J Surg Med. 2020;4(11):1077-1081.
DOI: 10.28982/josam.811687

Research article
Araştırma makalesi

Journal of Surgery and Medicine
e-ISSN=2602-2079

A novel approach in the diagnosis and follow-up of sarcoidosis

Sarkoidozun tanı ve takibinde yeni bir yaklaşım

Aydın Balcı [1], Suphi Aydın [2]

[1] Afyonkarahisar Health Sciences University, Department of Pulmonology, Afyonkarahisar, Turkey
[2] Afyonkarahisar Health Sciences University, Department of Chest Surgery, Afyonkarahisar, Turkey

ORCID ID of the author(s)
AB: 0000-0002-6723-2418
SA: 0000-0003-2102-0484

Corresponding author / Sorumlu yazar:
Aydın Balcı
Address / Adres: Afyonkarahisar Sağlık Bilimleri Üniversitesi, Göğüs Hastalıkları Anabilim Dalı, Afyonkarahisar, Türkiye
E-mail: draydnbalc@gmail.com

Ethics Committee Approval: Ethical approval was obtained from T.C Afyonkarahisar Health Sciences University Clinical Research Ethics Committee, dated 6/5/2020, number 2020/6. All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.
Etik Kurul Onayı: Etik onay, T.C Afyonkarahisar Sağlık Bilimleri Üniversitesi Klinik Araştırmalar Etik Kurulundan 05.06.2020 tarih, 2020/6 nolu numara ile alınmıştır. İnsan katılımcıların katıldığı çalışmalardaki tüm prosedürler, 1964 Helsinki Deklarasyonu ve daha sonra yapılan değişiklikler uyarınca gerçekleştirilmiştir.

Conflict of Interest: No conflict of interest was declared by the authors.
Çıkar Çatışması: Yazarlar çıkar çatışması bildirmemişlerdir.

Financial Disclosure: The authors declared that this study has received no financial support.
Finansal Destek: Yazarlar bu çalışma için finansal destek almadıklarını beyan etmişlerdir.

Published: 11/29/2020
Yayın Tarihi: 29.11.2020

Abstract

Aim: Sarcoidosis is characterized by the presence of non-caseous granulomas that can involve all organs, especially the lungs and mediastinal lymph nodes. No biomarker investigated in recent years appears to be specific for sarcoidosis. We aimed to investigate and evaluate the relationship between neutrophil-lymphocyte ratios (NLR), platelet-lymphocyte ratios (PLR), monocyte-lymphocyte ratios (MLR), eosinophil-lymphocyte ratios (ELR), and blood count parameters in sarcoidosis patients.

Methods: A total of 150 individuals comprising 97 sarcoidosis patients, and 53 controls, were included in the study. The data were recorded retrospectively. Chest X-ray findings were analyzed with regards to age, gender, body mass index, modified medical research concept (MMRC) dyspnea scale and respiratory function parameters. Blood count, NLR, PLR, MLR, eosinophil/basophil ratio (EBR) were evaluated in patients with sarcoidosis.

Results: Hemoglobin (g/dl) and lymphocyte count (103 /UL) values were significantly lower in sarcoidosis patients, while red blood cell distribution width standard deviation (RDW SD) (fl), neutrophil count (103 /UL), monocyte count (103 /UL), basophil count (103 /UL), NLR, PLR, MLR values were significantly higher compared to the control group. However, platelet (103 /UL), MPV and EBR values were similar.

Conclusion: Our study showed that MLR value, which was not previously used in sarcoidosis patients, is an important biomarker in the diagnosis of sarcoidosis, just as NLR.

Keywords: Sarcoidosis, Lymphadenopathy, Monocyte, Lymphocyte, Lung

Öz

Amaç: Sarkoidoz, akciğerler ve mediastinal lenf nodları başta olmak üzere tüm organları tutabilen non-kazeifiye granülomların varlığı ile karakterize bir hastalıktır. Yıllardır yapılan araştırmalarda sarkoidoz için spesifik bir biyobelirteç gösterilememiştir. Çalışmamızda, sarkoidoz hastalarında nötrofil-lenfosit oranları (NLO), trombosit-lenfosit oranları (PLR), monosit-lenfosit oranları (MLR), eozinofil-lenfosit oranları (ELR), kan sayım parametreleri arasındaki ilişkiyi araştırmayı ve çıkan sonuçları değerlendirmeyi amaçladık.

