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Relationship between monocytes to lymphocytes ratio and axial spondyloarthritis

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ABSTRACT

Background: Axial spondyloarthritis (axSpA) is a progressive, chronic, inflammatory skeletal disorder affecting the spine and sacroiliac joints. Many studies have shown that neutrophils, lymphocytes, monocytes, platelets, and red blood cells (RBCs) play important roles in the inflammatory process of axSpA. Neutrophils to lymphocytes ratio (NLR) and red blood cell distribution width (RDW) have been reported to be simple and inexpensive markers to indicate the disease activity of axSpA. However, the role of monocytes to lymphocytes ratio (MLR) and platelets to lymphocytes ratio (PLR) in axSpA was rarely mentioned.

Objective: The study's aim was to determine the role of MLR and PLR in axSpA patients and to investigate their relationships with disease severity.

Methods: AxSpA patients who fulfilled the Assessment in Ankylosing Spondylitis International Society classification criteria published in 2009 were enrolled in this study and divided into nonradiographic axial spondyloarthritis (nr-axSpA) group and ankylosing spondylitis (AS) group. Healthy age and gender-matched subjects were also enrolled as control group. MLR, PLR, NLR, RDW, C-reactive protein (CRP) level, and erythrocyte sedimentation rate (ESR) level were assessed. The correlation between the variables with finger-to-floor distance, Modified Schober test, and occiput-to-wall distance were tested with Pearson correlation. Furthermore, area under curve (AUC) value, sensitivity, specificity, and the optimal cutoff values were determined using receiver operating characteristic (ROC) curves.

Results: A total of 148 axSpA patients (67 nr-axSpA patients and 81 AS patients) and 58 healthy subjects were included in the study. The MLR, NLR, PLR, and RDW in axSpA group were higher than those in the control group ($P < 0.05$). Among them, MLR and RDW were highly increased in AS group compared with the nr-axSpA group ($P < 0.05$). MLR, NLR, PLR, and RDW were all positively correlated with ESR level and CRP level ($P < 0.05$). MLR and RDW were positively correlated with finger-to-floor distance and negatively correlated with Modified Schober test ($P < 0.05$). RDW was positively correlated with occiput-to-wall distance ($P < 0.05$). ROC curve results showed MLR yielded a higher AUC than NLR, PLR, and RDW ($P < 0.05$). In addition, the optimal cutoff value of MLR for axSpA was 0.22, with a specificity of 70.9% and sensitivity of 68.4%.

Conclusions: MLR was elevated in AS patients compared to nr-axSpA patients and had a close relationship with CRP level, ESR level, and spine movements. MLR may be a reliable, cost-effective, and novel potential parameter to evaluate disease severity in axSpA.

1. Introduction

Axial spondyloarthritis (AxSpA) is a progressive, chronic, inflammatory disease that mainly affects the axial skeleton and sacroiliac joints [1,2]. AxSpA includes nonradiographic axial spondyloarthritis (Nr-axSpA) and ankylosing spondylitis (AS), and Nr-axSpA is the early stages of the disease [3]. The common clinical manifestations of axSpA are chronic inflammatory back pain, sacroiliitis, spondylitis, and restrictions in spine movement [4]. Although the pathogenesis of axSpA is still unclear, about 90% of AS patients carry human leukocyte antigen (HLA)-B27. HLA-B27 is widely accepted as a routine clinical biomarker of AS [5]. However, with effective disease-modifying treatments such as

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tumor necrosis factor inhibitors becoming widely available for AS, early diagnosis is urgently required to reduce disease burden.

Many studies have shown that the immune and inflammatory systems are often activated in axSpA patients [6,7]. Serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels are increased in peripheral joint inflammation, which are useful biomarkers for determining the degree of inflammatory disease activity over time [8,9]. However, they have low sensitivity and specificity, with the limitations of short-term inflammatory activity and low discrimination ability. It has been reported that neutrophils, lymphocytes, monocytes, platelets, and red blood cells (RBCs) play important roles in the inflammatory process of axSpA [10–12]. Neutrophils to lymphocytes ratio (NLR) and red blood cell distribution width (RDW) have been reported to be simple and inexpensive markers to indicate the disease activity of axSpA [13,14]. Monocytes to lymphocytes ratio (MLR) and platelets to lymphocytes ratio (PLR), which can be easily calculated from the peripheral blood, have also been demonstrated to be novel systemic inflammatory indicators of disease severity in many diseases, such as Behçet's disease and cancer [15–17]. However, no study has focused on the role of MLR and PLR in axSpA.

Therefore, our study aims to investigate the role of MLR and PLR in axSpA patients and their relationships with disease severity.

2. Materials and methods

2.1. Participants characteristics

A total of 148 patients, fulfilling the 2009 Assessment in Ankylosing Spondylitis International Society classification criteria for the diagnosis of axSpA (male to female ratio: 116/32, mean 29.9 ± 8.8 years) and 58 healthy controls (male to female ratio: 43/15, mean 29.8 ± 6.9 years) between April 2016 and June 2017 were enrolled in the study. The enrolled AS patients fulfilled the modified 1984 New York criteria. Those who had malignancy, active infection, diabetes mellitus, hypertension, renal failure, and liver failure were excluded from the study. This study has been approved by the EC office of Guangdong Second Provincial General Hospital (2017-FSMY-009).

