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ORIGINAL RESEARCH

The Association Between Systemic Immune-Inflammation Index at Admission and Readmission in Patients with Bronchiectasis

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Purpose: Systemic Immune-Inflammation Index (SII), calculated by (neutrophils count × platelet count)/lymphocytes count, is a novel index of the local immune response and systemic inflammation response. The SII has been shown to play an important role in the prognosis of many diseases, including cardiovascular diseases, cancer and COPD. However, its role in the prognosis of bronchiectasis remains unclear and requires further investigation. This study aimed to investigate the association between SII and readmissions in patients with acute exacerbations of bronchiectasis.

Patients and Methods: We conducted a retrospective cohort study of all bronchiectasis patients admitted to the respiratory ward in Beijing Chaoyang Hospital from January 2020 to January 2022. Patients were classified into four groups according to the quartiles of $\log_2$(SII) at admission. The primary endpoint was readmission at 1-year follow up. Univariate and multivariate cox regression models were applied to investigate the relationship between SII and readmissions at 1-year follow up in patients with bronchiectasis.

Results: A total of 521 patients were included in our study. The median (IQR) SII at admission were 506.10 (564.84). Patients with higher SII tended to be older, male, past and current smokers, have lower BMI, and more dyspnea symptoms. They also had higher inflammatory markers and received a greater spectrum of antibiotics and more intravenous glucocorticoids. Higher SII at admission were independently associated with readmission in patients with acute exacerbations for bronchiectasis following confounder adjustment (OR =1.007; 95% CI, 1.003–1.011; p <0.001).

Conclusion: Patients with elevated SII levels were typically older males, often smokers, with lower BMI and increased dyspnea. They received more antibiotics and intravenous glucocorticoids. Higher SII at admission are associated with readmission in patients with acute exacerbations of bronchiectasis. SII has potential clinical value as a predictive biomarker for clinical outcomes in bronchiectasis, offering a valuable tool for management strategies.

Keywords: chronic respiratory disease, inflammation, prognosis

Introduction

Non-cystic fibrosis (non-CF) bronchiectasis is a chronic respiratory disease characterized by persistent airway infection and the presence of abnormal thickening and dilation of the bronchial wall.[1,2] Patients with bronchiectasis always suffer from chronic cough, sputum production and recurrent acute exacerbations, which may require admissions. Repeated admissions due to acute exacerbation of bronchiectasis are a major clinical problem that is associated with adverse clinical outcomes and economic outcomes.[3] Therefore, identifying those who are at risk of repeated admissions to prevent or delay progression of the disease is essential for doctors.

Airway and systemic inflammation are considered to be important mechanisms in the pathogenesis of non-CF bronchiectasis.[4–6] The pathogenesis of bronchiectasis is currently believed to begin with the bacterial colonization of

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the lower respiratory tract, which then causes an inflammatory response.[7] The recurrent inflammation and infection insults result in the damage to the airways and a vicious cycle of the airway injury.[8] Previous studies have demonstrated that high systematic inflammation markers including TNF-α, C-reactive protein (CRP) and high-sensitivity C-reactive protein (hs-CRP) were associated with the severity of bronchiectasis[9,10] and the risk of future exacerbations.[11,12]

Systematic Immune-Inflammation Index (SII), which was calculated using the formula: (neutrophils count × platelet count)/lymphocytes count, has been considered as a novel index to reflect the local immune response and systemic inflammation.[13,14] It was initially utilized to evaluate the prognostic outcomes of hepatocellular carcinoma (HCC). Elevated levels of SII have been associated with increased tumor recurrence rates and shorter survival time in patients diagnosed with HCC.[13] Due to the cost-effectiveness and accessibility of the SII, the utility of the SII has since expanded beyond HCC. Previous studies also demonstrated the association between SII and adverse outcomes in other malignant cancers such as colorectal cancer[14] and cervical cancer.[15] Several studies have investigated the relationship between SII levels and cardiovascular diseases, kidney disease and respiratory disease.[16–19] Of note, a recent study has demonstrated the predictive value of SII in hospitalizations in patients with stable bronchiectasis,[20] which indicate that SII has potential clinical application value not only in oncology but also in the assessment of prognosis in bronchiectasis.

To date, there were few studies have evaluated the association between SII and the prognosis of bronchiectasis. Thus, we performed a cohort study to investigate the association between SII and the readmission in patients with bronchiectasis.

Material and Methods

Study Design and Study Population

This was a single center retrospective cohort study involving patients with acute exacerbations of bronchiectasis. We retrospectively enrolled patients hospitalized with bronchiectasis exacerbation between January 2020 and January 2022 at Beijing Chaoyang Hospital. The inclusion criteria were as follows: (1) Aged 18 years or older; (2) Diagnosis of bronchiectasis by HRCT and accordingly clinical symptoms; (3) Admission for bronchiectasis exacerbation; (4) With complete data for neutrophil count, lymphocyte count and platelet count. We defined the diagnosis of bronchiectasis exacerbations based on the worsening of three or more of the six symptoms of cough, changes in sputum volume, purulent sputum, dyspnea or exercise tolerance, fatigue or discomfort, and hemoptysis for more than 48 hours requiring treatment.[1] The exclusion criteria were as follows: (1) Age <18 years old; 2) Lack of data on neutrophil count, lymphocyte count and platelet count; (3) Suffering from uncontrolled malignant tumors and concomitant pulmonary disease, eg interstitial lung disease, pleural disease and pulmonary embolism; (4) People with acute or chronic liver or renal insufficiency, heart failure and other significant medical conditions; (5) Use of systemic corticosteroid therapy 3 months before admission; (6) Lost to follow up.

