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ORIGINAL RESEARCH

The Clinical Value of the Neutrophil-to-Lymphocyte Ratio, the C-Reactive Protein-to-Albumin Ratio, the Systemic Inflammatory Index, and the Systemic Inflammatory Response Index in Patients with the Anti-Synthetase Syndrome

Liuyi Huang*, Xi Li*, Wei Zhou, Haiqing Zhu, Yuehong Lao, Xiaoxia Huang, Zhenjia Deng, Yuting Tang, Jian Wang

Department of Clinical Laboratory, the First Affiliated Hospital of Guangxi Medical University, Key Laboratory of Clinical Laboratory Medicine of Guangxi Department of Education, Nanning, Guangxi, 530021, People's Republic of China

*These authors contributed equally to this work

Correspondence: Jian Wang, Department of Clinical Laboratory, the First Affiliated Hospital of Guangxi Medical University, Key Laboratory of Clinical Laboratory Medicine of Guangxi Department of Education, No. 6 Shuangyong Road, Nanning, Guangxi, 530021, People's Republic of China, Email wangjian0771@163.com

Objective: There are no studies examining the role of the neutrophil-to-lymphocyte ratio (NLR), the C-reactive protein-to-albumin ratio (CAR), the systemic inflammatory index (SII), and the systemic inflammatory response index (SIRI) in anti-synthetase syndrome (ASS). We aim to compare NLR, CAR, SII, and SIRI in ASS and dermatomyositis/polymyositis (DM/PM), as well as to examine potential correlations between NLR, CAR, SII, and SIRI and clinical features and laboratory parameters in ASS.

Methods: Retrospective collection of data from 111 patients with ASS and 175 patients with DM/PM. A Spearman rank correlation analysis was utilized to analyze the correlation between NLR, CAR, SII, and SIRI and inflammatory indexes. Receiver operating characteristic (ROC) curves were used to assess the diagnostic value. Univariate logistic regression analysis was performed to assess risk factors for interstitial lung disease (ILD).

Results: Compared with DM/PM, NLR, CAR, SII, and SIRI were significantly greater in ASS patients ($p < 0.05$). NLR, CAR, SII, and SIRI were correlated with albumin, lactic dehydrogenase (LDH), C-reactive protein (CRP), ferritin, white blood cell (WBC), platelets, and myositis disease activity assessment visual analog scales (MYOACT) score ($p < 0.05$). The ROC curves analysis showed that NLR, SII, and SIRI were all highly predictive of the occurrence of ASS. Comparisons based on clinical characteristics showed elevated levels of NLR, CAR, SII, and SIRI in ASS patients with ILD, fever, and infection ($p < 0.05$). Univariate logistic regression analysis revealed that NLR, CAR, and SII were significant risk factors for ASS-ILD ($p < 0.05$).

Conclusion: The levels of NLR, CAR, SII, and SIRI were higher in ASS than in DM/PM and correlated with disease activity and specific clinical features. NLR, CAR, SII, and SIRI may be an aid in differentiating ASS from DM/PM and maybe promising biomarkers for ASS.

Keywords: the neutrophil-to-lymphocyte ratio, the C-reactive protein-to-albumin ratio, the systemic immune inflammation index, the systemic inflammation response index, anti-synthase syndrome

Introduction

Idiopathic inflammatory myopathy (IIM) mainly includes dermatomyositis (DM), polymyositis (PM), anti-synthetase syndrome (ASS), immune-mediated necrotizing myopathy (IMNM), inclusion body myositis (IBM).[1] DM is the most common subtype of IIM, accounting for about 30–40% of IIMs.[2] DM is characterized by proximal muscle weakness and

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rash. In addition, myositis-specific antibody (MSA) is found in 60% of DM.[3] Clinical signs of PM are dominated by muscle abnormalities, while skin inflammation is less typical.[4] The definition of PM remains controversial, with ASS and IMNM being categorized as PM before MSA was discovered.[3,5] ASS is a newly classified clinical subtype of IIM characterized by the presence of anti-aminoacyl transfer RNA synthetase (ARS), and eight different isoforms targeting ARS have been identified, including Jo-1, OJ, PL-7, PL-12, KS, EJ, Ha, and Zo.[6–8] Interstitial lung disease (ILD) is the most prevalent clinical symptom of ASS, however, other symptoms include arthritis, myositis, and systemic symptoms including fever. Compared to DM/PM, ASS-ILD is more common and severe, with more extensive pulmonary involvement and faster onset of pulmonary symptoms.[9] Although ASS shares many features with DM/PM, it has a distinctive serologic and clinical presentation. The European Neuromuscular Centre (ENMC) states that even though there is an overlap in clinical presentation between ASS and DM, ASS is a distinct subgroup separate from DM/PM.[10] However, there are no recognized classification criteria. Therefore, further search for relevant biomarkers that can identify IIM subtypes is necessary. Researchers around the world are exploring these factors in different contexts.

