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Original Scientific Paper

PATTERNS OF NEUTROPHIL TO LYMPHOCYTE RATIO CHANGE IN TWO INFLAMMATORY RHEUMATIC DISEASES: SYSTEMIC LUPUS ERYTHEMATOSUS AND RHEUMATOID ARTHRITIS

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SUMMARY – A high neutrophil to lymphocyte ratio (NLR) is a potential marker of systemic inflammation and predictor of worse outcomes in numerous diseases, but with no report on the pattern of change in NLR (changes in absolute neutrophil and lymphocyte counts with corresponding changes in NLR). Aim: to investigate the pattern of change in NLR in systemic inflammation. Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) were taken as examples of systemic inflammatory disorders. We included 146 SLE patients and 181 RA patients in this retrospective study. The following data were collected: leukocyte, neutrophil and lymphocyte counts and CRP for all patients; C3, C4, hemoglobin concentration and SLEDAI for SLE; swollen and tender joint counts and DAS28CRP for RA. NLR was calculated from absolute neutrophil and lymphocyte counts in peripheral blood and correlated with relevant markers of disease activity. In both diseases, NLR positively correlated with disease activity, but with different patterns: in SLE due to a decreased lymphocyte count without concomitant change in the neutrophil count and in RA due to an elevated neutrophil count without concomitant change in the lymphocyte count. When investigating NLR, it is important to also evaluate the pattern of change in NLR for its right interpretation and understanding in the context of disease pathogenesis.

Keywords: *systemic lupus erythematosus; rheumatoid arthritis; biomarkers; systemic inflammation; neutrophil to lymphocyte ratio*

Introduction

The neutrophil to lymphocyte ratio (NLR) has in recent years emerged as a potential marker of disease activity and predictor of outcome in numerous cardiovascular, malignant and autoimmune diseases

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and critically ill patients, with high NLR predicting a worse outcome[1–4]. However, the background of change in NLR in these conditions is unclear. It is considered that an increase in NLR reflects a systemic inflammatory response[1,5] and that it is a good biomarker of systemic inflammation, because it combines two different immune pathways; neutrophils (Ne), which represent nonspecific immunity, and lymphocytes (Ly), which represent specific immunity and have a role in regulating the immune response. Therefore, an increase in NLR can reflect either an up-regulation of the innate immune response (increase in Ne count), a down-regulation of a specific immune response, or an impaired regulatory function of Ly (decrease in Ly count). The pattern of change in NLR (changes in absolute Ne and Ly counts with corresponding changes in NLR) depends on the pathophysiological characteristics of the disease and their impact on Ne and Ly counts in peripheral blood. Therefore, an evaluation of the pattern of change in NLR would enable a better interpretation of the NLR value and its understanding in the context of disease pathogenesis. Some studies have tried to provide a pathophysiological explanation for the association between elevated NLR and worse outcomes, but these explanations are based on literature discussions without direct proof based on original data on the pattern of change in NLR[4,6–11]. For example, in cardiovascular patients, Ne mediate the inflammatory response to acute myocardial injury by releasing reactive oxygen species, myeloperoxidase and proteolytic enzymes which facilitate plaque disruption[12]. On the other hand, inflammation increases Ly apoptosis[13] and some Ly subsets (CD4) were found to be decreased after acute myocardial infarction and correlated with worse cardiovascular outcomes[14]. In cancer patients, disease progression and survival depend on the balance between cancer-associated inflammation and the host's anti-tumor immune response which is Ly dependent, as Ly play a key role in cytotoxic cell death and cytokine production that inhibit the proliferation and metastatic activity of cancer cells[8]. Elevated levels of Ly in peripheral blood and within primary tumors have been linked with a favorable prognosis[15]. Ne, on the other hand, have a pro-tumor effect by contributing to tumor-related angiogenesis, as they are the primary source of circulating angiogenesis regulating chemokines, growth factors and proteases[16]. Elevated NLR in cancer patients thus represents a win of the pro-tumor inflammatory response over the anti-tumor immune response[8]. One study associated stress with relative neutrophilia and concomitant relative lymphocytopenia in oncological ICU patients following abdominal surgery, systemic inflammation or sepsis, with the highest values of the Ne count and lowest values of the Ly count in the most severe cases[17]. Neuroendocrine system (cortisol, catecholamines, prolactin) and pro-inflammatory cytokines (TNF-alpha, caspase-3) cause margination and redistribution of Ly within the lymphatic system and accelerated apoptosis, resulting in lymphocytopenia. Neutrophilia is caused by the demargination of Ne, their delayed apoptosis and the stimulation of stem cells by stem growing factors (G-CSF)[17]. Improvement in clinical status was accompanied by a gradual increase in Ly and a concomitant decrease in the Ne count. To the best of our knowledge, this is the only study that provided proof of the pattern of change in NLR, but with one downside: the relative values of Ne and Ly counts were measured, which are less precise than the absolute values.