Data Collection

Data on demographics (age, sex, body mass index (BMI), and smoking status), the etiology of bronchiectasis (idiopathic, post-infective, post-tuberculosis and others), comorbidities (hypertension, diabetes, coronary heart disease, chronic obstructive pulmonary disease (COPD) and asthma), clinical symptoms (cough, sputum, hemoptysis and the modified Medical Research Council (mMRC) dyspnea score), laboratory results (white blood cell count (WBC), neutrophil count, lymphocyte count, platelet count, CRP, erythrocyte sedimentation rate (ESR), fibrinogen (Fbg), D-dimer, albumin (ALB), prealbumin (PAB), globulin (GLB), and albumin/globulin Ratio (A/G)), microbiologic results, radiologic results (Unilateral/Bilateral, the number of affected lobes and involvement of lobes), treatment (use of oxygen support and mechanical ventilation, use of antibiotics and use of intravenous glucocorticoids) and length of stay were collected retrospectively from medical records. Blood samples and culture samples were collected within 24 hours after admission. The peripheral neutrophil count, lymphocyte count and platelet count were reported as 10^9cells/L. SII was calculated using the equation as follows: SII = (neutrophils count × platelet count)/lymphocytes count. Two specialists visually scored the modified Reiff scores on lung windows of CT scans. The modified Reiff[21] score was scored based on lobe

involvement (calculating lingula as a separate lobe) and degree of dilation (tubular=1, varicose=2, cystic=3). The minimum was 0 and the maximum was 18.

Outcomes

The primary endpoint was readmission of bronchiectasis exacerbation (since discharge) at 1 year. The secondary endpoint was the number of readmissions at 1 year. An unscheduled readmission was recorded if a patient was readmitted to hospital or emergency department visits after discharge due to acute exacerbations of bronchiectasis. Patients were followed-up for 1 year after they were discharged from hospital. They were followed up every 3 months through face-to-face interviews and telephones. We will assess hospital readmissions from paper or electronic medical records. The study protocol was approved by the ethics committees of the Beijing Chaoyang hospital (2020-K-017) and written informed consent was obtained from all patients. Our study complies with the Declaration of Helsinki principles and conforms to ethical requirements.

Statistical Analysis

Statistical analysis was performed using SPSS v.26.0 and R v.4.3.2 for Windows. As the SII counts exhibited left-skewed distribution, data were log2-transformed to approximate normality. The log2 SII was divided into quartiles, from the lowest (Quartile 1) to the highest (Quartile 4). Normally distributed variables were expressed as mean ± standard deviation and non-normally distributed variables were summarized as medians with interquartile range (IQR). Differences between the four groups were tested with the one-way ANOVA test or Kruskal–Wallis test. Categorical variables were summarized as percentage and analyzed using the Chi-squared test or Fisher's exact test. Univariate and multivariate Cox proportional hazards regression analysis were performed to examine the association between SII and readmissions in patients with bronchiectasis. Variables included in the multivariate logistic regression analysis were selected based on the results of a univariate analysis (p-value less than 0.1). Restricted cubic spline analysis (RCS) with four knots was employed to investigate the potential non-linear relationship between SII and the risk of readmission in patients with bronchiectasis. A p-value <0.05 were considered statistically significant.

Results

Study Population and Baseline Characteristics

A total of 521 patients with bronchiectasis were included in our study, of whom 64.3% were female, with a median age of 61 years. The study flow chart was presented in Figure 1. The median (IQR) SII levels were 506.10 (564.84). All patients were divided into four groups based on the quartiles of $\log_2$(SII) levels: Quartile 1 (< 8.37), Quartile 2 (8.37 to 8.98), Quartile 3 (8.98 to 9.80), and Quartile 4 (> 9.80). The clinical and demographic characteristics of patients according to the quartiles of $\log_2$(SII) levels were shown in Table 1. There were statistical differences in terms of age, sex, BMI, smoking status, coronary heart disease, and mMRC scores ($p< 0.05$). Patients within Quartile 4 group tended to be older, male, past and current smokers, have lower BMI, and more dyspnea symptoms (evaluated by mMRC). The laboratory, microbiological, radiological characteristics and treatment of patients according to the quartiles of $\log_2$(SII) levels were shown in Table 2. Patients within Quartile 4 had higher WBC, neutrophil percentage, CRP, ESR, D-dimer, lower ALB and PAB. A greater proportion of patients in Quartile 4 received oxygen therapy, combined antibiotics, and intravenous glucocorticoids compared with those in Quartile 1 (all $p<0.05$). They also had longer hospital stays compared with those in Quartile 1 ($p=0.001$).

