

Advanced Lung Cancer Inflammation Index (ALI) as an Independent Predictor for Bronchiectasis Exacerbation Risks

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Purpose: Advanced lung cancer inflammation index (ALI), which is composed of the body mass index (BMI), serum albumin level, and blood neutrophil and lymphocyte levels, has been studied in various conditions, including cancers and non-malignant conditions, but not in bronchiectasis.

Patients and methods: A prospective cohort study of Chinese patients with non-cystic fibrosis (CF) bronchiectasis was conducted in Hong Kong to investigate the association between baseline ALI and the risk of bronchiectasis exacerbation. ALI was assessed as a continuous variable, in quartiles, and cutoff values were determined using receiver operator curve (ROC) analysis.

Results: A total of 148 Chinese patients were recruited, 60 of whom developed bronchiectasis exacerbation during the follow-up period. Lower baseline ALI was associated with an increased risk of bronchiectasis exacerbation in the follow-up period, with an adjusted odds ratio (aOR) of 1.06 (95% CI = 1.03–1.09, $p < 0.001$) for every 10-unit decrease. The first to third quartiles of ALI were also associated with a significantly increased risk of bronchiectasis exacerbation, with aOR of 15.525 (95% CI = 3.927–61.379) for Q1 ($p < 0.001$), 6.523 (95% CI = 1.730–24.599) for Q2 ($p = 0.006$), and 7.272 (95% CI = 1.902–27.800) for Q3 ($p = 0.004$). Patients with ALI less than 45.6 had a significantly increased risk of bronchiectasis exacerbation during the follow-up period, with an aOR of 3.829 (95% CI = 1.737–8.442) ($p < 0.001$).

Conclusion: ALI can independently predicting the risk of future exacerbation in patients with non-CF bronchiectasis. Lower ALI was associated with an increased risk of bronchiectasis exacerbation, with a proposed cutoff value of 45.6.

Keywords: advanced lung cancer inflammation index, biomarkers, bronchiectasis, bronchiectasis exacerbation

Introduction

Bronchiectasis is marked by persistent neutrophilic inflammation of the airways.^{1–4} Among its clinical manifestations, exacerbations are both frequent and significant. Data from the European Multicenter Bronchiectasis Audit and Research Collaboration (EMBARC) Bronchiectasis Registry indicate that approximately half of bronchiectasis patients experience two or more exacerbations each year.⁵ These exacerbations adversely affect morbidity, quality of life, and mortality, in addition to raising healthcare costs.^{6–14} To assess disease severity, two well-established scoring systems are commonly used: the Bronchiectasis Severity Index (BSI)^{6,15} and the FACED score, which predicts five-year all-cause mortality. FACED score was built based on factors including forced expiratory volume in one second (FEV₁), age, *Pseudomonas aeruginosa* colonization, disease extent and level of dyspnea; while body mass index (BMI) and exacerbation history were also included in BSI.^{15–18} However, these scoring tools primarily focus on clinical parameters and do not account for the inflammatory status of patients. Several inflammatory markers—such as high-sensitivity C-reactive protein, neutrophil-to-lymphocyte ratio (NLR), and systemic immune-inflammation index (SII)—have been investigated as

possible prognostic biomarkers in bronchiectasis.^{19–21} Nevertheless, these markers do not incorporate patients' clinical characteristics.

The advanced lung cancer inflammation index (ALI)—which incorporates BMI, albumin, and neutrophil-to-lymphocyte ratio (NLR)—is a systemic inflammation marker that was originally developed for patients with lung cancer.^{22,23} Its application has since broadened to include other types of cancer, such as esophageal, colorectal, pancreatic, and gastric cancers.^{24–27} More recently, ALI has also been proposed as a potential prognostic marker for non-malignant conditions, including hypertension, heart failure, coronary artery disease, diabetes mellitus, stroke, and chronic kidney disease (CKD).^{28–31} Recently, our group also reported that ALI could predict the risk of exacerbation of chronic obstructive pulmonary disease (COPD).³² There is similarities between COPD and bronchiectasis in the pathological mechanism while there are also major differences in these two diseases,³³ for example the sex of the patients involves (predominantly male in COPD and more female in bronchiectasis), etiology (smoking as the predominant cause of COPD while post-infective causes predominates in bronchiectasis), radiological features, clinical course and treatment modalities. Hence, it will be interesting to assess if ALI has the same prognostic role in bronchiectasis as in COPD, while the findings in COPD cannot be directly extrapolated to bronchiectasis patients.