Yöntem: Çalışmaya 97 sarkoidoz hastası, 53 kontrol olmak üzere toplam 150 kişi dahil edildi. Veriler geriye dönük olarak kaydedildi. Göğüs röntgeni bulguları yaş, cinsiyet, vücut kitle indeksi, modifiye tıbbi araştırma kavramı (Mmrc) dispne ölçeği ve solunum fonksiyon parametreleri dikkate alınarak analiz edildi. Sarkoidozlu hastalarda kan sayımı, NLR, PLR, MLR, eozinofil / bazofil oranı (EBR) değerlendirildi.

Bulgular: Sarkoidoz hastaları ile kontrol grubunun laboratuvar değerleri karşılaştırıldığında, sarkoidoz hastalarında hemoglobin (g/dl) değeri ve lenfosit sayısı (103 /UL) değerleri, kontrol grubuna göre anlamlı olarak düşük bulundu. Aksine, kırmızı kan hücresi dağılım genişliği standart sapması (RDW SD) (fl), nötrofil sayısı (103 /UL), monosit sayısı (103 /UL), bazofil sayısı (103 /UL), NLR, PLR, MLR değeri sarkoidoz hastalarınında kontrol grubuna göre anlamlı derecede yüksek bulundu. Trombosit (103 /UL), MPV ve EBR değerleri karşılaştırıldığında ise anlamlı bir fark gözlenmedi.

Sonuç: Bu çalışma bize, sarkoidoz hastalarında daha önce kullanılmayan MLR değerinin NLR değeri gibi sarkoidoz tanısında kullanılabilecek önemli bir biyobelirteç olabileceğini göstermiştir.

Anahtar kelimeler: Sarkoidoz, Lenfadenopati, Monosit, Lenfosit, Akciğer

Introduction

Sarcoidosis is a systemic disease of unknown etiology characterized by the presence of non-caseating granulomas which may involve all organs, especially the lungs and mediastinal lymph nodes. Having varying symptoms, the fact that many patients may be asymptomatic, and having clinical and radiological findings that might be confused with infection and malignancies lead to difficulties in diagnosis [1]. Diagnosis is made by considering clinical, radiological, laboratory findings, and the presence of non-caseating granulomatous inflammation, after excluding other probable pathologies [2]. Granuloma in sarcoidosis is characterized by multinucleated giant cells formed by monocyte-derived epithelioid histiocytes and CD41 T lymphocytes. A small number of cells in or near the granuloma are CD81 T lymphocytes, fibroblasts, regulatory T cells, and B lymphocytes [3]. Sarcoidosis is frequently diagnosed with suspicion arising from chest x-ray findings during routine examination [4]. Symptoms can range from cough, shortness of breath, chest pain, low-grade fever, fatigue, weight loss, and night sweating to Lofgren's Syndrome accompanied by bilateral hilar lymphadenopathy and erythema nodosum [5].

Pulmonary sarcoidosis can be examined in five radiological stages as follows: Stage 0: Chest x-ray is normal, Stage 1: Presence of only hilar and mediastinal lymphadenopathy, Stage 2: Presence of Lymphadenopathy (LAP) and pulmonary infiltration, Stage 3: Presence of pulmonary infiltration alone, Stage 4: Presence of pulmonary fibrosis. This staging gives us information about the prognosis of the disease [6]. Pulmonary involvement is not observed in stage 0 and stage 1 while spontaneous remission is observed in most cases. Therefore, treatment is planned only in symptomatic cases with organ involvement. Steroids are used in basic therapy. Immunosuppressive therapy and Anti-Tumor Necrosis Factor (TNF) agents might also be used in patients with severe clinical conditions [7].

In recent years, many studies have been conducted on serological biomarkers, pulmonary and breathing biomarkers, and bronchoalveolar lavage biomarkers for use in the diagnosis. However, they were found to have limited benefits and not applicable to sarcoidosis [8].

Studies conducted in recent years state that neutrophil/lymphocyte ratio (NLR), which shows changes in neutrophils and lymphocytes, might be a reliable biomarker for hematological parameters [8].

