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ORIGINAL RESEARCH

The Value of NLR and PLR in the Diagnosis of Rheumatoid Arthritis Combined with Interstitial Lung Disease and Assessment of Treatment Effect: A Retrospective Cohort Study

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Objective: This retrospective cohort study investigated the value of neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) in the diagnosis and treatment of rheumatoid arthritis complicated with interstitial lung disease (RA-ILD).

Methods: A total of 163 patients with newly diagnosed rheumatoid arthritis (RA) were enrolled, with 122 patients in the RA group and 41 patients in the RA-ILD group. The mean age of the RA group was 63.84 ± 8.53 years, with a male-to-female ratio of 14:47. The RA-ILD group had a mean age of 66.29 ± 12.72 years, with a male-to-female ratio of 13:28. During the 2-year follow-up period, 10 patients in the RA group developed interstitial lung disease (ILD).

Results: NLR and PLR were significantly higher in RA-ILD group than in RA group ($p < 0.05$). The optimal critical values of NLR and PLR for the diagnosis of RA-ILD were 3.15 and 152.62, the area under ROC curve was 0.615 and 0.61, the sensitivity was 72%, 62%, and the specificity was 54% and 64%. NLR and PLR were significantly increased after ILD during follow-up in RA patients but decreased after ILD in the predicted percentage of vital capacity (VC%), forced vital capacity (FVC%), forced expiratory volume in the first second (FEV1%) and carbon monoxide dispersion (DLcoSB%) ($p < 0.05$). Moreover, NLR and PLR decreased after treatment. While VC%, FVC%, FEV1%, and DLcoSB% increased after treatment ($p < 0.05$). NLR was negatively correlated with FVC% and DLcoSB% both before and after treatment. PLR was also significantly negatively correlated with FVC% and DLcoSB% before and after treatment ($p < 0.05$).

Conclusion: When NLR and PLR increase, we should be alert to the possibility of RA complicated with ILD, which can be used as an evaluation index of the treatment effect of RA-ILD.

Keywords: neutrophils, lymphocyte, platelets, the ratio, rheumatoid arthritis, interstitial lung disease

Introduction

Rheumatoid arthritis (RA) is a systemic immune disease with arthritis as its main manifestation and can involve multiple organs and systems. The prevalence of RA is estimated to range between 0.5% and 1% globally, with a female-to-male ratio of approximately 3:1. It is most commonly diagnosed in individuals between the ages of 30 and 60 years, with a higher incidence in women compared to men.[1] Interstitial lung disease (ILD) is one of the main manifestations of RA involving the lungs, and it is one of the main causes of exacerbation and even death in RA patients. The prevalence of RA-associated interstitial lung disease (RA-ILD) varies significantly depending on the detection methods and the cohorts studied. Studies employing high-resolution computed tomography (HRCT) or lung biopsy often report a higher prevalence of RA-ILD compared to those using more limited diagnostic methods such as routine chest X-rays or pulmonary function tests. For instance, a recent study highlighted that the prevalence of RA-ILD can range from 10% to 30%, depending on the diagnostic techniques and patient population.[2] However, the current diagnosis of RA-ILD relies mainly

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on clinical manifestations, imaging, lung function and histopathological examination, while there is a lack of clear clinical criteria for whether RA-ILD needs to be treated aggressively, and a similar lack of markers for assessing whether the treatment of RA-ILD is effective. The most common radiological and histopathological pattern of RA-ILD is that of common interstitial pneumonia (UIP), with radiological features of honeycomb, reticular and tractional bronchiectasis, predominantly basal and peripheral.[3,4]

The reliance on imaging in the diagnosis and treatment of RA-ILD has led to an increase in the cumulative dose of radiation and an increase in the incidence of tumors. Pulmonary function tests require high levels of operator and patient cooperation, with poor reproducibility and high errors. Histopathological examinations are invasive and not well accepted by patients. Markers that are currently considered to have applied value in the diagnosis of ILD, such as salivary liquefaction glycan chain antigen-6 (KL-6). Recent studies have found that the combined use of lung ultrasound (LUS) and KL-6 for screening and follow-up of ILD in patients with RA may be useful in clinical practice.[5] However, it is a cumbersome procedure and a non-clinical routine test. Therefore, it is important to study and discover a biological marker that is meaningful for RA-ILD diagnosis and treatment evaluation.

It is currently believed that NLR and PLR can be used as a biological marker for the diagnosis and monitoring of RA,[6] and their value in other connective tissue diseases is gradually being appreciated. However, NLR, PLR has been less studied in RA-ILD. This study focuses on the value of NLR, PLR in the diagnosis and evaluation of treatment effects in RA-ILD.

Methods

Study Design and Participants

This retrospective study included 163 newly diagnosed RA patients who attended the Department of Rheumatology and Immunology, Zibo First Hospital, Zibo city, Shandong province, China, from January 2018 to December 2020. Patients were consecutively recruited based on the inclusion and exclusion criteria. Among them, 122 cases were assigned to the RA group, and 41 cases to the RA-ILD group. During the 2-year follow-up period, 10 patients in the RA group developed ILD. Additionally, 17 patients with RA-ILD required treatment for ILD. The patients were further divided into three groups based on the timing of the diagnosis and treatment: (1) initial diagnosis group: initial diagnosis of RA and initial diagnosis of RA-ILD; (2) follow-up group: follow-up before the appearance of ILD and after the appearance of ILD; and (3) treatment group: before and after treatment for RA-ILD. The reporting of this study conforms to STROBE guidelines.

Eligibility Criteria

Inclusion Criteria

(1) Patients with a confirmed diagnosis of RA according to the 2010 ACR/EULAR classification criteria for RA;[7] (2) Age ≥18 years; (3) No previous history of ILD before RA diagnosis.

Exclusion Criteria

Patients with concurrent connective tissue diseases or other pulmonary disorders (eg, cardiac failure, tuberculosis) were excluded from the study.

Diagnosis of RA-ILD

The diagnosis of comorbid ILD was based on the following (1): the presence of symptoms such as dry cough and progressive dyspnea (2) the presence of typical manifestations of ILD such as lattice-like and hairy-glass-like on high-resolution CT (HRCT) of the chest (3) the pulmonary function manifested by restrictive ventilation or diffusion dysfunction.[8]

Clinical Information

Clinical and laboratory data, treatment protocols and outcomes of patients with RA, RA-ILD were collected. Clinical data included patients' gender, age of onset, number of painful joints and number of swollen joints. Laboratory tests included

routine blood tests (including NLR, PLR), liver function, rheumatoid factor (RF), anti-CCP antibody, sedimentation rate (ESR), C-reactive protein (CRP) and DAS28 score. Lung function included VC%, FVC%, FEV1% and DLcoSB%.

