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Original Article

Increased platelet to lymphocyte ratio is related to inflammation in patients with Takayasu arteritis

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Abstract: Objectives: Takayasu arteritis (TA) is a chronic inflammatory disease that involves the aorta and main branches. Platelet to lymphocyte ratio (PLR) has been regarded as an indicator to assess inflammatory state in related rheumatic diseases. However, the association between PLR and TA in the literature has not been fully understood. Thus, the aim of our study is to investigate a relationship between PLR and TA. Methods: This cross-sectional study involved 108 newly diagnosed TA patients who were admitted to the First Affiliated Hospital of Xinjiang Medical University from 2010 to 2015. Results: PLR were higher in active TA patients (a-TA) compared with na-TA (145.4 ± 53.25 *vs*. 104.4 ± 34.45, *P*<0.001). PLR was negatively correlated with lymphocyte count in patients with a-TA, and positively correlated with platelet count, hemoglobin and neutrophil to lymphocyte ratio (NLR). Interestingly, a positively correlation between PLR and C reactive protein (CRP) was observed in a-TA. However, there was no correlation between PLR and CRP in na-TA. Stepwise logistic regression analysis showed that PLR was associated with a-TA independently of erythrocyte sedimentation rate (ESR) and CRP. When Receiver operating characteristic (ROC) curves were used to identify the performance of PLR in assessing a-TA, the area under the curve was 0.743 (95% CI: 0.644-0.842, P<0.001) with the sensitivity and specificity of 82.6% and 55.5%, respectively. Conclusions: Our study suggests that increased PLR is associated with TA patients with active disease, and is correlated with CRP in active TA patients. These results indicate that PLR may be used as an indicator to assess disease activity and reflect active inflammation in patients with TA.

Keywords: Takayasu arteritis, platelet to lymphocyte ratio, C reactive protein

Introduction

Takayasu arteritis (TA) is a chronic inflammatory disease that involves the aorta and main branches [1]. Traditionally, erythrocyte sedimentation rate (ESR) and C reactive protein (CRP) have been used to determine the development of TA patients [2, 3]. Very recently, several inflammatory cytokines have been considered to be markers for estimating the inflammatory status of patients with TA, such as tumor necrosis factor (TNF), interleukin-6 (IL-6) and matrix metalloproteinases (MMP). Accumulating data have indicated that serum IL-6 and TNF are correlated with the disease activity in TA patients [4]. These results lead to a hypothesis that inflammation plays an important role in the pathogenesis of TA.

Platelet to lymphocyte ratio (PLR), a part of routine blood tests, is an easy calculated parameter. Previous studies have shown that increased PLR are associated with neoplastic diseases such as lung cancer, esophageal cancer and liver cancer [5-7]. Moreover, it has been reported that PLR is a better predictor than neutrophil to lymphocyte ratio (NLR) for survival in patients with epithelial ovarian cancer [8]. Increasing evidences indicated that PLR is correlated with patients with mitral annular calcification, end-stage renal disease, ovarian hyperstimulation syndrome and obstructive sleep apnea syndrome [9-12]. In some autoimmune diseases, PLR has been found to be associated with psoriatic arthritis and systemic lupus erythematosus [13, 14]. Previous studies have pointed that inflammatory status may be potential factor to

Table 1. Baseline information among the active patients, inactive patients and all patients with TA

	Total TA patients (N=108)	Active group (N=58)	Inactive group (N=50)	*P*-value
Age (y)	26.9 ± 9.71	24.5 ± 10.16	28.9 ± 8.95	0.020
Gender (M/F)	105	7/40	45/13	0.329
CRP (mg/L)	26.9 ± 9.71	17.3 ± 19.0	5.3 ± 4.11	<0.001
ESR (mm/h)	22.9 ± 16.93	35.9 ± 17.16	12.2 ± 5.01	<0.001
Neutrophil count ($\times 10^9$/L)	5.8 ± 2.24	6.1 ± 2.76	5.6 ± 1.72	<0.001
Lymphocyte count ($\times 10^9$/L)	2.3 ± 0.75	2.1 ± 0.66	2.5 ± 0.79	0.016
Platelet count ($\times 10^9$/L)	285.3 ± 93.88	332.0 ± 108.91	248.2 ± 56.40	<0.001
Hemoglobin (g/L)	118.1 ± 16.64	110.6 ± 16.86	124.1 ± 13.93	<0.001
NLR	2.5 ± 1.15	2.5 ± 1.18	2.5 ± 1.13	0.995
PLR	122.9 ± 48.25	145.4 ± 53.25	104.4 ± 34.45	<0.001