Unlike other inflammatory indices, ALI uniquely includes BMI, a simple and repeatable measurement, along with readily accessible blood-based biomarkers. This combination may provide a more holistic evaluation of systemic inflammation and body composition, both of which can be affected by severe illness. Notably, BMI is also a component of BSI, highlighting its prognostic significance in bronchiectasis. Additionally, serum albumin, another ALI component, reflects patients' nutritional status, which can be compromised in the presence of major diseases. Integrating serum albumin, BMI, and NLR into a single scoring system like ALI could therefore enhance prognostic accuracy.

Given that bronchiectasis is characterized by chronic inflammation, additional studies are needed to further elucidate the prognostic significance of ALI in this disease.

Methods

This was a prospective, single-center cohort study conducted in Hong Kong. A total of 150 Chinese patients with non-cystic fibrosis (non-CF) bronchiectasis who were being followed at the designated bronchiectasis or respiratory clinic of the Department of Medicine, Queen Mary Hospital (QMH), were prospectively enrolled between February 9, 2023, and July 13, 2023. Participants were monitored for the occurrence of bronchiectasis exacerbations until February 28, 2025. Patients were excluded if they had coexisting airway disease (asthma/COPD), traction bronchiectasis secondary to interstitial lung disease (ILD), bronchiectasis due to allergic bronchopulmonary aspergillosis (ABPA), or those who lost to follow up. To confirm diagnoses, the investigators reviewed medical records and relevant radiological findings, ensuring that each case met the international consensus criteria for both the radiological and clinical diagnosis of bronchiectasis in adults.³⁴ Patients' data were accessed via the Electronic Patient Record (ePR) system of the Hong Kong Hospital Authority, which includes information from both outpatient and inpatient visits. Available data encompassed demographics, clinical documentation, investigation results, and treatment details.

Demographic information, clinical data, and investigation results were extracted from ePR. The primary outcome of the study was bronchiectasis exacerbation. Exacerbation of bronchiectasis was defined according to the consensus criteria for pulmonary exacerbations in adults with bronchiectasis.³⁵ The criteria for bronchiectasis exacerbation included: [1] a worsening of ≥ 3 key symptoms for ≥ 48 hours, such as cough, sputum volume and/or consistency, sputum purulence, dyspnea and/or reduced exercise tolerance, fatigue and/or malaise, and hemoptysis; AND [2] a clinician's judgment that a change in the patient's bronchiectasis treatment was necessary.³⁵ The secondary outcome was hospitalized bronchiectasis exacerbation, defined as an exacerbation meeting the aforementioned criteria that required inpatient care for at least 24 hours. Regular use of pharmacotherapy for bronchiectasis was defined as the continuous use of these medications for a minimum of 12 months during the study period. Baseline FACED scores were calculated for each patient, incorporating the following components: F—forced expiratory volume in 1 second (FEV₁) in percentage predicted; A—age with cut-off at 70; C—chronic colonization by *Pseudomonas aeruginosa*; E—extent of bronchiectasis; and D—dyspnea (Assessed by Modified Medical Research Council (mMRC) Dyspnea Scale).¹⁷

ALI was calculated as follows: body mass index (kg/m^2) $\times$ serum albumin level (g/dL)/neutrophil-to-lymphocyte ratio (NLR). Patients were categorized into four groups according to the quartiles of their ALI values.

The parameters required for calculating the ALI were obtained during the recruitment visit, when the patient had been clinically stable for at least 30 days following their most recent exacerbation that necessitated antibiotic treatment. The study was approved by the Institutional Review Board (reference number UW 22–656).

Sample Size Calculation

There was no published study on the association between ALI and bronchiectasis exacerbation risks. However, there was a study on the association between ALI and postoperative complications in patients undergoing lung resection for bronchiectasis.³⁶ In this study, patients in the low ALI group had a higher proportion of requiring open thoracotomy (11.3% vs 38.8%) when compared to the high ALI group, which is a surrogate marker of negative outcome. Sample size calculation using the reported findings in this study suggested a sample size of 124 would have 95% power and an alpha of 0.05.

Statistical Analysis

Demographic and clinical variables were presented as actual frequencies or as means $\pm$ standard deviations. Baseline demographic and clinical characteristics were compared between patients with and without exacerbations during the follow-up period using two-sample *t*-test. Univariate and multi-variable logistic regression analysis were performed to assess the relationship between ALI and the risk of bronchiectasis exacerbation during follow-up. Age, baseline FACED score, sex, smoking status, use of bronchiectasis pharmacotherapy and the number of exacerbations in the preceding 1 year were included as covariates in the multi-variable analyses. Multi-collinearity among these variables was evaluated, with results provided in [Supplementary Table 1](#); no evidence of multi-collinearity was found. Analyses of ALI were performed in three ways: as a continuous variable, by quartile grouping, and using the optimal cut-off determined by receiver operating characteristic (ROC) analysis. A *p*-value of < 0.05 was considered statistically significant. All statistical analyses were conducted using IBM SPSS Statistics for Windows, Version 28.0.

