

Elevated neutrophil-lymphocyte ratio predicts vascular remodelling outcome in spontaneous isolated superior mesenteric dissection

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Abstract. – **OBJECTIVE:** The neutrophil-lymphocyte ratio (NLR) is a prognostic marker predicting in-hospital mortality and stent patency in vascular disorders. This study aimed to investigate whether the NLR obtained at admission can be used to predict vascular remodelling outcomes in spontaneous isolated superior mesenteric dissection (SISMAD) patients.

PATIENTS AND METHODS: A total of 109 consecutive SISMAD patients, admitted to a single centre between November 2017 and June 2019, were retrospectively enrolled. Demographics, comorbidities, imaging data, and follow-up results were recorded. NLR at admission was calculated from a routine hemogram. The study endpoint was complete vascular remodelling or follow-up deadline. Patients were divided into two groups: complete vascular remodelling (Group 1) and partial vascular remodelling (Group 2). All parameters, including NLR, were compared between the groups. Multivariate logistic regression analysis determined whether NLR is independent of vascular remodelling in SISMAD patients after conservative treatment.

RESULTS: Complete vascular remodelling of SISMAD occurred in 26 patients (23.9%) and partial remodelling in 83 patients (76.1%). Baseline NLR was significantly higher in the partial remodelling group than in the complete remodelling group [(6.32±2.10) vs. (4.90±2.12), $p=0.003$]. Complete remodelling was higher in the low NLR group than in the high NLR group [(15, 34.1%) vs. (11, 16.9%), $p=0.039$]. NLR (odd ratio [OR], 1.631; 95% confidence interval [CI], 1.027-2.592; $p=0.038$) and superior mesenteric artery-distal aorta angle (OR, 9.246; 95% CI, 2.217-38.560; $p=0.002$) were independent predictors of complete remodelling in multivariate logistic regression analysis. From the receiver operating characteristic curve, the best NLR cut-off value to predict complete vascular remodelling was 5.37, with 72.3% sensitivity and 69.2% specificity.

CONCLUSIONS: The inflammation marker NLR may predict worse vascular remodelling in SISMAD patients.

Key Words:

Neutrophil to lymphocyte ratio, Vascular remodelling, Arterial dissection, Superior mesenteric artery.

Introduction

Spontaneous Isolated Superior Mesenteric Artery Dissection (SISMAD) is a rare vascular disorder involving only the Superior Mesenteric Artery (SMA). The incidence of this condition is mainly concentrated in East Asian countries such as Korea, Japan, and China^{1,2}. SISMAD has recently become a frequently notified disorder, following improvements and imaging advancements by Computed Tomography Angiography (CTA). As recommended by the guidelines of the European Society of Vascular Surgery, conservative treatment is the first-line management for SISMAD³. After conservative treatment, should there be signs of intestinal ischaemia, such as persistent abdominal pain or peritoneal irritation, endovascular stent placement or open surgery should be immediately considered⁴⁻⁶. Many clinical studies have reported that the near- and medium-term success rate of SISMAD patients after conservative treatment is about 75–95%. However, for some patients, the follow-up CTA observations do not show vascular remodelling in the lumen of the SMA. In some patients, the imaging shows dissecting aneurysm dilatation or false lumen blood flow emerged during the follow-up period.

An increasing number of pathology studies have found that inflammatory processes are involved in vascular remodelling in SISMAD, which plays an important role in the initiation, progression, and prognosis of this disorder. The neutrophil to lymphocyte ratio (NLR) is an easily obtainable measure of inflammation based on the white blood cell count. This simple and inexpensive index has been extensively studied and has shown to predict results in patients with several forms of cardiovascular and cerebrovascular disease, and more recently in patients with various tumours. A high NLR predicts an increased incidence of pericardial effusion and in-hospital mortality in patients with type A aortic dissection⁷. Furthermore, a literature review of the past decade has revealed that a vital correlation exists between high NLR at admission and a poor prognosis⁸. However, the effect of NLR on SISMAD is still unknown, and thus far, there has been no research examining the relationship between NLR and vascular remodelling.

Predicting the occurrence of remodelling is of great value for assessing treatment options and prognosis in SISMAD patients. Identifying the risk factor for complete arterial remodelling of the mesenteric artery can also help decide the optimal strategies in the follow-up. Therefore, this study aimed to investigate the relationship between the pre-treatment NLR in SISMAD patients who received conservative therapy and their outcomes.

