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ARTICLE

A Correlation Between Prognostic Nutritional Index and Sarcopenia in Patients With Rheumatoid Arthritis

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Abstract

Aims/Background In rheumatoid arthritis (RA) patients, malnutrition and sarcopenia are commonly associated with poor prognosis. The prognostic nutritional index (PNI), which includes serum albumin levels and lymphocyte counts, reflects the nutritional and inflammatory status of the patient. Therefore, this study aims to assess the relationship between PNI and sarcopenia in RA and examine its role as a diagnostic tool.

Methods This retrospective study analysed data from 178 RA patients hospitalised at Affiliated Jinhua Hospital, Zhejiang University School of Medicine, between June 2023 and June 2025. Sarcopenia was diagnosed following the 2019 Asian Working Group for Sarcopenia (AWGS) criteria. Demographic, clinical, and laboratory data were collected, and PNI was calculated. Univariate and multivariate logistic regression analyses were performed to examine the association between PNI and sarcopenia, and receiver operating characteristic (ROC) curves were used to evaluate its diagnostic performance.

Results Out of the total 178, 56 (31.5%) patients were diagnosed with sarcopenia. Multivariate regression analysis indicated lower PNI as an independent risk factor for sarcopenia (odds ratio [OR] = 0.88, 95% confidence interval [CI]: 0.80–0.97, $p = 0.007$), indicating that each 1-point increase in PNI was associated with a 12% decrease in risk. Older age (OR = 1.07), longer RA disease duration (OR = 1.50), and higher C-reactive protein (CRP) (OR = 1.06) were also independent risk factors. A prediction model combining age, PNI, disease duration, and CRP showed excellent discriminatory ability for sarcopenia, with an area under the curve (AUC) of 0.92 (95% CI: 0.87–0.97, $p < 0.001$), a sensitivity of 95.1%, and a specificity of 80.4%.

Conclusion PNI is a simple, cost-effective measure that integrates nutritional (albumin) and inflammatory (lymphocyte) markers, facilitating early identification of RA patients at higher risk for sarcopenia and providing a basis for timely intervention.

Key words: nutritional assessment; prognostic nutritional index; sarcopenia; rheumatoid arthritis; body composition

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Introduction

Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterised by inflammatory joint damage, affecting about 1% of adults globally (Almutairi et al, 2021; Park et al, 2023). RA is diagnosed following the 2010 the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) classification criteria, which assess scores derived from four domains, including

joint involvement, serological markers, acute-phase reactants, and symptom duration, with a total score of ≥6 confirming RA (Kay and Upchurch, 2012): first-line therapeutic option usually involves conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), like methotrexate. Patients with inadequate response are then treated with biological agents such as anti-tumour necrosis factor inhibitors or targeted synthetic agents like tofacitinib. Additionally, rehabilitation measures such as joint exercises and physical therapy are recommended to preserve joint function (Singh, 2022).

Sarcopenia, a progressive loss of skeletal muscle mass and function, is common in RA patients and is associated with physical dysfunction, an increased risk of falls, diminished quality of life, and potentially worse disease outcomes. The prevalence of sarcopenia in RA patients ranges from 25.9% to 43.3%, driven by interrelated factors, including chronic inflammation, glucocorticoid exposure, reduced physical activity, and malnutrition (Hein et al, 2022; Lian et al, 2022). Nutritional status is crucial to the pathogenesis of sarcopenia; malnutrition accelerates muscle protein catabolism and suppresses synthesis, thereby amplifying the systemic impact of RA (Gumtorntip et al, 2025). Emerging evidence suggests that up to two-thirds of RA patients have inadequate dietary intake and are at risk of malnutrition; however, studies investigating nutritional status in RA patients remain limited (Cano-García et al, 2023).

The prognostic nutritional index (PNI), determined from serum albumin and lymphocyte counts, is a commonly used predictor of nutritional risk and clinical outcomes in patients with cancer and chronic diseases, as well as in surgical settings (Xie et al, 2022; Zeng et al, 2025). Because PNI reflects both nutritional status and the impact of inflammation on nutritional metabolism, it has strong clinical significance. In RA, lower PNI values are associated with higher disease risk and activity, as well as increased all-cause mortality (Gumtorntip et al, 2025; Öz et al, 2024; Wang et al, 2024). Furthermore, PNI has been recognised as an independent predictor of disease activity (Öz et al, 2024).