Follow-Up Status

All participants were followed for 2 years, during which the development of ILD in the RA group was tracked, and RA-ILD patients were treated for ILD as needed. Data from patients before and after the onset of ILD were collected to assess the changes in disease parameters and treatment response. The study flow diagram see Figure 1.

Statistical Analysis

The quantitative data of the two groups were analyzed using Independent- Samples *T* Test (IST). Paired-Samples *T* Test was used to analyze the quantitative data of the paired data. The qualitative data of the two groups were analyzed using the chi-square test. Non-parametric tests were used for skewed data and data with a small number of sample cases. Descriptive content was given as number of cases and percentages, mean ± Std. Deviation,

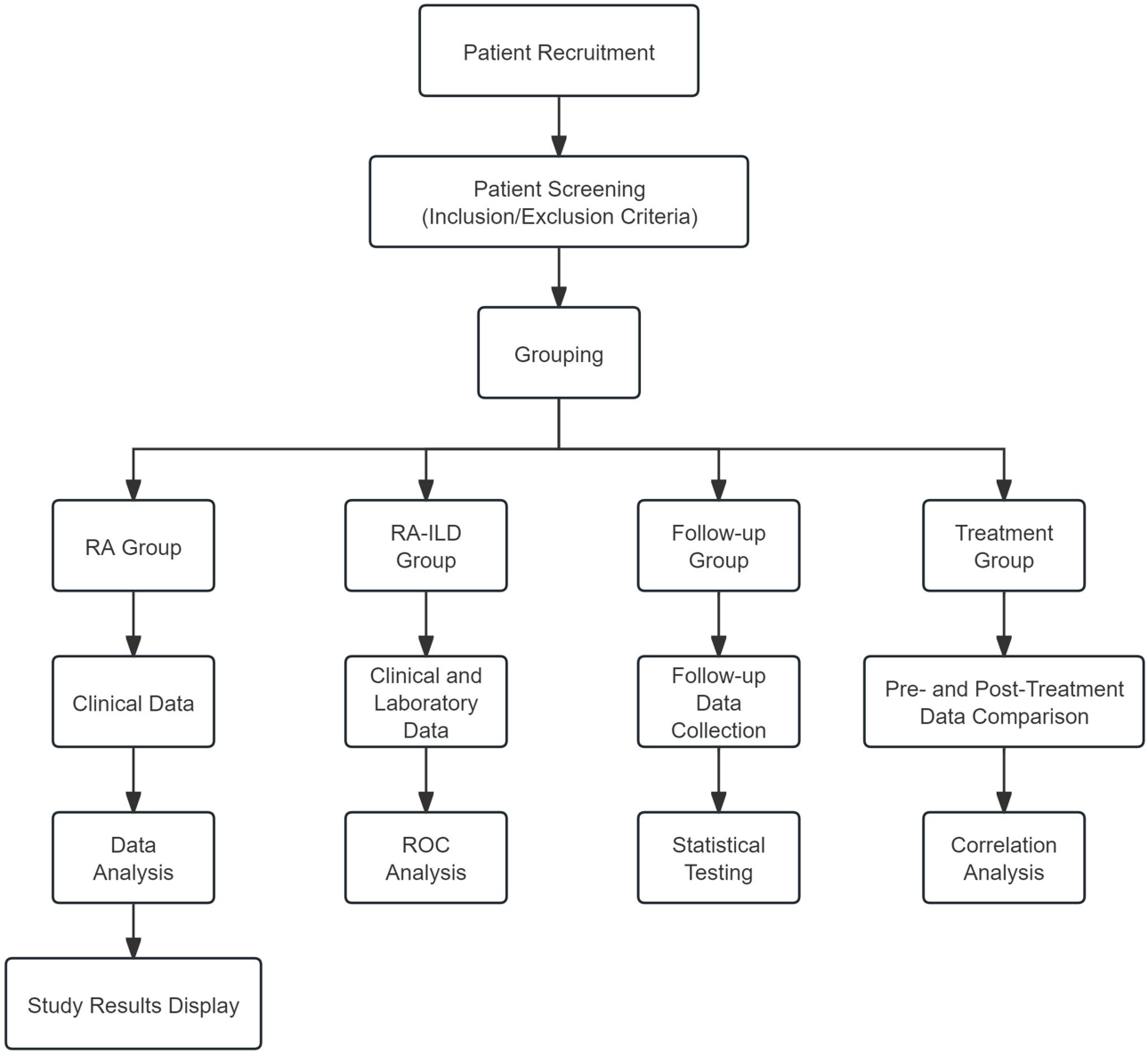

Figure 1 Study Flow Diagram.

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median (quartiles). Critical values were analyzed using ROC curves and correlations were analyzed using bivariate correlation analysis, all data were done using SPSS 26.0 software and $p < 0.05$ was considered statistically significant. Sample size calculation was based on the expected difference in NLR and PLR between the RA and RA-ILD groups, aiming for a statistical power of 80% with a significance level of 0.05.

Results

RA and RA-ILD Groups

The results in Table 1 showed that there were no statistically significant differences between RA and RA-ILD groups in age and gender, and there were neither no statistical differences in WBC, Hb, PLT, RDW (CV), PDW, CRP, RF, CAR, and DAS28 ($p > 0.05$). Whereas there were significant differences in NLR, PLR, RDW (SD), ALB, ESR in RA-ILD group compared with RA group ($p < 0.05$). Among them, NLR and PLR values in RA-ILD group were found to be significantly higher compared to RA group, and the optimal critical values of NLR and PLR for diagnosis of RA-ILD were 3.15 and 152.62, respectively, and the areas under the ROC curves were 0.615 and 0.61, with the sensitivities of 72% and 62%, and the specificities of 54% and 64%, respectively. These results indicate that while NLR and PLR have some potential as diagnostic markers for RA-ILD, their relatively low AUC values suggest they are not strong classifiers on their own (Figures 2 and 3).

Follow-Up Emergence of RA-ILD Group

Next, we compared the indicators of RA patients who developed an ILD during follow-up with those at their initial diagnosis. As shown in Table 2, there was a statistical difference between these two groups in Hb, ALB, NLR, PLR, DAS28, VC%, FVC%, FEV1%, and DLcoSB% ($p < 0.05$). NLR and PLR were significantly higher in patients with RA presenting with ILD during follow-up, while ALB, Hb, DAS28, VC%, FVC%, FEV1%, and DLcoSB% decreased after the presentation of ILD during follow-up. In addition, WBC, PLT, RDW (SD), RDW (CV), PDW, ESR, CRP, RF, and CAR showed no statistical differences ($p > 0.05$).