The neutrophil-to-lymphocyte ratio (NLR), the C-reactive protein-to-albumin ratio (CAR), the systemic inflammatory index (SII), and the systemic inflammatory response index (SIRI) are indicators of inflammation that have received much attention in recent years. Both the NLR and CAR are helpful indicators for autoimmune diseases.[11–15] In recent studies, NLR and CAR have been linked to survival and disease activity in DM/PM; additionally, NLR and CAR are risk factors for the development of ILD in IIM, are associated with high mortality in IIM-ILD, and can be used as serum biomarkers for IIM-ILD.[16–18] SII and SIRI have been recognized as two new biomarkers of inflammation that attempt to characterize the pro- and anti-inflammatory balance.[19] Additionally, there is a strong correlation between SIRI and SII and autoimmune diseases. For example, the SIRI and SII have been proposed as indicators for evaluating the disease activity in patients with Behcet disease or ankylosing spondylitis.[20,21] The above studies have demonstrated the importance of NLR, CAR, SII, and SIRI in disease diagnosis and prognostic evaluation. Although some of these metrics have been studied in DM/PM or IIM, they have never been used alone in the study of ASS. Whereas DM/PM and ASS have different pathogenesis, different inflammatory responses, and blood cell parameters are altered by inflammation, we speculate that NLR, CAR, SII, and SIRI are possible differences between the two. Therefore, we compared NLR, CAR, SII, and SIRI in ASS patients and DM/PM patients, explore whether these four metrics differ in ASS vs DM/PM, as well as investigated the diagnostic value and clinical significance of these four indices in ASS patients.

Materials and Methods

Patients

This study was approved by the Ethical Review Committee of the First Affiliated Hospital of Guangxi Medical University (2023-E755-01) and was consistent with the principles of the Declaration of Helsinki. All patients signed an informed consent form. Retrospectively, 381 patients who were diagnosed with IIM in the First Affiliated Hospital of Guangxi Medical University from 2020 to 2023 were collected, and all the patients were older than 18 years old. Based on exclusion criteria: no antibody testing; diagnosed with IBM or IMNM; patients with cancer and overlapping with other autoimmune diseases excluded (n=95). A total of 286 MSA-positive or MSA-negative patients were included in the study. In this study, the included patients were categorized into ASS (n=111) and DM/PM (n=175) groups according to MSA. Patients in the ASS group had ARS, which included anti-Jo-1, OJ, PL-7, PL-12, KS, EJ, Ha, and Zo, and patients in the DM/PM group had DM/PM-specific antibodies, which were DM/PM-specific and included anti-Mi-2, TIF1-γ, SAE, MDA5, NXP2, SRP, and HMGCR, and were also diagnosed with DM/PM when MSA-negative (Figure 1).[22,23] ASS was interpreted as positive for at least one ARS antibody and at least one triad of findings, including ILD, myositis, and arthritis.[24] Patients with DM/PM met Bohan and Peter's diagnostic criteria.[25,26] 155 age- and sex-matched participants undergoing physical examination were randomly selected as healthy controls (HCs).

Serum Antibody Detection

The assays of the MSA were assessed using linear immunoblotting assay (Centuryyis, Hangzhou, China) according to the manufacturer's protocol. The bands were scanned using EUROLineCamera (EUROIMMUN, Lubeck, Germany).

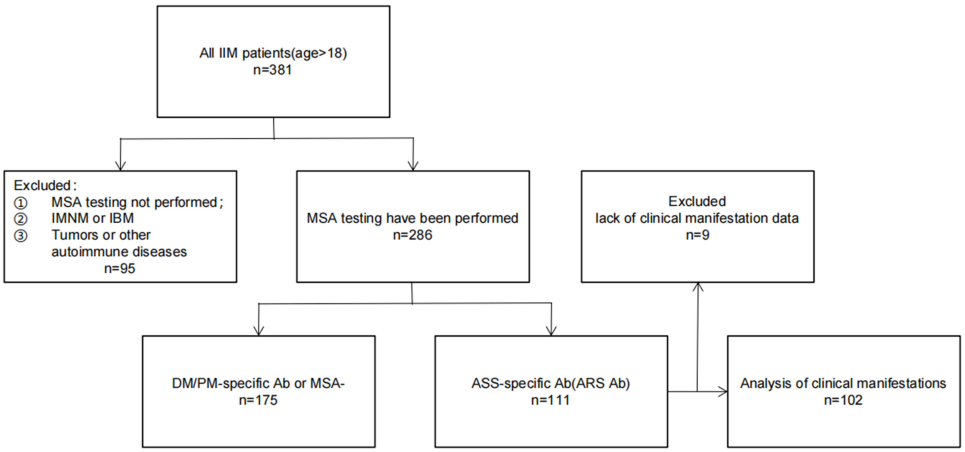


Figure 1 Flowchart illustrating the patients that were included and excluded from the study.
Abbreviations: IIM, idiopathic inflammatory myopathies; MSA, myositis-specific autoantibodies; IMNM, immune-mediated necrotizing myopathy; IBM, inclusion body myositis; DM, dermatomyositis; PM, polymyositis; ASS, anti-synthetase syndrome; Ab, antibody; ARS Ab, anti-aminoacyl transfer RNA synthetase antibody.

Assessment of Disease Activity

Myositis disease activity assessment visual analog scales (MYOACT)[27] score was used to assess myositis disease activity in all patients with IIM at the time of first admission by an experienced rheumatologist.

