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Research Article

Age-related differences in the association between nutritional–inflammatory indices and disease activity in rheumatoid arthritis

Romatoid artritte nütrisyonel–inflamatuvar indeksler ile hastalık aktivitesi arasındaki ilişkide yaşa bağlı farklılıklar

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Abstract

Aim: Rheumatoid arthritis (RA) is a chronic inflammatory disease in which inflammation and nutritional status jointly influence disease severity and prognosis. This study aimed to evaluate the relationships between nutritional–inflammatory indices—C-reactive protein–Albumin–Lymphocyte (CALLY) index, Prognostic Nutritional Index (PNI), Controlling Nutritional Status (CONUT) score, and Geriatric Nutritional Risk Index (GNRI)—and disease activity in patients with RA.

Material and Methods: Clinical and laboratory data of 199 RA patients who presented to the Rheumatology Outpatient Clinic between January 2024 and July 2025 were retrospectively analyzed. Disease activity was assessed using DAS28-CRP, CDAI, and SDAI scores. PNI, CONUT, CALLY, and GNRI values (for patients aged ≥60 years) were calculated, and their correlations with disease activity and nutritional parameters were examined.

Results: The study included 199 patients with a mean age of 53.4 ± 14.5 years, of whom 72.9% were female. The CALLY index showed strong negative correlations with disease activity indicators while the PNI showed weak-to-moderate negative correlations. The CONUT score was not significantly associated with disease activity. In the geriatric subgroup (≥60 years), correlations between all indices and disease activity were stronger, and GNRI was found to be negatively associated with both malnutrition risk and inflammatory activity.

Conclusion: The CALLY and PNI indices are reliable and practical laboratory markers that comprehensively reflect inflammatory burden and nutritional status in RA. GNRI appears clinically useful for assessing malnutrition and inflammation-related frailty, particularly in older patients. Incorporating nutritional–inflammatory indices into routine clinical evaluation may improve disease activity monitoring and facilitate more integrated patient management.

Keywords: CRP-albumin-lymphocyte (CALLY), rheumatoid arthritis, disease activity, geriatric nutritional risk index (GNRI)

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Öz

Amaç: Romatoid artrit (RA), inflamasyon ve beslenme durumunun birlikte hastalık şiddeti ve prognozu üzerinde etkili olduğu kronik inflamatuvar bir hastalıktır. Bu çalışmada RA'lı hastalarda nutrisyonel–inflamatuvar indeksler olan C-reactive protein–Albumin–Lymphocyte (CALLY), Prognostic Nutritional Index (PNI), Controlling Nutritional Status (CONUT) ve Geriatric Nutritional Risk Index (GNRI) skorlarının hastalık aktivitesiyle ilişkilerinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntem: Ocak 2024–Temmuz 2025 tarihleri arasında Romatoloji Polikliniği'ne başvuran 199 RA hastasının klinik ve laboratuvar verileri retrospektif olarak incelendi. Hastalık aktivitesi DAS28-CRP, CDAI ve SDAI skorlarıyla değerlendirildi. PNI, CONUT, CALLY ve ≥60 yaş için GNRI değerleri hesaplanarak hastalık aktivitesi ve nutrisyonel parametrelerle korelasyonları analiz edildi.

Bulgular: Çalışmaya dahil edilen 199 hastanın yaş ortalaması 53,4 ± 14,5 yıl olup, %72,9'u kadındı. CALLY indeksi DAS28-CRP ve SDAI dahil olmak üzere hastalık aktivitesi göstergeleriyle güçlü negatif korelasyonlar gösterirken, PNI zayıf ile orta düzeyde korelasyonlar gösterdi. CONUT skorunun hastalık aktivitesiyle anlamlı bir ilişkisi bulunmadı. Geriatrik grupta (≥60 yaş) tüm indeksler ile hastalık aktivitesi arasındaki korelasyonlar daha güçlü olup, GNRI'nin hem malnütrisyon riski hem de inflamatuvar aktiviteyle negatif ilişkili olduğu saptandı.

