the sample well on the test cartridge. The sample-loaded test cartridge was incubated at room temperature for 15 min. The results (values) were obtained using the AnyLab F1 measuring device. The linear range of MPO was 0.1–1000 $ng \cdot mL^{-1}$ [11].

CT protocol

Chest CT was performed using various multidetector row CT scanners, including a 64-slice CT scanner (Brilliance 64; Philips Healthcare, Cleveland, OH, USA), a dual-source CT scanner (Somatom Definition Flash; Siemens Healthcare, Forchheim, Germany) and a 256-slice CT scanner (IQon Spectral CT; Philips Healthcare). The scanning parameters were 120 kV tube voltage, automatic tube current modulation, 1 mm thickness, 1 mm increment, rotation time 0.5 s and 0.89 pitch. All CT images were reconstructed to 1 mm thickness and 1 mm intervals using a three-dimensional image program (Xelis; Infinitt Healthcare, Seoul, Republic of Korea). The scan data were directly displayed on the monitors of the Picture Archiving and Communication System. Both mediastinal (window width 400 HU; window level 20 HU) and lung (window width 1500 HU; window level −700 HU) window images were available on the monitors for analysis.

Statistical analysis

Data are presented as median (interquartile range (IQR)) for continuous variables and as frequency (percentage) for categorical variables. Continuous variables were compared using the Mann–Whitney U-test, and the Pearson Chi-squared test or Fisher's exact test was used for categorical variables, as appropriate. Spearman's rho (ρ) correlation method was used to evaluate whether the extent of MP was correlated with sputum MPO concentration. To evaluate whether the sputum MPO level was an independent factor associated with high MP, univariate and multivariate logistic regression analyses were performed. Adjusted odds ratios (aORs) and 95% confidence intervals were estimated after adjusting for potential confounding factors. In the multivariable logistic regression model, age, BMI, smoking status, microbiology, BHQ score, post-bronchodilator FEV_1 % pred, mMRC Dyspnoea scale, hs-CRP level, previous history of acute exacerbations and natural log-transformed level of sputum MPO concentration were adjusted. All tests were two-sided and p-values <0.05 were considered to indicate statistical

significance. All statistical analyses were performed using SPSS Statistics for Windows version 27.0 (IBM, Armonk, NY, USA).

Results

Baseline characteristics

Baseline characteristics of the 78 patients with bronchiectasis are shown in table 1. There were 59 (75.6%) and 19 (24.4%) participants in the low and high MP groups, respectively. Compared with the low MP group, the high MP group was older (median (IQR) 70 (65–75) *versus* 64 (59–70) years; p=0.031) and had lower BMI (median (IQR) 20.7 (18.8–21.3) *versus* 22.1 (19.5–23.7) $kg \cdot m^{-2}$; p=0.048) and lung function (p<0.05 for all spirometry parameters). The high MP group had higher white blood cell counts, neutrophil counts and hs-CRP levels than did the low MP group (p<0.05). In addition, sputum MPO concentration was significantly higher in the high MP group than in the low MP group (median (IQR) 152.7 (47.6–541.0) *versus* 40.2 (12.1–109.5) $ng \cdot mL^{-1}$; p=0.009). There were no significant intergroup differences in sex, smoking history, comorbidities, mMRC Dyspnoea scale, BHQ scores, long-term macrolide maintenance therapy or physiotherapy (p>0.05 for all variables).

Comparison of disease severity of bronchiectasis according to extent of MP

As shown in figure 1, regarding bronchiectasis severity, the median (IQR) modified Reiff score (12 (11–16) *versus* 7 (5–10); p<0.001), BSI (8 (7–12) *versus* 7 (5–9); p=0.064) and FACED score (3 (3–4) *versus* 2 (1–3); p=0.003) were higher in the high MP group than in the low MP group; however, the difference in BSI was not significant.

Association between extent of MP and sputum MPO concentration

As shown in figure 2, the high MP group had a significantly higher log-transformed MPO concentration than did the low MP group (median (IQR) 3.69 (2.49–4.70) *versus* 5.03 (3.86–6.29); p=0.004). Even for the non-transformed MPO concentration, the high MP group had a significantly higher MPO concentration than did the low MP group (median (IQR) 40.2 (12.1–109.5) *versus* 152.7 (47.6–541.0) $ng \cdot mL^{-1}$); p=0.009) (supplementary figure S1). Moreover, there was a significant positive correlation between the extent of MP and natural log-transformed sputum MPO concentration (ρ=0.313, p=0.009).