Definitions and Data Collection

Clinical manifestations and laboratory results of patients were collected. Clinical manifestations include (1) ILD, which is defined as a typical bilateral ground glass shadow or bilateral subpleural reticular to late fibrosis as determined by high-resolution computed tomography; (2) fever; (3) myalgia; (4) arthralgia; (5) rash: including gottron's sign/papule, helipcoter's rash, periorbital red rash, systemic rash; (6) infection; (7) cough. Disease-related laboratory parameters include (1) blood routine indexes; (2) inflammatory indicators. Only data from the first admission were included for patients with multiple admissions.

We calculated NLR, CAR, SII, and SIRI according to the following formula: NLR= neutrophils/lymphocytes; CAR=C-reactive protein/albumin; SII = platelets × neutrophils/lymphocytes; SIRI = monocytes × neutrophils/lymphocytes.

Statistical Analysis

Kolmogorov–Smirnov test evaluated the normality. For the presentation of the data, continuous variables that conform to a normal distribution mean ± standard deviation are represented, those that do not conform to a normal distribution are represented by median values (interquartile range), and categorical variables are represented by numbers (percentages). For statistical comparison of continuous variables, the independent sample *t*-test was used for normally distributed data, and the Mann–Whitney *U*-test was used for non-normally distributed data. The comparison of categorical variables was performed by chi-square test. Spearman rank correlation analysis was used to conduct the correlation analysis. Univariate logistic regression analysis was used to assess whether NLR, CAR, SII, and SIRI were risk factors for concomitant ILD in patients with ASS. The predictive power of NLR, CAR, SII, and SIRI in patients with ASS was evaluated using ROC curves. Using IBM SPSS version 26.0, GraphPad Prism 8.0.2, and PS (Adobe Photoshop 2023) software to handle all statistics. A p-value < 0.05 (bilateral) was considered statistically significant.

Results

Comparison of Demographic and Laboratory Features Between ASS and DM/PM

A total of 286 patients were found to be MSA-positive or MSA-negative, of whom 175 were diagnosed with DM/PM and 111 with ASS; these patients were included in the study (Figure 1). Table 1 demonstrates demographic and laboratory

Table 1 Demographic and Laboratory Features Between ASS and DM/PM

Items	ASS (N=111)	DM/PM (N=175)	P
Age (years)	55.14±12.70	51.40±14.28	0.025
Sex			
Male	27(24.32)	48(27.43)	0.561
Female	84(75.68)	127(72.57)	
Laboratory parameters			
Albumin, g/L	32.09±5.25	33.07±5.62	0.144
Globulin, g/L	34.30(30.00, 39.25)	31.70(27.50, 37.15)	0.006
CK, U/L	621.00(110.00, 2770.50)	336.00(79.00, 1737.00)	0.424
LDH, U/L	411.00(281.50, 667.25)	392.50(314.25, 622.75)	0.603
IgG, g/L	16.26(12.79, 20.20)	14.15(11.04, 17.40)	0.003
CRP, mg/L	16.83(2.20, 41.50)	5.50(1.92, 15.40)	<0.001
ESR, mm/h	33.50(20.00, 55.00)	26.00(13.50, 45.00)	0.025
Ferritin, ng/mL	671.97(244.31, 2190.32)	796.83(414.81, 2218.61)	0.214
WBC, $\times10^9$/L	10.39(7.35, 12.64)	6.36(4.57, 8.77)	<0.001
Platelets, $\times10^9$/L	327.00±104.41	248.00(189.00, 304.50)	<0.001
Neutrophil, $\times10^9$/L	7.55(5.00, 10.42)	4.58(2.95, 6.63)	<0.001
Lymphocyte, $\times10^9$/L	1.20(0.82, 1.86)	1.00(0.64, 1.40)	0.001
Monocyte, $\times10^9$/L	0.68±0.32	0.55(0.38, 0.76)	0.113
NLR	6.15(3.59, 9.93)	4.80(2.91, 7.31)	0.009
CAR	0.64(0.15, 1.47)	0.16(0.06, 0.52)	<0.001
SII	1893.38(920.08, 3152.65)	1076.47(667.55, 1889.55)	<0.001
SIRI	3.67(1.75, 6.43)	2.39(1.35, 4.36)	0.009
Myositis-specific autoantibodies			
Anti-Jo-1 antibody	74(66.67)	–	–
Anti-OJ antibody	3(2.70)	–	–
Anti-PL-7 antibody	8(7.21)	–	–
Anti-PL-12 antibody	9(8.11)	–	–
Anti-EJ antibody	14(12.61)	–	–
Anti-Ha antibody	3(2.70)	–	–
Anti-MDA5 antibody	–	75(42.86)	–
Anti-Mi-2 antibody	–	12(6.86)	–
Anti-TIF1-γ antibody	–	21(12.00)	–
Anti-NXP2 antibody	–	6(3.43)	–
Anti-SAE antibody	–	4(2.29)	–
Anti-SRP antibody	–	5(2.86)	–
Anti-HMGCR antibody	–	1(0.57)	–
Anti-PM-SCL75 antibody	–	6(3.43)	–
Anti-MSA negative	–	43(24.57)	–
Anti-Mi-2 + NXP2 antibody	–	1(0.57)	–
Anti-SRP + TIF1γ antibody	–	1(0.57)	–