Results

A total of 150 Chinese patients with non-CF bronchiectasis were recruited. Two subjects were excluded because they were unable to perform body measurements for BMI assessment owing to their poor mobility. Sixty patients developed exacerbations of bronchiectasis during the follow-up period, with 22 requiring hospitalization. The mean follow-up interval was 21.9 ± 2.6 months. The patient selection flow diagram is shown in [Figure 1](#).

Baseline Characteristics

The mean age of the include patients was 70.6 ± 10.0 years, with more females (71.6%) and never-smokers (88.5%). A total of 41 (27.7%) patients had *Pseudomonas aeruginosa* colonization. The mean baseline FEV₁ was 1.75 ± 0.52 L ($93.1 \pm 20.6\%$). A total of 83 patients (56.1%) had more than 2 lobes involved by bronchiectasis. The mean ALI was 48.9 ± 22.1 . The quartiles of ALI were Q1 (lowest): <343 ; Q2: 343–450; Q3: 450.1–577; Q4: > 577 . The results are summarized in [Table 1](#).

Optimal ALI Cut-off Value to Predict the Risk of Total Bronchiectasis Exacerbation and Hospitalized Bronchiectasis Exacerbation

ROC analysis was performed to determine the optimal cut-off value for ALI in predicting total bronchiectasis exacerbation. At a cutoff of 45.6, the area under the curve (AUC) was 0.713 (95% confidence interval [CI] = 0.631–0.795; $p < 0.001$). The corresponding sensitivity and specificity were 60.2% and 71.7%, respectively, with a Youden index of 0.319 ([Figure 2](#)).

ROC analysis was performed to determine the optimal cutoff value for ALI in predicting hospitalized bronchiectasis exacerbations. At the cut-off at 39.5, the AUC was 0.718 (95% CI = 0.610–0.826; $p = 0.001$). The corresponding sensitivity and specificity were 69.0% and 68.2%, respectively, with a Youden index of 0.372 ([Figure 3](#)).

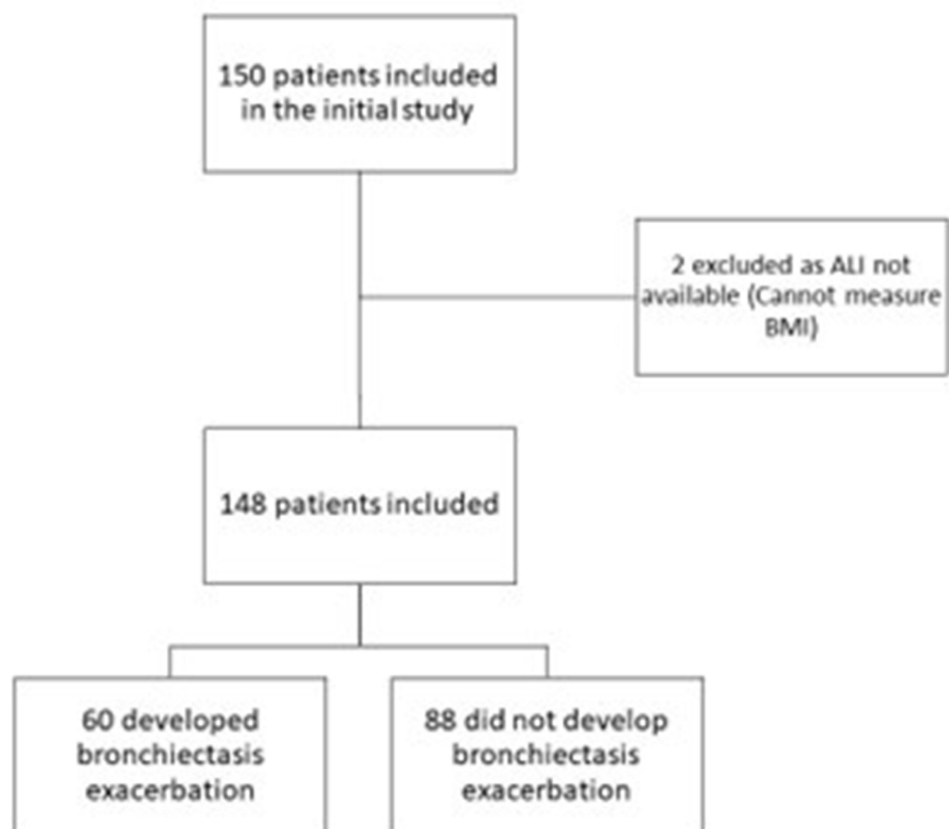


Figure 1 Patient selection flow diagram.