Sonuç: CALLY ve PNI, RA'da inflamatuvar yük ve beslenme durumunu bütüncül biçimde yansıtan güvenilir ve pratik laboratuvar belirteçleridir. GNRI, özellikle ileri yaş hastalarda malnütrisyon ve inflamasyona bağlı kırılganlığı değerlendirmede klinik açıdan yararlıdır. Nutrisyonel–inflamatuvar indekslerin rutin klinik değerlendirmelere entegrasyonu, hastalık aktivitesinin daha kapsamlı izlenmesine ve bütüncül hasta yönetimine katkı sağlayabilir.

Anahtar Kelimeler: CRP–albümin–lenfosit (CALLY), romatoid artrit, hastalık aktivitesi, geriatrik nutrisyonel risk indeksi (GNRI)

Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune and inflammatory disorder affecting approximately 0.5–1% of the global population, leading to progressive joint damage and systemic complications [1]. Regular assessment of disease activity is essential for monitoring treatment response and predicting prognosis [2]. In clinical practice, validated indices such as the Disease Activity Score-28 using CRP (DAS28-CRP), Clinical Disease Activity Index (CDAI), and Simplified Disease Activity Index (SDAI) are commonly used for this purpose [3].

Factors influencing disease activity are not limited to inflammatory processes; metabolic status, body composition, systemic inflammatory burden, and nutritional state also play important roles in disease severity and treatment response. Chronic inflammation can alter energy metabolism, protein and muscle synthesis, and immune responses, leading to a catabolic state and an increased risk of malnutrition. Conversely, malnutrition may exacerbate disease activity by enhancing inflammatory responses and impairing immune function [4]. This interaction can adversely affect disease severity and clinical outcomes, particularly in older patients. In recent years, the impact of nutritional status and malnutrition on the clinical course of RA has attracted increasing research interest [5].

Despite the growing recognition of the clinical importance of nutritional status in RA, there remains a need for objective and quantitative markers for its routine assessment. Several nutritional and inflammatory indices developed to objectively evaluate nutritional status have been investigated in RA and other chronic diseases. Among these, the Controlling Nutritional Status (CONUT) score—based on serum albumin, lymphocyte count, and total cholesterol levels—reflects the degree of malnutrition and has been reported to correlate positively with DAS28-ESR in RA patients [6].

The Prognostic Nutritional Index (PNI), calculated from serum albumin levels and lymphocyte count, reflects both nutritional and immunological status. Several studies have demonstrated its association with inflammatory activity and clinical outcomes in RA [7].

The recently proposed C-reactive protein–Albumin–

Lymphocyte (CALLY) index is a novel biomarker that integrates inflammatory burden (CRP), nutritional status (albumin), and immune response (lymphocytes) into a single formula. It has shown prognostic value in malignancies and chronic inflammatory diseases, though its clinical utility in RA remains limited and understudied [8]. In addition, the Geriatric Nutritional Risk Index (GNRI), commonly used in older adults, is considered a reliable tool for assessing malnutrition risk in the geriatric population. Age-related changes in immune function, increased comorbidity burden, and nutritional frailty may alter the clinical course of rheumatoid arthritis and modify biomarker profiles associated with inflammatory activity. In elderly patients with RA, nutritional deficiencies are more common and may exert additional adverse effects on inflammatory activity and clinical prognosis. Therefore, evaluating GNRI in geriatric RA patients may be valuable for identifying age-related pathophysiological differences and risk levels [9].

Comprehensive studies evaluating nutritional–inflammatory indices such as CONUT, PNI, CALLY, and GNRI together with RA disease activity scores (DAS28-CRP, CDAI, SDAI) remain limited in the current literature. This limitation highlights a significant knowledge gap regarding the integration of nutritional and inflammatory markers into clinical assessment. Given the limited evidence on the integration of nutritional–inflammatory indices into disease assessment, this study aimed to investigate the associations between CONUT, PNI, CALLY, and GNRI indices and disease activity in patients with rheumatoid arthritis, and to determine the potential effects of age on these relationships.