Outcomes

A total of 175 patients were readmitted within one year, with 135 of them experiencing one readmission and 40 having two or more readmissions. As illustrated in Figure 2, patients in Quartile 4 exhibited a significantly higher number of readmissions than those in other groups ($p < 0.001$). The KM survival curves (Figure 3) showed statistically significant differences among the four groups in readmission (Log rank test $P<0.001$). Patients in Quartile 4 (compared to Quartile 1) had a short relative time to readmission for acute exacerbations of bronchiectasis (mean estimate 325 days

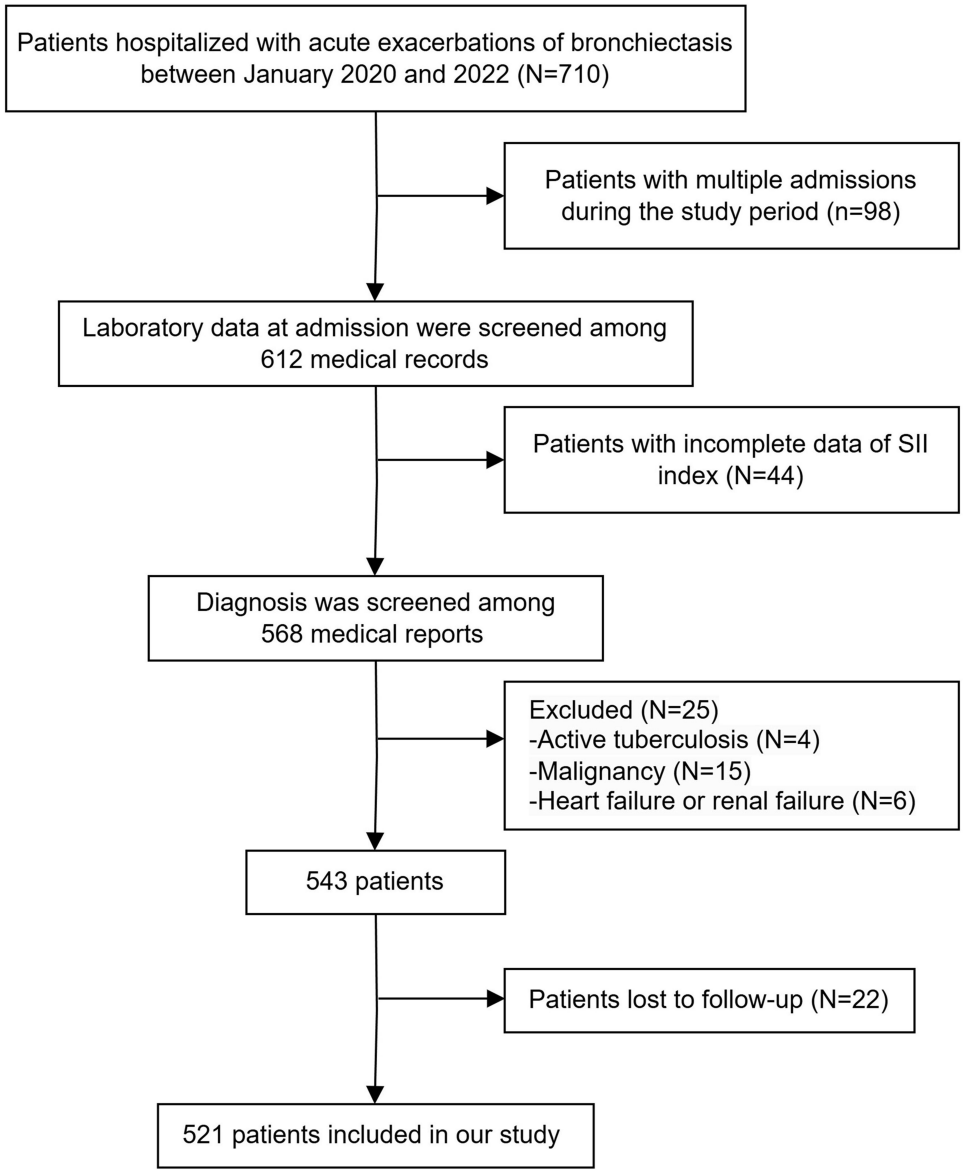

Figure 1 The flow chart of the study population.

versus 288 days). Univariate Cox proportional hazards regression analysis found that the following variables to be significantly associated with readmissions: older age, higher mMRC dyspnea scores, ALB, the number of acute of exacerbations in the previous year, infection with P. aeruginosa, the number of affected lobes and higher modified Reiff score (seen in Supplementary Table 1). As demonstrated in Table 3, elevated SII levels were significantly associated with an increased risk of readmissions in patients with bronchiectasis (odds ratio of 3.381 for quartile 4 vs 1, 95% confidence interval of 2.154 to 5.308, p for trend < 0.001). Higher SII levels remained significantly associated with increased risk of readmissions (odds ratio 2.618 for quartile 4 vs 1, 95% confidence interval 1.636 to 4.188, p for trend < 0.001) after adjustment for potential confounders, including age, BMI, mMRC, ALB, infection with P. aeruginosa, and modified Reiff scores. This study employed RCS analysis to investigate the association between log2(SII) levels and readmissions due to acute exacerbations in patients with bronchiectasis (seen in Figure 4). The results of the RCS analysis indicated a linear relationship between SII levels at admission and the risk of readmissions in patients with bronchiectasis (p for nonlinear = 0.399). A subgroup analysis was performed according to sex, and similar results were obtained.