Risk of Total Bronchiectasis Exacerbation and Baseline ALI

The lower baseline ALI, as a continuous variable, every ten-unit decrease was associated with an increased risk of total bronchiectasis exacerbation in the follow-up period, with an odds ratio (OR) of 1.05 (95% CI = 1.03–1.08, $p < 0.001$) and an adjusted OR (aOR) of 1.06 (95% CI = 1.03–1.09, $p < 0.001$).

Table 1 Baseline Demographic and Clinical Characteristics

	No Exacerbation (n = 88)	Exacerbation During Follow-Up (n = 60)	Whole Cohort (n = 148)	p-value
Age (years), mean $\pm$ SD	71.3 $\pm$ 10.1	69.4 $\pm$ 9.8	70.6 $\pm$ 10.0	0.26
Sex				0.26
Male	28 (31.8%)	14 (23.3%)	42 (28.4%)	
Female	60 (68.2%)	46 (76.7%)	106 (71.6%)	
Smoking status				0.11
Non-smoker	74 (84.1%)	57 (95.0%)	131 (88.5%)	
Ex-smoker	12 (13.6%)	3 (5.0%)	15 (10.1%)	

(Continued)

Table 1 (Continued).

	No Exacerbation (n = 88)	Exacerbation During Follow-Up (n = 60)	Whole Cohort (n = 148)	p-value
Current smoker	2 (2.3%)	0 (0%)	2 (1.4%)	
BMI (kg/m ²)	22.8 ± 5.6	21.5 ± 3.7	22.2 ± 1.9	0.11
FEV ₁ (L), mean ± SD	1.80 ± 0.52	1.68 ± 0.51	1.75 ± 0.52	0.20
FEV ₁ (% predicted), mean ± SD	96.6 ± 19.2	87.9 ± 21.8	93.1 ± 20.6	0.02*
FVC (L), mean ± SD	2.56 ± 0.71	2.34 ± 0.68	2.47 ± 0.70	0.08
FVC (% predicted), mean ± SD	101.8 ± 17.0	93.6 ± 20.0	98.5 ± 18.6	0.02*
FEV ₁ /FVC ratio (%), mean ± SD	70.5 ± 9.7	71.6 ± 11.4	70.9 ± 10.4	0.55
FACED score, mean ± SD	1.98 ± 1.20	2.20 ± 1.61	2.07 ± 1.38	0.34
Extent of bronchiectasis (Number of lobes involved)				0.89
1	18 (20.5%)	11 (28.3%)	29 (19.6%)	
2	23 (26.1%)	13 (21.7%)	36 (24.3%)	
3	28 (31.8%)	20 (33.3%)	48 (32.4%)	
4	10 (11.4%)	10 (16.7%)	20 (13.5%)	
5	9 (10.2%)	6 (10.0%)	15 (10.1%)	
<i>Pseudomonas aeruginosa</i> colorization	13 (14.8%)	28 (46.7%)	41 (27.7%)	<0.001*
mMRC dyspnoea scale				0.60
0	26 (29.5%)	20 (33.3%)	46 (31.1%)	
1	41 (46.6%)	22 (36.7%)	63 (42.6%)	
2	17 (19.3%)	14 (23.3%)	31 (20.9%)	
3	4 (4.5%)	3 (5.0%)	7 (4.7%)	
4	0 (0%)	1 (1.7%)	1 (0.7%)	
Exacerbations in past 12 months	4 (4.5%)	7 (11.7%)	11 (7.4%)	0.11
Baseline platelet count (x10 ⁹ cells/L), mean ± SD	231 ± 64	242 ± 59	236 ± 62	0.29
Baseline neutrophil count (x10 ⁹ cells/L), mean ± SD	3.46 ± 1.16	4.47 ± 1.32	3.87 ± 1.32	<0.001*
Baseline lymphocyte count (x10 ⁹ cells/L), mean ± SD	1.77 ± 0.53	1.87 ± 0.59	1.81 ± 0.56	0.31
Baseline albumin (g/dL), mean ± SD	4.4 ± 0.3	4.2 ± 0.4	4.3 ± 0.4	<0.001*
ALI, mean ± SD	55.5 ± 24.5	39.2 ± 13.3	48.9 ± 22.1	<0.001*
Treatment				
ICS	7 (8.0%)	30 (33.0%)	37 (25.0%)	<0.001*
Macrolide	3 (3.4%)	8 (13.3%)	11 (7.4%)	0.024*
Inhaled antibiotics	0 (0%)	1 (1.7%)	1 (0.7%)	0.22

Notes: * statistically significant.