Materials and Methods

This retrospective study included patients diagnosed with rheumatoid arthritis (RA) who presented to the Rheumatology Outpatient Clinic for routine follow-up between January 2024 and July 2025. Inclusion required the availability of detailed physical examination findings specifically, the number of tender, swollen, and painful joints to enable accurate disease activity assessment. Patients with missing data, pregnancy, chronic kidney or liver disease, active malignancy under chemotherapy or radiotherapy, or primary hematologic disorders were excluded. A total of 199 patients met the criteria. Demographic and clinical data (age, sex, height, weight, disease duration, and joint counts), as well as laboratory parameters (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP], albumin, total cholesterol, and complete blood count) were retrieved from electronic records. Disease activity was evaluated using DAS28-CRP, CDAI, and SDAI scores.

Disease Activity Scores

DAS28-CRP reflects disease activity based on tender and swollen joint counts (28 joints), CRP level, and patient global assessment; higher scores indicate greater inflammation [10]. CDAI, based solely on clinical parameters—joint counts and patient/physician global assessments—is a practical tool that excludes laboratory measures. SDAI adds the CRP value to CDAI components, incorporating both clinical and laboratory findings [11].

Nutritional and Inflammatory Indices

Nutritional–inflammatory status was assessed using the following indices:

Prognostic Nutritional Index (PNI): [10 × albumin (g/dL) + 0.005 × total lymphocyte count (per mm^3)]. Lower PNI values indicate poorer nutritional and immunologic status [7].

Controlling Nutritional Status (CONUT) Score: Based on albumin (0–6), lymphocyte (0–3), and cholesterol (0–3) scores; total 0–12, with higher values reflecting more severe malnutrition [12].

C-reactive protein–Albumin–Lymphocyte (CALLY) Index: [Albumin (g/dL) × lymphocytes (/μL) / CRP (mg/dL) × 10^4]. Higher values indicate better nutrition and lower inflammatory burden [13].

GNRI was calculated according to the method described by Bouillanne et al. [14], using the following formula: GNRI = [1.489 × albumin (g/L) + 41.7 × (actual body weight / ideal body weight)]. Ideal body weight was estimated using the Lorentz formula, and GNRI was computed for patients aged ≥60 years, defined as the geriatric group according to prior literature [14,15].

PNI, CONUT, CALLY, and (for ≥60 years) GNRI values were analyzed in relation to DAS28-CRP, CDAI, and SDAI scores.

This study was approved by the Ethics Committee of KTO Karatay University Faculty of Medicine (approval number: 2025/015, dated September 25, 2025). The study was conducted in accordance with the principles of the Declaration

of Helsinki. Data were collected retrospectively by reviewing electronic medical records and laboratory findings of patients. No direct contact with patients was made and no interventional procedures were performed. Therefore, individual informed consent was not required.

Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics, Version 27.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were expressed as frequency (n), percentage (%), mean ± standard deviation, median, and interquartile range. The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Differences between categorical variables were analyzed with the chi-square (χ^2) test. For comparisons of continuous variables, the independent samples t-test was used for normally distributed data, while the Mann–Whitney U test was applied for non-normally distributed data. Correlations between continuous variables were evaluated using Pearson or Spearman correlation analyses, as appropriate. A p-value of <0.05 was considered statistically significant, and results were reported with 95% confidence intervals.

Results

General Demographic, Clinical and Laboratory Characteristics

The study included 199 patients with rheumatoid arthritis, with a mean age of 53.4 ± 14.5 years; 72.9% were female. Patients were stratified into two subgroups according to age: younger (n = 127) and geriatric (n = 72, ≥60 years). The mean ages of the younger and geriatric groups were 45.1 ± 10.5 and 68.1 ± 6.7 years, respectively ($p < 0.001$). No significant differences were found between the groups in terms of sex distribution or body mass index (BMI) ($p > 0.05$). The rates of seropositivity were comparable between the geriatric (69%) and younger (66.7%) groups ($p = 0.73$). Laboratory findings revealed significantly higher erythrocyte sedimentation rate (24 [29.7] mm/h vs. 12 [17] mm/h; $p < 0.001$) and CRP levels (0.46 [1.4] mg/dL vs. 0.31 [0.53] mg/dL; $p = 0.009$) in the geriatric group, while serum albumin levels were lower (4.20 ± 0.35 g/dL vs. 4.39 ± 0.29 g/dL; $p < 0.001$).