Platelet/lymphocyte ratio (PLR) was investigated in sarcoidosis patients, and a significant relationship was detected between the diagnosis of sarcoidosis and lung parenchymal involvement [9].

NLR and PLR activities are affected by many chronic diseases and inflammatory conditions, such as cardiovascular diseases and malignancies. An increase in these parameters suggests poor prognosis while a decrease suggests a good prognosis [10]. It has been shown that low NLR and PLR values in patients with lung cancer indicate increased response to chemotherapy and might be associated with a good prognosis [11].

In this study, we aimed to investigate and evaluate the relationship between neutrophil-lymphocyte ratios (NLR), platelet-lymphocyte ratios (PLR), monocyte-lymphocyte ratios (MLR), eosinophil-lymphocyte ratios (ELR), and blood count parameters in sarcoidosis patients.

Materials and methods

A total of 150 individuals, 97 sarcoidosis patients and 53 healthy individuals, were included in this study. The data of sarcoidosis patients and the control group were retrospectively evaluated in terms of age, gender, body mass index (BMI), presence of chronic disease, smoking, modified medical research council dyspnea scale (MMRC), and pulmonary function parameters. The classification of sarcoidosis patients was made as follows: Stage 0: Chest x-ray is normal, Stage 1: Presence of only hilar and mediastinal lymphadenopathy, Stage 2: Presence of Lymphadenopathy (LAP) and pulmonary infiltration, Stage 3: Presence of pulmonary infiltration alone, Stage 4: Presence of pulmonary fibrosis. Pulmonary involvement is not observed in stages 0 and 1, which were named the “early-stage group” while those with lung parenchymal involvement constitute Stages 3 and 4, “the advanced stage group”. Blood count, neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), monocyte/lymphocyte ratio (MLR), and eosinophil/basophil ratio (EBR) values of the sarcoidosis patients in various stages were compared with other participants of the study. The “Receiver Operator Characteristics Curve” (ROC) analysis method was used to determine which of these parameters were more specific and sensitive for this disease.

Complete blood counts were measured by spectrophotometry/impedance. Venous blood samples were drawn into ethylenediaminetetraacetic acid tubes and sent to the laboratory. Hemoglobin (g/dl), hematocrit (%), red blood cell distribution width standard deviation (RDW SD), platelet count (10^3 /UL), mean platelet volume (MPV), neutrophil count (10^3 /UL), lymphocyte count (10^3 /UL), monocyte count (10^3 /UL), basophil count (10^3 /UL), eosinophil count (10^3 /UL), NLR, PLR, MLR, and ELR results were noted.

Pulmonary function tests (PFTs) were performed by 3 experienced technicians in the pulmonary function test laboratory. The following conditions were met by the participants: Not taking antihistamines for at least 3-4 days, not having received cromolyn and short-acting bronchodilator therapy for at least 8 hours, not having received long-acting bronchodilator and long-acting theophylline and nedocromil therapy for at least 48 hours and not taking leukotriene receptor antagonists (LTRAs) for at least 24 hours. They were asked not to consume any tea, coffee, fizzy drinks, or chocolate on the day of the test. Participants were rested for 5 minutes before the test.

Statistical analysis

SPSS v20 program was used in statistical analysis. Data were shown as mean (standard deviation), number of individuals, and percentage. The compliance of quantitative data to normal distribution was assessed with Kolmogorov-Smirnov, and Shapiro - Wilk tests, and graphical evaluations. Student's t-test was used to compare the two groups of normally distributed quantitative data, and the Mann-Whitney U test was utilized to compare the two non-normally distributed data groups. Pearson's

chi-square test and Fisher's exact test were used for the comparison of qualitative data. Relationships between variables were analyzed using Spearman correlation analysis. ROC (Receiver Operator Characteristics Curve) analysis was used to measure the sensitivity and specificity continuous variables.

Results

A total of 150 individuals, 97 sarcoidosis patients and 53 healthy individuals (control group) were included in this study. Among sarcoidosis patients, 55 (56.7%) were female and 42 (43.3%) were male. In the control group, 34 (64.2%) were female and 19 (35.8%) were male. The mean ages of the sarcoidosis patients and the control group were 59.64 (19.07) years and 34.20 (5.93) years, respectively. Body mass index (BMI) (kg /cm^2) was 25.21 (18.21-39.84) among sarcoidosis patients and 24.09 (19.82-35.19) in the control group. The modified medical research council dyspnea scale (MMRC) scores were 2 (0-3) and 1 (0-1) among the sarcoidosis patients and the control group, respectively (Table 1). Fifty-three (54.6%) sarcoidosis patients were classified as Stage 1, 36 (37.1%), as Stage 2, 6 (6.2%), as Stage 3 and 2 (2.1%), as Stage 4.