Note: Data are presented as numbers (percentages), mean ± standard deviation, or median values (interquartile range).
Abbreviations: ASS, anti-synthetase syndrome; DM, dermatomyositis; PM, polymyositis; CK, creatine kinase; LDH, lactic dehydrogenase; IgG, immunoglobulin G; CRP, C-reactive protein; ESR, erythrocyte sedimentation; WBC, white blood cell; NLR, the neutrophil-to-lymphocyte ratio; CAR, the C-reactive protein-to-albumin ratio; SII, the systemic inflammatory index; SIRI, the systemic inflammatory response index.

features between ASS and DM/PM. Inflammatory biomarkers such as globulin ($p = 0.006$), IgG ($p = 0.003$), CRP ($p < 0.001$), and ESR ($p = 0.025$) showed significant differences between ASS and DM/PM. Albumin, CK, LDH, and ferritin did not show statistically significant differences between the two. Compared with DM/PM, NLR (6.15 [3.59–9.93] vs 4.80 [2.91–7.31], $p = 0.009$), CAR (0.64 [0.15–1.47] vs 0.16 [0.06–0.52], $p < 0.001$), SII (1893.38 [920.08–3152.65] vs 1076.47 [667.55–1889.55], $p < 0.001$) and SIRI (3.67 [1.75–6.43] vs 2.39 [1.35–4.36], $p = 0.009$) were significantly greater in ASS patients.

NLR, CAR, SII, and SIRI Were Associated with the Disease Activity of ASS

As shown in Figure 2, Spearman correlation analysis showed that NLR, CAR, SII, and SIRI were positively correlated with the MYOACT score in ASS patients ($r = 0.503$, $p < 0.001$; $r = 0.470$, $p < 0.001$; $r = 0.421$, $p < 0.001$; $r = 0.332$, $p = 0.001$). Among them, NLR has the strongest correlation with the MYOACT score.

Table 2 correlation analysis shows that NLR, CAR, SII, and SIRI were positively correlated with albumin, lactic dehydrogenase (LDH), C-reactive protein (CRP), ferritin, white blood cell (WBC), and platelets ($p < 0.05$). In addition to NLR and SII, CAR, and SIRI are also associated with erythrocyte sedimentation (ESR) ($p < 0.05$).

The Predictive Ability of NLR, SII, and SIRI for ASS

155 age- and sex-matched physical examination participants were randomized to healthy controls (HCs). The ROC curve for CAR could not be assessed because of the lack of CRP data for healthy controls. The ROC curve was used to analyze the predictive ability of NLR, SII, and SIRI for ASS patients. According to the ROC curves, the ideal critical values for NLR, SII, and SIRI as ASS indicators were 3.01, 667.96, and 1.51, and each of the three had a sensitivity and specificity greater than 80% and 90%, respectively. The combined diagnosis of NLR, SII, and SIR (NLR-SII-SIRI) had a better diagnostic value than either indicator alone, with an area under the curve (AUC) of 0.956 (95% CI: 0.926–0.986), a sensitivity of 92.8%, and a specificity of 93.5% (Figure 3).

