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, platelets, lymphocytes, and monocytes, hemoglobin (HGB) levels, and the neutrophil:lymphocyte ratio (NLR), platelet:lymphocyte ratio (PLR), and monocyte:lymphocyte ratio (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 $26.00 \pm 25.63$ mm/h and CRP was $18.25 \pm 24.06$ 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.
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
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,
which provides information about immune system elements. The NLR, PLR, and MLR have all been reported to be simple markers to indicate the disease activity of axSpA. In our study, we found that WBC, neutrophil, and monocyte counts, as 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 0.493, 86.1%, and 56.7%, respectively. 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.

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

| Parameter | 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       | 0.506| 0.392–0.641  | 0.796 | 69.500               | 16.7%       | 94.4%       |
| CRP       | 0.563| 0.443–0.682  | 0.318 | 7.800                | 63.9%       | 52.9%       |

### 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.
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. 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. 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**

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