Table 1: Demographic features of patients in the study

	Sarcoidosis (N=97)	Control (N=53)	Total (N=150)	*P*-value
Gender				
Female N	55 (56.7%)	34 (64.2%)	89 (100%)	
Male N	42 (43.3%)	19 (35.8%)	61 (100%)	
Age	59.64 (19.07)	34.20 (5.93)	48.03 (18. 07)	<0.001
Height (cm)	169 (153-187)	174 (160-180)	168 (150-187)	0.364
Weight (kg)	78 (48-102)	75 (58-98)	75 (48-102)	0.143
BMI (kg/cm^2)	25.21 (18.21-39.84)	24.09 (19.82-35.19)	25.43 (17.82-39.84)	0.028
MMRC	2 (0-3)	1 (0-1)	1 (0-3)	<0.001
Smoking status (years)	22 (3-56)	15 (8-30)	22 (3-56)	0.170
Smoking (persons)	32 (33%)	14 (26.4%)		
Comorbid disease	26 (26.8%)	0		
Sarcoidosis stage				
Stage 1	53 (54.6%)	-	53 (54.6%)	
Stage 2	36 (37.1%)	-	36 (37.1%)	
Stage 3	6 (6.2%)	-	6 (6.2%)	
Stage 4	2 (2.1%)	-	2 (2.1%)	

BMI: Body mass index, MMRC: Modified Medical Research Council Dyspnea Scale

A total of 9 (25%) patients from stage 2, 4 (75%) patients from stage 3, and 1 (50%) patient from stage 4 had the history of steroid treatment while 1 patient from stage 4 was still on steroid therapy.

Eye involvement of sarcoidosis was detected in 3 patients. All patients with eye involvement were Stage 2. Lymph node involvement was observed in all 53 Stage 1 patients, all 36 Stage 2 patients, and in 1 (50%) Stage 4 patient. None of the patients in Stage 3 had lymph node involvement. None of the patients had liver or neurological involvement. A total of 9 (17%) patients in stage 1, 16 (44.4%) patients in stage 2, and 1 (50%) patient in stage 4 had chronic diseases such as hypertension, diabetes mellitus, and cardiovascular diseases. None of the stage 3 sarcoidosis patients had any chronic diseases.

Patients without lung involvement had early-stage (53 patients) while patients with lung parenchymal involvement were considered to have advanced-stage (44 patients) sarcoidosis. Among pulmonary function parameters such as % FEV1, % FVC, and % FEV1 / FVC, FVC (LT) and FEV1 / FVC values of sarcoidosis patients were decreased significantly compared to the control group (Table 2).

There was a significant decrease in the pulmonary parameters of advanced-stage sarcoidosis patients when compared with early-stage sarcoidosis patients (Table 3).

Hemoglobin (g/dl) values and lymphocyte count (103 /UL) were significantly lower in sarcoidosis patients, while red blood cell distribution width standard deviation (RDW SD) (fl), neutrophil count (103 /UL), monocyte count (103 /UL), basophil count (103 /UL), NLR, PLR, MLR values were significantly higher compared to the control group. However, platelet (103 /UL), MPV and EBR values were similar (Table 4).

Table 2: Comparison of PFT values in sarcoidosis patients and control group

Respiratory Function Test Values	Sarcoidosis (N=97)	Control (N=53)	Total (N=150)	*P*-value
FEV1 (LT)	3.13(1.07)	3.42(0.80)	3.23(0.99)	0.091
FVC (LT)	3.71(1.21)	4.13(0.99)	3.86(1.15)	0.032
FEV1/FVC	79.53(9.06)	83.45(7.85)	80.92(8.83)	0.009