Table 1 Baseline Clinical Characteristics of Patients Stratified by log2 SII Quartile

	SII					
	Total Patients (N=521)	**Q1 (N=131)**	**Q2 (N=130)**	**Q3 (N=130)**	**Q4 (N=130)**	**P value**
Age, y	61(53,67)	59(52,64)	61(49,65)	60(53,67)	63(55,70)	0.006
Age group						0.004
≤40 years	48(9.2)	17(13.0)	18(13.8)	8(6.2)	5(3.8)	
41–64 years	303(58.2)	83(63.3)	74(56.9)	76(58.5)	70(53.8)	
≥65 years	170(32.6)	31(23.7)	38(29.2)	46(35.4)	55(42.3)	
Sex, F, n (%)	335(64.3)	94(71.8)	88(67.7)	86(66.2)	67(51.5)	0.004
BMI, kg/m2	22.0(19.3,24.6)	22.3(19.4,25.0)	23.0(20.0,25.2)	22.1(19.2,24.2)	20.9(18.2,23.9)	<0.001
Smoking status, n (%)						0.007
Never	418(80.2)	107(81.7)	108(83.1)	109(83.1)	94(72.3)	
Past	63(12.1)	10(7.6)	11(8.5)	14(10.8)	28(21.5)	
Current	40(7.7)	14(10.7)	11(8.5)	7(5.4)	8(6.2)	
Exacerbations in previous year	98(18.8)	24(18.3)	29(22.3)	21(16.2)	24(18.5)	0.647
Etiology, n (%)						0.107
Idiopathic	137(26.3)	36(27.5)	41(31.8)	29(22.3)	31(23.8)	
Post-infective	325(62.5)	82(62.6)	71(55.0)	94(72.3)	78(60.0)	
Post-tuberculosis	34(6.5)	6(4.6)	10(7.8)	5(3.8)	13(10.0)	
Others	24(4.6)	7(5.3)	7(5.4)	2(1.5)	8(6.2)	
Comorbidities, n (%)						
Hypertension	121(23.2)	24(18.3)	35(26.9)	26(20.0)	36(27.7)	0.173
Diabetes	109(20.9)	27(20.6)	37(28.5)	22(16.9)	23(17.7)	0.088
Coronary heart disease	39(7.5)	5(3.8)	17(13.1)	7(5.4)	10(7.7)	0.025
COPD	11(2.1)	1(0.8)	1(0.8)	3(2.3)	6(4.6)	0.126
Asthma	44(8.4)	13(9.9)	6(4.6)	11(8.5)	14(10.8)	0.297
Clinical symptoms, n (%)						
Cough	515(98.8)	130(99.2)	130(100)	128(98.5)	127(97.7)	0.350
Sputum production	484(92.9)	125(95.4)	117(90.0)	123(94.6)	119(91.5)	0.273
Hemoptysis	186(35.7)	48(36.6)	57(43.8)	43(33.1)	38(29.2)	0.086
mMRC ≥2	208(39.9)	43(32.8)	45(34.6)	47(36.2)	73(56.2)	<0.001
Time since the diagnosis, y	3(0,15)	2(0,11)	4(0,19)	3(0,20)	5(0,13)	0.366

Notes: Data are presented as median (IQR) for continuous variables and number (percentage) for categorized variables.
Abbreviations: BMI, body mass index; SII, systemic immunity-inflammation index; COPD, chronic obstructive pulmonary disease; mMRC, modified British medical research council.

Table 2 The Laboratory, Microbiologic and Radiologic Variables Stratified by log2 SII Quartile