Patients and Methods

Study Population

This study retrospectively analysed the data from 109 consecutive SISMAD patients admitted to the Subei People Hospital between November 2017 and June 2019. Patients were excluded if they 1) manifested bowel infarction or arterial rupture and underwent primary invasive treatment, 2) presented with involvement of another artery, such as an aortic dissection, or 3) had acute coronary syndrome, active infection, chronic inflammatory disease, or malignancy. All patients had an acute onset of abdominal pain. The diagnosis of SISMAD was based on abdominal CTA (Figure 1) and the patients' clinical manifestation. Patients were divided into two groups: those with complete remodelling (26 patients) and those with partial remodelling (83 patients) according to their follow-up results at the endpoint. Patient in-

formation including baseline characteristics (age, sex, history of hypertension, diabetes mellitus, hyperlipidemia, coronary artery disease, abdominal surgery, and smoking), length of hospital stay, follow-up duration, treatments, clinical manifestations, and radiographic findings (Yun's classification, SMA-distal aorta angle, distance from the SMA ostium to the beginning of the dissection, dissection length, and true lumen stenosis >70%) were gathered from the medical databases. The radiographic type was determined from the initial CTA and based on Yun's classifications (Figure 2): Type I dissection with both entry and re-entry; Type IIa dissection with a patent true lumen but no re-entry site in the false lumen; Type IIb dissection with a patent true lumen and thrombosed false lumen, and Type III dissection with occlusion of the SMA⁹. This study was approved by the Ethics Committee of the People's Hospital of North Jiangsu. Approval number of the Ethics Committee of the People's Hospital of North Jiangsu is 2018072.

Definition

Complete vascular remodelling was defined as complete resorption of the false lumen thrombosis, the disappearance of blood flow, and morphological recovery of the correct cavity shape and hemodynamics without residual stenosis or occlusion. Partial remodelling was defined as partial resorption of the false lumen thrombosis and residue of the false lumen thrombosis visible on images, or improved stenosis in the true lumen but with residual stenosis or intramural thrombus on CTA (Figure 1). All laboratory data were determined using peripheral venous blood obtained 1 to 3 days before conservative management at the vascular surgery ward during hospitalisation. Total white blood cell, neutrophil, lymphocyte, monocyte, and platelet counts, and red blood cell distribution width were measured using an automated blood cell counter. The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count.

Treatment

All patients were routinely treated conservatively after admission. Conservative treatment included close observation, pain control (intravenous nonsteroidal anti-inflammatory drugs or narcotic analgesics), strict blood pressure control ($\leq 120/80$ mmHg), bowel rest and fasting (intravenous fluid therapy or total parenteral nutrition therapy), antiplatelet therapy (daily oral adminis-