However, direct evidence associating PNI with sarcopenia in RA is limited, and systematic assessments of PNI as an independent predictor of sarcopenia are scarce. A retrospective study addressing this gap could clarify this link and support PNI as a novel and convenient screening tool to guide tailored nutritional interventions, improve prognosis, and reduce healthcare burden. Incorporating PNI assessment into RA management could enhance collaboration between nutrition science and rheumatology, expand the application of PNI to autoimmune diseases, and lay a theoretical groundwork for developing PNI-based nutritional risk prediction models in RA.

Methods

Study Design

This retrospective study included RA patients hospitalised at Affiliated Jinhua Hospital, Zhejiang University School of Medicine, between June 2023 and June 2025. Inclusion criteria for patient selection were as follows: (1) fulfillment of the

2010 EULAR revised classification criteria for RA (Aletaha et al, 2010; Scott et al, 1987); (2) age ≥18 years; and (3) ability to complete evaluation of muscle mass, grip strength, and gait speed/physical function as required by the 2019 Asian Working Group for Sarcopenia (AWGS) criteria (Chen et al, 2020). Exclusion criteria included: (1) coexisting active malignancy, severe hepatic or renal failure, hematologic or autoimmune diseases, or complications affecting muscle metabolism; (2) use of glucocorticoids or other immunosuppressive drugs within the last 6 months, or presence of drug-induced myasthenia gravis; (3) major trauma or surgery within the past 3 months; (4) hospitalisation for infection or acute infection within the past month; (5) recipient of nutritional interventions or significant dietary changes within the past 3 months; (6) limited activity hindering completion of physical assessment; and (7) incomplete clinical data.

The study protocol was approved by the Medical Ethics Review Committee of Affiliated Jinhua Hospital, Zhejiang University School of Medicine (Approval No. 20252300101). Because the study involved anonymised retrospective data, the requirement for informed consent was waived by the Medical Ethics Review Committee of Affiliated Jinhua Hospital, Zhejiang University School of Medicine. All procedures strictly adhered to the Declaration of Helsinki.

The study initially recruited 220 patients. However, 16 patients were excluded due to comorbidities affecting muscle metabolism, five for recent surgery, eight for drug-induced myopathy that hindered completion of physical assessments, and 13 for missing PNI or sarcopenia data. Ultimately, 178 individuals with RA were included in the final analysis (Fig. 1).

