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Clinical significance of the monocyte:lymphocyte ratio for ankylosing spondylitis patients with thoracolumbar kyphotic deformities

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Abstract

Purpose: This study aimed to determine the clinical significance of the monocyte:lymphocyte ratio (MLR) in ankylosing spondylitis (AS) patients with thoracolumbar kyphotic deformity.

Methods: Ninety AS patients and 45 healthy controls were retrospectively enrolled. AS patients were divided into thoracolumbar kyphotic deformity (AS deformity) and spine normal (AS normal) groups. Blood parameters including C-reactive protein and erythrocyte sedimentation rate were determined. Receiver operating characteristic (ROC) curves and binary logistic regression analysis were conducted.

Results: Counts of white blood cells, neutrophils, and monocytes, and the neutrophil:lymphocyte ratio, platelet:lymphocyte ratio, and MLR were significantly higher in the AS than the control group. ROC curve results showed that the MLR yielded a higher area under the curve (AUC) value than other parameters, compared with controls. The MLR and monocyte count were higher in the AS deformity group than the AS normal group. ROC curve results indicated that the MLR yielded a higher AUC value than other parameters, compared with the AS normal group. Logistic regression suggested that the MLR was an independent predictor for thoracolumbar kyphotic deformity.

Conclusions: The MLR was elevated in AS patients, and was shown to be an independent predictor for thoracolumbar kyphotic deformity.

Keywords

Monocyte to lymphocyte ratio, ankylosing spondylitis, thoracolumbar kyphotic deformity, clinical significance, predictor, logistic regression, receiver operating characteristic curve

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Introduction

Ankylosing spondylitis (AS) is a progressive and chronic inflammatory autoimmune disease characterized by axial skeleton and sacroiliac joint involvement.[1,2] Although 90% of AS patients carry human leukocyte antigen B27, the pathogenesis of AS is not yet clear.[3] Thoracolumbar kyphotic deformity is a disabling condition affecting more than 30% of AS patients that places a huge burden on patients and their families.[4] In recent years, the early application of tumor necrosis factor inhibitors (TNFi) have changed the outcomes and the prognosis of AS patients.[5] Therefore, means of obtaining an earlier diagnosis of AS are urgently required.

Currently, magnetic resonance imaging (MRI) is widely used to determine the disease activity and prognosis of AS.[6] Biochemical markers such as C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) in combination with MRI help to specify patients at risk and to determine the appropriate drug usage.[7,8] Blood parameters including numbers of neutrophils, platelets, lymphocytes, and monocytes, hemoglobin (HGB) levels, and the neutrophil:lymphocyte ratio (NLR), platelet:lymphocyte ratio (PLR), and monocyte:lymphocyte ratio (MLR) have been proposed as indicators of systemic inflammation.[9,10] In particular, the NLR, PLR, and MLR were proposed as simple and inexpensive markers to indicate the disease activity of axial spondyloarthritis (axSpA).[11,12] However, no studies have focused on the clinical importance of blood parameters for AS patients with thoracolumbar kyphotic deformity.

Therefore, this study retrospectively examined counts of neutrophils, lymphocytes, platelets, monocytes, HGB, and the NLR, PLR, and MLR in AS patients and determined their diagnostic value for AS patients with thoracolumbar kyphotic deformity.

Materials and methods

Participant characteristics

Ninety AS patients, fulfilling the modified 1984 New York criteria, and 45 healthy subjects were enrolled in the study between May 2015 and May 2018. AS patients were further divided into the thoracolumbar kyphotic deformity (AS deformity, $n = 36$) group and the spine normal (AS normal, $n = 54$) group. Patients were excluded from the study if they had any of the following: malignancy, active infection, diabetes mellitus, hypertension, renal failure, or rheumatic disease. This study was approved by the Ethics Committee of Guangdong Provincial People's Hospital, and all subjects provided their informed consent for participation.