Factors associated with MP

In univariate analysis, natural log-transformed sputum MPO concentration (OR 1.60 (95% CI 1.10–2.33)), mMRC Dyspnoea scale (OR 1.75 (95% CI 0.95–3.32)) and hs-CRP (OR 1.17 (95% CI 0.99–1.38)) were positively associated with high MP, whereas BMI (OR 0.77 (95% CI 0.62–0.97)) and post-bronchodilator FEV_1 % pred (OR 0.95 (95% CI 0.91–0.98)) were negatively associated with high MP. In multivariate analyses, natural log-transformed MPO concentration (aOR 1.60 (95% CI 1.06–2.42)), post-bronchodilator FEV_1 % pred (aOR 0.95 (95% CI 0.91–0.99)) and modified Reiff score (aOR 1.44 (95% CI 1.17–1.77)) were significantly associated with high MP (table 2).

Discussion

In this study, we compared disease severity in bronchiectasis according to the extent of MP and evaluated whether MPO concentration was independently associated with MP in patients with bronchiectasis. Our study showed that disease severity measured by the FACED score and modified Reiff score is significantly higher in patients with more MP on the CT scan compared to those with less MP. In addition, we showed that sputum MPO concentration correlated with MP and was an independent marker associated with MP in bronchiectasis, suggesting its potential role as a biomarker that reflects the extent of MP.

The correlation between MP and severity of bronchiectasis has been highlighted in several studies. For example, MP on chest CT has been demonstrated to be associated with lower BMI, worse lung function, more acute exacerbations and systemic inflammation in patients with bronchiectasis [30, 31]. Supporting these results, our study also provided evidence of a positive association between the degree of mucus obstruction and increased disease severity in bronchiectasis. This was reflected in BSI and FACED score, which are comprehensive tools for assessing bronchiectasis severity and predicting future outcomes of bronchiectasis, such as the risk of future exacerbations, hospitalisations and mortality [16, 32, 33]. Accordingly, MP on chest CT should not be regarded as a mere marker of symptom burden (a high amount of sputum), but should be considered as an active chest CT biomarker reflecting the current severity of bronchiectasis. Although more studies are needed to confirm the role of MP on chest CT in predicting future outcomes, our findings, showing a significant correlation between MP and BSI and FACED score, suggest its potential role in predicting poor outcomes. MP on chest CT may also indicate a new therapeutic phenotype; specifically, patients with thick hypersecretion of mucus or those who have difficulties in sputum expectoration may exhibit MP on chest CT. In such patients, a more extensive airway