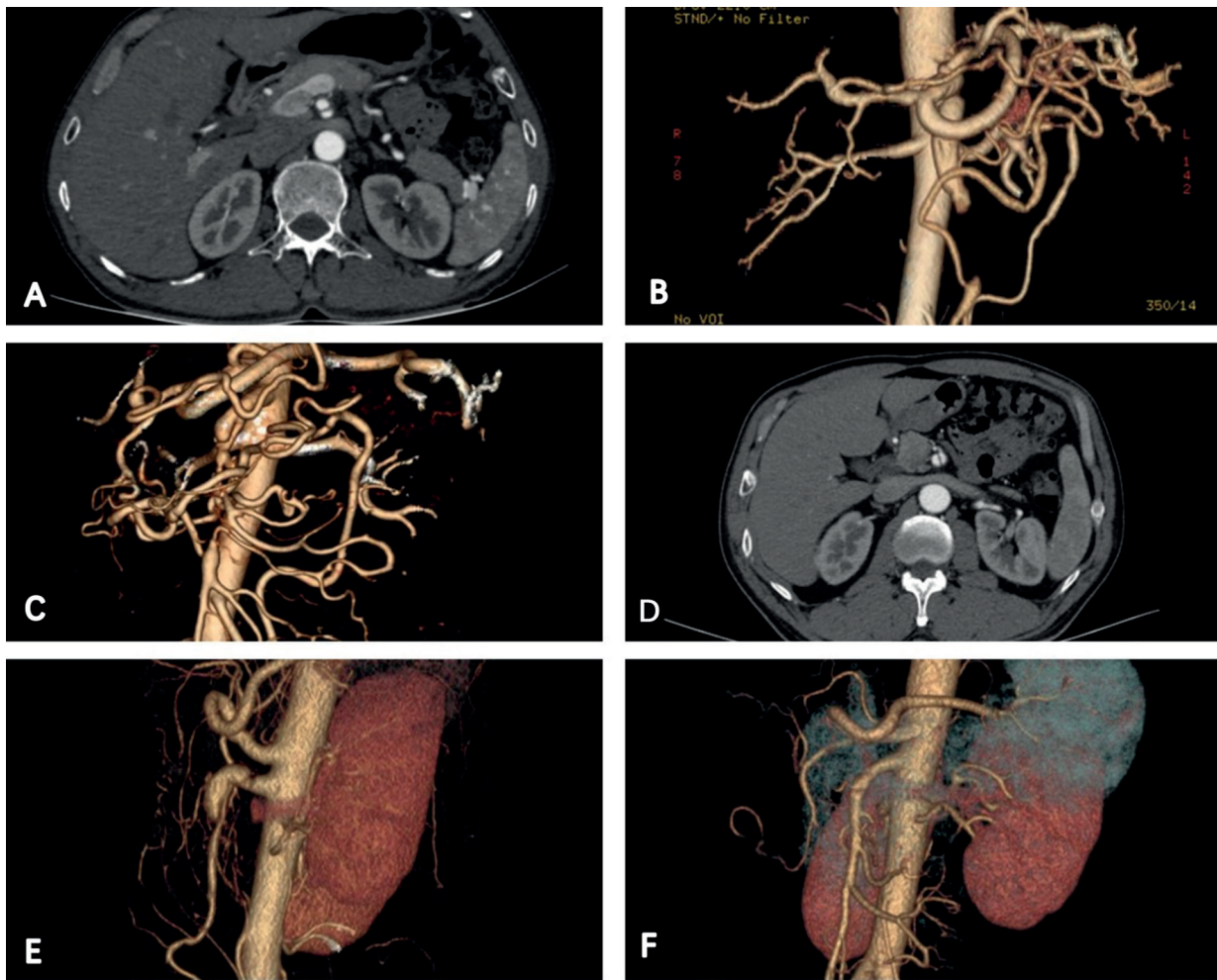


Figure 1. A 54-year-old man presented with acute and moderate epigastric pain that had lasted for approximately 10 h, and CTA showed the SMA separated by intimal flap (*white arrow head*) (A). CTA demonstrates the dissection, and the true lumen is compressed by the aneurysmal dilated false lumen (B). CTA at 13 months demonstrates that partial remodelling had occurred (*white arrow head*) (C). A 49-year-old man with acute middle upper abdominal and back pain that had for 2 days (D). CTA demonstrates isolated dissection of the SMA and the true lumen is stenosis compressed by the false lumen (*white arrow head*) (E). Complete remodelling of the SISMA was seen on CTA 1 year later (*white arrow head*) (F).

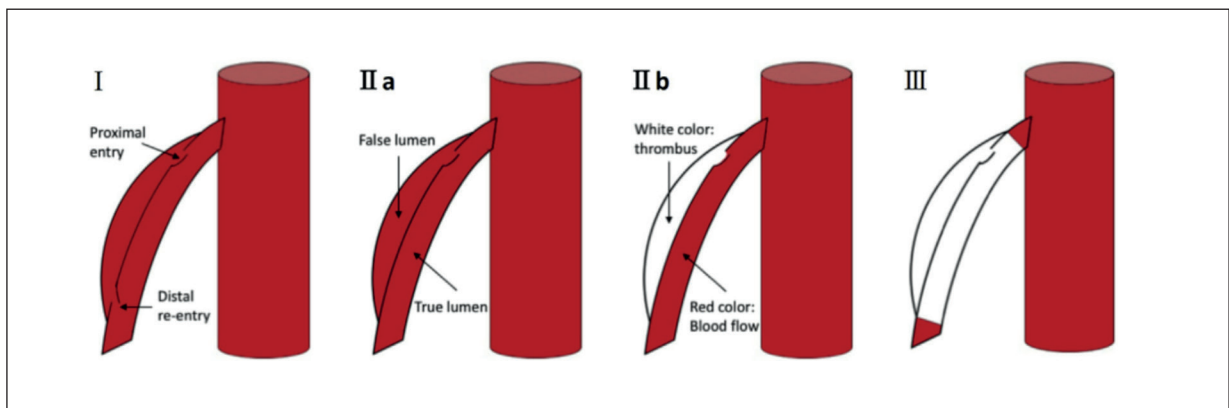


Figure 2. Angiographic classification of spontaneous isolated superior mesenteric artery dissection (SISMA)⁹.

tration of 100 mg aspirin, Garbagnate Milanese, MI, Italy), and anticoagulation therapy (4,000 U twice per day subcutaneous injection of low molecular weight heparin, Sanofi (Beijing) Pharmaceutical Co. LTD, Beijing, China). Conservative treatment was maintained until abdominal pain was relieved or disappeared.

Follow-up

Patients were required to attend outpatient clinic visits at 3 months, 6 months, 1 year, and annually thereafter. Both clinical and outpatient clinical follow-up outcomes and vascular remodelling were recorded by two vascular surgeons. All patients were identified and assessed by CTA in our outpatient clinic. In this study, the primary endpoints were the observed vascular remodelling or the follow-up deadline (April 2020).

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics software, version 26.0 (SPSS Corp., Armonk, NY, USA). Continuous variables are presented as means and standard deviations, with Student's *t*-test and Mann-Whitney U test used for comparisons between groups. Fisher exact test ($n < 5$) or the Chi-square test was used for comparing categorical variables. Multivariable analysis (logistic) was performed to identify the independent risk factors for vascular remodelling of SIS-MAD. Multivariate logistic analysis was also performed to assess the independent role of NLR on the risk of vascular remodelling in SIS-MAD patients. A two-sided *p*-value < 0.05 was considered statistically significant in all analyses. Receiver operating characteristics (ROC) curves were drawn to determine the sensitivity and specificity of NLR in predicting vascular remodelling outcomes.