In this study, two autoimmune inflammatory diseases, systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), were taken as examples for an investigation of the pattern of change in NLR in systemic inflammation. In both SLE and RA, the immune system recognizes the body's specific antigens as foreign bodies with a subsequent activation of both branches of the immune system; the innate and adaptive immune response. SLE is characterized by the formation of autoantibodies to nuclear components, which leads to the formation of immune complexes, complement activation and an inflammatory response which can affect any organ system. Hematological disturbances are among common SLE manifestations with lymphopenia being the most common white blood cell disturbance, which also correlates with disease activity[18]. In RA, a major effector mechanism is through cellular immunity, with monocytes, neutrophils and fibroblasts being the main responsible factors for joint destruction[19]. Most previous studies have found a positive correlation between NLR and disease activity in SLE and RA[3,20,21], but none have reported on the pattern of change in NLR.

The aim of this study was to investigate the pattern of change in NLR (changes in absolute Ne and

Ly counts with corresponding changes in NLR) in systemic inflammation. We expect that this study will contribute to the understanding of the pattern of change in NLR in systemic inflammation generally, and in SLE and RA particularly. To elucidate the background of change in NLR in active disease, NLR was correlated with other parameters of inflammation and disease activity in SLE and RA.

Materials and methods

Subjects

This retrospective study encompassed SLE and RA patients who were treated at Dubrava University Hospital (the coordinator of the study) and University Hospital Centre Zagreb, both centers in Zagreb, Croatia, between March 2006 and June 2016. All SLE patients fulfilled the 1997 American College of Rheumatology (ACR) Revised Criteria for Classification of SLE[22]. All RA patients diagnosed before 2010 fulfilled the American Rheumatism Association 1987 revised criteria for the classification of RA[23] and those diagnosed after that year the 2010 ACR/European League against Rheumatism (EULAR) Classification Criteria for RA[24]. The new criteria have higher sensitivity but lower specificity, facilitating the detection of early RA[25]. All RA patients diagnosed before 2010 fulfilled both sets of criteria. The following data were collected consecutively from medical records: component complement 3 (C3) and 4 (C4), leukocyte count, Ne count, Ly count, C-reactive protein (CRP), hemoglobin concentration and the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)[26] score for SLE; and leukocyte count, Ne count, Ly count, CRP, swollen and tender joint count and Disease Activity Score 28 for Rheumatoid Arthritis with CRP (DAS28CRP)[27] for RA. Patients with a current infection or malignant disease were excluded from the study. The final number of included patients was N = 146 for SLE and N = 181 for RA. The patients were divided in two groups; a group in remission and a group with active disease with a cut-off value of SLEDAI = 3 and DAS28CRP = 2.6 for SLE and RA, respectively. The number of patients in remission and with active disease was 42 and 104 for SLE, and 49 and 132 for RA. Also, the patients were divided in two groups according to whether or not they received glucocorticoid treatment at the time the data were recorded. The number of patients in the glucocorticoid group and no glucocorticoid group was 108 and 35 for SLE and 100 and 78 for RA (three RA patients were excluded from this analysis because they had just started or discontinued glucocorticoid treatment). Additionally, since SLE patients on glucocorticoid treatment received a higher glucocorticoid dosage, we divided them into three subgroups based on the dose taken at the time the data were recorded. The first group included 49 SLE patients on 2-8 mg, the second 42 SLE patients on 12-28 mg and the third group 17 SLE patients on 32-80 mg of methylprednisolone or equivalent daily dose (three SLE patients receiving glucocorticoids were excluded from this analysis because their dosage was unknown). In RA patients receiving glucocorticoids, the highest dose was 12 mg of methylprednisolone or equivalent daily dose. The study was approved by the Ethics committee of Dubrava University Hospital, the coordinator of the study.