Clinical and laboratory assessments

Biochemical measurements of fresh material were performed as part of routine clinical treatment. Blood samples were obtained during the fasting state. Patient age, sex, and clinical features were recorded. Counts of white blood cells (WBCs), neutrophils, monocytes, platelets, lymphocytes, HGB, and CRP and ESR were recorded. The NLR, PLR, and MLR were calculated.

Statistical analysis

Database management and statistical analyses were performed with SPSS 13.0 software (SPSS Inc., Chicago, IL, USA). Continuous variables were presented as means ± standard deviation (SD), and categorical variables were indicated as numbers (n) and percentages (%). Comparisons of study parameters were performed using Student's *t* tests, while qualitative variables were assessed with Chi square tests. The area under the curve (AUC) value, optimal cutoff value, sensitivity, and specificity were

determined using receiver operating characteristic (ROC) curves. Binary logistic regression analysis was conducted to evaluate the risk factors of thoracolumbar kyphotic deformity. A P value <0.05 was accepted as significant.

Results

Basic characteristics of AS patients and healthy controls

Counts of WBCs, neutrophils, and monocytes, as well as the NLR, PLR, and MLR were significantly higher in the AS group than in the control group, while HGB levels were significantly lower ($P < 0.05$). The ESR was 26.00 ± 25.63 mm/h and CRP was 18.25 ± 24.06 mg/L in the AS group (Table 1).

The MLR had a high diagnostic value for AS

ROC curve results showed that the MLR yielded a higher AUC value [0.746 (95% confidence interval [CI]: 0.661–0.832)] than other parameters, compared with the control group. The optimal cutoff value of the MLR for AS was 0.279, with a sensitivity of 47.2% and a specificity of 91.2% (Figure 1 and Table 2).

The MLR was higher in AS patients with thoracolumbar kyphotic deformities

Blood parameters were compared between the AS deformity group and AS normal group, and the MLR, and WBC and monocyte counts were shown to be significantly higher in the AS deformity group than the AS normal group ($P < 0.05$; Table 3).

The MLR had a high diagnostic value for AS patients with thoracolumbar kyphotic deformities

The ROC curve was used to evaluate the diagnostic value of blood parameters for AS deformities. The MLR was found to yield a higher AUC value [0.764 (95% CI: 0.667–0.860)] than other parameters, compared with the AS normal group. The optimal cutoff value of the MLR was 0.271, with a sensitivity of 75.0% and a specificity of 68.0% (Figure 2 and Table 4).

Table 1. Demographic features and laboratory findings of the participants.

	Control (n = 45)	AS (n = 90)	*P* value
Age (years)	30.04 ± 7.19	30.24 ± 10.06	0.895
Sex (male/female)	35/10	74/16	0.537
WBC ($\times 10^9$/L)	6.45 ± 1.19	7.65 ± 2.30	**<0.001**
Neutrophil ($\times 10^9$/L)	3.49 ± 0.83	4.69 ± 2.30	**<0.001**
Lymphocyte ($\times 10^9$/L)	2.29 ± 0.54	2.17 ± 0.68	**0.202**
Monocyte ($\times 10^9$/L)	0.46 ± 0.15	0.65 ± 0.47	**0.001**
Platelet ($\times 10^9$/L)	262.78 ± 42.29	291.36 ± 90.96	0.018
Hemoglobin (g/dL)	145.20 ± 16.15	133.49 ± 16.77	**<0.001**
NLR	1.60 ± 0.48	2.39 ± 1.39	**<0.001**
PLR	119.02 ± 28.88	150.46 ± 109.12	**0.060**
MLR	0.21 ± 0.07	0.31 ± 0.22	**<0.001**
ESR (mm/h)	–	26.00 ± 25.63	
CRP (mg/L)	–	18.25 ± 24.06	

WBC, white blood cell; NLR, neutrophil:lymphocyte ratio; PLR, platelet:lymphocyte ratio; MLR, monocyte:lymphocyte ratio; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein. They mean *P* value <0.05.