In clinical assessments, physician global assessment scores were significantly higher in geriatric patients (27.5 [30] vs. 10 [30]; $p = 0.001$), whereas patient global assessment scores did not differ significantly ($p = 0.50$). Regarding disease activity, DAS28-ESR, SDAI, and CDAI scores were all significantly higher in the geriatric group ($p = 0.01$, $p = 0.01$, and $p = 0.05$, respectively). Evaluation of nutritional and inflammatory indices showed that the geriatric group had a significantly lower CALLY index (1.6 [4.2] vs. 2.9 [7.3]; $p = 0.003$) and a markedly reduced PNI score (42 ± 3.55 vs. 43.9 ± 2.95; $p < 0.001$). No significant difference was observed in CONUT scores between the groups ($p = 0.18$). Comparisons of demographic, clinical, laboratory, and nutritional characteristics for the total cohort and the age-based subgroups are summarized in Table 1.

Correlation Analyses

In the overall cohort, the CALLY index showed significant inverse correlations with indicators of disease activity. Strong negative correlations were observed with Physician Global Assessment, DAS28-ESR, DAS28-CRP, SDAI, and CDAI scores, and a moderate negative correlation with Patient Global Assessment.

Regarding nutritional parameters, the CALLY index demonstrated a moderate positive correlation with PNI and a weak negative correlation with CONUT score.

In subgroup analyses by age, the direction of correlations remained consistent, though the associations tended to be stronger in the geriatric group. In this group, the CALLY index was strongly and inversely correlated with Physician Global Assessment, DAS28-CRP, SDAI, and CDAI scores, while showing moderate-to-strong positive correlations with PNI and GNRI (Table 2).

In the overall cohort PNI showed negative correlations with disease activity parameters, including weak inverse associations with Physician Global Assessment, DAS28-ESR, DAS28-CRP, and SDAI, and a very weak one with CDAI. PNI was moderately positively correlated with the CALLY index and weakly negatively correlated with the CONUT score.

In subgroup analyses, similar trends were observed, with stronger correlations in the geriatric group. In this subgroup, PNI demonstrated moderate negative correlations with Physician Global Assessment, DAS28-ESR, DAS28-CRP, and SDAI, and weakly negative correlation with CDAI. PNI also showed strong positive correlations with GNRI and CALLY indices (Table 2).

The CONUT score was calculated in 104 patients due to missing cholesterol data. Among these, 89 were in the young subgroup, whereas only 15 were in the geriatric group. Because the number of geriatric patients with available CONUT data was

insufficient for meaningful analysis, correlation analyses were conducted only for the total cohort and the young subgroup.

In the overall cohort, the CONUT score showed weak but statistically significant negative correlations with the CALLY index and PNI. In the young subgroup, a weak inverse correlation was also observed between CONUT score and age. No significant correlations were found between the CONUT score and disease activity indices, including DAS28, SDAI, and CDAI, in either the total or young groups (Table 4).

In the geriatric rheumatoid arthritis group, GNRI was significantly associated with both disease activity and nutritional status indicators. It showed moderate-to-strong negative correlations with Physician Global Assessment and moderate negative correlations with DAS28-ESR, DAS28-CRP, SDAI, and CDAI scores. GNRI also demonstrated strong positive correlations with PNI and CALLY indices (Figure 1).