2.2. Clinical and laboratory assessments

Age, gender, clinical features, HLA-B27 values, number of white blood cells (WBCs), neutrophils, monocytes, platelets, lymphocytes, RBCs, hemoglobin level, RDW, CRP level, and ESR level were recorded. MLR, PLR, and NLR were calculated.

2.3. Statistical analysis

Database management and statistical analyses were performed with SPSS 13.0. Continuous variables were presented as mean ± standard deviation, and categorical variables were indicated as number (n) and percent (%). Comparisons of the study parameters were performed using Student's *t*-tests, while qualitative variables were assessed with Chi square tests. Pearson correlation analysis was carried out to test the correlation of the data. Furthermore, sensitivity and specificity were compared using the receiver operating characteristic (ROC) curve. A P value < 0.05 was accepted as significant.

3. Results

3.1. Basic characteristics of axSpA patients and healthy subjects

A total of 148 axSpA patients and 58 healthy subjects were included in the study. There was no statistically significant difference between the two groups in terms of age and gender. The number of WBCs, neutrophils, monocytes, platelets, and RDW in the axSpA group were higher than those in the control group, while the number of lymphocytes, RBCs, and hemoglobin level were lower ($P < 0.05$). The disease duration was (5.6 ± 5.9) years, ESR level was (32.3 ± 30.4) mm/h, CRP level was (17.5 ± 22.5) mg/L, HLB-27 positive rate was 73.80%, finger-to-floor distance was (11.8 ± 14.2) cm, occiput-to-wall distance was (1.5 ± 4.2) cm, and Modified Schober test was (4.5 ± 1.7) cm in axSpA patients (Table 1).

Table 1
Demographic features and laboratory findings of the participants.

	Control (n = 58)	axSpA (n = 148)	*P*
Age (years)	29.78 ± 6.87	29.86 ± 8.77	0.949
Gender (male/female)	43/15	116/32	0.514
WBC ($\times 10^9$/L)	6.59 ± 1.44	7.32 ± 1.94	**0.004**
Neutrophils ($\times 10^9$/L)	3.52 ± 1.02	4.45 ± 1.65	< **0.001**
Lymphocytes ($\times 10^9$/L)	2.40 ± 0.66	2.11 ± 0.73	**0.009**
Monocytes ($\times 10^9$/L)	0.45 ± 0.16	0.58 ± 0.21	< **0.001**
Platelets ($\times 10^9$/L)	264.72 ± 57.29	293.68 ± 87.45	**0.006**
Hemoglobin (g/dL)	145.41 ± 15.44	133.44 ± 19.70	< **0.001**
RBC ($\times 10^{12}$/L)	5.06 ± 0.60	4.82 ± 0.56	**0.008**
RDW (%)	12.96 ± 1.24	13.30 ± 1.53	**0.112**
MLR	0.20 ± 0.07	0.28 ± 0.10	< **0.001**
NLR	1.55 ± 0.52	2.39 ± 1.53	< **0.001**
PLR	115.67 ± 30.71	155.47 ± 78.68	< **0.001**
ESR (mm/h)		32.34 ± 30.36	
CRP (mg/L)		17.54 ± 22.54	
Disease duration (years)		5.57 ± 5.88	
HLB-27 positive rate (%)		73.80%	
Finger-to-floor distance (cm)		11.77 ± 14.15	
Occiput-to-wall distance (cm)		1.46 ± 4.15	
Modified Schober test (cm)		4.45 ± 1.74	

3.2. MLR, PLR, NLR, and RDW were increased in axSpA patients

The MLR, PLR, NLR, and RDW were 0.28 ± 0.10, 155.5 ± 78.7, 2.4 ± 1.5, and 13.3 ± 1.5, respectively, in the axSpA group and 0.20 ± 0.07, 115.7 ± 30.7, 1.6 ± 0.5, and 13.0 ± 1.2 in the control group. These differences were statistically significant (P *all* < 0.05) (Table 1).

3.3. MLR and RDW were increased in AS patients

In the 148 axSpA patients, 67 patients belong to the nr-axSpA group, and 81 patients belong to the AS group. Comparison of variables between the two groups showed that MLR, RDW, number of WBCs, monocytes, and platelets, ESR level, CRP level, HLB-27 positive rate, disease duration, finger-to-floor distance, and occiput-to-wall distance significantly increased in the AS group, while the hemoglobin level and Modified Schober test decreased (P *all* < 0.05). There was no statistically significant difference between groups in terms of age, neutrophils number, lymphocytes number, RBCs, NLR, or PLR. (Table 2).

3.4. MLR and RDW were associated with ESR level, CRP level, and spine activity

MLR, PLR, NLR, and RDW were all positively correlated with ESR level ($r = 0.324$, $P < 0.001$; $r = 0.443$, $P < 0.001$; $r = 0.291$, $P < 0.001$; $r = 0.342$, $P < 0.001$, respectively) and CRP level ($r = 0.428$, $P < 0.001$; $r = 0.451$, $P < 0.001$; $r = 0.350$, $P < 0.001$; $r = 0.316$, $P < 0.001$, respectively). MLR and RDW were positively correlated with finger-to-floor distance ($r = 0.202$, $P = 0.015$; $r = 0.317$, $P < 0.001$, respectively) and negatively correlated with Modified Schober test ($r = -0.254$, $P = 0.002$; $r = -0.287$, $P < 0.001$, respectively). RDW was also positively correlated with occiput-to-wall distance ($r = -0.285$, $P = 0.001$) (Table 3).