RA-ILD Treatment Group

The results as presented in Table 3 and showed that the values of NLR, PLR and ESR in RA-ILD patients were decreased after treatment, while ALB, VC%, FVC%, FEV1% and DLcoSB% were increased after treatment, and all of them were statistically significantly different ($p < 0.05$). However, WBC, Hb, PLT, RDW (SD), RDW (CV), PDW, CRP, RF and CAR values did not change significantly after treatment compared to before treatment ($p > 0.05$).

Table 1 Comparison of Data Between RA and RA-ILD Groups

Groups	Case	Age $\bar{x} \pm s$	Male		WBC (×109/L)	Hb (g/L)	PLT (×109/L)	ALB
			case	%	M (P25, P75)	M (P25, P75)	M (P25, P75)	M (P25, P75)
RA	122	63.84±8.53	28	23.00	6.9 (5.69, 8.44)	126 (112, 137)	271 (230.5, 335.25)	36.2 (33.68, 38.33)
RA-ILD	41	66.29±12.72	13	31.70	7.05 (5.55, 8.53)	119 (112, 133.5)	258 (228.5, 299.5)	33.7 (31.5, 36)
χ2/t/z		−1.208	1.250		−0.153	−1.416	−0.962	−3.334
p value		0.232	0.264		0.878	0.157	0.336	0.001
Groups	**Case**	**ESR**	**CRP**		**NLR**	**PLR**	**CAR**	**DAS28**
		M (P25, P75)	**M (P25, P75)**		**M (P25, P75)**	**M (P25, P75)**	**M (P25, P75)**	$\bar{x} \pm s$
RA	122	33 (17, 58.25)	11.55 (3.18, 39)		2.42 (1.72, 3.33)	140.11 (120.23, 179.59)	0.31 (0.09, 1.1)	4.9±1.39
RA-ILD	41	53 (29.5, 76)	14 (5.8, 52.3)		3.17 (2.08, 3.89)	163.46 (126.96, 227.67)	0.47 (0.17, 1.48)	5.19±1.65
t/z		−2.508	−1.218		−2.213	−2.113	−1.425	−1.098
p value		0.012	0.223		0.027	0.035	0.154	0.274

Abbreviations: RA, rheumatoid arthritis; RA-ILD, rheumatoid arthritis with interstitial lung disease; WBC, white blood cells; Hb, hemoglobin; PLT, platelets; ALB, albumin; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio; PLR, platelet/lymphocyte ratio; CAR, C-reactive protein/albumin ratio; DAS28: disease activity score in rheumatoid arthritis.

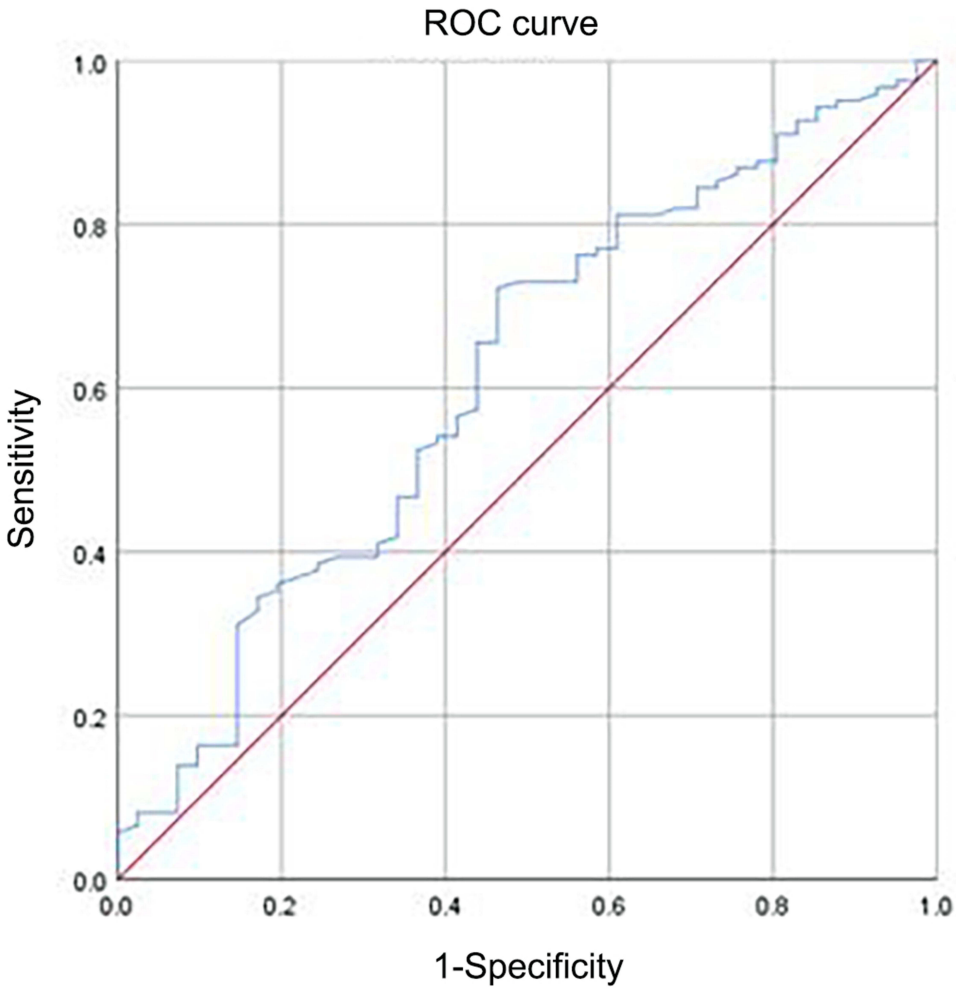

Figure 2 Working curve of subjects with RA-ILD diagnosed by NLR.

Further, correlation analysis was also studied. It was found that NLR was negatively correlated with FVC% value ($r = -0.983$, $p < 0.05$) and DLcoSB% ($r = -0.865$, $p < 0.05$) before treatment. After treatment NLR was negatively correlated with FVC% ($r = -0.738$, $p < 0.05$) as well as DLcoSB% ($r = -0.982$, $p < 0.05$). A negative correlation was detected between PLR with FVC% as well as DLcoSB before treatment ($r = -0.551$ and -0.532, $p < 0.05$), and A negative correlation also was found between PLR with FVC% as well as DLcoSB after treatment ($r = -0.838$ and -0.636, $p < 0.05$) (Figure 4–11).