Abbreviations: SD, standard deviation; mL, milliliter; FEV₁, forced expiratory volume in one second; FVC, forced vital capacity; ICS, inhaled corticosteroid; AUC, area under the curve; LS, least squares; NE, not estimable.

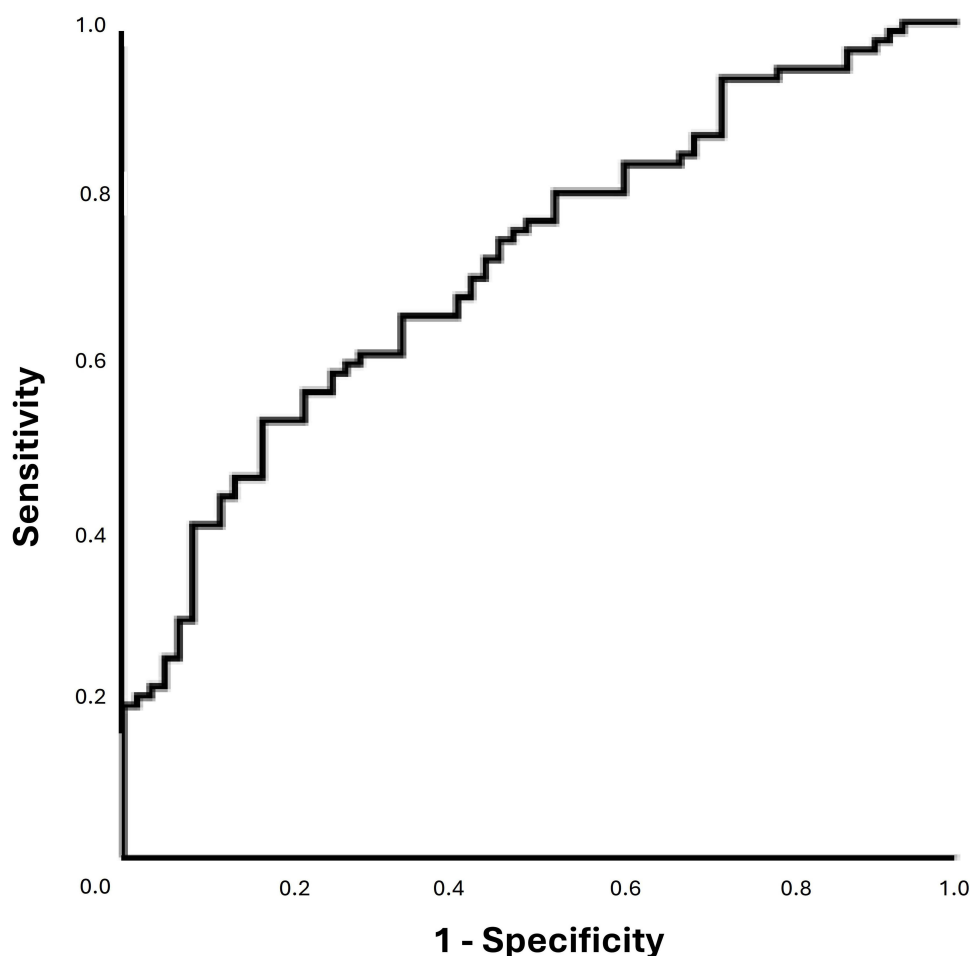


Figure 2 Receiver Operating Curve (ROC) for ALI and risk of total bronchiectasis exacerbation.

Q1 to Q3 of ALI, when compared with Q4 (highest quartile), were associated with a significantly increased risk of total bronchiectasis exacerbation during the follow-up period, with OR of 9.389 (95% CI = 2.977–29.600; $p < 0.001$) for Q1, 6.063 (95% CI = 1.935–18.994; $p = 0.002$) for Q2, and 4.364 (95% CI = 1.384–13.761; $p = 0.012$) for Q3 (Table 2).

The aORs were 15.525 (95% CI = 3.927–61.379; $p < 0.001$) for Q1, 6.523 (95% CI = 1.730–24.599; $p = 0.006$) for Q2 and 7.272 (95% CI = 1.902–27.800; $p = 0.004$) for Q3.

Patients with ALI less than 45.6 (cut-off value determined by ROC analysis) had a significantly increased risk of total bronchiectasis exacerbation during the follow-up period, with an OR of 3.830 (95% CI = 1.892–7.755; $p < 0.001$) and aOR of 3.829 (95% CI = 1.737–8.442; $p < 0.001$).