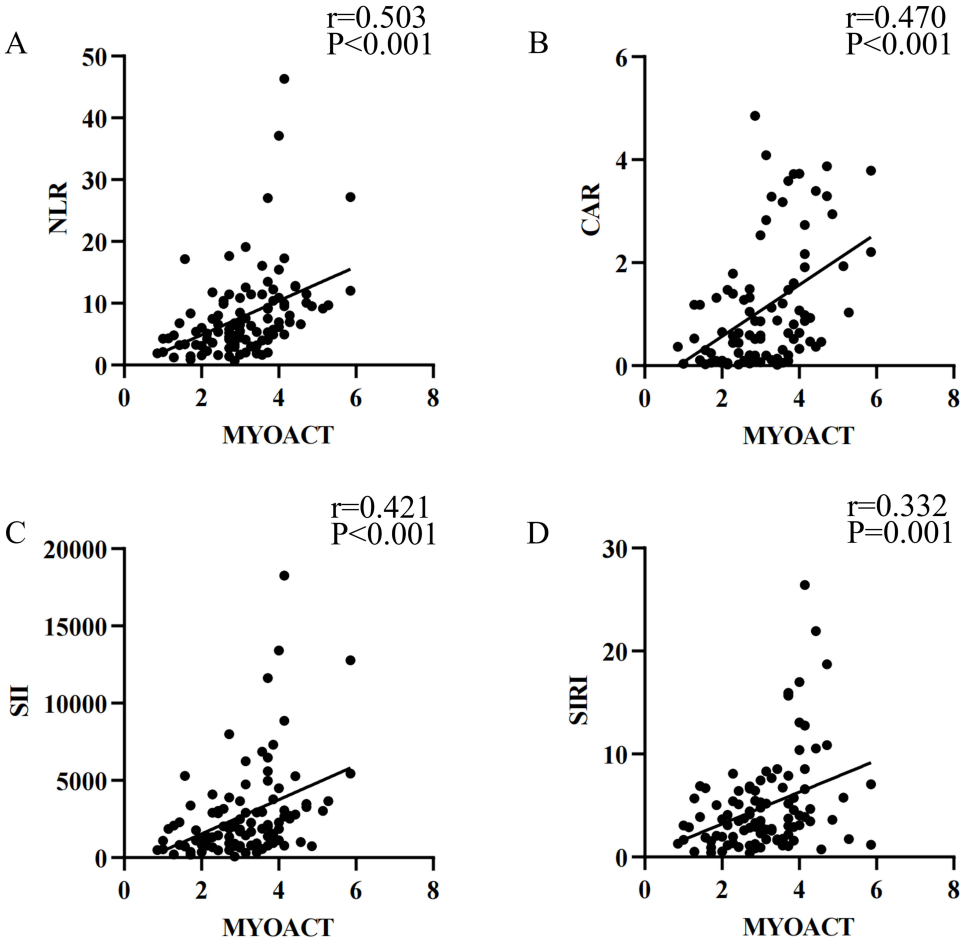


Figure 2 Correlation between MYOACT score and NLR, CAR, SII, and SIRI in ASS.
Notes: (**A**) Shows NLR and MYOACT score. (**B**) Shows CAR and MYOACT score. (**C**) Shows SII and MYOACT score. (**D**) Shows SIRI and MYOACT score.
Abbreviations: MYOACT, myositis disease activity assessment visual analog scales; NLR, the neutrophil-to-lymphocyte ratio; CAR, the C-reactive protein-to-albumin ratio; SII, the systemic inflammatory index; SIRI, the systemic inflammatory response index; ASS, anti-synthetase syndrome.

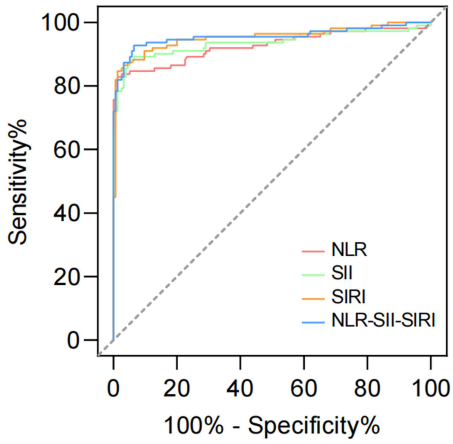
Table 2 Correlation Between Disease Activity Markers and NLR, CAR, SII, and SIRI in ASS

Activity Markers	r, P			
	NLR	**CAR**	**SII**	**SIRI**
Albumin, g/L	−0.378, <0.001	−0.497, <0.001	−0.427, <0.001	−0.400, <0.001
Globulin, g/L	0.134, 0.165	0.026, 0.806	0.180, 0.062	0.018, 0.853
LDH, U/L	0.314, 0.001	0.364, <0.001	0.341, <0.001	0.204, 0.036
CRP, mg/L	0.537, <0.001	0.991, <0.001	0.502, <0.001	0.432, <0.001
ESR, mm/h	0.173, 0.070	0.475, <0.001	0.159, 0.096	0.202, 0.035
Ferritin, ng/mL	0.511, <0.001	0.612, <0.001	0.440, <0.001	0.509, <0.001
WBC, $\times 10^9$/L	0.533, <0.001	0.421, <0.001	0.603, <0.001	0.585, <0.001
Platelets, $\times 10^9$/L	0.307, 0.001	0.211, 0.039	0.625, <0.001	0.263, 0.005
NLR	–	0.542, <0.001	0.909, <0.001	0.720, <0.001
CAR	0.542, <0.001	–	0.519, <0.001	0.448, <0.001
SII	0.909, <0.001	0.519, <0.001	–	0.688, <0.001
SIRI	0.720, <0.001	0.448, <0.001	0.688, <0.001	–

Abbreviations: NLR, the neutrophil-to-lymphocyte ratio; CAR, the C-reactive protein-to-albumin ratio; SII, the systemic inflammatory index; SIRI, the systemic inflammatory response index; ASS, anti-synthetase syndrome; LDH, lactic dehydrogenase; CRP, C-reactive protein; ESR, erythrocyte sedimentation; WBC, white blood cell.

Comparison of NLR, CAR, SII, and SIRI According to Manifestations in ASS

Clinical manifestations of 102 patients with ASS were collected, and 9 cases were excluded due to incomplete data (Figure 1). Figure 4 shows the correlation between NLR, CAR, SII, SIRI, and disease manifestations in ASS. Compared with ASS patients without fever or infections, NLR, CAR, SII, and SIRI were significantly enhanced in ASS patients with fever or infections ($p < 0.05$). Compared with ASS patients without ILD, NLR, CAR, and SII were significantly enhanced in ASS patients with ILD ($p < 0.05$), But there was no difference in SIRI between the two groups ($p = 0.085$). However, NLR, CAR, SII, and SIRI did not correlate with clinical features such as myalgia, arthralgia, rash, and cough.