Results

Comparison of Clinical Baseline Data

A total of 109 SIS-MAD patients were included in this study, including 91 men (83.5%) and 18 women (16.5%). The age distribution of the patients was 39–79 (52.67 ± 7.89) years. The mean follow-up duration was 20.21 (range 13–26) months. The clinical data and demographic characteristics of the patients are shown in Table I. Patients were divided into a complete vascular remodelling group and a partial remodelling group based on their vascular remodelling results at the

endpoint follow-up. In this study, there were 26 cases in the complete vascular remodelling group and 83 cases in the partial remodelling group. There were no statistically significant differences in age, sex, body mass index, complications, smoking history, and clinical manifestations between the two groups. Complications included hypertension, diabetes mellitus, coronary heart disease, hyperlipidemia, and a history of abdominal surgery, with a higher incidence of hypertension (53/109, 48.6%) and smoking (43/109, 39.4%). The main clinical manifestations were abdominal pain (104/109, 95.4%), nausea/vomiting (41/109, 37.6%), diarrhea (12/109, 11.0%), and abdominal distension (15/109, 13.8%). According to the optimal truncation value of the NLR, patients were divided into two groups. Group A had 65 patients with $NLR > 5.37$, and Group B had 45 patients with $NLR \leq 5.37$. The outcomes of vascular remodelling in Group A (11, 16.9%) and Group B (15, 34.1%) were statistically significant ($p = 0.039$). The baseline characteristic comparisons between Group A and Group B are shown in Table II.

Comparison of Imaging Data

Based on Yun classification, 10.1% (11/109) had type I SIS-MAD, 37.6% (41/109) had type IIa SIS-MAD, 44.0% (48/109) had type IIb SIS-MAD, and 8.3% (9) had type III SIS-MAD (Table I). In terms of the image classification, there was no statistical difference between the complete vascular remodelling group and the partial remodelling group ($p = 0.868$). By collecting and analysing the relevant data of abdominal CTA, the SMA-distal aorta angle in the complete vascular remodelling group was smaller than that in the partial remodelling group ($51.16 \pm 1.18^\circ$ vs. $57.35 \pm 4.01^\circ$, $p < 0.001$). The length of the dissection in the complete vascular remodelling group (41.39 ± 3.24 mm) was less than that in the partial remodelling group (42.42 ± 3.02 mm). The true lumen stenosis $> 70\%$ in the complete vascular remodelling group and partial remodelling group was 10 (38.5%) and 34 (41.0%), respectively. The distance from the SMA ostium to the beginning of the dissection in the complete vascular remodelling group and partial remodelling group was 19.04 ± 1.08 mm vs. 19.37 ± 2.47 mm ($p = 0.989$), respectively.

Comparison of Laboratory Data

The neutrophil count in the complete vascular remodelling group was significantly lower than

Table I. Baseline Clinical Characteristics and Demographics of the study patients^a.

Variables	Total (n = 109)	Complete remodelling (n = 26)	Partial remodelling (n = 83)	p-value ^b
Age, mean ± SD, (years)	52.67 ± 7.89	51.96 ± 6.95	52.89 ± 8.19	0.602
Gender, male, n (%)	91 (83.5)	21 (80.8)	70 (84.3)	0.763
BMI, mean ± SD, (kg/m ²)	21.83 ± 1.76	21.90 ± 1.76	21.81 ± 1.77	0.754
Clinical presentation, n (%)				
Abdominal pain	104 (95.4)	24 (92.3)	80 (96.4)	0.591
Nausea/vomiting	41 (37.6)	8 (30.8)	33 (39.8)	0.490
Diarrhea	12 (11.0)	3 (11.5)	9 (10.8)	0.921
Abdominal distention	15(13.8)	4 (15.4)	11 (13.3)	0.752
Smoking, (n%)	43 (39.4)	9 (34.6)	34 (41.0)	0.649
Comorbidities, n (%)				
Hypertension	53 (48.6)	11 (42.3)	42 (50.6)	0.506
Diabetes mellitus	18 (16.5)	5 (19.2)	13 (15.7)	0.763
Coronary artery disease	14 (12.8)	4 (15.4)	10 (12.0)	0.738
Hyperlipidemia	17 (15.2)	5 (19.2)	12 (14.5)	0.547
Abdominal surgery	9 (8.3)	2 (7.7)	7 (8.4)	0.905
Hospitalization days, n (d)	7.08 ± 1.48	7.18 ± 1.39	7.05 ± 1.51	0.256
Anticoagulation therapy, n (%)	103 (94.5)	24 (92.3)	79 (95.6)	0.627
Blood pressure control, n (%)	77 (70.6)	17 (65.4)	60 (72.3)	0.622
Yun's classification, n (%)				0.868
Type I	11 (10.1)	3 (11.5)	8 (9.6)	
Type IIa	41 (37.6)	9 (34.6)	32 (38.6)	
Type IIb	48(44.0)	11(42.3)	37 (44.6)	
Type III	9 (8.3)	3 (11.5)	6 (7.2)	
SMA-distal aorta angle (°)	55.88 ± 4.43	51.16 ± 1.18	57.35 ± 4.01	0.001c
Distance from the SMA ostium to the beginning of the dissection (mm)	19.29 ± 2.22	19.04 ± 1.08	19.37 ± 2.47	0.989
Dissection length (mm)	42.17 ± 3.09	41.39 ± 3.24	42.42 ± 3.02	0.121
True lumen stenosis > 70%, n (%)	44 (40.4)	10 (38.5)	34 (41.0)	0.820
Follow-up time, months	20.21 ± 3.06	20.04 ± 3.04	16.38 ± 3.72	0.742
Laboratory test results				
Neutrophil count (10 ⁹ /L)	6.58 ± 2.45	6.13 ± 2.63	6.72 ± 2.38	0.380
Lymphocyte count (10 ⁹ /L)	1.22 ± 0.55	1.29 ± 0.31	1.20 ± 0.61	0.158
Monocyte count (10 ⁹ /L)	0.41 ± 0.20	0.41 ± 0.20	0.40 ± 0.27	0.714
Platelet count (10 ⁹ /L)	196.82 ± 75.18	205.88 ± 63.50	193.98 ± 78.62	0.294
Red cell distribution width	12.62 ± 0.66	12.69 ± 0.68	12.60 ± 0.65	0.554
NLR	5.97 ± 2.19	4.90 ± 2.12	6.32 ± 2.10	0.003
MLR	0.44 ± 0.41	0.36 ± 0.23	0.47 ± 0.45	0.539
RPR	7.60 ± 5.09	6.80 ± 2.37	7.85 ± 5.66	0.368