Risk of Hospitalized Bronchiectasis Exacerbation and Baseline ALI

A lower baseline ALI as a continuous variable was associated with an increased risk of hospitalization bronchiectasis exacerbation during the follow-up period, with an OR of 1.005 (95% CI = 1.002–1.009; $p = 0.003$) and an aOR of 1.005 (95% CI = 1.001–1.009; $p = 0.018$) for every unit increase.

Q1 (lowest quartile) of ALI, compared with Q4 (highest quartile), was associated with a significantly increased risk of bronchiectasis exacerbation during the follow-up period, with OR of 11.571 (95% CI = 1.383–96.808; $p = 0.024$) for Q1, 9.931 (95% CI = 1.175–84.038; $p = 0.035$) for Q2, and 4.364 (95% CI = 0.464–41.056; $p = 0.198$) for Q3.

The aORs were 12.033 (95% CI = 1.279–113.217; $p = 0.030$) for Q1; 6.927 (95% CI = 0.748–64.1841; $p = 0.088$) for Q2 and 45.257 (95% CI = 0.521–53.025; $p = 0.159$) for Q3 (Table 3).

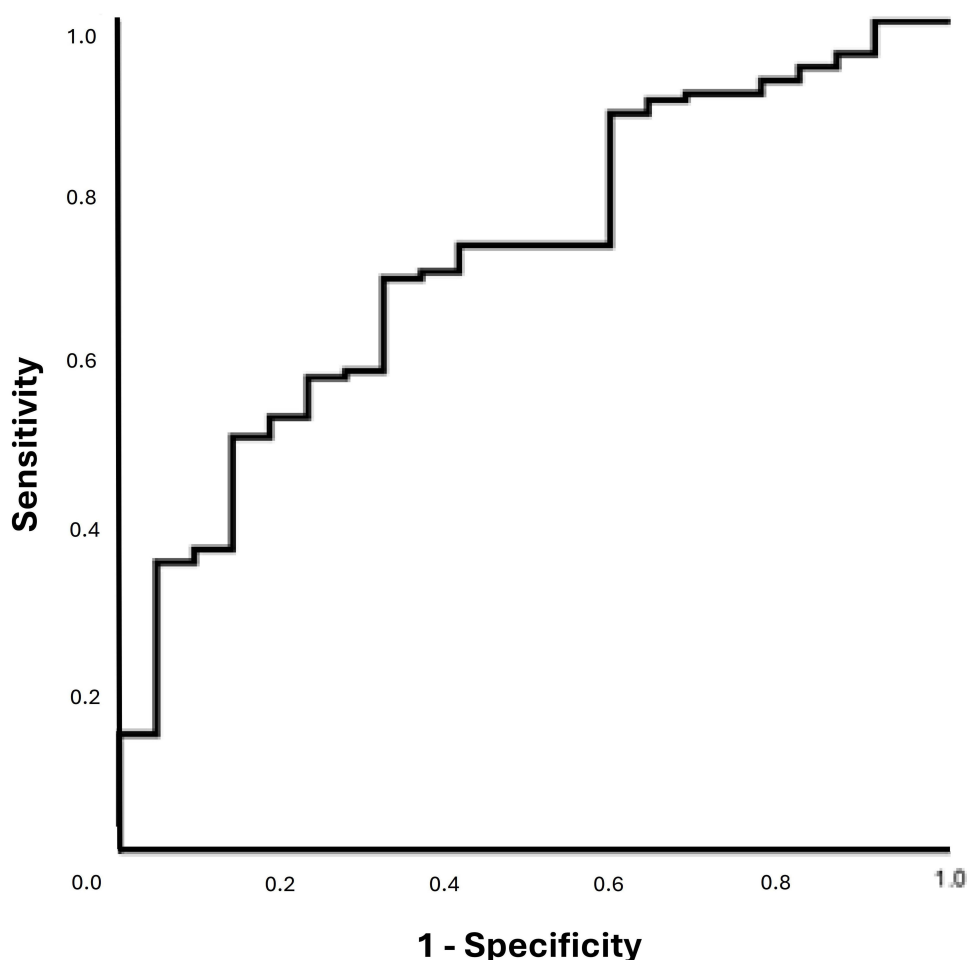


Figure 3 Receiver Operating Curve (ROC) for ALI and risk of hospitalized bronchiectasis exacerbation.

Patients with ALI less than 39.2 (the cut-off value determined by ROC analysis) had a significantly increased risk of hospitalization bronchiectasis exacerbation during the follow-up period, with an OR of 4.053 (95% CI = 1.570–10.461; $p = 0.004$) and an aOR of 4.517 (95% CI = 1.434–14.227; $p = 0.010$).