Variable	AUC	P	95%CI	Sensitivity(%)	Specificity(%)	Cut-off
NLR	0.927	<0.001	0.889-0.965	82.9	98.7	3.01
SII	0.936	<0.001	0.900-0.973	88.3	94.8	667.96
SIRI	0.953	<0.001	0.924-0.982	84.7	98.7	1.51
NLR-SII-SIRI	0.956	<0.001	0.926-0.986	92.8	93.5	0.24

Figure 3 The predictive ability of NLR, SII, SIRI, and NLR-SII-SIRI for ASS.
Abbreviations: NLR, the neutrophil-to-lymphocyte ratio; SII, the systemic inflammatory index; SIRI, the systemic inflammatory response index; ASS, anti-synthetase syndrome; AUC, area under the curve.

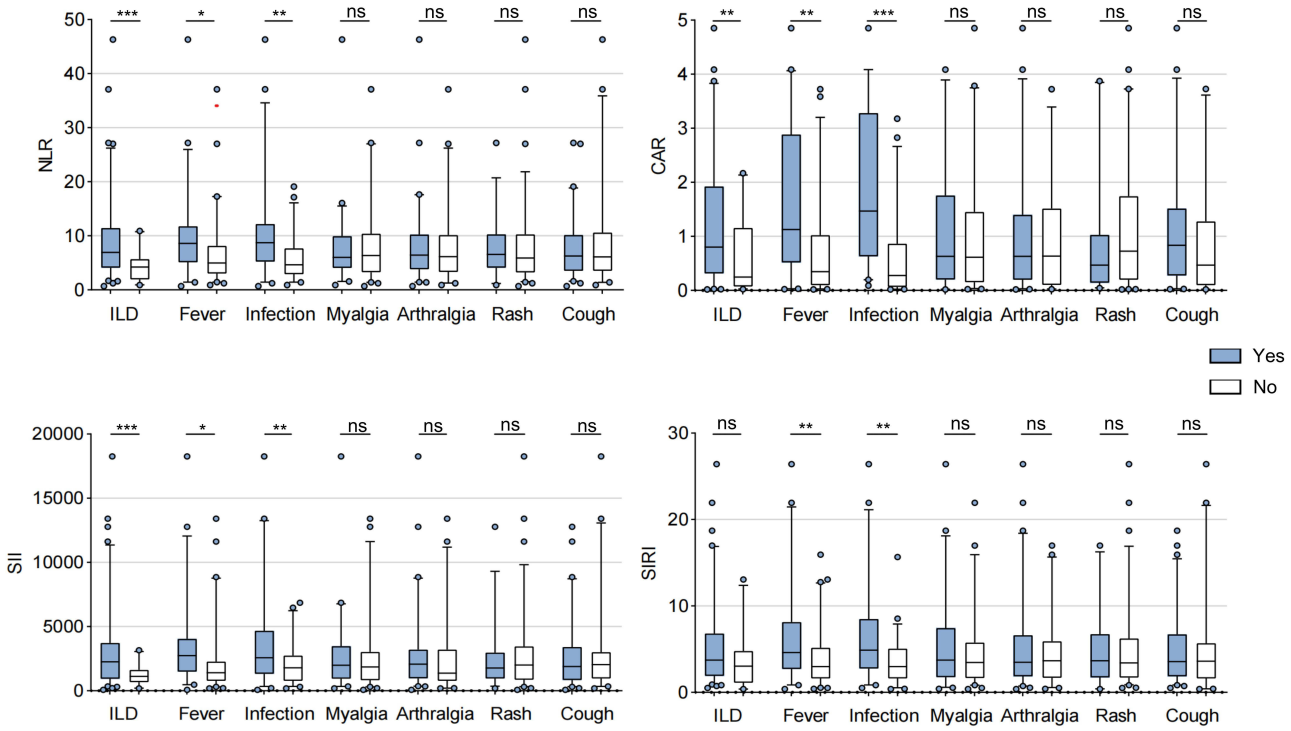


Figure 4 Comparison of NLR, CAR, SII, and SIRI according to manifestations in ASS.
Notes: Yes and No denote presence and absence, respectively. *P < 0.05, **P < 0.01, ***P < 0.001.
Abbreviations: NLR, the neutrophil-to-lymphocyte ratio; CAR, the C-reactive protein-to-albumin ratio; SII, the systemic inflammatory index; SIRI, the systemic inflammatory response index; ASS, anti-synthetase syndrome; ILD, interstitial lung disease.

Diagnostic Value of NLR, CAR, SII, and SIRI for ASS-ILD

Since ILD is the most common clinical symptom in ASS patients and seriously affects the survival of ASS patients. Therefore, we evaluated the effects of NLR, CAR, SII, and SIRI on ASS-ILD. Binary logistic regression analysis was used to determine the risk factors for ASS-ILD (Table 3). Univariate logistic regression analysis revealed that NLR (OR = 1.254, 95% CI: 1.065–1.476, p = 0.007), CAR (OR = 2.084, 95% CI: 1.057–4.110, p = 0.034), and SII (OR = 1.001, 95% CI: 1.000–1.001, p = 0.005) were significant risk factors for ILD. Therefore, we plotted ROC curves to evaluate the diagnostic value of NLR, CAR, and SII for ASS-ILD. The optimal cutoff value for NLR, CAR, and SII for detecting ILD was 6.48 (AUC = 0.725; sensitivity: 56.8%; specificity: 85.7%; p = 0.002), 0.32 (AUC = 0.658; sensitivity: 75.4%; specificity: 60.0%; p = 0.033), and 2209.36 (AUC = 0.730; sensitivity: 51.9%; specificity: 95.2%; p = 0.001). An evaluation of the diagnostic value of the combination of three (NLR-CAR-SII) gave an AUC of 0.770 (sensitivity: 75.4%; specificity: 75.0%; p < 0.001) (Figure 5).