FEV1: Forced expiratory volume in the 1st second, FVC: Forced vital capacity

Table 3: Comparison of PFT values in early and advanced sarcoidosis patients

Respiratory Function Test Values	Sarcoidosis Early Stage (N=53)	Sarcoidosis Advanced Stage (N=44)	*P*-value
FEV1 (LT)	3.50(0.91)	2.69(1.10)	<0.001
FVC (LT)	4.03(1.06)	3,33(1.29)	0.004
FEV1/FVC	81.46(8.31)	77.21(9.46)	0.021

FEV1: Forced expiratory volume in the 1st second, FVC: Forced vital capacity

Table 4: Mean laboratory values of the study and control groups

Laboratory Values	Sarcoidosis (N=97)	Control (N=53)	Total (N=150)	*P*-value
Hemoglobin (g/dL)	13.40(1.92)	14.07(2.05)	13.64(1.98)	0.047
Hematocrit (%)	71.85(5.08)	43.08(5.35)	42.29(5.19)	0.167
Red Cell Distribution Width (RDW SD)	43.90(35.10-71.60)	40.80 (36.90-47.70)	42.50 (35.10-71.60)	<0.001
Platelet (10^3/UL)	260 (73-496)	258 (150-487)	259 (73-496)	0.995
Mean Platelet Volume (MPV)	10.00(1.16)	10.27(1.04)	10.10(1.12)	0.170
Neutrophil (10^3/UL)	21 (1-51)	13 (1-41)	5.09 (2.01-23.62)	<0.001
Lymphocytes (10^3/UL)	1.88 (0.26-8.44)	2.18 (1.38-4.14)	2.06 (0.26-8.44)	0.017
Monocyte (10^3/UL)	0.60 (0.14-2.10)	0.48 (0.23-0.94)	0.57 (0.14-2.10)	0.003
Basophil (10^3/UL)	0.05 (0.01-0.43)	0.03 (0.01-0.12)	0.04 (0.01-0.43)	0.019
Eosinophil (10^3/UL)	0.14 (0.01-1.86)	0.12 (0.01-0.53)	0.13 (0.01-1.86)	0.138
Neutrophil Lymphocyte Ratio (NLR)	2.79 (0.85-42.19)	1.77 (0.67-4.79)	2.31 (0.67-42.19)	<0.001
Platelet/Lymphocyte Ratio (PLR)	127.95 (24.88-1350.00)	117.75 (55.84-278.15)	121.10 (24.88-1350)	0.03
Monocyte/Lymphocyte Ratio (MLR)	0.31 (0.07-1.26)	0.23 (0.11-0.43)	0.27 (0.07-1.26)	<0.001
Eosinophil/Basophil Ratio (EBR)	4.25 (0.10-93.00)	3.85 (0.33-21.00)	4 (0.10-93)	0.750

There was a significant increase in lymphocyte (10^3 /UL) values and a significant decrease in the PLR of patients in the advanced stage. No significant differences were detected in other values (Table 5).

Table 5: Comparison of laboratory data of early and advanced sarcoidosis patients

Laboratory Values	Sarcoidosis Early Stage (N=53)	Sarcoidosis Advanced Stage (N=44)	*P*-value
Hemoglobin (g/dL)	13.13(2.00)	13.72(1.78)	0.137
Hematocrit (%)	41.33(5.28)	42.48(4.80)	0.269
Red Cell Distribution Width (RDW SD)	44.30 (35.10-68.90)	43.50 (36.40-71.60)	0.210
Platelet (10^3/UL)	264 (73-437)	248 (166-496)	0.401
Mean Platelet Volume (MPV)	10.12(1.29)	9.86(1.05)	0.262
Neutrophil (10^3/UL)	24 (1-51)	18 (1-41)	0.261
Lymphocytes (10^3/UL)	1.73 (0.26-8.44)	2.10 (0.59-5.00)	0.036
Monocyte (10^3/UL)	0.60 (0.14-1.18)	0.60 (0.23-2.10)	0.312
Basophil (10^3/UL)	0.04 (0.01-22)	0.01 (0.01-0.43)	0.120
Eosinophil (10^3/UL)	0.14 (0.01-1.86)	0.21 (0.01-0.70)	0.459
Neutrophil / Lymphocyte Ratio (NLR)	2.88 (1.15-42.90)	2.39 (0.85-12.49)	0.062
Platelet / Lymphocyte Ratio (PLR)	149.77 (24.88-1350.00)	119.78 (50.82-502.27)	0.020
Monocyte / Lymphocyte Ratio (MLR)	0.33 (0.12-1.26)	0.31 (0.07-1.06)	0.674
Eosinophil / Basophil Ratio (EBR)	4.00 (0.01-93.00)	4.33 (0.10-15.00)	0.994

When ROC analysis was performed in terms of NLR, the confidence interval was 0.748 (0.669-0.826) and the cut-off value was 2.148. Its sensitivity and specificity were 70.1% and 69.8%, respectively (Figure 1). These values were statistically significant (P<0.01).