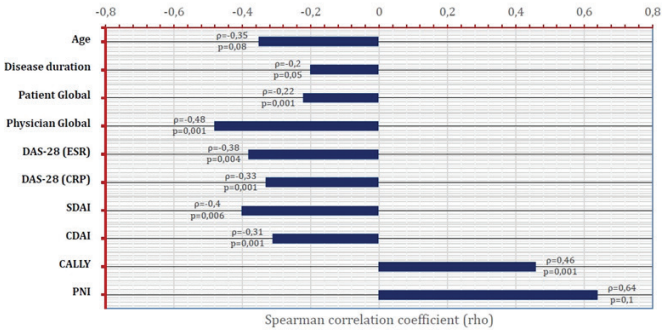

Figure 1. The correlation of GNRI with clinical and nutritional parameters (Geratrics Group). (Abbrev.: DAS: Disease Activity Score; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; CALLY: CRP–Albumin–Lymphocyte Index; PNI: Prognostic Nutritional Index; GNRI: Geriatric Nutritional Risk Index. Forest plot illustrating the correlation coefficients (ρ) and corresponding p-values between the Geriatric Nutritional Risk Index (GNRI) and various clinical and nutritional parameters in elderly patients with rheumatoid arthritis. Bars to the left of the zero line indicate negative correlations, while those to the right indicate positive correlations).

Table 1. Demographic, clinical, and nutritional characteristics by age group in rheumatoid arthritis.

Parameters	Total Group (n=199)	Young Group (n=127, n=89 for CONUT)	Geriatric Group (n=72)	p value
Age, years	53.4±14.5	45.09±10.5	68.1±6.7	<0.001
Female sex, n (%)	145 (%72.9)	95 (%74)	50 (%69)	0.41
BMI, kg/m^2	28±5.7	28±6.3	28±4.3	0.99
Disease duration, months	72 (103)	60 (92)	132 (168)	0.001
*Seropositivity (n = 197),n (%)	133 (%67.5)	84 (%66.7)	49 (%69)	0.73
ESR, mm/h	17 (23)	12 (17)	24 (29.7)	<0.001
CRP, mg/dL	0.36 (0.62)	0.31 (0.53)	0.46 (1.4)	0.009
Albumin, g/dL	4.32±0.32	4.39±0.29	4.20±0.35	<0.001
Lymphocyte count, ×10^9/L	2.23±0.72	2.26±0.71	2.16±0.73	0.33
Cholesterol mg/dL (n=104)	185.9±37.4	186.2±38.9	185.5±35.4	0.93
Patient Global Assessment	45 (45)	40 (45)	50 (38.7)	0.50
Physician Global Assessment	15 (30)	10 (30)	27.5(30)	0.001
DAS-28 (ESR) score	2.75 (3,06)	2.5 (2.36)	3.1(3)	0.01
DAS-28 (CRP) score	2.17 (2,8)	2 (2.5)	2.5 (3.1)	0.06
SDAI score	10.5 (22)	9.4 (20.8)	18.9 (30.4)	0.01
CDAI score	6 (17.5)	6 (14.5)	8.7 (18.6)	0.05
CALLY	2.6 (6.05)	2.9 (7.3)	1.6 (4.2)	0.003
PNI	43.2±3.2	43.9±2.95	42±3.55	<0.001
*CONUT (n=104)	1(1)	1(1)	-	0.18
GNRI	-	-	115.8±10.5	-

Abbrev.: BMI: Body Mass Index; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; DAS: Disease Activity Score; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; CALLY: CRP–Albumin–Lymphocyte Index; PNI: Prognostic Nutritional Index; CONUT: Controlling Nutritional Status; GNRI: Geriatric Nutritional Risk Index; Data are presented as mean ± standard deviation (SD) for normally distributed variables and as median (interquartile range, IQR) for non-normally distributed variables. Albumin values were recorded in g/dL. For GNRI calculations, albumin was converted to g/L (1 g/dL = 10 g/L), while for CALLY calculations albumin was used in g/dL.

*Seropositivity was defined as positivity for RF or anti-CCP antibodies.

*CONUT score was calculated in 104 patients (89 young, 15 geriatric); due to limited geriatric sample size, subgroup comparisons were not performed.