^aData are expressed as mean±standard deviation for normally distributed data and percentage for categorical variables, ^bChi-square test, Student's *t*-test and Mann-Whitney U test, ^c*p* < 0.001, ^dDefined as serial blood pressure measurements >140/90 mmHg; ^e Defined as fasting blood glucose test result at or >7.0 mmol/L or a random blood test result at or >11.1 mmol/L; ^fDefined as history of increased low-density lipoprotein or triglycerides. *Abbreviations*: NLR: Neutrophil-lymphocyte ratio, MLR: Monocyte-Lymphocyte ratio, RPR: Red cell distribution width-Platelet ratio, BMI: Body mass index (kg/m²); SMA: superior mesenteric artery.

that in the partial remodelling group. In comparison, the lymphocyte count was significantly higher than that in the partial remodelling group (Figure 3). The NLR of the complete vascular remodelling group was significantly lower than that of the partial remodelling group (*p*=0.003). There was no significant difference in monocyte-lymphocyte ratio and platelet-lymphocyte ratio between the two groups (Table I).

Multi-Factor Analysis of Vascular Remodelling

Multivariate logistic regression analysis with vascular remodelling as the dependent variable and hypertension, smoking, SMA-distal aorta angle, the true lumen stenosis >70%, Yun's classification, and NLR as independent variables showed that NLR (odds ratio [OR]=1.631, 95% confidence interval [CI]=1.027–2.592,

Table II. Demographic and clinical characteristics of population with NLR > 5.37 and NLR ≤ 5.37.

Variables	Total (n = 109)	NLR		p-value ^a
		> 5.37 (n = 64)	≤ 5.37 (n = 45)	
Age, (years)	52.67 ± 7.89	53.56 ± 9.04	52.05 ± 6.98	0.555
Gender, male, n(%)	91 (83.5)	53 (82.8)	38 (84.4)	0.821
BMI, (kg/m ²)	22.16 ± 1.78	21.99 ± 1.77	22.18 ± 1.78	0.274
Smoking, n(%)	43 (39.4)	28 (43.8)	15 (33.3)	0.273
Dissection length(mm)	42.17 ± 3.09	42.58 ± 3.07	41.60 ± 3.07	0.076
Distance from the SMA ostium to the beginning of the dissection (mm)	19.29 ± 2.22	19.39 ± 2.32	19.15 ± 2.10	0.602
SMA-distal aorta angle (°)	55.88 ± 4.43	56.01 ± 4.20	55.69 ± 4.77	0.513
True lumen stenosis > 70%, n (%)	44 (40.4)	27 (42.2)	17 (37.8)	0.644
Yun's classification ^a , n (%)				0.750
Type I	11 (10.1)	5 (7.8)	6 (13.3)	
Type IIa	41 (37.6)	26 (40.6)	15 (33.3)	
Type IIb	48 (44.0)	28 (43.8)	20 (44.4)	
Type III	9 (8.3)	5 (7.8)	4 (8.9)	
Anticoagulation therapy, n (%)	103 (94.5)	60 (92.3)	43 (97.7)	0.398
Blood pressure control, n (%)	77 (70.6)	47 (72.3)	30 (68.2)	0.643
Neutrophil count (10 ⁹ /L)	6.58 ± 2.45	7.11 ± 2.30	5.83 ± 2.47	0.010
Lymphocyte count (10 ⁹ /L)	1.22 ± 0.55	1.00 ± 0.39	1.54 ± 0.60	0.001 ^b
SMA Complete remodelling	26 (23.9)	11 (16.9)	15 (34.1)	0.039