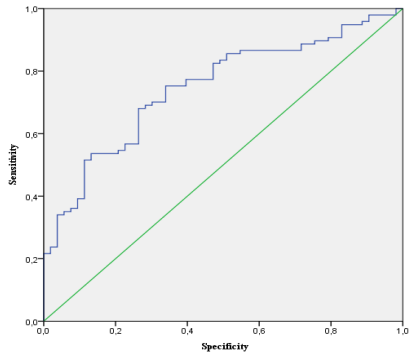

Figure 1: NLR Receiver Operator Characteristics Curve (ROC) Chart

According to ROC analysis results, the confidence interval, cut-off value, sensitivity, and specificity of MLR were 0.733 (0.655-0.812), 0.257, 68.1%, and 68.8%, respectively (P<0.01) (Figure 2).

According to ROC analysis, the confidence interval, cut-off value, sensitivity and specificity of PLR were 0.607 (0.514-0.701), 120.548, 54.6%, and 54.7%, respectively (P=0.03) (Figure 3).

ROC analysis of EBR revealed that the confidence interval, cut-off value, sensitivity and specificity were 0.475 (0.379-0.572), 3.928, 53.6%, and 50.9%, respectively, none of which were significant (P=0.619) (Figure 4).

The sensitivity and specificity of the NLR and PLR values were remarkably close to each other and statistically significant.

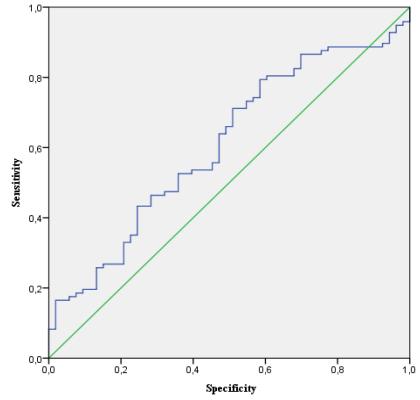

Figure 2: MLR Receiver Operator Characteristics Curve (ROC) Chart

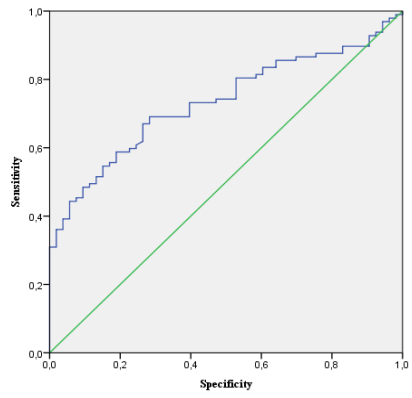

Figure 3: PLR Receiver Operator Characteristics Curve (ROC) Chart

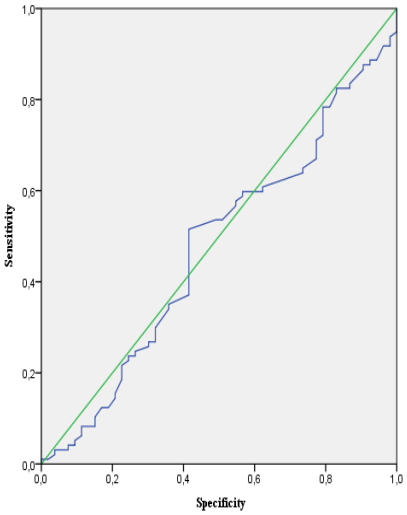

Figure 4: EBR Receiver Operator Characteristics Curve (ROC) Chart

This study has proven that MLR can be used instead of NLR in the diagnosis and follow-up for sarcoidosis patients. PLR values were also statistically significant; however, their sensitivity and specificity were lower than those of NLR and MLR. EBR values were not statistically significant and they were not helpful in the diagnosis of sarcoidosis (Figure 5).