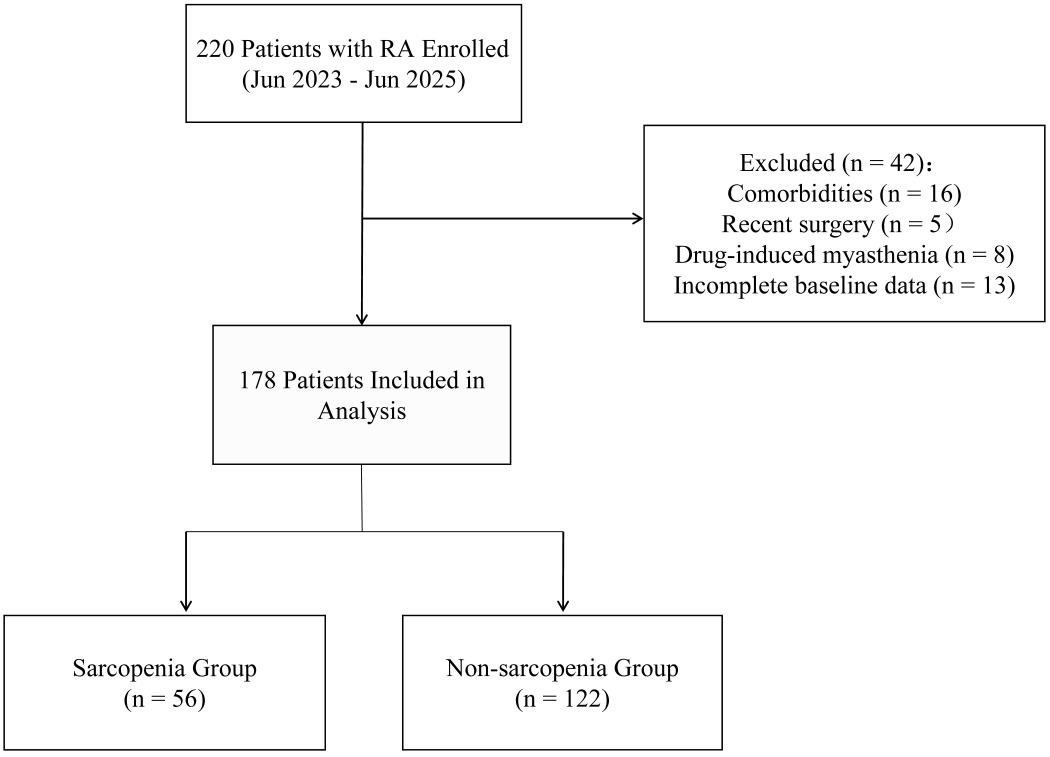

Fig. 1. A flow chart of study design and patient selection. RA, rheumatoid arthritis.

Data Collection

Clinical data were retrospectively obtained from the hospital's electronic medical records. Examined variables included demographics (age, sex, body mass index [BMI], smoking history, alcohol consumption), comorbidities (hypertension, diabetes mellitus, dyslipidemia), RA-specific measures (disease duration, rheumatoid factor [RF] status, anti-cyclic citrullinated peptide antibody [ACPA] status, Disease Activity Score 28 with CRP [DAS28-CRP], Disease Activity Score 28 with ESR [DAS28-ESR]), laboratory parameters (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR], white blood cell count, neutrophil count, lymphocyte count, red blood cell count, hemoglobin, platelet count, total serum protein, albumin, urea, creatinine, uric acid, triglycerides, total cholesterol, high-density lipoprotein cholesterol [HDL-C], and low-density lipoprotein cholesterol [LDL-C]).

All measurements were based on the first laboratory and clinical assessments upon admission. Serum albumin and other biochemical parameters, including total protein, urea, creatinine, uric acid, triglycerides, total cholesterol, HDL-C, and LDL-C, were determined using an AU5800 automated biochemistry analyser (Beckman Coulter, Inc., Brea, CA, USA). CRP levels were quantified by a high-sensitivity immunoturbidimetric assay, and the erythrocyte sedimentation rate (ESR) was assessed using the standard Westergren method. Both CRP and ESR assays were performed according to the manufacturers' instructions (Siemens Healthineers, Erlangen, Germany).

Disease Activity Assessment and Handgrip Strength Measurement

Disease activity was assessed with the 28-joint Disease Activity Score (DAS28) system, using DAS28-CRP (Inoue et al, 2007) and DAS28-ESR (Prevoo et al, 1995). Each score includes the number of swollen and tender joints out of 28 predefined joints, a patient's overall health evaluation on Visual Analog Scale (VAS), and either CRP (mg/L) or ESR (mm/h). DAS28 scores were calculated using the following formulas:

$$\mathrm{DAS28-CRP} = 0.56 \times \sqrt{\mathrm{TJC28}} + 0.28 \times \sqrt{SJC28} + 0.36 \times \ln(CRP + 1) + 0.014 \times GH + 0.96$$

$$DAS28 - ESR = 0.56 \times \sqrt{TJC28} + 0.28 \times \sqrt{SJC28} + 0.70 \times \ln(ESR) + 0.014 \times GH$$

Where TJC28 is the number of tender joints, SJC28 is the number of swollen joints, and GH is the patient's overall health VAS score (0–100 mm).

All joint assessments were independently performed by two trained rheumatologists, and the average value was used for statistical analysis. According to the AWGS consensus, disease activity was graded as follows: DAS28 score >5.1 indicates high disease activity, $3.2 <$ DAS28 ≤ 5.1 moderate activity, $2.6 <$ DAS28 ≤ 3.2 low activity, and DAS28 ≤ 2.6 clinical remission.

Handgrip strength (HGS, kg) of the dominant hand was quantified with a digital hand dynamometer (model SH5003, Sehan Corp., Masan, Korea). The participants were seated with the elbow flexed to 90° and the forearm in a neutral posture between pronation and supination. Three consecutive trials were performed with

the dominant hand, and the mean value was recorded as the participant's maximal HGS. All measurements were conducted by a single trained examiner to ensure consistency and reliability.