	SII					
	Total Patients (N=521)	**Q1 (N=131)**	**Q2 (N=130)**	**Q3 (N=130)**	**Q4 (N=130)**	**P value**
WBC (×109 mL−1)	6.4(5.1,8.0)	5.1(4.4,6.3)	5.9(4.9,6.8)	6.6(5.8,7.7)	8.4(6.9,10.9)	<0.001
Neutrophils (×109 mL−1)	3.8(2.9,5.2)	2.6(2.1,3.3)	3.4(2.7,3.9)	4.2(3.6,5.1)	6.3(5.1,9.3)	<0.001
Lymphocytes (×109 mL−1)	1.7(1.3,2.2)	2.1(1.6,2.5)	1.9(1.6,2.3)	1.7(1.4,2.0)	1.2(0.8,1.6)	<0.001
Platelets (×109 mL−1)	241(199,294)	198(169,230)	238(203,278)	263(213,296)	299(241,364)	<0.001
CRP, mg/ L	0.61(0.29,2.1)	0.37(0.23,0.70)	0.42(0.25,0.86)	0.69(0.31,2.03)	2.43(0.86,8.59)	<0.001
ESR, mm/h	15(6,32)	9(3,20)	10(5,18)	16(7,30)	35(16,55)	<0.001
D-Dimer, ng/mL	360(231,678)	282(176,466)	282(225,444)	351(233,670)	796(404,1555)	<0.001
ALB, g/L	38.7(36.4,41.1)	39.2(37.7,41.1)	39.5(37.6,41.6)	38.7(36.5,41.3)	37.0(34.1,39.4)	<0.001
GLB, g/L	28.4(25.5,31.9)	27.5(24.9,30.1)	28.2(25.2,31.3)	27.9(25.6,31.1)	30.3(27.4,35.0)	<0.001
A/G	1.4(1.2,1.6)	1.4(1.2,1.7)	1.4(1.2,1.6)	1.4(1.2,1.6)	1.2(1.0,1.4)	<0.001
PAB, mg/dl	0.18(0.13,0.23)	0.20(0.16,0.24)	0.21(0.16,0.24)	0.18(0.13,0.24)	0.13(0.07,0.20)	<0.001

(*Continued*)

Table 2 (Continued).

	SII					
	Total Patients (N=521)	**Q1 (N=131)**	**Q2 (N=130)**	**Q3 (N=130)**	**Q4 (N=130)**	**P value**
Patients with positive bacteria cultures, n (%)	137(26.3)	31(23.7)	31(23.8)	33(25.4)	42(32.3)	0.342
P. aeruginosa	94(18.0)	24(18.3)	17(13.1)	23(17.7)	30(23.1)	0.220
Others	48(9.2)	9(6.9)	15(11.5)	12(9.2)	12(9.2)	0.635
Unilateral/Bilateral	154/367	39/92	49/81	36/94	30/100	0.073
Involvement of lobes, n (%)						
Left upper lobe	198(38.0)	46(35.1)	45(34.6)	52(40.0)	55(42.3)	0.505
Lingula	304(58.3)	74(56.3)	66(50.8)	81(62.3)	83(63.8)	0.126
Left lower lobe	329(63.1)	72(55.0)	83(63.8)	90(69.2)	84(64.6)	0.113
Right upper lobe	308(59.1)	75(57.3)	72(55.4)	80(61.5)	81(62.3)	0.615
Right middle lobe	292(56.0)	72(55.0)	70(53.8)	73(56.2)	77(59.2)	0.837
Right lower lobe	321(61.6)	76(58.0)	72(55.4)	87(66.9)	86(66.2)	0.137
The number of affected lobes	3(2,5)	3(2,4)	3(1,5)	4(2,5)	4(2,5)	0.082
The modified Reiff score	4(2,7)	4(2,6)	4(2,7)	5(2,8)	5(3,8)	0.118
Treatment, n (%)						
Oxygen	264(54.4)	57(46.3)	55(47.8)	64(51.6)	88(71.5)	<0.001
Mechanical ventilation						
Non-invasive mechanical ventilation	17(3.5)	3(2.4)	4(3.5)	3(2.4)	7(5.7)	0.460
Invasive mechanical ventilation	1(0.2)	0(0.0)	0(0.0)	0(0.0)	1(0.8)	0.400
Antibiotics	495(95.0)	121(92.4)	122(93.8)	125(96.2)	127(97.7)	0.201
Antibiotics use ≥2	283(54.3)	52(39.7)	58(44.6)	74(56.9)	99(76.2)	<0.001
Intravenous glucocorticoids	20(3.8)	0(0.0)	3(2.3)	7(5.4)	10(8.6)	0.005
Length of stay, d	11(8,14)	10(8,13)	11(8,13)	11(8,13)	12(9,16)	0.001

Notes: Data are presented as median (IQR) for continuous variables and number (percentage) for categorized variables.
Abbreviations: WBC, white blood cell; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ALB, albumin; GLB, globulin; PAB, prealbumin.

Subgroup Analysis

We also performed subgroup analysis to further ascertain the association between SII and readmissions in particular subpopulations (seen in Figure 5). In all subgroups, SII was significantly associated with readmission in patients with bronchiectasis (all p<0.05). When stratified by subgroups defined by age, sex, smoking status, BMI and ALB, there was