Discussion

In this study, we found that NLR, CAR, SII, and SIRI were elevated in ASS patients compared to DM/PM patients. In patients with ASS, the four inflammatory markers (NLR, CAR, SII, and SIRI) correlated with various laboratory markers such as albumin, LDH, CRP, and ferritin, as well as with clinical manifestations such as ILD, fever, and infection. NLR, CAR, SII, and SIRI had good diagnostic values.

Previous studies have shown that DM and ASS have significantly different pathologic mechanisms, that ASS muscle biopsies display peri fascicular necrosis, whereas DM patients exhibit peri fascicular atrophy.[28] The mechanisms of occurrence are also not the same. IFN -I - related proteins (MxA, RIG-I, and ISG15) are highly expressed in the blood, skin, and tissues of patients with DM and low or moderately expressed in ASS.[29] They also respond differently to treatment. Previous studies have shown that patients with MDA5+ DM have a higher incidence of RP-ILD, which progresses quickly and has a poorer prognosis. In contrast, ASS - ILD is usually responsive to treatment.[30] Anti-ARS

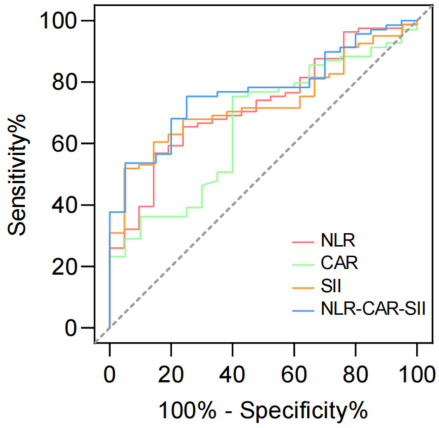
Table 3 Univariate Logistic Regression Analysis of ILD in ASS

Variable	OR (95% CI)	P
NLR	1.254 (1.065–1.476)	0.007
CAR	2.084 (1.057–4.110)	0.034
SII	1.001 (1.000–1.001)	0.005
SIRI	1.159 (0.975–1.377)	0.094

Abbreviations: ILD, interstitial lung disease; ASS, anti-synthetase syndrome; NLR, the neutrophil-to-lymphocyte ratio; CAR, the C-reactive protein-to-albumin ratio; SII, the systemic inflammatory index; SIRI, the systemic inflammatory response index.

antibodies have been linked to improved treatment response and increased survival.[31] Thus, identifying ASS and DM/PM helps clinicians with treatment and prognosis prediction. In the absence of MSA, it is often difficult to differentiate between the two diseases clinically. Although they show differences in muscle pathology, this does not constitute a "gold standard" for identification, and exploring this "gold standard" is a challenge for the medical field. Considering that they are different entities, the identification of serum biomarkers can help to understand the pathogenesis of the disease better and differentiate between DM and ASS. In this study, we compared NLR, CAR, SII, and SIRI levels in DM/PM and ASS. The results showed that NLR, CAR, SII, and SIRI levels were elevated in ASS patients compared to DM/PM patients, which indicated that NLR, CAR, SII, and SIRI were able to distinguish well between ASS and DM/PM. They hold promise as markers to aid in the identification of ASS and DM. The critical point to confirm the diagnosis of ASS is the precise detection of ARS, but MSA is not popular; some hospitals need to send out a third-party cooperative company for testing; compared with routine blood and biochemical indicators, MSA is expensive and the time to get the results is long, the NLR, CAR, SII, and SIRI are easy and quick to detect, and can even be monitored dynamically. So the test of NLR, CAR, SII, and SIRI is vital.

Our results suggest that NLR, CAR, SII, and SIRI may be helpful markers for assessing disease activity in patients with ASS. Here we present this conclusion based on two points: first, NLR, CAR, SII, and SIRI were positively correlated with MYOACTscore. MYOACT score was proposed as a tool for assessing myositis disease activity in 2004 and has been widely used to determine myositis disease activity.[27,32–34] Secondly, there was a significant correlation



Variable	AUC	P	95%CI	Sensitivity(%)	Specificity(%)	Cut-off
NLR	0.725	0.002	0.615-0.835	56.8	85.7	6.48
CAR	0.658	0.033	0.528-0.787	75.4	60.0	0.32
SII	0.730	0.001	0.630-0.831	51.9	95.2	2209.36
NLR-CAR-SII	0.770	<0.001	0.669-0.871	75.4	75.0	0.71