TABLE 1 Baseline characteristics of the participants

	Total (n=78)	MP ⩽9 (n=59)	MP >9 (n=19)	p-value
Age, years	67 (59–71)	64 (59–70)	70 (65–75)	0.031
Male	42 (53.8)	34 (57.6)	8 (42.1)	0.238
BMI, kg·m^{-2}	21.2 (19.4–23.3)	22.1 (19.5–23.7)	20.7 (18.8–21.3)	0.048
Smoking history				0.159
Never-smoker	55 (70.5)	39 (66.1)	16 (84.2)	
Current or ex-smoker	23 (29.5)	20 (33.9)	3 (15.8)	
mMRC Dyspnoea scale	1 (1–2)	1 (0–1)	1 (1–2)	0.059
BHQ score	60.1 (53.5–68.2)	60.8 (53.5–70.8)	58.8 (50.1–63.6)	0.134
Physiotherapy	10 (12.8)	8 (13.6)	2 (10.5)	1.000
Long-term macrolide maintenance therapy	13 (16.7)	10 (16.39)	3 (15.8)	0.906
Post-bronchodilator spirometry				
FVC, L	2.5 (2.0–3.0)	2.7 (2.3–3.1)	2.0 (1.7–2.6)	0.003
FVC, % pred	73 (65–84)	78 (70–88)	65 (62–73)	0.001
FEV_1, L	1.8 (1.3–2.1)	1.9 (1.4–2.2)	1.3 (0.9–1.6)	0.002
FEV_1, % pred	66 (53–82)	73 (58–88)	53 (46–65)	0.001
FEV_1/FVC ratio	71 (59–76)	72 (61–76)	64 (53–71)	0.015
Microbiology	54 (69.2)			
Pseudomonas aeruginosa	17 (21.8)	13 (22.0)	4 (21.1)	1.000
Others	37 (47.4)	26 (44.1)	11 (57.9)	0.294
Acute exacerbation				
Acute exacerbations in the prior year, n	1 (0–2)	1 (0–2)	1 (0–2)	0.244
Severe acute exacerbations in the prior year, n	0 (0–1)	0 (0–1)	0 (0–1)	0.517
Acute exacerbations during follow-up, n	1 (0–1)	1 (0–1)	1 (0–1)	0.852
Severe exacerbations during follow-up, n	0	0	0	0.787
Laboratory findings				
WBC count, L^{-1}	7080 (5940–8650)	6530 (5600–7895)	9715 (7818–11 348)	<0.001
Neutrophil count, μL^{-1}	4281 (3172–5879)	4025 (3078–4796)	6602 (4716–9248)	<0.001
hs-CRP, mg·dL^{-1}	0.4 (0.2–1.8)	0.3 (0.1–1.4)	1.2 (0.4–3.7)	0.011
Sputum MPO concentration, ng·mL^{-1}	51.2 (16.2–50.7)	40.2 (12.1–109.5)	152.7 (47.6–541.0)	0.009
Comorbidities				
Hypertension	11 (14.1)	11 (18.6)	0	0.057
COPD	27 (34.6)	20 (33.9)	7 (36.8)	0.815
Asthma	9 (11.5)	5 (8.5)	4 (21.1)	0.210
Diabetes mellitus	12 (15.4)	10 (16.9)	2 (10.5)	0.720
Cardiovascular disease	16 (20.5)	12 (20.3)	4 (21.1)	1.000
Neurological disease	5 (6.4)	4 (6.8)	1 (5.3)	1.000
Malignancy	5 (6.4)	3 (5.1)	2 (10.5)	0.590
Connective tissue disease	7 (9.0)	6 (10.2)	1 (5.3)	1.000
Previous history of tuberculosis	26 (33.3)	19 (32.2)	7 (36.8)	0.709
Previous history of pertussis	6 (7.7)	6 (10.2)	0	0.327
NTM-PD	21 (26.9)	16 (27.1)	5 (26.3)	1.000
Extent of bronchiectasis, n BP segments				<0.001
1–5	21 (26.9)	21 (35.6)	0	
6–9	23 (29.5)	23 (39.0)	0	
> 9	34 (43.6)	15 (25.4)	19 (100)	
Extent of MP, n BP segments				<0.001
Absent	1 (1.3)	1 (1.7)	0	
1–5	37 (47.4)	37 (62.7)	0	
6–9	21 (26.9)	21 (35.6)	0	
>9	19 (24.4)	0	19 (100)	
Time duration between MPO and chest CT, days	98 (15–205)	98 (11–176)	126 (16–287)	0.322

Data are presented as median (interquartile range) or n (%), unless otherwise stated. MP: mucus plugging; BMI: body mass index; mMRC: modified Medical Research Council; BHQ: Bronchiectasis Health Questionnaire; FVC: forced vital capacity; FEV_1: forced expiratory volume in 1 s; WBC: white blood cell; hs-CRP: high-sensitivity C-reactive protein; MPO: myeloperoxidase; NTM-PD: non-tuberculous mycobacterial pulmonary disease; BP: bronchopulmonary; CT: computed tomography.

clearance technique or the use of hypertonic saline may be helpful. Therefore, understanding MP in terms of disease severity, progression and future outcomes in bronchiectasis could pave the way for more personalised treatment plans; future studies are needed in this regard.