Methods

A complete blood count with differential was performed on a Siemens ADVIA 2120i high-volume hematology analyzer. CRP, C3 and C4 were analyzed on an Olympus AU 2700 plus analyzer. NLR was calculated from the absolute Ne and Ly counts in peripheral blood (NLR = absolute Ne count/absolute Ly count).

Statistical analysis

The Kolmogorov-Smirnov test was used to assess the normality of distribution of the investigated parameters. All parameters in our study were non-normally distributed ($P < 0.05$). Numerical variables were expressed as median values with interquartile range and categorical variables as counts and percentages. Differences between groups for non-normally distributed parameters were tested with the Mann-Whitney and Kruskal-Wallis test for two and more groups, respectively. Differences between groups for categorical variables were tested with the chi-square test. Spearman's correlation was used to analyze the association between the studied parameters. The values of $P < 0.05$ were considered statistically significant. Statistical analysis was done using the IBM SPSS Statistics 23.0 program (International Business Machines Corp., New York, USA).

Table 1. Demographic characteristics of the SLE and RA patient groups.

		SLE (N=146)	RA (N=181)	*P*-value
Sex	Male	17 (12%)	42 (23%)	<0.001
	Female	129 (88%)	139 (77%)	
Age (years)		41 (31-57)	57 (50-63)	<0.001
Duration of the disease (years)		6 (1-15)	2 (0-9)	0.003

The number of male and female patients is expressed as a count and percentage, *P* for chi-square test. Patients' age and length of the disease are expressed as median values and interquartile range, *P* for Mann-Whitney test.

Results

The demographic characteristics of the SLE and RA patient groups are shown in Table 1. The SLE group contained more female patients ($P < 0.001$), younger patients ($P > 0.001$) and patients with a longer duration of the disease ($P = 0.003$) than the RA group.

Differences in clinical characteristics between the group in remission and the group with active disease are shown in Tables 2 and 3 for SLE and RA, respectively. In SLE, there was no difference in NLR and Ly count between groups ($P = 0.062$ and $P = 0.166$, respectively). In RA, a significant difference in NLR and Ne count was found between the group in remission and the group with active disease, where the Ne count was higher ($P = 0.018$ and $P < 0.001$, respectively). In both the SLE and RA groups, the Ne count was in the reference interval, regardless of disease activity. The Ly count in RA was in the reference interval, while in SLE it was below the reference interval, also regardless of disease activity. Differences in Ne and Ly counts and NLR between patients receiving glucocorticoids and patients not receiving them at the moment the data were recorded are shown in Tables 4 and 5 for SLE and RA, respectively. In SLE, a significant difference in the Ne count was found between the two groups, with the Ne count being higher in patients receiving glucocorticoids ($P = 0.002$), while no difference was found in the Ly count and NLR. In RA, no difference in Ne and Ly

Table 2. Differences between the group in remission and the group with active disease in patients with SLE with a cut-off value of SLEDAI = 3.