^aChi-square test, Student's *t*-test and Mann-Whitney U test; ^b*p*<0.001. Abbreviations: SMA: superior mesenteric artery.

p=0.038) and SMA (OR=9.246, 95% CI=2.217–38.560, *p*=0.002) were independent influencing factors (Table III).

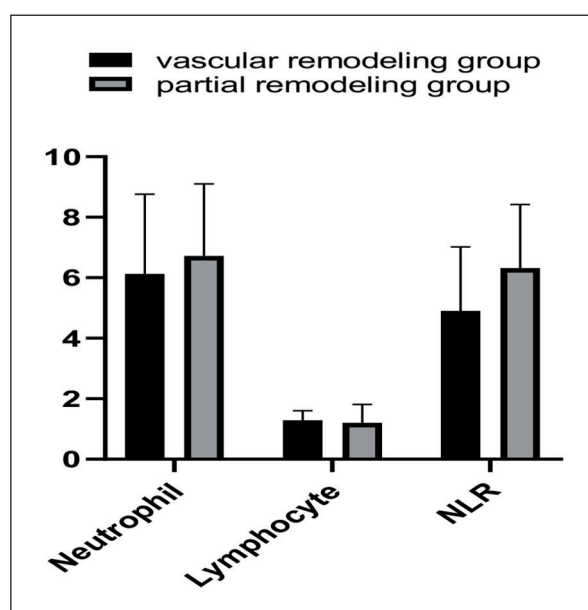


Figure 3. Histograms of laboratory parameters and NLR in vascular remodelling group and partial remodelling group.

ROC Curve of NLR

Baseline NLR and vascular remodelling were used for subject performance profile analysis to determine the NLR threshold. The area under the ROC curve was 0.735, the optimal cut-off value of the NLR was 5.37, and the sensitivity and specificity were 72.3% and 69.2%, respectively (Figure 4). Therefore, patients were divided into two groups according to the optimal cut-off value NLR at 5.37: the high NLR group (NLR>5.37) and the low NLR group (NLR≤5.37). There was a statistically significant difference in complete vascular remodelling between the high NLR group (11/64, 16.9%) and the low NLR group (15/45, 34.1%; *p*=0.039, Table II).

Discussion

To the best of our knowledge, our study is the first to examine the relationship between NLR and SISMAD patients. Our study found that an elevated NLR was strongly associated with mesenteric artery remodelling and that the NLR of the complete vascular remodelling group was lower than that of the incomplete vascular remodelling group. Our study also suggested that higher NLR levels contributed to a higher

Table III. Multivariate analysis of factors affecting vascular remodelling in SISMD patients.

Parameters	OR	95CI	p-value
Hypertension	0.844	0.139-5.119	0.854
Smoking	1.074	0.128-9.031	0.948
SMA-distal aorta angle	9.246	2.217-38.560	0.002
True lumen stenosis >70%	1.174	0.123-11.216	0.889
Yun's classification	0.833	0.310-2.237	0.717
NLR	1.631	1.027-2.592	0.038

Abbreviations: NLR: Neutrophil-lymphocyte ratio, SMA: superior mesenteric artery.

superior mesenteric artery-distal aorta angle (SAA). Moreover, the NLR showed a significant positive correlation with clinical presentation, which impacts the quality of life in SISMD patients. Furthermore, a higher NLR was indicative of higher one-year mortality. The multi-factor analysis showed that NLR and SAA were independent influencing factors of SISMD. In the present study, we used a ROC curve analysis to determine the NLR value with the highest specificity and sensitivity that correlated with vascular remodelling. The NLR is an easily obtained and inexpensive indicator that may have predictive validity in SISMD prognosis. The ROC curve also showed that NLR had a high degree of sensitivity and specificity in predicting artery remodelling of SISMD patients. A higher NLR was also associated with a higher

risk of rupture and the progression of dissecting aneurysm, which is in line with previous studies. SISMD patients who had not undergone vascular remodelling had poorer clinical outcomes¹⁰.