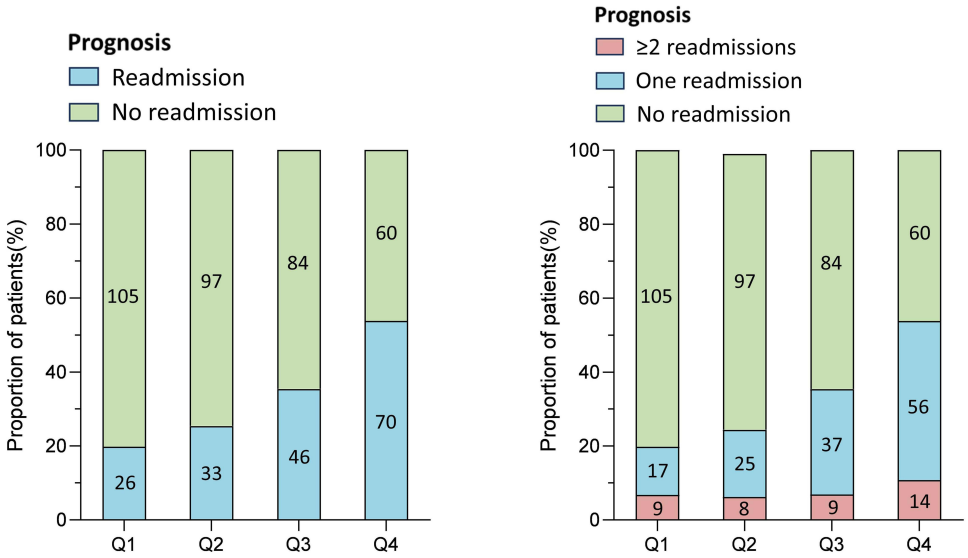

Figure 2 The number of readmissions in patients with bronchiectasis according to quartiles of log2SII.

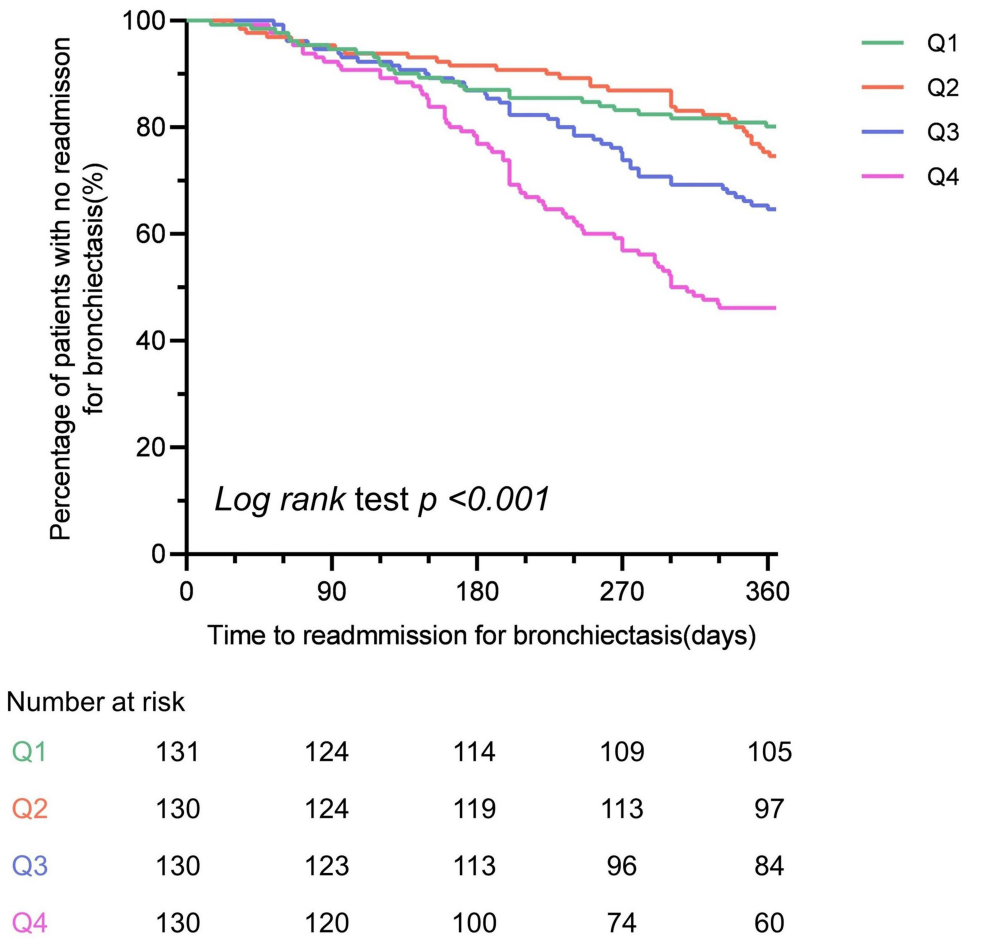

Figure 3 The Kaplan–Meier curve for readmissions according to quartiles of log2SII.

no evidence of heterogeneity in the association (p for interaction >0.05). However, when stratified by age, slightly more patients in the older subgroup were readmitted during the 1-year follow up (38.5% for the ≥60-years subgroup and 27.5% for the <60 years subgroup).