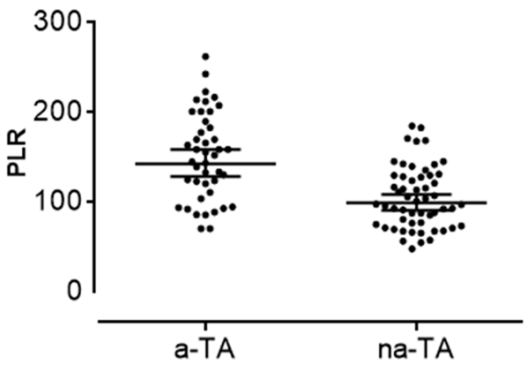

Figure 1. PLR were higher in a-TA compared with na-TA (P<0.001).

correlate the relationship between PLR and rheumatic diseases [15, 16]. In addition, a strong association of PLR with polymyositis has been reported by Peng et al. [17]. PLR in fact has been regarded as an indicator to assess inflammatory state in related rheumatic diseases. However, the association between PLR and TA in the literature has not been fully understood, which leads to an interest with respect to PLR in patients with TA. Thus, the aim of our study is to investigate a relationship between PLR and TA.

Patients and methods

This cross-sectional study involved 108 newly diagnosed TA patients who were admitted to the First Affiliated Hospital of Xinjiang Medical University from 2010 to 2015. The diagnosis for TA was based on the diagnostic criteria from American Rheumatism Association [18]. The disease activity in patients with TA was defined according to the National Institutes of Health criteria [19]. The patients with following diseases and/or situations were excluded: cardiovascular disease, hematological disorder, infectious disease, liver and kidney dysfunction, cancer and mental illness. We retrospectively extracted demographic and laboratory data of all patients, including neutrophil count, lymphocyte count, platelet count, hemoglobin, CRP and ESR. The blood routine tests were evaluated using the Sysmex XN-1000 automatic blood instrument (Sysmex Inc., Japan).

This clinical research complied with Helsinki Declaration and had been approved by the Institutional Review Board in the First Affiliated Hospital of Xinjiang Medical University, and obtained the informed consents of all patients.

Statistical analysis

The data analysis was performed by using SPSS16.0 (SPSS Inc, Chicago, IL, USA) statistical software. Continuous variables were showed as means ± SD. The Kolmogorov-Smirnov test was used to determine the normal distribution. Differences between the two groups were assessed by student's t-test, Mann-Whitney U test and X test. The correlation between the laboratory parameters was analyzed using Spearman correlation. Multivariate logistic regression analysis was performed to determine the factors associated with active TA patients (a-TA). The performance of variables was estimated by receiver operating characteristic (ROC) curves. P<0.05 was accepted as statistically significant.

Results

A total of 108 TA patients were included in this study. All clinical data and laboratory data for a-TA and na-TA were outlined in **Table 1**. At baseline, age, CRP, ESR, platelet count and

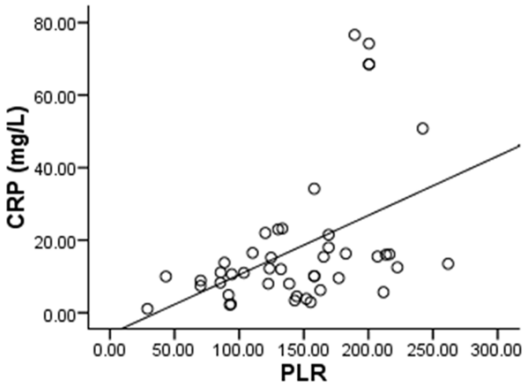

Figure 2. Scatter plot showed a positively correlation between PLR and CRP in a-TA.

Table 2. Multivariate logistic regression analysis between laboratory parameters and a-TA

	p-value	OR	95% CI
CRP (mg/L)	<0.001	2.230	1.145-3.580
ESR (mm/h)	<0.001	1.278	1.008-2.568
PLR	0.001	1.820	1.230-2.872