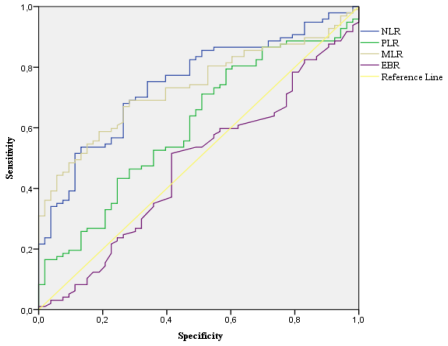

Figure 5: Comparison of ROC Charts

Discussion

The lung is affected in more than 90% of sarcoidosis patients [12]. A biomarker that is specific to sarcoidosis has not been identified yet. However, in clinical studies, hematological changes such as leukopenia, leukocytosis, anemia, eosinophilia, lymphopenia, thrombocytopenia were observed [13].

Angiotensin-converting enzyme (ACE) is produced from the epithelioid cells of granulomas in sarcoidosis, and the increase in ACE levels may be significant in terms of the diagnosis of sarcoidosis [14]. However, an increase in the ACE level is also observed in Gaucher disease, tuberculosis, hyperthyroidism, and fungal infections [15]. Therefore, this test is not sensitive enough for the diagnosis of sarcoidosis.

Dirican et al. [9] suggested that MPV values were higher in sarcoidosis patients compared to the control group and there was no significant difference in the MPV values of the stages of sarcoidosis.

Gupta et al. [13] detected lymphopenia in 26.66% of sarcoidosis patients and stated that the most common hematological abnormality was lymphopenia.

The reason lymphopenia is thought to be the accumulation of CD4+ T lymphocytes around the granulomas and their antiproliferative effect on effector T lymphocytes [16].

MPV values of sarcoidosis patients and controls did not significantly differ in our study. Similarly, there was no significant difference in MPV values of early and advanced-stage sarcoidosis patients.

The RDW-SD, hemoglobin, neutrophil, lymphocyte, monocyte, and basophil levels of sarcoidosis patients significantly differed from those of the controls.

Although published clinical studies show that NLR can be an objective measurement for hematological parameters, it is affected by malignancies, cardiovascular diseases, and many inflammatory conditions, which raises doubts about its prognostic value [8].

In our study, there was a significant difference between sarcoidosis patients and the control group in terms of NLR value. There was no statistically significant difference between early and advanced stage sarcoidosis patients.

Mirsaeidi et al. [9] reported that the cut-off value was around 3.5 while sensitivity and specificity were 50.0% and 78.0%, respectively. It was concluded in same study that NLR and PLR values of sarcoidosis patients with parenchymal involvement were significantly higher, and cut off values were 2.4 and 158, respectively.

In our study, NLR and PLR values were statistically significant in sarcoidosis patients, like the studies in the literature. We determined that the cut off value for NLR was 2.148, and sensitivity and specificity were 70.1% and 69.8%, respectively, while for PLR, the same parameters were 120.548, 54.6%, and 54.7%, respectively.

In our study, we detected that MLR values of sarcoidosis patients significantly differed from those of controls, however, MLR values of early and advanced stage sarcoidosis patients were similar.

The confidence interval, sensitivity, and specificity of NLR values and MLR values were remarkably close to each other and significant in sarcoidosis patients.

In previous studies, MLR values were not investigated in sarcoidosis patients. Our study is the first to evaluate this parameter in this patient group.

Limitations

The rarity of sarcoidosis limited the number of patients included in the study.

Conclusions

This study showed that confidence intervals, sensitivity, and specificity of MLR was close to those of NLR among sarcoidosis patients. Therefore, we think that MLR can be used instead of NLR in the diagnosis and follow-up of this disease. In addition, EBR did not prove to be a reliable prognostic marker in pulmonary sarcoidosis.