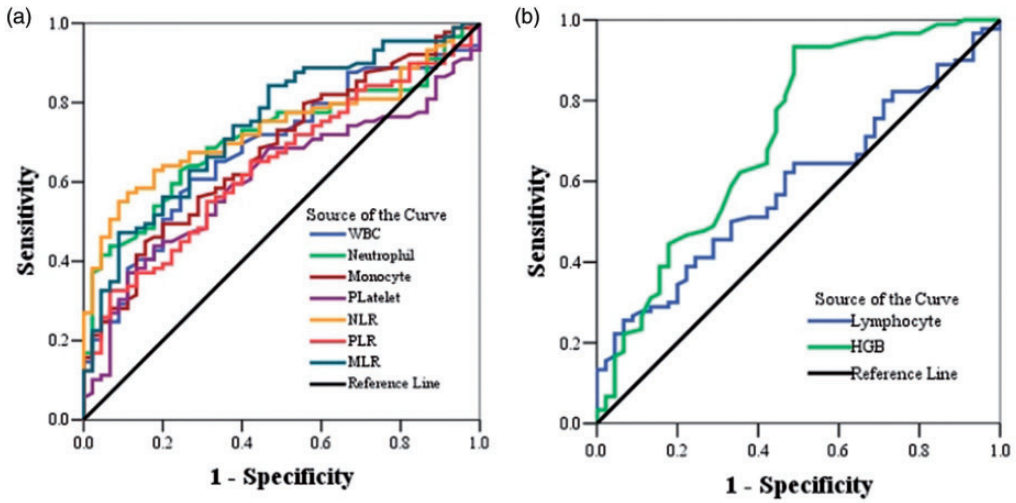

Figure 1. The ROC curve was used to evaluate the diagnostic value of blood parameters for AS. ROC, receiver operating characteristic; AS, ankylosing spondylitis.

Table 2. ROC curve evaluation of the diagnostic value of blood parameters for AS.

	AUC	95% CI	*P*	Optimal cutoff value	Sensitivity	Specificity
WBC	0.682	0.590–0.773	**0.001**	6.695	60.7%	73.3%
Neutrophil	0.714	0.628–0.800	**<0.001**	3.935	62.9%	75.6%
Monocyte	0.678	0.586–0.770	**0.001**	0.573	49.4%	80.0%
Platelet	0.608	0.512–0.704	0.042	292.5	43.8%	82.3%
Lymphocyte	0.589	0.492–0.686	**0.093**	1.725	25.6%	93.4%
HGB	0.715	0.618–0.812	**<0.001**	151.5	93.3%	51.2%
NLR	0.735	0.653–0.818	**<0.001**	2.156	57.3%	88.9%
PLR	0.642	0.548–0.736	**0.008**	127.301	55.1%	68.9%
MLR	0.746	0.661–0.832	**<0.001**	0.279	47.2%	91.2%

ROC, receiver operating characteristic; AS, ankylosing spondylitis; AUC, area under the curve; CI, confidence interval; WBC, white blood cell; HGB, hemoglobin; NLR, neutrophil:lymphocyte ratio; PLR, platelet:lymphocyte ratio; MLR, monocyte:lymphocyte ratio.

Binary logistic regression analysis of factors independently associated with thoracolumbar kyphotic deformity

Logistic regression analysis was used to reveal the association of the MLR, WBC and monocyte counts, the ESR, and CRP with thoracolumbar kyphotic deformities of AS. The MLR was found to be an independent predictor for thoracolumbar kyphotic deformity (EXP (B) = 2.418, 95% CI (1.110–5.421), $P = 0.038$), compared with the AS normal group (Table 5).

Discussion

Because TNFi is becoming increasingly widely available for AS treatment, earlier diagnosis and disease activity assessment are crucial for reducing the disease

Table 3. Comparison of variables between patients with and without thoracolumbar kyphotic deformities.