Figure 5 ROC curve of NLR, CAR, SII, and NLR-CAR-SII for the diagnosis of ASS-ILD.
Abbreviations: ROC, receiver operating characteristic; NLR, the neutrophil-to-lymphocyte ratio; CAR, the C-reactive protein-to-albumin ratio; SII, the systemic inflammatory index; ASS, anti-synthetase syndrome; ILD, interstitial lung disease; AUC, area under the curve.

between NLR, CAR, SII, and SIRI with indicators of disease inflammatory activity. In addition, NLR, SII, and SIRI have good diagnostic values in ASS. ROC curve analysis showed that the area under the NLR, SII, and SIRI curves was more significant than 0.9. The AUC of the combined diagnosis of the three was also as high as 0.956, with a sensitivity and specificity of more than 90%. In summary, our study enriches the current epidemiological evidence on NLR, CAR, SII, and SIRI with ASS, but we must admit that their influencing factors are more numerous, and the reliability and validity may vary depending on the particular disease and individual case.

ILD has been reported to occur in 67–100% of ASS patients.[35] In the present study, the incidence of ILD in patients with ASS was 81/102 (79.4%), which is consistent with the reported results. In addition, several studies have shown that ILD is the leading cause of death in patients with ASS.[36] Especially in patients with rapidly progressive interstitial lung disease (RP-ILD), who are resistant to conventional therapy, resulting in rapid progression and a poor prognosis.[37,38] Therefore, it is crucial to recognize ASS-ILD. NLR and SII have been shown to reflect the presence, progression, and prognosis of ILD, with an increased risk of concomitant interstitial lung disease when NLR values exceed 2.3–2.5.[39,40] In our study, NLR was significantly higher in ASS-ILD relative to patients without ILD. In the present study, NLR, CAR, and SII are independent risk factors for ASS-ILD and have a good diagnostic value for ASS-ILD, which is consistent with the findings of Pei Zhou,[41,42] suggesting that these three biomarkers can identify ASS-ILD and reflect lung parenchymal inflammation.

Our study showed that NLR, CAR, SII, and SIRI were elevated in infected and febrile patients, which may be because the organism is in a state of inflammation, and the inflammatory response promotes the release of immune cells and inflammatory factors.[43] However, a sustained inflammatory response ultimately depletes the immune system, which supports elevated neutrophils and decreased albumin.[44] Additionally, in some cases, such as infections, lymphocytes leave the bloodstream and accumulate in affected tissues, such as lung tissues.[45] Migration of lymphocytes leads to a decrease in peripheral lymphocytes, which in turn leads to an elevation of NLR, SII, and SIRI. However, there is a clear causal relationship between infection and fever. One article reported a significant correlation between fever and poor prognosis in DM/PM.[46] Taken together, NLR, CAR, SII, and SIRI help to identify patients with ASS with concomitant ILD, fever, and infection, which may improve patient survival.

We did not find studies of SII and SIRI in myositis. SII is considered more reliable and reflective of inflammation than PLR and NLR.[47] As can be seen from our ROC curve, SII (AUC=0.936) has a more substantial predictive power than NLR (AUC=0.927), suggesting that elevated platelets have a role in predicting the occurrence of ASS.[48] Some articles have shown that platelets are increasingly identified as critical regulators of the inflammatory response and can accelerate the inflammatory state.[49] SIRI is like SII and combines three parameters: neutrophils, lymphocytes, and monocytes. Monocytes are the circulating precursors of macrophages and dendritic cells. In patients with ASS, macrophages and dendritic cells are prominent in muscle biopsies.[50] As can be seen from the formula, monocytes play a role in SIRI. To our great surprise, the area under the curve of SIRI was as high as 0.953, which was superior to that of NLR (AUC=0.927) versus SII (AUC=0.936), so the role of SIRI in ASS is worthwhile. Both SII and SIRI include three blood cell parameters, which are more stable than individual blood cell parameters, which are simple in structure and susceptible to environmental and sample management differences.

There are some limitations to this study. Firstly, both DM/PM and ASS are rare diseases, so the overall sample size was small. In particular, the sample that could be collected for ASS without ILD was small, and performing multivariate logistic regression analysis as well as adjusting for confounders was limited, and further expansion of the sample size is needed in future studies. Secondly, this was a cross-sectional study with no follow-up assessment of SII and SIRI levels after treatment. Thirdly, because we belong to a tertiary care hospital, only some patients diagnosed with IIM were primary patients, and some were already on glucocorticoids or immunosuppressants at the time of enrollment, which may have affected the study results. Fourthly, our samples were all from one center, and all participants were Chinese patients; the association of these results may need to be validated in populations in other countries.

Conclusion

In conclusion, we found that compared with DM/PM patients, ASS patients had higher levels of NLR, CAR, SII, and SIRI, which had specific diagnostic values for ASS. Elevated levels of NLR, CAR, SII, and SIRI in ASS patients were associated with ILD, fever, infection, and disease activity.

Compliance with Ethical Standards

This study was approved by the Ethical Review Committee of the First Affiliated Hospital of Guangxi Medical University (2023-E755-01) and was consistent with the principles of the Declaration of Helsinki. All patients signed an informed consent form.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis, and interpretation, or in all these areas; 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 agree 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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