Characteristics	SLEDAI ≤ 3 (N=42)	SLEDAI > 3 (N=104)	*P*-value
C3 (g/L)	1.03 (0.82-1.13)	0.73 (0.54-0.92)	<0.001
C4 (g/L)	0.18 (0.13-0.26)	0.11 (0.06-0.19)	<0.001
Leukocyte count ($x10^9$/L)	6.8 (5.3-8.8)	6.8 (4.6-10.1)	0.844
Neutrophil count ($x10^9$/L)	4.63 (3.37-6.34)	4.62 (3.31-7.41)	0.7
Lymphocyte count ($x10^9$/L)	1.12 (0.78-2.08)	1.09 (0.67-1.6)	0.166
NLR	2.88 (2.15-6.15)	4.65 (2.75-7.06)	0.062
Hemoglobin (g/L)	127 (107-138)	116 (100-131)	0.049
CRP (mg/L)	3.1 (1.125-11.2)	4.5 (1.175-12.675)	0.534
SLEDAI	2 (0-2)	9 (6-14)	<0.001

Results are given as median values and interquartile range, *P* for the Mann-Whitney test. C3, C4 – complement component 3, 4. NLR – neutrophil to lymphocyte count. CRP – C-reactive protein. SLEDAI – Systemic Lupus Erythematosus Disease Activity Index

Table 3. Differences between the group in remission and the group with active disease in patients with RA with a cut-off value of DAS28CRP = 2.6.

Characteristics	DAS28CRP ≤ 2.6 (N=49)	DAS28CRP > 2.6 (N=132)	*P*-value
Leukocyte count (x10^9/L)	6.7 (4.7-8.3)	7.9 (6.3-9.9)	0.001
Neutrophil count (x10^9/L)	4.0 (2.63-5.33)	5.3 (4.1-7.2)	<0.001
Lymphocyte count (x10^9/L)	1.66 (1.15-2.22)	1.6 (1.27-2.2)	0.691
NLR	2.39 (1.4-4.08)	3.1 (1.96-4.54)	0.018
CRP (mg/L)	1.6 (0.45-4.0)	9.45 (2.8-24.5)	<0.001
Swollen joint count	0	4 (1-11)	<0.001
Tender joint count	0 (0-1)	8 (3-18)	<0.001
DAS28CRP	2.0 (1.39-2.315)	4.655 (3.405-6.005)	<0.001

Results are given as median values and interquartile range, *P* for the Mann-Whitney test. NLR – neutrophil to lymphocyte ratio. CRP – C-reactive protein. DAS28CRP – Disease Activity Score-28 for Rheumatoid Arthritis with CRP.

Table 4. Differences between the group that received glucocorticoid treatment and the group that did not in patients with SLE.

Characteristics	Glucocorticoid treatment (N=108)	No glucocorticoid treatment (N=35)	*P*-value
Leukocyte count (x10^9/L)	7.4 (5.3-10.3)	5.0 (4.1-7.4)	0.002
Neutrophil count (x10^9/L)	5.2 (3.7-7.44)	3.5 (2.82-5.1)	0.002
Lymphocyte count (x10^9/L)	1.1 (0.7-1.83)	1.04 (0.7-1.5)	0.617
NLR	4.49 (2.55-7.13)	3.92 (2.04-5.75)	0.106

Results are given as median values and interquartile range, *P* for the Mann-Whitney test. NLR – neutrophil to lymphocyte ratio.

Table 5. Differences between the group that received glucocorticoid treatment and the group that did not in patients with RA.

Characteristics	Glucocorticoid treatment (N=100)	No glucocorticoid treatment (N=78)	*P*-value
Leukocyte count (x10^9/L)	8.1 (6.1-9.9)	7.3 (6.1-9.1)	0.22
Neutrophil count (x10^9/L)	5.23 (3.63-7.5)	4.75 (3.6-6.1)	0.243
Lymphocyte count (x10^9/L)	1.64 (1.2-2.22)	1.6 (1.3-2.12)	0.844
NLR	2.71 (1.75-5.24)	3.05 (1.95-3.96)	0.943

Results are given as median values and interquartile range, *P* for the Mann-Whitney test. NLR – neutrophil to lymphocyte ratio.

counts and NLR was found between the two groups. In SLE subgroups with different glucocorticoid dosage, there was an increase in Ne count that was more prominent with dose increase (see supplement material).