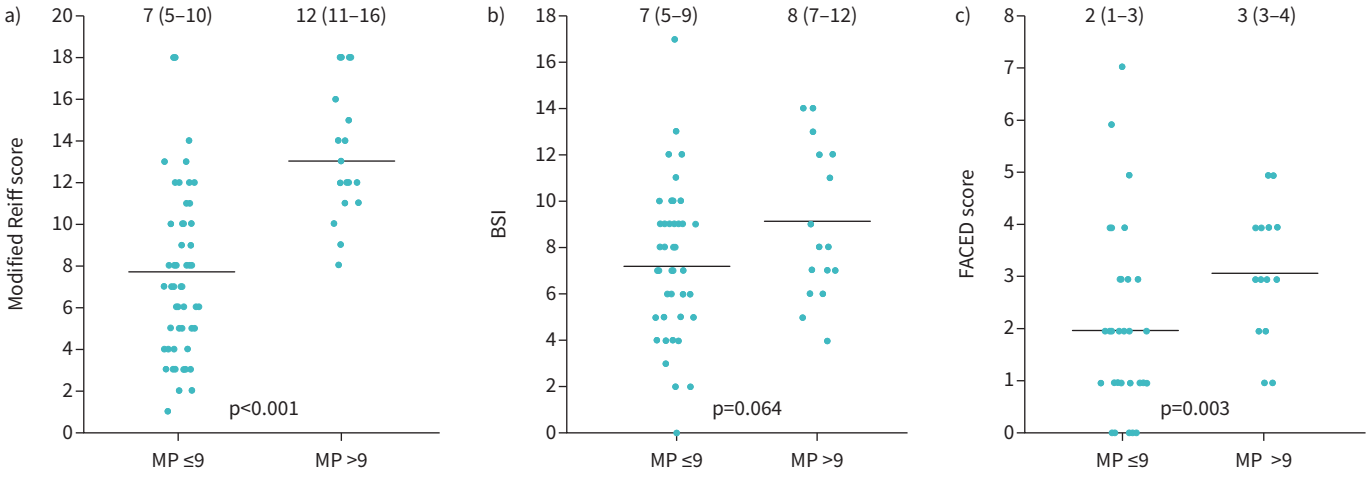

FIGURE 1 Comparison between mucus plugging (MP) of bronchiectasis and a) modified Reiff score, b) Bronchiectasis Severity Index (BSI) and c) FACED (percentage predicted Forced expiratory volume in 1 s, Age, Chronic colonisation of *Pseudomonas aeruginosa*, Extension and Dyspnoea) score. Data values are presented as median (interquartile range).

The most notable finding in our study was that sputum MPO concentration was an independent marker correlating with the extent of MP. Previously, Regelmann *et al.* [34] showed that as sputum MPO activity increased in patients with cystic fibrosis, the Brasfield chest radiograph score and FEV_1 worsened. Additionally, MPO activity in blood neutrophils affects airway injury and airflow obstruction in patients with cystic fibrosis [35]. Our findings augment this understanding by explicitly linking the extent of MP, a critical but often underexplored physical manifestation of bronchiectasis, with elevated concentration of MPO, a marker of neutrophil activation. This correlation not only reinforces the pivotal role of neutrophils in the pathophysiology of bronchiectasis but also suggests that monitoring MPO concentration could provide a more direct assessment of disease severity, specifically relating to airway obstruction by MP. By drawing a parallel to cystic fibrosis, in which a similar pattern of increased neutrophilic inflammation correlates with lung damage, our study underscores the potential common pathways involved in the management of these chronic conditions. Thus, our research not only aligns with but also extends the

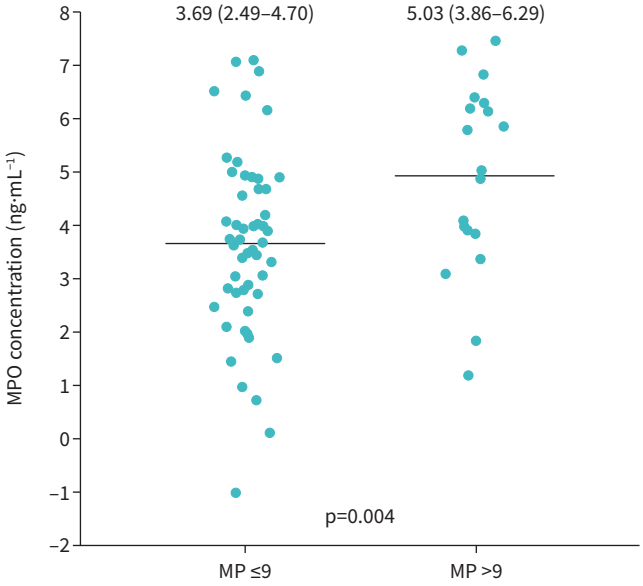

FIGURE 2 Comparison of sputum myeloperoxidase (MPO) concentration between the low and high mucus plugging (MP) groups. MPO concentration was natural log transformed. Data values are presented as median (interquartile range).