Discussion

ILD is a common complication of RA and can cause serious consequences. At present, the following problems exist in the diagnosis and treatment of RA-ILD as follow: 1. Failure to detect ILD in time: It is crucial to detect ILD early during the initial diagnosis of RA and during follow-up, especially because RA is a chronic disease, and patients may develop ILD at any stage of their illness. Timely detection is important because various RA treatments can affect the lungs and even lead to pulmonary fibrosis. Early detection allows for the adjustment of treatment plans to avoid severe consequences. In addition, the role of biological disease-modifying antirheumatic drugs (bDMARDs), such as TNF-alpha inhibitors, IL-6 inhibitors, and Rituximab, in the management of RA-ILD needs to be better understood. Some bDMARDs, particularly TNF-α inhibitors, have been shown to potentially exacerbate pulmonary complications, including ILD, by promoting lung inflammation. However, IL-6 inhibitors, such as tocilizumab, may show promise in controlling pulmonary symptoms due to their role in modulating immune responses and reducing inflammation in RA patients. The effect of these drugs on ILD, including potential exacerbation or improvement, warrants further

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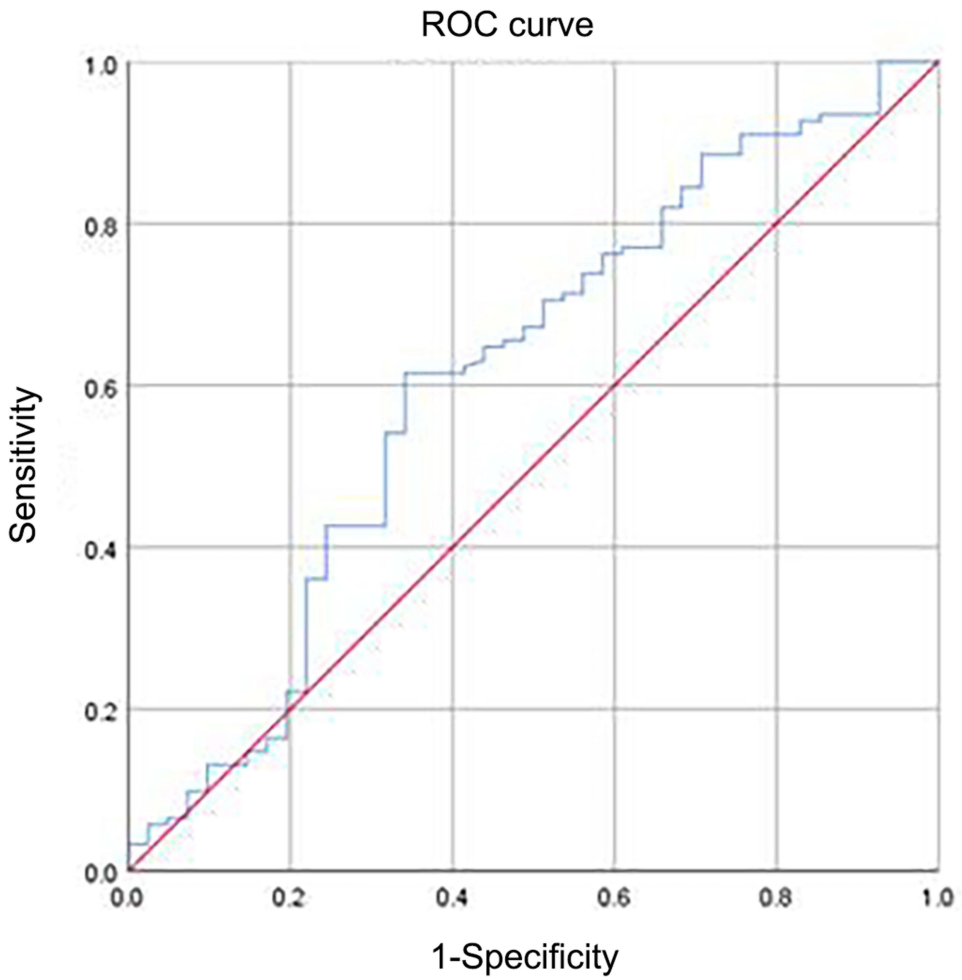

Figure 3 Working curves of subjects with RA-ILD diagnosed by PLR.

investigation. 2. The assessment of therapeutic efficacy: For patients with RA-ILD who require active intervention, a simple, effective, and economical method of assessing treatment efficacy is essential. Current assessments rely on clinical symptoms, physical examination, chest CT, and lung function tests, which inevitably cause delays in diagnosis, and impose a significant economic burden on patients. Frequent chest CT examinations may also result in radiation exposure. Therefore, there is a need for alternative, non-invasive diagnostic and evaluation methods. In this context, NLR and PLR, as simple and cost-effective inflammatory markers, could potentially be used for the early diagnosis of RA-ILD and for monitoring treatment outcomes. Research on how these markers correlate with disease activity and response to therapy could significantly impact clinical practice in RA-ILD management.

NLR, PLR is a routine test, simple and easy to obtain, which is relevant in autoimmune diseases to assess disease activity.[9] In RA, NLR has a clear relationship with disease activity and even with treatment response. In particular, the increase of NLR is a predictor of poor treatment effect of TNF-α inhibitors, and may be related to the withdrawal of TNF-α inhibitors.[8–14] Increased NLR is an independent predictor of increased risk of long-term death in RA patients.[15] Although multiple studies have confirmed that NLR in RA patients are significantly higher than those in healthy controls,[16–18] indicating that NLR has application value in the diagnosis of RA, but research conclusions are inconsistent, and other studies have also confirmed that there is no statistical difference in NLR between RA and control group,[18,19] this indicates that NLR is of limited significance in RA diagnosis.It has been found in recent years that PLR can also be utilized for the diagnosis, activity prediction, and prognostic assessment of rheumatic diseases.[20–22]The mechanism may be that more than 50% of neutrophils are produced by the bone marrow and are in the first line of the defense system. It is

Table 2 Comparison of Data from 9 RA Patients Who Presented with ILD During Follow-up with Those at the Time of Initial Diagnosis

Groups	WBC (×109/L)	Hb (g/L)	PLT (×109/L)	ALB	RF
RA	7.47 (5.81,11.44)	127 (115.5, 141.5)	275 (233, 348)	34.9 (30.6,37.05)	101 (58.6, 476.5)
RA-ILD	7.81 (5.92,8.14)	107 (80.5, 137.5)	204 (186, 366.5)	31.4 (29.25,34.65)	190.1 (127.05, 498.65)
Z value	−1.362	−2.134	−0.296	−2.666	−0.889
p value	0.173	0.033	0.767	0.008	0.374
Groups	**ESR**	**CRP**	**NLR**	**PLR**	**CAR**
RA	34 (25.5,61)	23.7 (9.35,52.6)	2.72 (1.74,4.40)	142.04 (95.29, 195.22)	0.75 (0.26,1.52)
RA-ILD	23 (12.5,91.5)	13.8 (8.35,81.1)	4.71 (3.93,5.93)	375.21 (130.50, 409.47)	0.48 (0.27,2.47)
Z value	−0.178	−0.415	−2.310	−2.192	−0.415
p value	0.859	0.678	0.021	0.028	0.678
Groups	**DAS28**	**VC%**	**FVC%**	**FEV1%**	**DLcoSB%**
RA	6.38 (5.86,6.70)	91.1 (82,95.8)	89.3 (75.4,91.1)	77.2 (72,89)	75.6 (62.85,81.6)
RA-ILD	3.19 (1.87,3.66)	65.3 (58.8,80.6)	62.8 (56.65,78.55)	55.3 (45,71.3)	39.6 (33.1,50.05)
Z value	−2.666	−2.429	−2.310	−2.429	−2.666
p value	0.008	0.015	0.021	0.015	0.008