Correlations between the investigated parameters are shown in Tables 6 and 7 for SLE and RA, respectively. In both SLE and RA, a weak positive correlation was found between NLR and the disease activity index, SLEDAI ($\rho = 0.165$, $P = 0.046$) and DAS28CRP ($\rho = 0.254$, $P = 0.001$), respectively. In SLE, a weak negative correlation was found between Ly count and SLEDAI ($\rho = -0.173$, $P = 0.037$), while

Table 6. Correlations between investigated parameters in patients with SLE (N = 146).

		NLR	SLEDAI*
Neutrophil count	ρ	-	-0.011
	P-value	-	0.891
Lymphocyte count	ρ	-	-0.173
	P-value	-	0.037
NLR	ρ	1	0.165
	P-value		0.046
CRP	ρ	0.233	-0.002
	P-value	0.005	0.978
C3	ρ	0.013	-
	P-value	0.872	-
C4	ρ	0.015	-
	P-value	0.862	-
Hemoglobin	ρ	-0.162	-0.264
	P-value	0.051	0.001

*Correlations between SLEDAI and C3, C4 were not calculated since both parameters are included in the SLEDAI score.

NLR – neutrophil to lymphocyte count. CRP – C-reactive protein. C3, C4 – complement component 3, 4. SLEDAI – Systemic Lupus Erythematosus Disease Activity Index.

Table 7. Correlations between investigated parameters in patients with RA (N=181).

		NLR	DAS28CRP*
Neutrophil count	ρ	-	0.328
	P-value	-	<0.001
Lymphocyte count	ρ	-	0.022
	P-value	-	0.772
NLR	ρ	1	0.254
	P-value		0.001
CRP	ρ	0.326	-
	P-value	<0.001	-
Swollen joint count	ρ	0.177	-
	P-value	0.018	-
Tender joint count	ρ	0.152	-
	P-value	0.042	-
DAS28CRP*	ρ	0.254	1
	P-value	0.001	

*Correlations between DAS28CRP and swollen joint count, tender joint count and CRP were not calculated since these parameters are included in the DAS28CRP score.

NLR – neutrophil to lymphocyte ratio. CRP – C-reactive protein. DAS28CRP – Disease Activity Score-28 for Rheumatoid Arthritis with CRP.

no correlation was found between Ne count and SLEDAI (ρ = -0.011, *P* = 0.891). In RA, a weak positive correlation was found between Ne count and DAS28CRP (ρ = 0.328, *P* < 0.001), while no correlation was found between Ly count and DAS28CRP (ρ = 0.022, *P* = 0.772). In both SLE and RA there was a weak positive correlation between NLR and CRP (ρ = 0.233, *P* = 0.005 and ρ = 0.326, *P* < 0.001, respectively). In SLE, NLR weakly negatively correlated with hemoglobin concentrations, but without statistical significance (ρ = -0.162, *P* = 0.051), while no correlation was found between NLR and C3 and C4 (ρ = 0.013, *P* = 0.872 and ρ = 0.015, *P* = 0.862, respectively). In RA, NLR weakly positively correlated with the swollen and tender joint count (ρ = 0.177, *P* = 0.018 and ρ = 0.152, *P* = 0.042, respectively).

Discussion

The aim of our study was to investigate the pattern of change in NLR (changes in absolute Ne and Ly counts with corresponding changes in NLR) in systemic inflammation generally. The two autoimmune inflammatory diseases taken as examples of systemic inflammatory disorders were systemic lupus erythematosus and rheumatoid arthritis, and the aim of the study was to investigate changes in NLR in specific terms of these diseases.