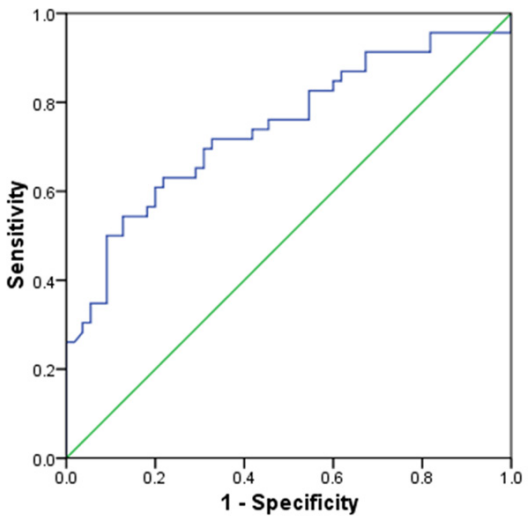

Figure 3. A receiver operating characteristic (ROC) curves for PLR in estimating patients with a-TA.

hemoglobin were found to be statistically significant between a-TA and na-TA, as shown in **Figure 1**, PLR was higher in a-TA compared with na-TA (145.4 ± 53.25 *vs.* 104.4 ± 34.45, *P*<0.001). PLR was negatively correlated with lymphocyte count, and positively correlated with platelet count, hemoglobin and NLR in patients with a-TA. Interestingly, a positively correlation between PLR and CRP was observed in a-TA, as shown in **Figure 2**. However, there was no correlation between PLR and CRP in na-TA.

Stepwise logistic regression analysis showed that PLR was associated with a-TA independently of ESR and CRP (**Table 2**). The area under the curve was 0.743 (95% CI: 0.644-0.842, P<0.001) with the sensitivity and specificity of 82.6% and 55.5% when receiver operating characteristic (ROC) curves were used to identify the performance of PLR in assessing a-TA, as shown in **Figure 3**.

Discussion

PLR is a useful marker to assess subclinical inflammation in peripheral blood, it is consist of information in regard to platelet and lymphocyte count, which may can avoid an acute alteration compared with single platelet and lymphocyte count for the assessment of inflammation in patients with TA. There were several remarkable findings to this study. We demonstrated that PLR was increased in a-TA compared with na-TA, and was associated with a-TA in logistic regression analysis. Importantly, increased PLR was positively correlated with CRP in a-TA.

Previous studies provided evidences that systemic or chronic inflammation is associated with increased platelet. Elevated PLR has been demonstrated to be associated with ulcers in patients with critical limb ischemia, patients with end stage renal disease and subclinical inflammation in atherosclerosis patients [10, 20, 21]. Thus, we can know the PLR not only shows the state of coagulation, but also reflects the inflammatory status. In fact, PLR as an available parameter in the blood routine tests is an objective measured value, which could be less affected by subjective factors of clinicians. In addition, there are no additional costs for PLR measurement compared with CRP, ESR and imaging findings. In the present study, we suggested that PLR is independently associated with a-TA, indicating increased PLR is an index to reflect disease activity in patients with TA.

Inflammatory cytokine is a potential factor to stimulate thrombocytopoiesis [22]. It has been demonstrated in previous trials that IL-6 and TNF are associated with disease activity in TA patients [4], and the levels of CRP and IL-18 are

increased in patients with active TA [23]. Klingei M.H et al. [24] observed that some inflammatory factors such as IL-1, IL-6 and IL-11 were involved in the pathogenesis of TA, which results in increased platelet in patients with TA. Immune and inflammatory factors may also cause elevated platelet in some autoimmune diseases, including rheumatoid arthritis, systemic lupus erythematosus and inflammatory bowel disease [14, 15, 25]. Similarly, increased platelet count has been reported to be associated with the disease severity in psoriasis patients [26]. The mechanism probably explains that aortic lesions may cause higher inflammatory response by aggregating inflammatory cytokines, which produced a relatively large platelet by stimulating megakaryocyte proliferation. In contrast, lymphocyte is reduced in immune disease since inflammatory response and excessive apoptosis simultaneously [27]. Indeed, reduced lymphocyte has been suggested in some diseases such as type 2 diabetes, acute pancreatitis and acute coronary syndromeor [28-30]. Moreover, decreased lymphocyte in peripheral circulation has been reported in patients with Behcet' s disease, inflammatory bowel disease and vestibular neuritis [31-33]. Thus, elevated PLR may be explained by active inflammatory status in patients with TA.

There were several limitations in this study. First, our study did not assess the value of PLR in patients undergoing anti-inflammatory treatment. In addition, a small sample size should be noted in the present study. Finally, increased PLR were not estimated in TA subgroups. However, our study suggests that increased PLR is associated with TA patients with active disease, and is correlated with CRP in active TA patients. These results indicate that PLR may be used as an indicator to assess disease activity and reflect active inflammation in patients with TA.

Disclosure of conflict of interest

None.

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