TABLE 2 Logistic regression analysis of factors associated with mucus plugging

	Univariate analysis		Multivariable analysis	
	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI)	p-value
MPO concentration[#] (per 1 ln increase)	1.60 (1.10–2.33)	0.015	1.60 (1.06–2.42)	0.025
Age, years (per 1 year increase)	1.03 (0.97–1.10)	0.342	1.00 (0.93–1.06)	0.875
BMI, $kg \cdot m^{-2}$ (per 1 $kg \cdot m^{-2}$ increase)	0.77 (0.62–0.97)	0.023	0.80 (0.64–1.02)	0.066
Smoking status (yes *versus* no)	0.33 (0.08–1.29)	0.111	0.30 (0.07–1.27)	0.102
Microbiology				
Pseudomonas aeruginosa (yes *versus* no)	0.64 (0.16–2.63)	0.538	0.37 (0.08–1.74)	0.206
Others (yes *versus* no)	2.18 (0.71–6.72)	0.175	2.03 (0.62–6.65)	0.241
BHQ score (per 1 point increase)	0.94 (0.89–1.00)	0.053	0.96 (0.90–1.02)	0.179
Post-bronchodilator FEV_1, % pred (per 1% pred increase)	0.95 (0.91–0.98)	0.004	0.95 (0.91–0.99)	0.036
mMRC Dyspnoea scale (per 1 point increase)	1.75 (0.92–3.32)	0.089	1.27 (0.62–2.63)	0.513
hs-CRP, $mg \cdot dL^{-1}$ (per 1 $mg \cdot dL^{-1}$ increase)	1.17 (0.99–1.38)	0.068	1.15 (0.97–1.36)	0.098
Previous history of acute exacerbation	0.38 (0.11–0.24)	0.107	0.28 (0.08–1.03)	0.055
Modified Reiff score	1.47 (1.20–1.80)	<0.001	1.44 (1.17–1.77)	0.001

MPO: myeloperoxidase; BMI: body mass index; BHQ: Bronchiectasis Health Questionnaire; FEV_1: forced expiratory volume in 1 s; mMRC: modified Medical Research Council; hs-CRP: high-sensitivity C-reactive protein. [#]: natural log transformed.

existing literature highlighting the potential of MPO as a target for therapeutic intervention and as a biomarker for the clinical monitoring of bronchiectasis, especially in terms of MP.

Although our study provides insightful findings regarding the association of the extent of MP with disease severity and sputum MPO concentration in bronchiectasis, it is important to acknowledge its limitations. First, the sample size was relatively small and, thus, may not be sufficient to capture the full spectrum of variability in patients with bronchiectasis. Furthermore, in this study, MP was not associated with an increased rate of baseline acute exacerbation as well as future acute exacerbation. Future studies with larger sample sizes are needed to evaluate MP and acute exacerbation. Second, although our study suggests a correlation between MP and sputum MPO concentration, it could not establish a causal relationship. Further studies are required to evaluate the causal relationship between MP and sputum MPO concentration. Third, our study design initially aimed to collect sputum samples within 3 days from the date of CT acquisition. However, the actual time duration between these two procedures was highly variable due to patient preferences and hospital resource constraints. This variability is a significant limitation of our study, which is a retrospective analysis of prospectively collected data. Fourth, since our study enrolled subjects who could produce spontaneous sputum, there was inevitable bias.

Conclusions

In conclusion, our study demonstrated that the extent of MP reflects disease severity and correlates with sputum MPO concentration in patients with bronchiectasis. Specifically, the sputum MPO concentration was independently associated with an increased extent of MP, suggesting a potential role of MPO in the pathogenesis of MP.

Data availability: The data supporting this study's findings are available from the corresponding author upon reasonable request.

Provenance: Submitted article, peer reviewed.

Ethics statement: Consent to participate was obtained from all participants and the study was approved by the Institutional Review Board of Chungbuk National University Hospital (IRB number 2020-03-008). The study was conducted in accordance with the principles of the Declaration of Helsinki.

Author contributions: S-H. Kim: data curation, methodology, investigation, formal analysis and writing (original draft, review and editing). K.M. Lee: writing (original draft, review and editing). J.Y. Yoo: supervision, data curation and writing (review and editing). K.J. Chae: supervision and writing (review and editing). G-H. Kim: formal analysis

and writing (review and editing). J.Y. Cho: supervision and writing (review and editing). N.M. The: supervision and writing (review and editing). E-G. Kim: funding acquisition, supervision and writing (review and editing). J-K. Choi: supervision and writing (review and editing). K.H. Choe: data curation, supervision and writing (review and editing). H. Lee: conceptualisation, methodology, visualisation and writing (original draft, review and editing). B. Yang: conceptualisation, formal analysis, funding acquisition, methodology, visualisation and writing (original draft, review and editing).

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