Our results show that NLR correlated with markers of systemic inflammation and disease activity in RA (CRP, DAS28CRP) and some (CRP, SLEDAI), but not all (hemoglobin concentration, C3, C4) such markers in SLE. These findings correspond to some[20,28,29], but not all[3,30] previous studies of NLR in

SLE and RA. We analyzed the possible effect of glucocorticoid treatment on Ne and Ly counts and NLR, which showed that, in SLE, the Ne count was higher in patients receiving glucocorticoids and it followed the dose-response pattern (supplement material), but there was no effect on the Ly count or on NLR. In RA, glucocorticoid treatment showed no effect on any of the aforementioned parameters. Due to the retrospective cross-sectional design of our study, these results represent only the effect of the actual glucocorticoid dose on Ne and Ly counts and NLR at the time the data were recorded.

The novelty of our study was the investigation of the pattern of change in NLR (changes in absolute Ne and Ly counts with corresponding changes in NLR) in SLE and RA. Our results for RA, both from the comparison of disease activity groups and correlation analysis, clearly show that NLR was higher in patients with active disease than in those in remission, and it increased with disease activity (DAS28CRP) due to an increase in Ne count with irrelevant changes in Ly count (Table 7). Regarding NLR in SLE, our results were ambiguous. Although there was no difference in NLR between the group with active disease and the group in remission ($P = 0.062$), the results of the correlation analysis indicate that NLR was higher in patients with active disease, which is consistent with some previous studies[20]. Moreover, a correlation analysis in SLE showed that NLR increased with disease activity (SLEDAI) due to a decrease in Ly count with irrelevant changes in Ne count (Table 6), as opposed to the change noticed in RA. These findings indicate that the pattern of change in NLR can be different in different diseases, reflecting their pathogeneses. Since none of the previous studies have investigated the pattern of change in NLR, we cannot compare our results to the results of any previous studies. Regarding SLE, we hypothesized that the increase in NLR with disease activity could be due to the relative decrease in Ly count, since lymphopenia is the most common white blood cell count disturbance in SLE, which also correlates with disease activity[18]. Regarding RA, literature findings stress the role of Ne in the initiation and perpetuation of RA[31], which could account for the pattern of change in NLR in RA (increased with disease activity due to an increase in Ne count with irrelevant changes in Ly count). Additionally, none of the previous studies described neutrophilia or neutropenia as a manifestation of RA. The results of our study are in line with this, with the Ne count being within the reference interval in both groups of RA patients; both with active disease and in remission. Also, the Ly count was below the reference interval in both groups of SLE patients. These findings indicate that even a small change in Ne with a corresponding change in NLR could reflect disease activity in RA and, similarly, a small change in Ly count with a corresponding change in NLR could reflect disease activity in SLE.

In conclusion, NLR was increased in active disease versus remission in both SLE and RA, but the pattern was different – in SLE due to a decreased Ly count without concomitant change in Ne count, and in RA due to an elevated Ne count without concomitant change in Ly count. We can point out that, when investigating NLR, it is also important to evaluate the pattern of change in NLR for a precise interpretation and understanding of the NLR value in the context of disease pathogenesis. One of the limitations of our study was its retrospective cross-sectional design without a follow-up of the patients, which is why we could not analyze the pattern of change of NLR value during the course of the disease and correlate it to the change of disease activity and inflammatory markers in the same patient. Also, we could not analyze the effect of the duration of the disease, the effect of cumulative disease activity, nor the effect of the duration of glucocorticoid treatment or cumulative glucocorticoid dose on NLR.