Discussion

To the best of our knowledge, this is the first report on the role of ALI in predicting the risk of exacerbation of bronchiectasis. The findings were observed when ALI was assessed as a continuous variable, in quartiles and as a cut-off

Table 2 Baseline ALI Level in Quartile and Risk of Total Bronchiectasis Exacerbation

Quartile	OR	95% CI	p-value	aOR	95% CI	p-value
Q1 (n = 37)	9.389	2.977–29.600	<0.001	15.525	3.927–61.379	<0.001
Q2 (n = 37)	6.063	1.935–18.994	0.002	6.523	1.730–24.599	0.006
Q3 (n = 37)	4.364	1.384–13.761	0.012	7.272	1.902–27.800	0.004
Q4 (n = 37; Reference group)	–	–	–	–	–	–

Notes: Factors adjusted in multiple logistic regression: age, baseline FACED score, sex, smoking status, bronchiectasis pharmacotherapy, and number of bronchiectasis exacerbations in the past 12 months.

Abbreviations: OR, Odds ratios, aOR, adjusted odds ratio; CI, confidence interval; OR, Odds ratio.

Table 3 Baseline ALI Level in Quartile and Risk of Hospitalized Bronchiectasis Exacerbation

Quartile	OR	95% CI	p-value	aOR [^]	95% CI	p-value
Q1* (n = 37)	11.571	1.383–96.808	0.024	12.033	1.279–113.217	0.030
Q2 (n = 37)	9.931	1.175–84.038	0.035	6.927	0.748–64.1841	0.088
Q3 (n = 37)	4.364	0.464–41.056	0.198	45.257	0.521–53.025	0.159
Q4 (n = 37; Reference group)	–	–	–	–	–	–

Notes: * statistically significant; [^] Factors adjusted in multiple logistic regression: Age, baseline FACED score, sex, smoking status, bronchiectasis pharmacotherapy, and number of bronchiectasis exacerbations in the past 12 months.
Abbreviations: OR, Odds ratios, aOR, adjusted odds ratio; CI, confidence interval; OR, Odds ratio.

value determined by ROC. ALI was associated with both total and hospitalized exacerbations. Our results indicate that this easily accessible marker may have a role in predicting outcomes in bronchiectasis.

Although different scoring systems and biomarkers have been proposed for bronchiectasis, they have their own limitations. The BSI and FACED scores are well validated and most often used. However, these studies have mainly focused on established outcomes, such as the extent of bronchiectasis and bacterial colonization. However, the inflammatory state of bronchiectasis was not assessed using these scoring systems. BSI and FACED mainly based on the established outcomes in bronchiectasis like extent, lung function and colonization of bacteria, which are rather stable over time. BMI is included in BSI but not FACED. ALI has the advantage of incorporating inflammatory markers and BMI, which can reflect the dynamic process in bronchiectasis. It may also serve as the tool to monitor bronchiectasis, by observing the changes in BMI and inflammatory markers with time. While NLR, SII, and hs-CRP have been shown to predict bronchiectasis exacerbations, these biomarkers did not consider the nutritional status of patients with bronchiectasis. These markers only measure the inflammatory component but not BMI which is an important parameter, reflecting the nutritional status of these patients. ALI can serve as a simple, easily repeatable, and comprehensive biomarker of bronchiectasis. The calculation of ALI uses NLR in the denominator to represent inflammatory status, especially neutrophilic inflammation, which is a hallmark of bronchiectasis. BMI and albumin, forming the numerator, are essential nutritional indicators that often decline as chronic respiratory diseases progress.³⁷ By incorporating systemic inflammation and nutritional parameters within a single scoring system, clinicians can easily prognosticate and monitor these patients. ALI can potentially serve as a simple and meaningful marker to reflect nutritional and inflammatory markers in bronchiectasis. Our study also suggested that ALI can predict bronchiectasis exacerbation as a continuous variable, in quartiles, and at a cut-off value, as determined by ROC analysis. In short, a lower ALI, which can result from worse nutritional status, a higher degree of neutrophilic inflammation, or both, is associated with an increased risk of bronchiectasis exacerbation.

However, ALI did have its own disadvantages. While ALI included important and easily available nutritional and inflammatory markers, it did not include other well reported prognostic factors in bronchiectasis, such as lung function, symptoms and bacterial colonization. Also, whether replacing NLR with SII, or adding hs-CRP to it may enhance its prognostic role is also worth assessing. In the future, it is worthwhile to assess the incorporation of ALI into FACED/BSI to enhance the performance of these well reporting scoring systems.