Abbreviations: WBC, white blood cells; Hb, hemoglobin; PLT, platelets; ALB, albumin; RF, Rheumatoid Factor; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio; PLR, platelet/lymphocyte ratio; CAR, C-reactive protein/albumin ratio; DAS28, disease activity score in rheumatoid arthritis; VC%, vital capacity as a percentage of predicted value; FVC%, forced vital capacity as a percentage of predicted value; FEV1%, Forced Expiratory Volume in the first second as a percentage of predicted value; DLcoSB%, carbon monoxide diffusion as a percentage of predicted value.

Table 3 Comparison of RA-ILD Pre- and Post-Treatment Data

Groups	WBC (×109/L)	Hb (g/L)	PLT (×109/L)	ALB	RF
RA-ILD Pre-treatment	6.14±2.19	120.94±11.32	233.75±72.33	33.02±2.96	101 (58.6, 476.5)
RA-ILD treatment	5.83±2.47	121.75±11.2	214.81±68.27	34.84±2.54	190.1 (127.05, 498.65)
t value	0.441	−0.28	1.353	−2.461	−0.889
p value	0.665	0.783	0.196	0.026	0.374
Groups	**ESR**	**CRP**	**NLR**	**PLR**	**CAR**
RA-ILD Pre-treatment	41.81±29.73	13.02±14.83	3.23±1.39	174.32±63.04	0.75 (0.26,1.52)
RA-ILD treatment	28.63±20.78	9.78±14.09	2.28±1.23	131.95±59.4	0.48 (0.27,2.47)
t value	2.256	0.837	2.688	4.429	−0.415
p value	0.039	0.416	0.017	0.000	0.678
Groups	**DAS28**	**VC%**	**FVC%**	**FEV1%**	**DLcoSB%**
RA-ILD Pre-treatment	6.38 (5.86,6.70)	75.64±9.69	83.36±9.23	60.89±8.48	54.45±11.82
RA-ILD treatment	3.19 (1.87,3.66)	82.03±5.59	91.18±10.11	64.01±5.76	77.23±9.53
t value	−2.666	−4.11	−2.973	−2.548	−7.210
p value	0.008	0.001	0.009	0.022	0.000

Abbreviations: WBC, white blood cells; Hb, hemoglobin; PLT, platelets; ALB, albumin; RF, Rheumatoid Factor; ESR, erythrocyte sedimentation rate; CRP, C-reactive protein; NLR, neutrophil to lymphocyte ratio; PLR, platelet/lymphocyte ratio; CAR, C-reactive protein/albumin ratio; DAS28, disease activity score in rheumatoid arthritis; VC%, vital capacity as a percentage of predicted value; FVC%, forced vital capacity as a percentage of predicted value; FEV1%, Forced Expiratory Volume in the first second as a percentage of predicted value; DLcoSB%, carbon monoxide diffusion as a percentage of predicted value.

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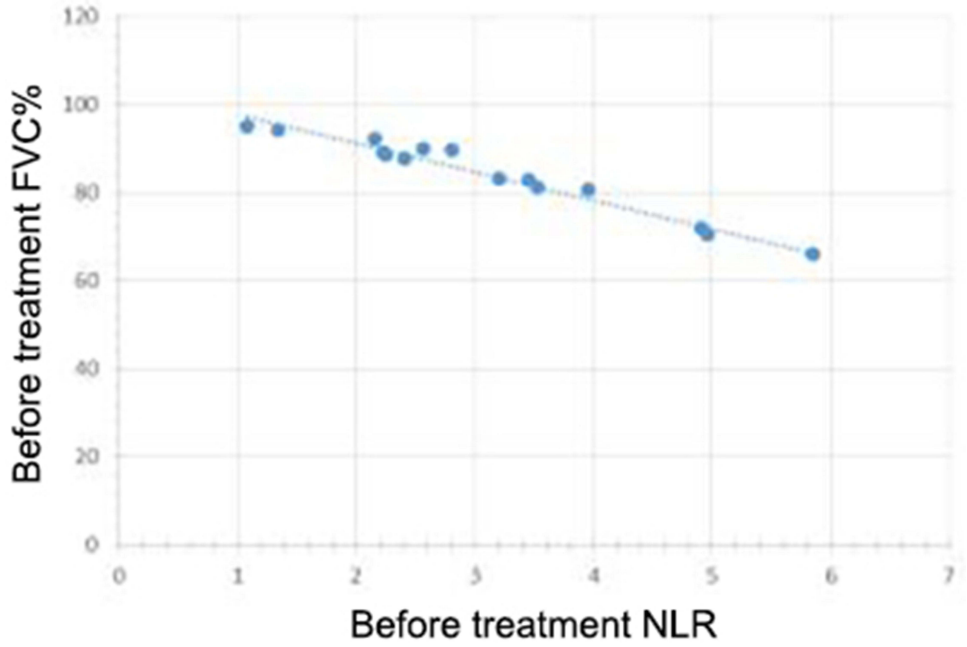

Figure 4 Correlation between NLR and FVC% before treatment.