Calculation of PNI

The PNI was calculated from serum albumin levels and the peripheral lymphocyte count using the following formula (Shi et al, 2023):

$$\text{PNI} = \text{Albumin}\,(\text{g/L}) + 5 \times \text{Lymphocyte count}\left(\times 10^9/\text{L}\right)$$

Diagnostic Criteria for Sarcopenia

Sarcopenia was diagnosed following the 2019 AWGS criteria and defined as age-related loss of muscle mass combined with low muscle strength and/or poor physical performance (Chen et al, 2020). In this study, muscle strength was assessed using an electronic dynamometer; low muscle strength was defined as a handgrip $<$28 kg in men and $<$18 kg in women. Physical performance was assessed using a 6-meter walking speed test, with a gait speed below 1.0 m/s indicating low performance. Muscle mass was assessed using bioelectrical impedance analysis (BIA); low muscle mass was defined as an appendicular skeletal muscle mass index (ASMI) $<$7.0 kg/m^2 for men and $<$5.7 kg/m^2 for women. Sarcopenia was diagnosed when low muscle mass was observed together with either diminished muscle strength or reduced physical performance.

Sample Size Calculation

Sample size was calculated in PASS 2023 (NCSS, LLC., Kaysville, UT, USA) for a binary logistic regression model using a two-sided α of 0.05 and a statistical power (1-β) of 0.80. As per previous research evidence, the prevalence of sarcopenia in RA patients was found to be 30% (Li et al, 2021), and the minimum clinically significant odds ratio (OR) was set at 2.5. This estimated a required cohort of at least 167 participants.

Furthermore, model stability was examined using the events per variable (EPV) criterion (Peduzzi et al, 1996). The multivariable model incorporated five independent variables, with at least 50 sarcopenia cases expected, yielding an EPV of 10, which meets the recommended methodological standards. Consequently, a cohort of 178 individuals was included in the final analysis, satisfying both statistical power and model robustness requirements.

Statistical Analysis

All statistical analyses were conducted using SPSS (version 27.0; IBM Corp., Armonk, NY, USA) and R (version 4.4.2; R Foundation for Statistical Computing, Vienna, Austria). Normality across continuous variables was examined using the Shapiro-Wilk test, and homogeneity of variance was assessed using Levene's test. Variables following a normal distribution were expressed as mean $\pm$ standard deviation and compared using an independent-samples t-test. Non-normally distributed variables were presented as median (interquartile range) and analysed with

the Mann-Whitney U test. Categorical variables were summarised as frequencies (percentages) and compared using the chi-square test.

Variables achieving a p-value of <0.05 in univariate logistic regression were incorporated into the multivariate model. To minimise collinearity, components of the PNI, such as albumin and lymphocyte count, were excluded. Multicollinearity was determined using the variance inflation factor (VIF), with VIF <10 considered acceptable. Receiver operating characteristic (ROC) curves were generated to assess the predictive performance of PNI, and the Youden index was applied to identify the optimal cutoff for sensitivity, specificity, and predictive accuracy. All statistical tests were two-sided, and a p-value of <0.05 was considered statistically significant.

Results

Comparison of Baseline Characteristics Between Sarcopenia and Non-Sarcopenia Groups

Out of 178 RA patients, 56 (31.5%) had sarcopenia (Table 1). Sarcopenia patients were older ($p = 0.039$) and had a longer disease duration ($p < 0.001$) than the non-sarcopenia group. Furthermore, they showed poorer nutritional and muscle status, as evidenced by lower BMI, handgrip strength, serum albumin, hemoglobin, and PNI (all $p < 0.05$). Moreover, the sarcopenia group had higher inflammatory burden and disease activity, with elevated white blood cell count, CRP, ESR, DAS28-CRP, and DAS28-ESR, along with lower lymphocyte counts (all $p < 0.05$). There were no statistically significant between-group differences in sex distribution, smoking or alcohol history, common comorbidities, rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (ACPA) status, or other laboratory parameters ($p > 0.05$).