Table 3 The Association Between SII and Readmission in Patients with Bronchiectasis

	Crude Model (Model 1)		Partially Adjusted Model (Model 2)		Fully Adjusted Model (Model 3)	
	OR (95% CI)	***p* value**	**OR (95% CI)**	***p* value**	**OR (95% CI)**	***p* value**
SII/100	1.009(1.006–1.013)	<0.001	1.009(1.006–1.013)	<0.001	1.007(1.003–1.011)	<0.001
Log_2(SII) quartiles						
Q1	Reference		Reference		Reference	
Q2	1.246(0.745–2.084)	0.401	1.237(0.740–2.067)	0.418	1.128(0.671–1.898)	0.650
Q3	1.900(1.174–3.073)	0.009	1.818(1.123–2.944)	0.015	1.671(1.027–2.717)	0.039
Q4	3.381(2.154–5.308)	<0.001	3.133(1.989–4.934)	<0.001	2.618(1.636–4.188)	<0.001
p for trend	<0.001		<0.001		<0.001	

Notes: Model 1, no covariates were adjusted. Model 2, age was adjusted. Model 3, age, BMI, mMRC, ALB, Infection with P. aeruginosa, modified Reiff scores and number of acute exacerbations in previous year were adjusted.

Abbreviations: 95% CI, 95% confidence interval; OR, odds ratio; SII, systemic immunity-inflammation index; BMI, body mass index; mMRC, modified Medical Research Council; ALB, albumin.

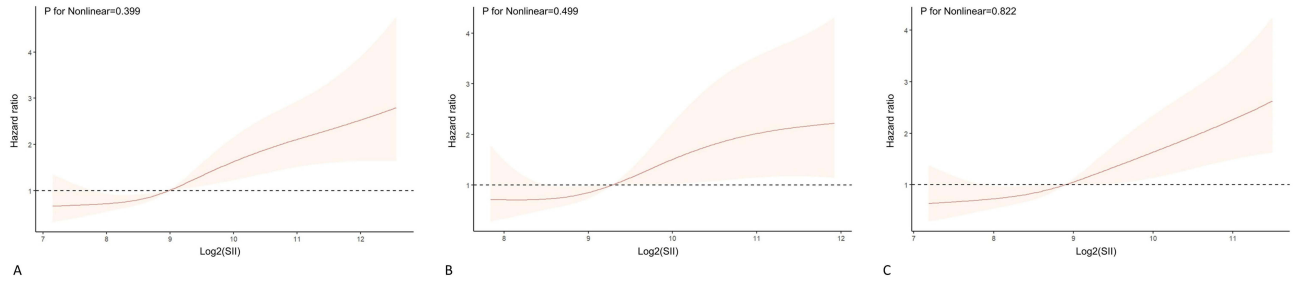

Figure 4 Testing for readmissions according to the levels of the systemic immune-inflammation index (SII) on a continuous scale. Model adjusted for age, BMI, mMRC, ALB, Infection with P. aeruginosa, modified Reiff scores and number of acute exacerbations in previous year. Hazard ratios are represented by solid lines and 95% confidence intervals are represented with colored components. (**A**) RCS for all patients (**B**) RCS for male patients (**C**) RCS for female patients.
Abbreviations: BMI, body mass index; mMRC, modified Medical Research Council; ALB, albumin.

Subgroup	Readmission Case/Total	Adjusted Hazard Ratio (95%CI)	P for interaction
All patients	175/521	1.413(1.264-1.580)	
Age			0.266
<60 yr	64/233	1.309(1.069-1.603)	
>=60 yr	111/288	1.498(1.304-1.720)	
Sex			0.781
Male	64/186	1.328(1.109-1.590)	
Female	111/335	1.475(1.278-1.701)	
Smoking			0.292
Non smokers	138/418	1.447(1.275-1.642)	
Past and Current smokers	37/103	1.376(1.067-1.776)	
BMI			0.692
<18.5 kg/m2	38/93	1.345(1.077-1.681)	
18.5-25 kg/m2	104/314	1.448(1.252-1.675)	
>25kg/m2	33/114	1.724(1.229-2.420)	
ALB			0.105
<3.5 g/L	40/85	1.258(1.037-1.528)	
>=3.5 g/L	135/436	1.523(1.328-1.747)	

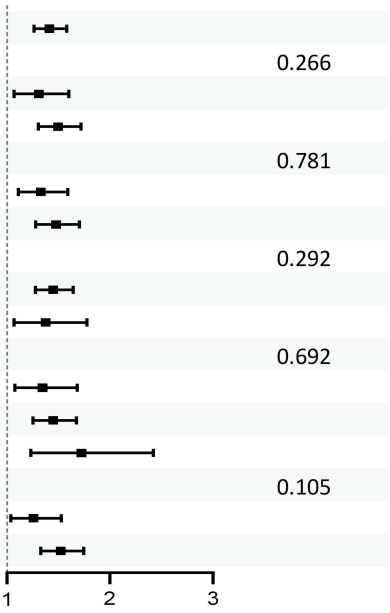

Figure 5 The association between SII and readmission in patients with bronchiectasis by different subgroups. Adjusted for age, sex, smoking status, BMI, and ALB except subgroup variable.
Abbreviations: SII, systemic immunity-inflammation index; BMI, body mass index; ALB, albumin.

Discussion

To the best of our knowledge, this is one of the first studies to demonstrate an association between SII and prognosis associated with bronchiectasis. Our study showed a linear positive relationship between SII levels and readmissions in patients with acute exacerbations of bronchiectasis even after adjusting for various potential confounders, which may indicate SII as a useful biomarker for the prognosis of bronchiectasis patients.