	AS normal (n = 54)	AS deformity (n = 36)	*P*
WBC	7.26 ± 2.12	8.3523 ± 2.46	**0.049**
Neutrophil ($\times 10^9$/L)	4.50 ± 1.96	4.97 ± 1.86	0.261
Lymphocyte ($\times 10^9$/L)	2.07 ± 0.59	2.25 ± 0.76	0.214
Monocyte ($\times 10^9$/L)	0.51 ± 0.20	0.86 ± 0.65	**0.003**
Platelet ($\times 10^9$/L)	286.87 ± 99.66	298.08 ± 76.93	0.570
HGB	135.44 ± 15.48	130.56 ± 18.37	0.177
NLR	2.43 ± 1.66	2.32 ± 0.89	0.708
PLR	157.66 ± 137.31	139.66 ± 39.05	0.446
MLR	0.25 ± 0.09	0.40 ± 0.32	**0.011**
ESR	24.34 ± 23.13	28.50 ± 29.14	0.454
CRP	17.73 ± 24.73	19.04 ± 23.33	0.802

WBC, white blood cell; HGB, hemoglobin; NLR, neutrophil:lymphocyte ratio; PLR, platelet:lymphocyte ratio; MLR, monocyte:lymphocyte ratio; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

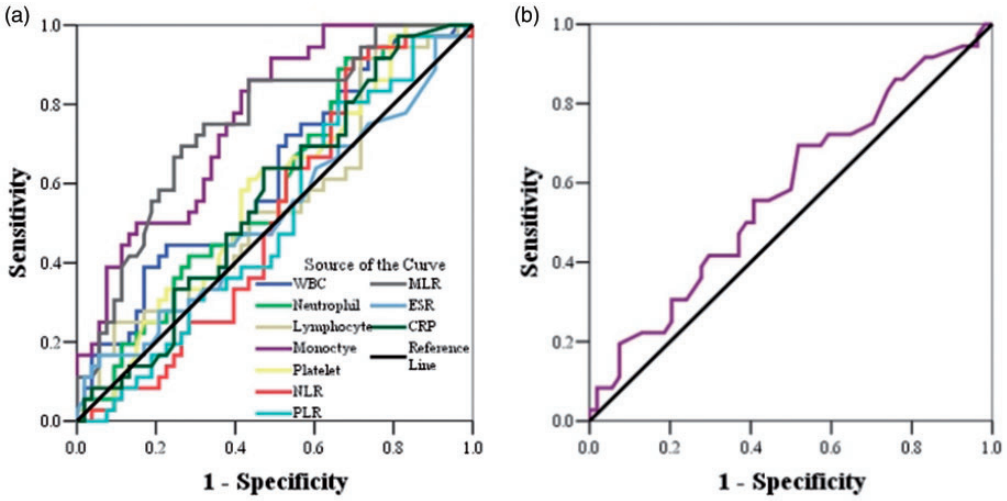

Figure 2. The ROC curve was used to evaluate the diagnostic value of blood parameters for AS patients with thoracolumbar kyphotic deformities. ROC, receiver operating characteristic; AS, ankylosing spondylitis.

burden. The present study was designed to assess the clinical significance of blood parameters for AS patients with thoracolumbar kyphotic deformities. Our results indicated that the MLR is elevated in AS patients, and that it has a higher diagnostic value for patients with thoracolumbar kyphotic deformities. Thus, the MLR is an independent predictor for thoracolumbar kyphotic deformity.

Complete blood counts are an easy, inexpensive, routine examination technique,

Table 4. ROC curve evaluation of the diagnostic value of blood parameters for AS patients with thoracolumbar kyphotic deformities.