Univariate Logistic Regression Analysis of Sarcopenia-Associated Risk Factors

Univariate logistic regression analysis (Table 2) revealed that higher PNI scores were significantly associated with a lower risk of sarcopenia (OR = 0.83, 95% confidence interval [CI]: 0.77–0.89, $p < 0.001$), indicating a 17% reduction in risk per 1-point increase in PNI. Other protective nutritional and immunological markers included serum albumin (OR = 0.81, $p < 0.001$), BMI (OR = 0.90, $p = 0.009$), lymphocyte count (OR = 0.46, $p = 0.012$), and hemoglobin (OR = 0.96, $p = 0.027$). Conversely, older age (OR = 1.03, $p = 0.041$), longer disease duration (OR = 1.46, $p < 0.001$), higher CRP (OR = 1.05, $p = 0.003$), higher ESR (OR = 1.02, $p = 0.011$), higher DAS28-ESR (OR = 1.23, $p = 0.012$), higher DAS28-CRP (OR = 1.24, $p = 0.024$), and elevated white blood cell count (OR = 1.23, $p = 0.035$) were each significantly associated with increased risk.

Multivariate Logistic Regression Analysis of Sarcopenia-Associated Risk Factors

Significant variables from univariate analysis ($p < 0.05$) were incorporated into a multivariate logistic regression model to identify independent sarcopenia risk

Table 1. Baseline characteristics of RA patients.

Variable	Total (n = 178)	Non-sarcopenia (n = 122)	Sarcopenia (n = 56)	Statistic	*p*-value
Age, years	58.52 ± 10.87	57.39 ± 10.66	61.00 ± 10.98	$t = -2.08$	0.039
Female, n (%)	157 (88.20)	106 (86.89)	51 (91.07)	$\chi^2 = 0.65$	0.421
BMI, kg/m^2	23.61 ± 4.23	24.18 ± 4.09	22.36 ± 4.30	$t = 2.72$	0.007
RA duration, years	8.15 (5.80, 11.35)	6.70 (5.23, 8.90)	13.30 (10.17, 18.77)	$Z = -7.75$	<0.001
Smoking, n (%)	26 (14.61)	18 (14.75)	8 (14.29)	$\chi^2 = 0.01$	0.935
Alcohol, n (%)	17 (9.55)	12 (9.84)	5 (8.93)	$\chi^2 = 0.04$	0.848
Hypertension, n (%)	44 (24.72)	27 (22.13)	17 (30.36)	$\chi^2 = 1.40$	0.237
Diabetes, n (%)	19 (10.67)	12 (9.84)	7 (12.50)	$\chi^2 = 0.29$	0.593
Dyslipidemia, n (%)	50 (28.09)	34 (27.87)	16 (28.57)	$\chi^2 = 0.01$	0.923
Grip strength, kg	19.32 ± 3.09	21.11 ± 1.82	15.41 ± 0.88	$t = 28.15$	<0.001
CRP, mg/L	4.95 (1.52, 17.75)	3.05 (1.40, 14.90)	7.50 (2.22, 25.33)	$Z = -2.55$	0.011
ESR, mm/h	30.15 (12.60, 50.55)	24.20 (12.38, 45.60)	39.05 (14.78, 58.85)	$Z = -2.03$	0.043
DAS28-CRP	2.95 (1.44, 4.03)	2.73 (1.19, 3.53)	3.31 (2.64, 4.19)	$Z = -2.88$	0.004
DAS28-ESR	3.59 (1.90, 4.68)	3.31 (1.63, 4.30)	4.09 (3.06, 4.97)	$Z = -2.75$	0.006
ACPA positive, n (%)	128 (71.91)	90 (73.77)	38 (67.86)	$\chi^2 = 0.66$	0.415
RF positive, n (%)	134 (75.28)	93 (76.23)	41 (73.21)	$\chi^2 = 0.19$	0.665
White blood cell counts, 10^9/L	5.93 ± 1.66	5.75 ± 1.52	6.32 ± 1.87	$t = -2.15$	0.033
Neutrophils, 10^9/L	3.86 ± 1.12	3.76 ± 1.08	4.07 ± 1.18	$t = -1.72$	0.087
Lymphocytes, 10^9/L	1.92 ± 0.58	2.00 ± 0.54	1.76 ± 0.63	$t = 2.60$	0.010
Red blood cell counts, 10^{12}/L	4.07 ± 0.38	4.10 ± 0.36	4.01 ± 0.43	$t = 1.50$	0.136
Platelets, 10^9/L	236.57 ± 61.20	234.94 ± 60.20	240.12 ± 63.71	$t = -0.52$	0.602
Hemoglobin, g/L	123.48 ± 8.42	124.44 ± 8.81	121.41 ± 7.13	$t = 2.44$	0.016
Total protein, g/L	67.96 ± 5.20	68.35 ± 4.41	67.13 ± 6.57	$t = 1.27$	0.209
Albumin, g/L	43.54 ± 4.13	44.54 ± 4.12	41.37 ± 3.26	$t = 5.53$	<0.001
Urea, mmol/L	5.02 ± 0.83	4.95 ± 0.87	5.16 ± 0.70	$t = -1.61$	0.109
Creatinine, μmol/L	50.91 ± 9.34	51.60 ± 10.12	49.41 ± 7.21	$t = 1.65$	0.102
Uric acid, μmol/L	246.50 ± 56.58	243.51 ± 53.66	253.02 ± 62.49	$t = -1.04$	0.299
Triglycerides, mmol/L	1.31 ± 0.44	1.29 ± 0.45	1.36 ± 0.42	$t = -0.88$	0.380
Cholesterol, mmol/L	4.85 ± 0.92	4.81 ± 0.99	4.94 ± 0.77	$t = -0.90$	0.370
HDL-C, mmol/L	1.23 ± 0.21	1.24 ± 0.23	1.21 ± 0.17	$t = 0.82$	0.413
LDL-C, mmol/L	2.89 ± 0.89	2.86 ± 0.85	2.93 ± 0.96	$t = -0.46$	0.646
PNI	53.16 ± 5.22	54.53 ± 4.87	50.17 ± 4.71	$t = 5.60$	<0.001