Previous research has demonstrated that exacerbations of bronchiectasis are associated with a significant escalation in both airway and systemic inflammation,[22] which contributes to disease progression. Repeated exacerbations exert a detrimental impact on the quality of life, lung function and mortality.[23,24] Patients with severe exacerbations invariably necessitate hospitalization. Identifying high-risk patients of future exacerbations or admissions by rapid, economical, and accurate methods is very important for enhancing the prognosis and optimizing the treatment strategies for these patients. Currently, there is a dearth of validated laboratory biomarkers for bronchiectasis, and the optimal methods for assessing clinical status, treatment response and prognosis remain elusive.

The SII emerges as a novel biomarker that reflects systemic inflammation at a low cost, making it a promising indicator for clinical applications. Previous studies have shown that patients with COPD exhibiting elevated levels of SII levels are at an increased risk of respiratory failure and all-cause mortality.[16,25,26] Given that bronchiectasis and COPD are both chronic respiratory inflammatory diseases, it is imperative to explore the potential role of SII in bronchiectasis. In this study, we found a significant association between elevated SII and an increased risk of readmission in patients with bronchiectasis. The specific mechanism of the relationship between high SII and readmission in patients with bronchiectasis is still unclear. Bronchiectasis is predominantly a neutrophilic inflammatory disease and is a disorder driven by interplay of inflammation, pathogen and environment.[27] Extensive studies indicate neutrophils as the predominant cell type in sputum, bronchoalveolar lavage (BAL) fluid and blood from patients with bronchiectasis.[28–30] which plays a crucial role in the disease severity and progression. During the inflammation, the number of neutrophils increased due to persistent neutrophil recruitment and impaired neutrophil apoptosis and clearance by macrophages,[28,31] thus resolving inflammation and eliminate pathogens. Lymphocytes which act as a major component of the adaptive immune system, are also very crucial for immunity. Platelets, traditionally recognized for their role in hemostasis and thrombosis, have been characterized as inflammatory cells that contribute to host defense against infection.[32] Uysal et al[33] found that the mean platelet volume (MPV) levels were significantly lower in children with bronchiectasis during acute exacerbations compared with those in a stable state. Aliberti et al also reported that elevated platelet count was associated with disease severity, hospitalizations due to acute exacerbations, diminished quality of life and mortality in stable bronchiectasis.[34]

We speculate the SII at admission may indicate the inflammatory burden and potential disease severity in patients with bronchiectasis. SII is more comprehensive than neutrophils, lymphocytes, platelets themselves and could provide a new perspective on the systemic inflammatory in patients with bronchiectasis.

In this study, we found patients with higher SII levels tended to have prolonged hospital stays, a greater variety of antibiotics and treatment of ICS, indicating these patients were at higher levels of airway and systematic inflammation and were in a critical clinical condition. Elevated neutrophils have historically been considered to reflect increased systemic inflammation and to be associated with a higher bacterial load. Although we did not find significant difference in the positive rate of bacteria culture between the two groups, we did identify a trend towards a higher sputum culture positive rate of Pseudomonas aeruginosa in bronchiectasis patients with higher SII levels. We also found patients with higher SII levels presented with more dyspnea symptoms. The reason for this is not difficult to understand as in clinical evidence, SII levels may reflect inflammation of the airways and cause the worsening of respiratory symptoms.

In this study, we found patients with higher SII tended to be older, male and past and current smokers. Numerous studies have demonstrated that the levels of inflammatory markers such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-alpha) and CRP, exhibit an age-related increase in healthy individuals and patients with acute infections,[35,36] which can support our findings. There is enough evidence indicating that smoking is closely associated with an inflammatory response, which affects both cell-mediated and humoral immune functions, and induces the release of pro-inflammatory factors such as TNF-alpha, IL-1 and IL-6.[37]

In this study, we also found patients with higher SII levels had lower BMI and lower ALB, suggesting that these patients are more susceptible to malnutrition. Elevated inflammatory indicators such as CRP were independently associated with low ALB levels,[38] which can indirectly confirm our results. Previous studies demonstrated that BMI, albumin and prealbumin was significantly associated with disease severity and radiological severity (evaluated by Reiff scores) and clinical outcomes,[39,40] which may also explain poor outcomes in patients with high SII levels.

This study has several limitations. First, it is a single-center retrospective study, which inevitably leads to selection bias. Further multicenter studies are required to investigate the relationship between SII levels and readmissions in patients with acute exacerbations of bronchiectasis. Second, the neutrophil, lymphocyte, and platelet counts are measured at one time point at admission, which may not fully reflect the long-term status or capture the dynamic fluctuations of SII levels over time.

Conclusion

In conclusion, patients with higher SII levels tended to be older, male, past and current smokers, have lower BMI, and more dyspnea symptoms. They also had higher inflammatory markers and received a greater spectrum of antibiotics and more intravenous glucocorticoids. Higher SII at admission were significantly associated with readmissions in patients with bronchiectasis. SII has potential clinical value as a predictive biomarker for clinical outcomes in bronchiectasis, offering a valuable tool for management strategies.

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Disclosure

The authors report no conflicts of interest in this work.

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