Table 2. Correlations between CALLY index and clinical variables by age group.

Variables	All patients (n=199)		Young Group (n=127, n=89 for CONUT)		Geriatric Group (n=72)	
	rho	**p-value**	**rho**	**p-value**	**rho**	**p-value**
Age, years	-0.26	<0.001	-0.14	0.09	-0.25	0.03
BMI, kg/m^2	-0.13	0.05	-0.30	<0.001	0.23	0.05
Disease duration, months	-0.13	0.05	-0.08	0.34	-0.07	0.54
Patient Global Assessment	-0.28	<0.001	-0.23	0.009	-0.39	0.001
Physician Global Assessment	-0.61	<0.001	-0.52	<0.001	-0.72	<0.001
DAS-28 (ESR) score	-0.53	<0.001	-0.42	<0.001	-0.63	<0.001
DAS-28 (CRP) score	-0.63	<0.001	-0.57	<0.001	-0.71	<0.001
SDAI score	-0.69	<0.001	-0.62	<0.001	-0.81	<0.001
CDAI score	-0.41	<0.001	-0.32	<0.001	-0.54	<0.001
PNI	0.33	<0.001	0.17	0.05	0.51	<0.001
*CONUT (n=104)	-0.21	0.02	-0.10	0.43	-	-
GNRI	-	-	-	-	0.46	<0.001

Abbrev.: BMI: Body Mass Index; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; DAS: Disease Activity Score; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; PNI: Prognostic Nutritional Index; CONUT: Controlling Nutritional Status; GNRI: Geriatric Nutritional Risk Index.

Correlation coefficients were calculated using Pearson or Spearman methods according to the distribution characteristics of the variables.

*CONUT score was calculated in 104 patients (89 young, 15 geriatric); due to limited geriatric sample size, subgroup comparisons were not performed.

Table 3. Correlations between PNI and clinical variables by age group.

Variables	All patients (n=199)		Young Group (n=127, n=89 for CONUT)		Geriatric Group (n=72)	
	rho	**p-value**	**rho**	**p-value**	**rho**	**p-value**
Age, years	-0.32	<0.001	-0.16	0.06	-0.30	0.01
BMI, kg/m^2	0.08	0.23	0.04	0.59	0.18	0.11
Disease duration, months	-0.10	0.15	0.05	0.55	-0.18	0.11
Patient Global Assessment	-0.11	0.09	-0.03	0.67	-0.23	0.04
Physician Global Assessment	-0.28	<0.001	-0.14	0.11	-0.44	<0.001
DAS-28 (ESR) score	-0.28	<0.001	-0.15	0.08	-0.40	<0.001
DAS-28 (CRP) score	-0.20	0.003	-0.09	0.30	-0.33	0.004
SDAI score	-0.26	<0.001	-0.11	0.19	-0.41	<0.001
CDAI score	-0.17	0.01	-0.06	0.46	-0.27	0.02
CALLY	0.33	<0.001	0.17	0.05	0.51	<0.001
*CONUT (n=104)	-0.24	0.01	-0.17	0.16	-	-
GNRI	-	-	-	-	0.64	<0.001

Abbrev.: BMI: Body Mass Index; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; DAS: Disease Activity Score; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; CALLY: CRP–Albumin–Lymphocyte Index; PNI: Prognostic Nutritional Index; CONUT: Controlling Nutritional Status; GNRI: Geriatric Nutritional Risk Index.

Correlation coefficients were calculated using Pearson or Spearman methods according to the distribution characteristics of the variables.

*CONUT score was calculated in 104 patients (89 young, 15 geriatric); due to limited geriatric sample size, subgroup comparisons were not performed.

Table 3. Correlations between PNI and clinical variables by age group.