SISMD vascular remodelling refers to no severe residual stenosis or occlusion of the SMA true lumen, no false lumen, or complete resorption of false lumen thrombosis¹¹⁻¹³. Vascular remodelling is a complex pathological process involving a variety of cells. Inflammation and oxidative stress are the main driving forces of vascular remodelling. The inflammatory response mechanism involved in vascular remodelling is complex and there is currently no unified theory. Based on our results, we found that vascular remodelling is strongly associated with inflammation, which is in line with the literature^{14,15}. Current theories suggest that inflammation is involved in and accelerates the apoptosis of vascular smooth muscle cells and the degradation of the extracellular matrix during the vascular remodelling of SISMD. Many studies have shown that when the dissection occurs, neutrophils, macrophages, mast cells, and T cells infiltrate to different degrees^{16,17}. When SISMD occurs, abnormal changes occur in the number and morphology of plasma white blood cells, and an additional inflammatory response is activated to promote the accumulation of inflammatory cells in the damaged vessels. Inflammatory cells such as neutrophils, lymphocytes, and monocytes can release various proteolytic enzymes, matrix metalloproteinases, and other inflammatory factors such as interleukin-2, nuclear factor-kB, and interleukin-6. The recruitment of inflammatory cells produces extracellular matrix degradation, additional infiltration of inflammatory cells, increased endothelial cell damage, and inhibition of vascular remodelling¹⁸⁻²⁰. Neutrophils mediate the response of various factors, including arachidonic acid metabolites, platelet-aggravating factors, cytotoxic oxygen-derived free radicals,

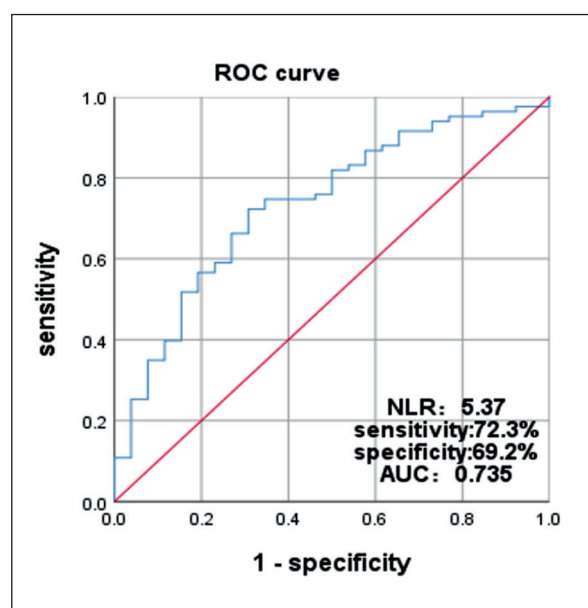


Figure 4. Receiver-operating characteristic curve of the neutrophil-lymphocyte ratio for predicting vascular remodelling of SISMD.

hydrolytic enzymes, and acid phosphatases¹⁸⁻²¹. In contrast, lymphocytes regulate inflammatory responses and have anti-atherosclerosis effects, and promote vascular remodelling, among which regulatory T cells (lymphocyte subclass) may have an inhibitory effect on atherosclerosis²². Low lymphocyte numbers may represent immunosuppression or a physiological stress state, which is often associated with poor overall prognosis of patients²³. This value is less susceptible to acute physiological inflammation by calculating the NLR, rather than applying changes in the single-cell count²⁴.

The NLR predicts adverse events in other disorders, including arteriosclerosis obliterans²⁵, acute stroke²⁶, and cancer²⁷. NLR also has been used as an alternative marker of inflammation and to predict mortality for cardiovascular and non-cardiovascular diseases²⁸⁻³¹. Several previous studies have explored the association between NLR and prognosis of dissection^{7,32-34}. However, studies on NLR and SISMAAD vascular remodelling are currently lacking, and, to our knowledge, our study is the first to do so. Karakoyun et al³⁵ and Bedel et al³⁶ found that NLR can be used as an indicator of the incidence of pericardial effusion and in-hospital mortality in patients with acute aortic dissection. Kalkan et al³⁴ divided 184 patients with type A aortic dissection into two groups based on NLR. They found that the high NLR group was more likely to experience adverse events such as major bleeding, nosocomial infection, multiple organ failure, and in-hospital death. A retrospective study of 123 patients with type I aortic dissection found that NLR was significantly increased, and the prognosis for vascular remodelling was worse in the group with higher mortality³². Additionally, Kordzadeh et al²³ found that high NLR was an independent influence factor for morbidity rather than mortality within 30 days after the rupture of abdominal aortic aneurysm repair. Our results showed that the NLR of patients in the incomplete remodelled group was significantly higher than that in the complete remodelled group; therefore, high NLR may be a simple indicator of poor prognosis of SMA dissection. It is unclear whether increased inflammatory levels predate SISMAAD and affect long-term vascular remodelling or whether they are merely a response to SISMAAD. Regardless of this relationship's direction, our results suggest that poorer vascular remodelling is more likely to occur with increased inflammation. NLR may have significant clinical value in the prognos-

tic outcome of SISMAAD. However, there is an absence of such studies; thus, some prospective studies are needed to confirm its value.