References

1. Soto-Gomez N, Peters JI, Nambiar AM. Diagnosis and Management of Sarcoidosis. Am Fam Physician. 2016;93(10):840-8.
2. Hunninghake GW, Costabel U, Ando M, Baughtman R, Cordier JF, du Bois R, et al. ATS/ERS/WASOG statement on sarcoidosis. American Thoracic Society/European Respiratory Society/World Association of Sarcoidosis and other Granulomatous Disorders. Sarcoidosis, Vasc Diffus lung Dis Off J WASOG. 1999;16(2):149-73.
3. Baughman RP, Culver DA, Judson MA. A concise review of pulmonary sarcoidosis. Am J Respir Crit Care Med. 2011;183(5):573-81. doi: 10.1164/rccm.201006-0865CI
4. Statement on sarcoidosis. Joint Statement of the American Thoracic Society (ATS), the European Respiratory Society (ERS) and the World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) adopted by the ATS Board of Directors and by the E. Am J Respir Crit Care Med. 1999;160(2):736-55. doi: 10.1164/ajrccm.160.2.ats4-99
5. Jain R, Yadav D, Puranik N, Guleria R, Jin J-O. Sarcoidosis: Causes, Diagnosis, Clinical Features, and Treatments. J Clin Med. 2020;9(4). doi: 10.3390/jcm9041081
6. Sulica R, Teirstein AS, Kakarla S, Nemani N, Behnegar A, Padilla ML. Distinctive clinical, radiographic, and functional characteristics of patients with sarcoidosis-related pulmonary hypertension. Chest. 2005;128(3):1483-9. doi: 10.1378/chest.128.3.1483
7. Baughman RP, Lower EE, Drent M. Inhibitors of tumor necrosis factor (TNF) in sarcoidosis: who, what, and how to use them. Sarcoidosis, Vasc Diffus lung Dis Off J WASOG. 2008;25(2):76-89.
8. Ocal N, Dogan D, Ocal R, Tozkoparan E, Deniz O, Ucar E et al. Effects of radiological extent on neutrophil/lymphocyte ratio in pulmonary sarcoidosis. Eur Rev Med Pharmacol Sci. 2016;20(4):709-14.
9. Yalnız E, Karadeniz G, Üçsular FD, Erbay Polat G, Şahin GV. Predictive value of platelet-to-lymphocyte ratio in patients with sarcoidosis. Biomark Med. 2019;13(3):197-204. doi: 10.2217/bmm-2018-0252
10. Akboga MK, Canpolat U, Yuksel M, Yayla C, Yılmaz S, Turak O et al. Platelet to lymphocyte ratio as a novel indicator of inflammation is correlated with the severity of metabolic syndrome: A single center large-scale study. Platelets. 2016;27(2):178-83. doi: 10.3109/09537104.2015.1064518
11. Liu D, Jin J, Zhang L, Li L, Song J, Li W. The Neutrophil to Lymphocyte Ratio May Predict Benefit from Chemotherapy in Lung Cancer. Cell Physiol Biochem Int J Exp Cell Physiol Biochem Pharmacol. 2018;46(4):1595-605. doi: 10.1159/000489207
12. Baughman RP, Teirstein AS, Judson MA, Rossman MD, Yeanger JRH, Brenıtz EA et al. Clinical characteristics of patients in a case control study of sarcoidosis. Am J Respir Crit Care Med. 2001;164(10 Pt 1):1885-9. doi: 10.1164/ajrccm.164.10.2104046
13. Gupta D, Rao VM, Aggarwal AN, Garewal G, Jindal SK. Haematological abnormalities in patients of sarcoidosis. Indian J Chest Dis Allied Sci. 2002;44(4):233-6.
14. Silverstein E, Pertschuk LP, Friedland J. Immunofluorescent localization of angiotensin converting enzyme in epithelioid and giant cells of sarcoidosis granulomas. Proc Natl Acad Sci U S A. 1979;76(12):6646-8. doi: 10.1073/pnas.76.12.6646
15. Lieberman J, Nosal A, Schlessner A, Sastre-Foken A. Serum angiotensin-converting enzyme for diagnosis and therapeutic evaluation of sarcoidosis. Am Rev Respir Dis. 1979;120(2):329-35. doi: 10.1164/arrd.1979.120.2.329
16. Loke WSJ, Herbert C, Thomas PS. Sarcoidosis: Immunopathogenesis and Immunological Markers. Int J chronic Dis. 2013;2013:928601. doi: 10.1155/2013/928601.

This paper has been checked for language accuracy by JOSAM editors.
The National Library of Medicine (NLM) citation style guide has been used in this paper.