Variables	All patients (n=104)		Young Group (n=89)	
	rho	p-value	rho	p-value
Age, years	-0.01	0.90	-0.25	0.04
BMI, kg/m^2	-0.11	0.22	-0.10	0.40
Disease duration, months	0.03	0.75	-0.04	0.70
Patient Global Assessment	0.02	0.80	0.01	0.91
Physician Global Assessment	0.01	0.84	-0.06	0.62
DAS-28 (ESR) score	-0.03	0.73	-0.10	0.42
DAS-28 (CRP) score	0.01	0.89	-0.04	0.72
SDAI score	0.04	0.68	-0.03	0.76
CDAI score	0.03	0.74	0.004	0.97
CALLY	-0.21	0.02	-0.10	0.43
PNI	-0.24	0.01	-0.17	0.16

BMI: Body Mass Index; ESR: Erythrocyte Sedimentation Rate; CRP: C-Reactive Protein; DAS: Disease Activity Score; SDAI: Simplified Disease Activity Index; CDAI: Clinical Disease Activity Index; CALLY: CRP–Albumin–Lymphocyte Index; PNI: Prognostic Nutritional Index; CONUT: Controlling Nutritional Status; GNRI: Geriatric Nutritional Risk Index.

Correlation analyses were performed using Pearson or Spearman methods according to the distribution characteristics of the variables.

*CONUT score was calculated in 104 patients (89 young, 15 geriatric); due to limited geriatric sample size, subgroup comparisons were not performed.

Discussion

In this study, the relationships between nutritional–inflammatory indices (CALLY, PNI, CONUT, and GNRI) and disease activity were investigated in patients with rheumatoid arthritis, and the potential influence of age on these associations was also evaluated. The findings of this study suggest that parameters reflecting nutritional status are associated with disease activity, particularly among geriatric patients.

The strong negative correlations between the CALLY index and disease activity indicators (DAS28, SDAI, CDAI, and Physician Global Assessment) suggest that this parameter reflects both inflammatory burden and overall nutritional status. In RA, increased inflammatory activity accelerates protein catabolism, leading to reduced albumin levels, impaired immune response, and decreased lymphocyte counts. By integrating these variables, the CALLY index provides a comprehensive reflection of the detrimental impact of inflammation on nutritional status. In this study, CALLY values showed a marked inverse relationship with SDAI and DAS28-CRP scores, indicating that the index declines as inflammatory activity increases. These results imply that the CALLY index may serve as a potential clinical indicator of disease activity in RA. Evidence regarding its use in rheumatoid arthritis remains limited. One of the few studies in this area, conducted by Zhang et al. (2025), similarly reported that lower CALLY scores were associated with increased mortality and systemic inflammation, consistent with the present findings. Collectively, these observations suggest that the CALLY index could be a useful parameter not only for assessing inflammatory activity but also for predicting long-term prognosis [8].

In this study, PNI showed weak-to-moderate negative correlations with DAS28-CRP, SDAI, and CDAI scores in the overall cohort, with these associations becoming more pronounced in the geriatric subgroup. As a parameter derived from serum albumin and lymphocyte count, PNI reflects both nutritional reserves and immune competence. The observed decrease in PNI values with increasing inflammatory activity suggests that nutritional capacity declines as inflammation progresses. These findings are consistent with the results reported by Öz et al. (2024), who demonstrated that lower PNI values were associated with higher DAS28 and SDAI scores, indicating increased disease activity [7]. The more pronounced associations in elderly patients may be explained by age-related changes in immune function, reduced albumin synthesis, and an enhanced inflammatory response, all of which could contribute to lower PNI levels.

The CONUT score showed weak but significant negative correlations with CALLY and PNI. However, no significant association was found with disease activity indices, including DAS28, SDAI, and CDAI, suggesting that this index may not adequately reflect inflammatory activity in RA. This finding contrasts with the results of Kılıç et al. [6], who reported a positive correlation between CONUT score and DAS28-ESR in patients with RA. In our study, the lack of a significant association between CONUT and disease activity parameters may be primarily attributed to the limited number of patients in whom the CONUT score could be calculated, as cholesterol data were unavailable

for a substantial proportion of the cohort. This reduced sample size, particularly in the geriatric subgroup, likely decreased the statistical power to detect meaningful correlations.