In previous studies, complete vascular remodelling occurs in approximately 25%–30% of SISMAAD patients undergoing conservative treatment^{37,38}. In this study, the vascular remodelling rate was 23.9% in the study population. According to previous studies, SISMAAD vascular remodelling is associated with dissection length, the diameter of SMA, true lumen stenosis, the absence of a false lumen with blood flow, and the presence of symptoms³⁸⁻⁴¹. The role of inflammation in SISMAAD remodelling pathogenesis has been studied for some time, but to a much lesser extent than in SAA, and the distance and true lumen stenosis. In this study, only SAA and NLR were found to be independent influencing factors for SISMAAD vascular remodelling. Patients were more likely to suffer from SISMAAD and obtain a worse outcome in pathological progression in the larger SAA group⁴². It is of note that our conclusion is inconsistent with previous studies. We speculated that the reason might be that the patients included in this study had a longer overall period from onset to prognosis, and there were some deviations in the early imaging data compared with the recent imaging data, making it difficult to obtain significant statistical significance. However, we cannot exclude the influence of other factors in this study on the vascular remodelling of SISMAAD.

The current study also found that complete remodelling of the mesenteric artery occurs more in type IIb SISMAAD patients than in type IIa SISMAAD patients [9 (34.6%) vs. 11 (42.3%), respectively]. The type IIa SISMAAD has a patent false lumen, and thrombosis of the patent false lumen is the first procedure in SMA remodelling. In type IIb SISMAAD this procedure is omitted because a patent false lumen is not present. Therefore, it takes more time for type IIa SISMAAD to achieve complete vascular remodelling, resulting in a decrease in the proportion of remodelling. For type IIa SISMAAD patients, early antithrombotic therapy is more beneficial for false lumen thrombosis and accelerates the process of vascular remodelling. At present, there are some conflicting opinions regarding the use of antithrombotic when SISMAAD patients received initial treatment after admission. Ahn et al⁴³ conducted a meta-analysis of 842 patients, both symptomatic and asymptomatic. The meta-analysis found no significant difference in morphological progress between the

antithrombotic group and the non-antithrombotic group. The success rate of conservative treatment in the two groups was similar. However, another meta-analysis described the effectiveness of antithrombotic therapy in which the majority of patients achieved complete remodelling and better results in SMA morphological progress after antithrombotic therapy³⁸. In addition, Han et al⁴⁴ conducted an 8-year follow-up of 52 symptomatic SIS-MAD patients and found that anticoagulant or antiplatelet therapy can cause a higher complete vascular remodelling rate in the natural prognosis of SIS-MAD. Based on these results, 94.5% of patients received initial anticoagulant therapy in our current treatment strategy. No correlation was found between antithrombotic therapy and vascular remodelling in our study. The effect of anticoagulant or antiplatelet therapy, which is based on conservative treatment on vascular remodelling, remains unclear for us and needs to be validated by a systematic review or randomised controlled trial in future studies.

Additionally, in our study, the patients with higher NLR were men and had a longer history of smoking, which is similar to the epidemiology of SIS-MAD⁴⁵. In our risk factors analysis among SIS-MAD patients who were free from intervention or surgical treatment, inflammation and SAA were the only independent influence factors, while surprisingly, tobacco, smoking, and hypertension were less important. Karaolani et al⁴⁶ found through meta-analysis that SIS-MAD usually occurred in middle-aged men with a history of smoking. Perhaps further research will be needed in the future to prove the link between smoking and remodelling, and we cannot conclude that there is no link between smoking and vascular remodelling based on current research. The NLR contains important information regarding the patient's inflammatory condition. Mesenteric artery remodelling is a common phenomenon that occurs in the natural course of SIS-MAD and appears to lead to better clinical outcomes⁴⁷. Therefore, our study demonstrated that determining NLR can help identify patients who may need readmission or have a higher chance of partial remodelling within one year, which provides a more accurate follow-up in these patients who had SIS-MAD, and thus NLR may serve as a useful biomarker to guide treatment and management.

The current study has limitations, which need to be taken into consideration when interpreting the results. First, with the development of

CTA imaging technology, more and more SIS-MAD cases have been found in recent years even though SIS-MAD is a rare vascular disease. Our study sample were patients who were retrospectively enrolled from our database, which is small and might cause some selection bias. Second, we only assessed NLR, without considering other vital inflammatory markers, such as high sensitivity C-reactive protein and interleukin-6, since they were not routinely measured in our hospital. Finally, the absence of dynamic level assessment of NLR levels in our study needs to be considered.

Conclusions

We provided evidence that NLR is an effective marker for vascular remodelling in SIS-MAD patients who underwent conservative therapy. This study suggests that SIS-MAD patients with a higher NLR have a worse prognosis. When the NLR >5.37, SIS-MAD patients are more likely to suffer from partial vascular remodelling than patients with NLR ≤5.37.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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Fan Wu and Guo Hong made a substantial contribution to research design or the acquisition and analysis of data; Fan Wu, YanChun Chen and Guo Hong drafted the paper or revised it critically. Xi Cheng Zhang has given approval of the submitted and final versions. All Authors had access to the full paper, read and approved the manuscript's final version.

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