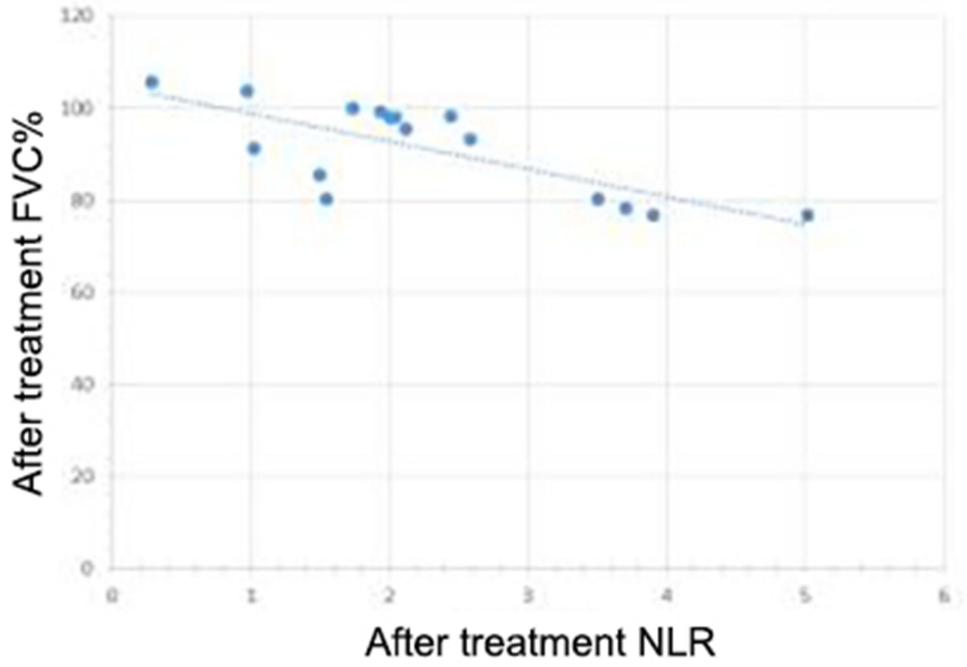

Figure 5 Correlation between NLR and FVC% after treatment.

associated with the production of many lytic enzymes, free oxygen radicals, and cytokines;[23] cytokines play a very important role in the pathogenesis of many inflammatory diseases, and neutrophils and platelets are involved in the production of these cytokines, which in turn activate neutrophils and platelets.[24,25] It has been shown that platelets also play an active role in inflammation and modulate the immune system.[26,27] Throughout the process, it can be observed that the control of lymphocyte apoptosis is compromised.[28] A high neutrophil count indicates the presence of persistent non-specific inflammatory processes, while a low lymphocyte count indicates a relatively compromised immune

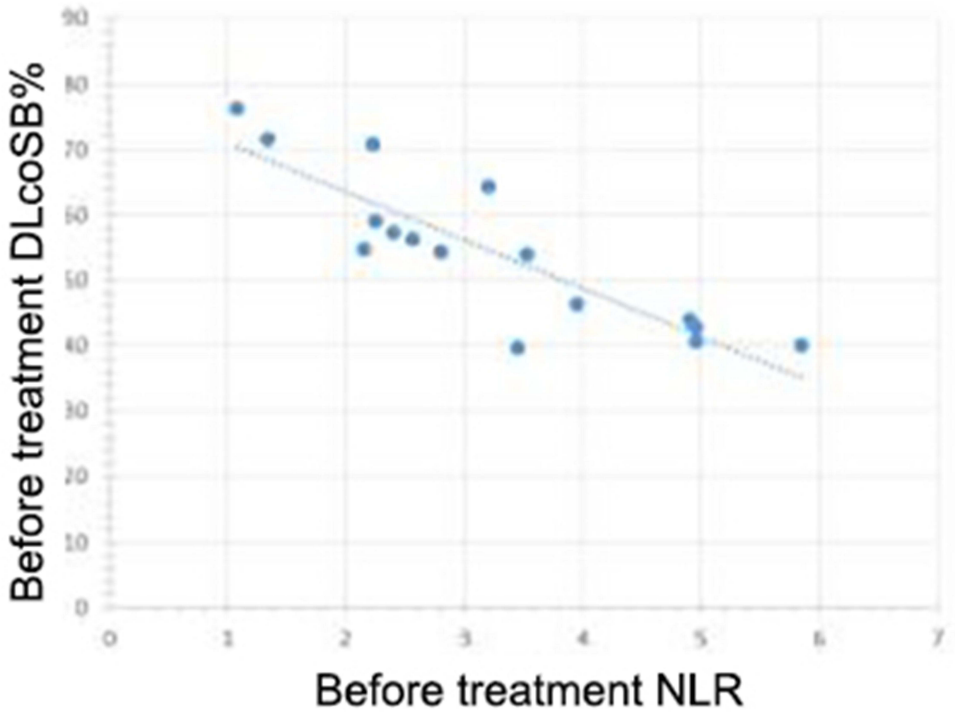

Figure 6 Correlation between NLR and DLcoSB% before treatment.

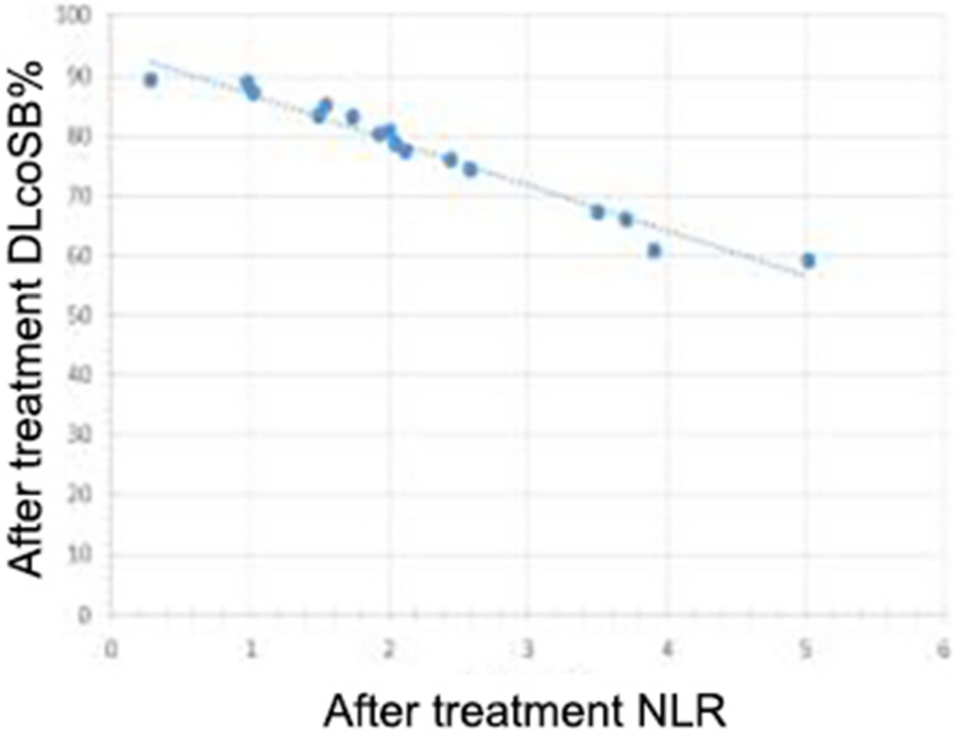

Figure 7 Correlation between NLR and DLcoSB% after treatment.