In the geriatric RA group, GNRI showed moderate-to-strong negative correlations with disease activity. This finding highlights the impact of malnutrition and inflammation on clinical outcomes in older patients. Higher levels of inflammatory markers (ESR and CRP) and lower serum albumin concentrations observed in the geriatric group suggest that increased inflammatory activity and nutritional decline progress in parallel with advancing age, potentially contributing to greater disease severity. Similarly, in the study by Cano-García et al. (2023), impaired nutritional status was identified in approximately one-third of elderly patients with RA, and this condition was reported to be associated with higher disease activity and lower quality of life [9]. GNRI appears to be a reliable tool for assessing malnutrition risk in the geriatric population and may provide valuable insights into predicting clinical outcomes associated with disease activity in RA. Moreover, the stronger correlations observed between all indices (particularly CALLY, PNI, and GNRI) and disease activity in the geriatric group suggest that age may act as a modifying factor in the inflammation–nutrition balance. With aging, processes such as sarcopenia, protein–energy malnutrition, and low-grade systemic inflammation contribute to increased frailty, thereby enhancing the clinical relevance of nutritional indices, particularly in the elderly RA population [16,17]. The present findings suggest that incorporating nutritional–inflammatory indices into routine clinical assessment may be beneficial, especially for older patients with RA.

This study has several limitations. Its single-center, retrospective design limits the ability to establish causal relationships. In addition, detailed data on dietary habits or nutritional questionnaires were not available, preventing a comprehensive assessment of the patients' actual nutritional status. Another important limitation is the incomplete availability of cholesterol data, which allowed the CONUT score to be calculated in only 104 patients in the entire cohort and in 89 patients within the young subgroup; therefore, analyses could not be performed for the geriatric group. This restricted sample size reduced the statistical power for correlation analyses and may have contributed to the lack of significant associations observed for the CONUT score. However, the study included a heterogeneous RA population covering a wide age range. While previous studies have typically evaluated nutritional–inflammatory indices separately, the present research analyzed these indices comparatively within the same cohort. Furthermore, subgroup analyses based on age allowed a detailed comparison between younger and geriatric patients, providing insight into the potential role of age in the interaction between inflammation and nutrition. With these aspects, this study adds to the limited body of evidence evaluating age-related differences in nutritional–inflammatory indices among patients with rheumatoid arthritis.

In conclusion, this study demonstrated that nutritional–inflammatory indices, particularly CALLY, PNI, and GNRI, are significantly associated with disease activity in patients with rheumatoid arthritis. Among these, the CALLY index showed the strongest relationship with disease activity parameters, suggesting that it may serve as a practical marker reflecting both inflammatory burden and nutritional status. The associations were more pronounced in geriatric patients, underscoring the influence of age on the interplay between inflammation and nutrition. From a clinical standpoint, integrating these easily obtainable indices into routine evaluation may support physicians in more accurately assessing disease activity and monitoring nutritional–inflammatory status, particularly in older adults.These findings highlight the importance of incorporating simple, laboratory-based nutritional indices into the clinical evaluation of rheumatoid arthritis, especially in older individuals, to better capture disease activity and overall health status. Future prospective, multicenter studies with larger sample sizes and comprehensive nutritional assessments are warranted to confirm these results and to clarify the prognostic utility of these indices in long-term disease management. Furthermore, future AI-driven research may refine and integrate these indices into automated models for predicting disease activity and guiding personalized treatment strategies.

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Ethical Approval and Informed Consent

This study was approved by the Ethics Committee of KTO Karatay University Faculty of Medicine (approval number: 2025/015, dated September 25, 2025).

Authors' Contributions

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contributed to the conceptualization of the study. Data curation was performed by Selma Özlem Çelikdelen and Rümeysa Ertürk. Formal analysis was conducted by Reyhan Bilici. Investigation was carried out by Selma Özlem Çelikdelen and Reyhan Bilici. Writing and editing of the manuscript were performed by Selma Özlem Çelikdelen. Supervision was provided by Reyhan Bilici.

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