Exacerbation of bronchiectasis is one of the most common sequelae. Assessing patients' risk of bronchiectasis exacerbation is crucial when considering new drug treatments.^{38–40} The use of scoring systems and biomarkers will facilitate clinicians to stratify the exacerbation of the disease and offer timely management. These findings suggest that ALI has potential as an independent prognostic factor in forecasting exacerbations in bronchiectasis. The observed values in this study can be explained by the fact that ALI incorporates factors representing both the pathophysiology and general health of bronchiectasis patients. This also underscores the need for clinicians to focus on both disease severity and the nutritional decline—evident through low BMI and albumin—that accompanies chronic inflammation in bronchiectasis. Whether nutritional support and therapy can help bronchiectasis patients is also worth studying, but the importance of

maintaining good overall health status should not be overemphasized. The simplicity of ALI makes it a practical tool for routine evaluation and serial monitoring of disease progression in bronchiectasis patients.

Knowing the role of various biomarkers, such as ALI, in relation to the prognosis of bronchiectasis, such as exacerbation risk, they can be incorporated into a new scoring system. The addition of biomarkers, including ALI, to the new scoring system could provide insight into patients' nutritional and inflammatory states and aid in predicting outcomes such as the risk of exacerbations. This could help clinicians to better understand the severity and risks of bronchiectasis by incorporating disease extent, nutritional status, and inflammatory markers into this novel scoring system, which can more precisely affect bronchiectasis in multiple dimensions. Apart from exacerbation risks, symptoms, quality of life, lung function, and survival should be assessed using this scoring system.

Our study had some limitations. First, it involved the QMH as the only center. QMH, a tertiary medical center in Hong Kong affiliated with The University of Hong Kong, houses a respiratory unit that receives referrals from healthcare facilities across the region. It also features a dedicated bronchiectasis clinic for comprehensive management of patients with bronchiectasis. Second, lung function tests were performed at different time points in the different patients. Only one ALI measurement was obtained from the included patients during the recruitment visit. As BMI and blood parameters can change over time, serial ALI measurements and assessment of their role in bronchiectasis should be considered in a separate study. A follow up study on serial ALI measurement and the long-term outcome such as development of other system complications, evolution of bronchiectasis over time and mortality shall be considered. Only Chinese patients were included in this study, which affects their generalizability. While baseline FACED score was adjusted, which included *Pseudomonas aeruginosa* colonization as one of the component, the colonization from other micro-organisms were not measured by FACED score with potential residual confounding. Using BSI instead of FACED score may overcome this issue as it includes the colonization from other micro-organisms as the component. But it also introduced the potential issue of multi-collinearity as BMI is also included in BSI. Finally, the study included only a small number of participants. Having a small sample size and low event number resulted in a wide CI in the results reported, despite statistical significance being reached. A large-scale study, especially multi-national multi-centre study involving patients of different ethnicities and clinical characteristics, is important to test the observations noted in this study. Ideally, the results should be validated using an external data source to confirm the findings of this study.

Conclusion

ALI has the potential to serve as a biomarker for predicting exacerbation risk in bronchiectasis patients. Reduced ALI was associated with an elevated risk of exacerbation in bronchiectasis patients. The proposed cut-off value was 45.6 for bronchiectasis exacerbation and 39.2 for hospitalized bronchiectasis exacerbation. The prognostic significance of ALI in bronchiectasis should be confirmed through external validation in a separate cohort.

Data Sharing Statement

All available data are presented in the manuscript and no additional data are provided. Due to the ethical restrictions imposed by the Institutional Review Board (IRB) regulations and rules on patient data privacy in this study, supporting research data were not available upon request.

Ethical Approval and Informed Consent

This study was approved by the Institutional Review Board of the University of Hong Kong and the Hospital Authority of Hong Kong West Cluster (UW 22-656). Informed consent was obtained from all the participants. This study was conducted in accordance with the principles of the Declaration of Helsinki. The study was reported in accordance with the RECORD reporting guidelines.

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Author Contributions

Conceptualization: W.C.K.; Methodology: W.C.K.; Validation: S.S.K.C., T.C.C.T.; Formal analysis: W.C.K.; Investigation: W.C.K., E.P.H.C.; Data Curation: W.C.K.; Writing - Original Draft: W.C.K., E.P.H.C., S.S.K.C., T.C.C.T., J.C.M.H.; Writing - Review & Editing: W.C.K., E.P.H.C., S.S.K.C., T.C.C.T., J.C.M.H.; Visualization: W.C.K., E.P.H.C., J.C.M.H.; Supervision: J.C.M.H.; Project administration: W.C.K., J.C.M.H.

All authors took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agreed to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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