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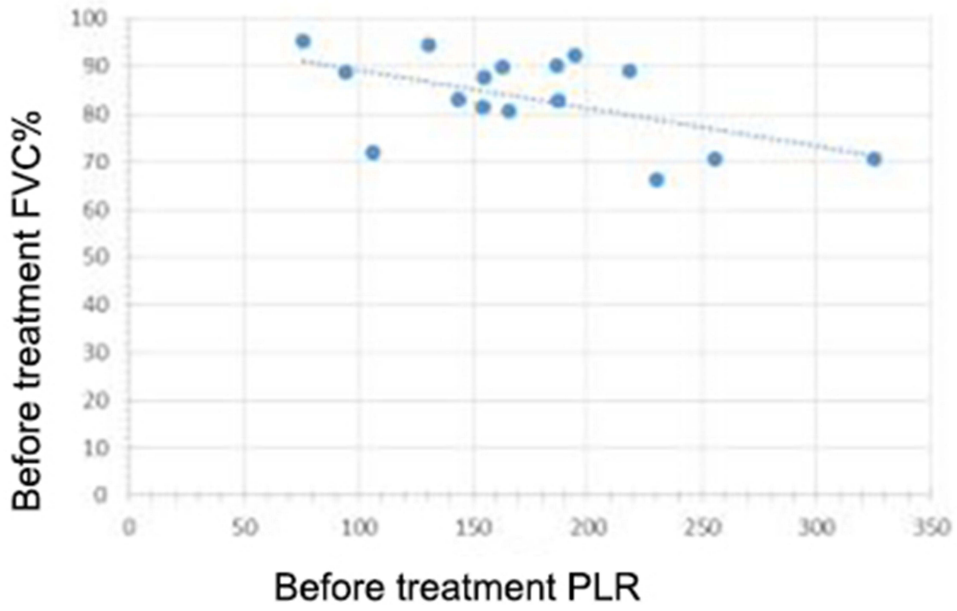

Figure 8 Correlation between PLR and FVC% before treatment.

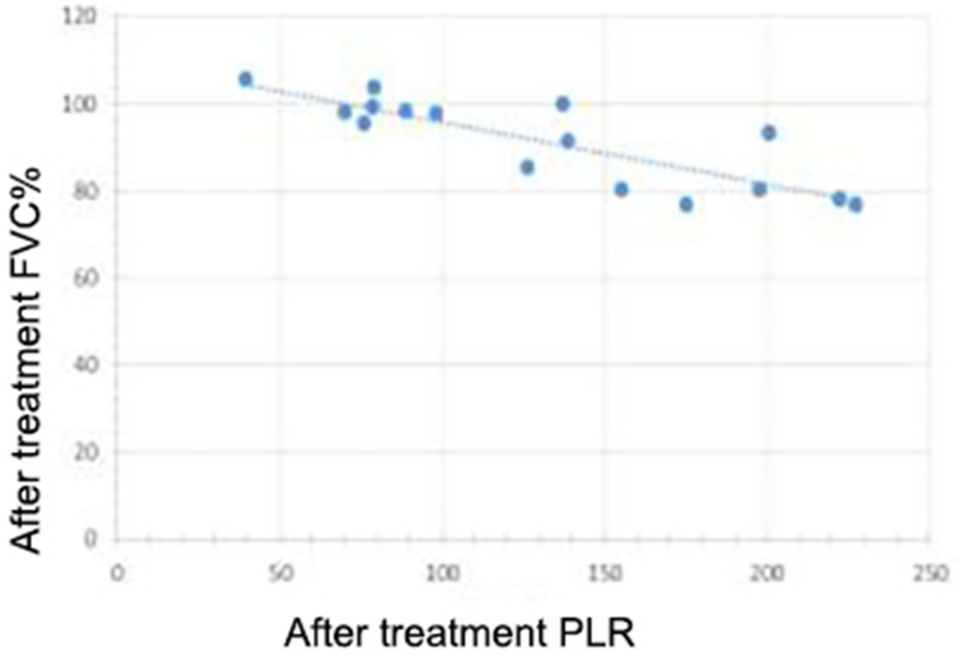

Figure 9 Correlation between PLR and FVC% after treatment.

system.[29] In RA, this process is more obvious. Innate immune dysregulation and persistent inflammatory response play a key role in the pathogenesis of RA.[30,31] Neutrophils are the first reactant of RA immune response and inflammation,[31] and can play a role as antigen-presenting cells in presenting antigen and activating T cells to perpetuate immune response and inflammation.[32] Elevated PLT count is strongly associated with acute phase reactants and pro-inflammatory substances. During the progression of RA, PLTs increase in response to the release of inflammatory cytokines such as IL-1β, IL-6, and tumor necrosis factor-α (TNF-α) and the production of thrombopoietin and granulocyte colony-stimulating factor (CSF).[33–35] Due to inflammation-induced changes in neutrophils, platelets, and lymphocytes, NLR

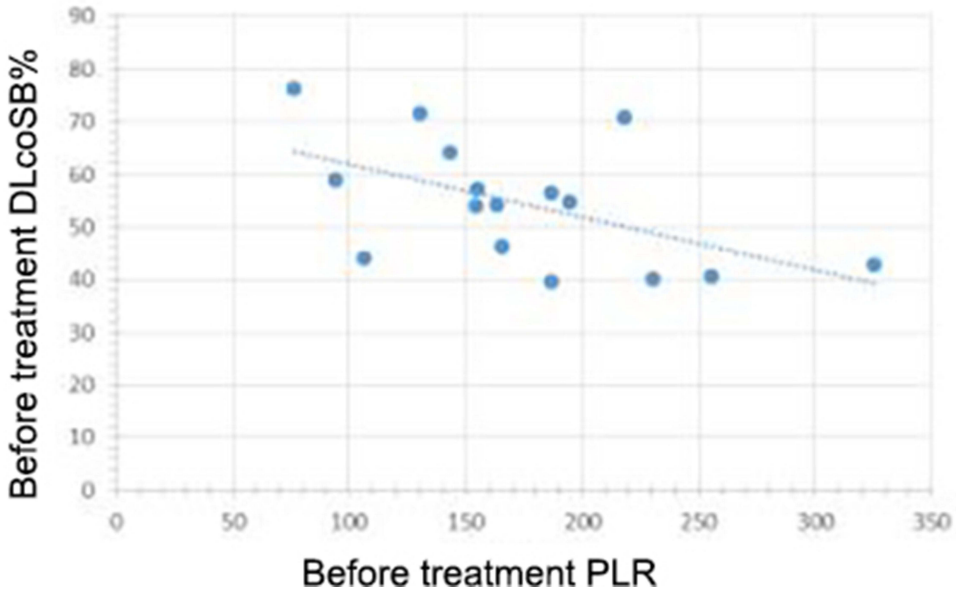

Figure 10 Correlation between PLR and DLcoSB% before treatment.