	AUC	95% CI	*P*	Optimal cutoff value	Specificity	Sensitivity
WBC	0.619	0.501–0.737	0.058	8.080	44.4%	774%
Neutrophil	0.583	0.463–0.702	0.188	3.330	91.7%	32.1%
Lymphocyte	0.546	0.423–0.669	0.462	0.493	86.1%	56.7%
Monocyte	0.750	0.648–0.852	**<0.001**	0.493	86.1%	56.7%
Platelet	0.572	0.453–0.691	0.250	201.500	97.2%	20.8%
HGB	0.579	0.458–0.700	0.208	140.500	69.4%	48.2%
NLR	0.515	0.394–0.635	0.815	1.471	91.7%	30.2%
PLR	0.508	0.387–0.628	0.900	113.207	80.6%	34.0%
MLR	0.764	0.667–0.860	**<0.001**	0.271	75.0%	68.0%
ESR	0.516	0.392–0.641	0.796	69.500	16.7%	94.4%
CRP	0.563	0.4431–0.682	0.318	7.800	63.9%	52.9%

ROC, receiver operating characteristic; AS, ankylosing spondylitis; AUC, area under the curve; CI, confidence interval; WBC, white blood cell; HGB, hemoglobin; NLR, neutrophil:lymphocyte ratio; PLR, platelet:lymphocyte ratio; MLR, monocyte:lymphocyte ratio; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Table 5. Binary logistic regression analysis of factors independently associated with thoracolumbar kyphotic deformity.

Risk factor	EXP (B) (CI95%)	*P* value
WBC	0.883 (0.368–1.874)	0.685
Monocyte	1.530 (0.688–3.127)	0.525
MLR	2.418 (1.110–5.421)	**0.038**
ESR	1.641 (0.690–3.205)	0.619
CRP	1.718 (0.892–3.514)	0.191

WBC, white blood cell; MLR, monocyte:lymphocyte ratio; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

which provides information about immune system elements.[10,12] The NLR, PLR, and MLR have all been reported to be simple markers to indicate the disease activity of axSpA.[9,10] In our study, we found that WBC, neutrophil, and monocyte counts, we well as the NLR, PLR, and MLR were significantly higher in the AS group than the control group, while HGB levels were significantly lower. ROC curve analysis showed that the MLR and NLR yielded a higher AUC value. The optimal cutoff value for the MLR for AS was 0.279, with a sensitivity of 47.2% and a specificity of 91.2%, while values for the NLR were 2.156, 57.3%, and 88.9%, respectively. The AUC and sensitivity of the MLR and NLR were lower than reported previously,[11] which could be explained by differences in inclusion criteria. An explanation for the observed relationship between higher levels of NLR and MLR with AS is not yet clear. However, it has been reported that interleukin (IL)-1α may play a role in inflammation and lead to an increased NLR.[13] Additionally, Contis found that neutrophils displayed a gene expression signature of oxidative stress in rheumatoid arthritis (RA), leading to mitochondrial DNA release and enhanced progression of joint damage.[14]

Our present study also found that monocyte counts and the MLR were higher in the AS deformity group than the AS normal group, while ROC curve results indicated that monocytes and the MLR had a higher AUC than other variables. Optimal cutoff values for monocytes and the MLR were 0.493 and 0.271, sensitivity was 86.1% and 75.0%, and specificity was 56.7% and

68.0%, respectively. Logistic regression analysis suggested that the MLR was an independent predictor for thoracolumbar kyphotic deformity (EXP (B) = 2.418, 95% CI 1.110–5.421, $P = 0.038$).

An elevated MLR is defined as an increased monocyte and decreased lymphocyte count. Monocytes can differentiate into a wide range of terminally differentiated cells that perform versatile functions during inflammation.[15,16] Monocytes and macrophages are thought to produce tumor necrosis factor-α and IL-6, and to be the source of cells becoming osteoclasts in RA.[17]

Although this is the first demonstration that the MLR has a highest diagnostic value for AS deformity than other parameters, our study has some limitations. First, it was a single-center study with a relatively small sample size. Second, we only used spot parameters for the analysis, rather than follow-up values. Therefore, further controlled studies are needed to validate the clinical value of blood parameters for AS.

Based on the results of the present study, the MLR is elevated in AS patients compared with controls, and has a higher diagnostic value for AS patients with thoracolumbar kyphotic deformities. Thus, the MLR is an independent predictor for thoracolumbar kyphotic deformity.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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