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Sažetak

UZORCI PROMJENE NEUTROFILNO-LIMFOCITNOG OMJERA U DVA UPALNA REUMATSKA POREMEĆAJA: SUSTAVNOG ERITEMSKOG LUPUSA I REUMATOIDNOG ARTRITISA

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Povećani neutrofilno-limfocitni omjer (NLR) potencijalni je pokazatelj sustavne upale u brojnim stanjima i prediktor lošeg ishoda, međutim obrazac njegove promjene (promjene u apsolutnom broju neutrofila i limfocita s posljedičnom promjenom NLR-a) dosad nije istražen. Cilj ovog retrospektivnog istraživanja bio je utvrditi obrazac promjene NLR-a u sustavnoj upali. Sustavni eritemski lupus (SLE) i reumatoidni artritis (RA) uzeti su kao primjeri sustavnog upalnog poremećaja. Uključeni su bolesnici sa SLE (N = 146) i RA (N = 181). Prikupljeni su sljedeći podaci: broj leukocita, neutrofila i limfocita te CRP za sve bolesnike; C3, C4, koncentracija hemoglobina i SLEDAI za SLE; broj otečenih i bolnih zglobova te DAS28CRP za RA. NLR je izračunat iz apsolutnog broja neutrofila i limfocita u perifernoj krvi i koreliran s odgovarajućim pokazateljima aktivnosti bolesti. U obje bolesti NLR je pozitivno korelirao s aktivnosti bolesti, ali uz drugačiji obrazac njegove promjene: u SLE zbog sniženog broja limfocita, a istovremeno nepromijenjen broj neutrofila, a u RA zbog povišenog broja neutrofila uz istovremeno nepromijenjen broj limfocita. Pri utvrđivanju NLR-a važno je istražiti i obrazac njegove promjene radi ispravnog tumačenja i razumijevanja NLR-a u kontekstu patogeneze bolesti.

Ključne riječi: *sustavni eritemski lupus; reumatoidni artritis; biomarkeri; sustavna upala; neutrofilno-limfocitni omjer*

Supplement table. Differences between groups based on glucocorticoid dosage (mg of methylprednisolone or equivalent daily dose) in SLE patients. Also, every glucocorticoid subgroup was compared to the no-glucocorticoid group.

Characteristics	**0 mg (N=35)**	**2-8 mg (N=49)**	**12-28 mg (N=42)**	**32-80 mg (N=17)**	***P*-value$_1$**
Leukocyte count ($x10^9$/L)	5.0 (4.1-7.4)	6.7 (5.3-9.4) P_2=0.01	7.4 (5.0-8.8) P_2=0.049	12.3 (5.6-14.3) P_2=0.001	0.001
Neutrophil count ($x10^9$/L)	3.5 (2.82-5.1)	4.83 (3.68-6.88) P_2=0.014	4.98 (3.64-6.36) P_2=0.02	9.0 (4.12-12.0) P_2=0.001	0.001
Lymphocyte count ($x10^9$/L)	1.04 (0.7-1.5)	1.05 (0.7-1.98) P_2=0.66	1.14 (0.63-1.63) P_2=0.914	1.28 (0.7-1.93) P_2=0.354	0.835
NLR	3.92 (2.04-5.75)	3.75 (2.43-6.76) P_2=0.454	5.1 (2.67-6.85) P_2=0.115	5.57 (3.63-11.1) P_2=0.036	0.15

Results are given as median values and interquartile range, P_1 for the Kruskal-Wallis test, P_2 for the Mann-Whitney test. NLR – neutrophil to lymphocyte ratio.

A significant difference in Ne count was found between SLE groups on different glucocorticoid dosage (P_1 = 0.001) and when each glucocorticoid subgroup was compared to the no glucocorticoid group (P_2 = 0.014, P_2 = 0.02 and P_2 = 0.001 for 2-8 mg, 12-28 mg and 32-80 mg subgroups, respectively), with an increase in Ne count across dose increase. No difference in Ly count and NLR value was found between the groups (P_1 = 0.835 and P_1 = 0.15, respectively). Also, no difference in Ly count and NLR was found when each glucocorticoid subgroup was compared to the no glucocorticoid group, except for the subgroup of patients on 32-80 mg of methylprednisolone (or equivalent) daily dose, which had a higher NLR value than the no glucocorticoid group (P_2 = 0.036).