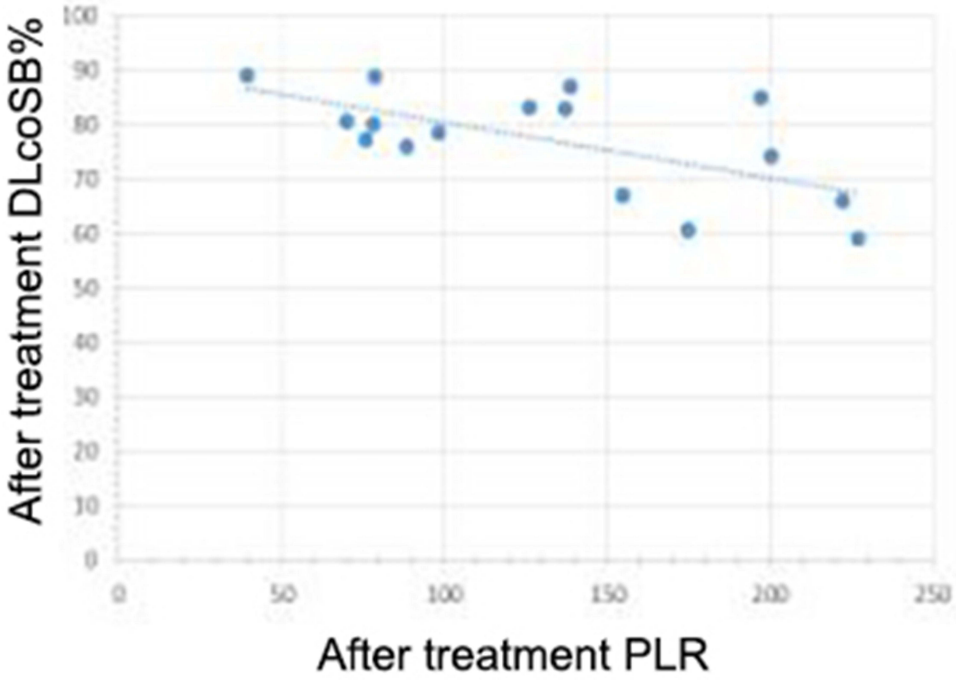

Figure 11 Correlation between PLR and DLcoSB% after treatment.

and PLR have become inflammatory markers. There are no studies on the role of NLR and PLR in the assessment of treatment outcome in RA-ILD.

In order to solve the problems of diagnosis and assessment of treatment effect, three control groups were designed to clarify whether NLR and PLR could be used as a diagnostic basis for RA presenting with ILD through whether NLR and PLR were statistically significant in RA and RA-ILD groups at the time of initial diagnosis and whether they were found to be statistically significant in the ILD group during the follow up compared with that at the time of initial diagnosis.

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Whether NLR and PLR were statistically significant before and after treatment in RA-ILD group was used to clarify whether NLR and PLR could be used as an assessment of the treatment effect of RA-ILD.

In the RA and RA-ILD groups, DAS28 was not statistically different between the two groups, while NLR and PLR were statistically different, and NLR and PLR were significantly higher when ILD occurred. In previous studies, it was shown that RA affected the expression of NLR and PLR,[36] while ILD affected the expression of NLR and PLR,[37] and the present study showed that the effect of ILD on NLR and PLR was more pronounced, therefore, it appeared in the present study that there was no significant difference in RA activity between the two groups, but there was a significant difference in NLR and PLR, which was in accordance with the literature.

The optimal cut-off values of NLR and PLR for the diagnosis of RA-ILD in this study were 3.15 and 152.62, and the area under the ROC curve was 0.615 and 0.61, a sensitivity of 72% and 62%, and a specificity of 54% and 64%. It was consistent with the literature reports. In the follow-up group, NLR, PLR, DAS28, VC%, FVC%, FEV1%, and DLcoSB% were statistically different ($p < 0.05$), except for those related to pulmonary function, which were statistically significant, and after the development of ILD, NLR and PLR were elevated, and DAS28 was decreased, suggesting that in the presence of RA activity significantly lower, NLR and PLR were elevated and the difference was statistically significant, again suggesting a more pronounced effect of ILD on NLR and PLR. There are no other studies that have examined the presence of ILD as a change in NLR and PLR during follow-up. The above 2 groups of studies also suggested that the correlation between ILD and NLR, PLR might be stronger when RA activity on NLR, PLR is considered. Therefore, the possibility of ILD should be considered in RA patients with significantly elevated NLR and PLR.[38]

In the treatment group, the differences in NLR, PLR, ESR, ALB, VC%, FVC%, FEV1%, and DLcoSB% were statistically significant ($p < 0.05$), and the related indexes of lung function, like VC%, FVC%, FEV1%, and DLcoSB% increased after treatment, indicating effective treatment and improvement of ILD. Among them, FVC and DLcoSB are important indicators for assessing ILD. The concomitant decrease in NLR and PLR indicated that the decrease in NLR and PLR correlated with the increase in VC%, FVC%, FEV1%, and DLcoSB%. Further correlation studies showed that pre-treatment NLR was significantly negatively correlated with FVC% and DLcoSB%; and post-treatment NLR was also significantly negatively correlated with FVC% and DLcoSB%. Before treatment PLR became negatively correlated with FVC% and DLcoSB%; while after treatment PLR became significantly negatively correlated with FVC% and DLcoSB%. It showed that NLR and PLR were in good agreement with FVC% and DLcoSB%. In the treatment of RA-ILD, NLR and PLR were significantly correlated with FVC and DLcoSB, which can be used as an assessment method for treatment.

Limitations of this study remain. The sample size was relatively small, and the follow-up period was short, which did not allow for a comprehensive exploration of the subsequent onset of ILD.

Policy and Future Research Directions

This study highlights the potential of NLR and PLR in the early diagnosis and monitoring of RA-ILD. Although their sensitivity and specificity are not high, elevated NLR and PLR levels in RA patients should raise suspicion for ILD, and these markers can be used as a cost-effective diagnostic tool. Future research should explore larger multicenter clinical trials to further validate the role of NLR and PLR in RA-ILD diagnosis, prognosis, and treatment evaluation. Additionally, there is a need to investigate the effect of bDMARDs, such as TNF-α inhibitors and IL-6 inhibitors, on NLR and PLR dynamics, as well as their role in managing RA-ILD. Research focused on the interaction between drug therapy and inflammatory markers could guide more personalized and effective treatment strategies for RA-ILD patients.

Conclusion

In conclusion, NLR and PLR are meaningful for the diagnosis of RA-ILD, although the sensitivity and specificity are not high, but the presence of elevated NLR and PLR in RA patients suggests that we are alerted to the possibility of the emergence of ILD; there is a significant difference between NLR and PLR before and after the treatment of RA-ILD, and they are negatively correlated with FVC% and DLcoSB%, which can be used as an RA-ILD assessment index of treatment effect.

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Disclosure

The authors report no conflicts of interest in this work.

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