Abbreviations: RA, rheumatoid arthritis; BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; DAS28-CRP, Disease Activity Score 28 with CRP; DAS28-ESR, Disease Activity Score 28 with ESR; ACPA, anti-cyclic citrullinated peptide antibody; RF, rheumatoid factor; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PNI, prognostic nutritional index.

Table 2. Univariate logistic regression of sarcopenia-related risk factors.

Variable	β	SE	Z	p-value	OR (95% CI)
Sex					
Male					1.00 (Reference)
Female	0.43	0.54	0.80	0.424	1.54 (0.53–4.44)
Smoking					
No					1.00 (Reference)
Yes	–0.04	0.46	–0.08	0.935	0.96 (0.39–2.37)
Alcohol					
No					1.00 (Reference)
Yes	–0.11	0.56	–0.19	0.848	0.90 (0.30–2.69)
Hypertension					
No					1.00 (Reference)
Yes	0.43	0.36	1.18	0.239	1.53 (0.75–3.13)
Diabetes					
No					1.00 (Reference)
Yes	0.27	0.51	0.53	0.594	1.31 (0.49–3.53)
Dyslipidemia					
No					1.00 (Reference)
Yes	0.03	0.36	0.10	0.923	1.04 (0.51–2.09)
ACPA positive					
No					1.00 (Reference)
Yes	–0.29	0.35	–0.81	0.416	0.75 (0.38–1.50)
RF positive					
No					1.00 (Reference)
Yes	–0.16	0.37	–0.43	0.665	0.85 (0.41–1.76)
Age	0.03	0.02	2.04	0.041	1.03 (1.01–1.07)
BMI	–0.11	0.04	–2.63	0.009	0.90 (0.83–0.97)
RA duration	0.38	0.06	6.15	<0.001	1.46 (1.30–1.65)
CRP	0.04	0.02	2.99	0.003	1.05 (1.02–1.08)
ESR	0.02	0.01	2.55	0.011	1.02 (1.01–1.03)
DAS28-ESR	0.21	0.08	2.52	0.012	1.23 (1.05–1.45)
DAS28-CRP	0.22	0.10	2.25	0.024	1.24 (1.03–1.51)
White blood cell counts	0.21	0.10	2.11	0.035	1.23 (1.01–1.50)
Neutrophils	0.25	0.15	1.70	0.089	1.29 (0.96–1.72)
Lymphocytes	–0.78	0.31	–2.52	0.012	0.46 (0.25–0.84)
Red blood cell counts	–0.67	0.45	–1.49	0.137	0.51 (0.21–1.24)
Hemoglobin	–0.04	0.02	–2.21	0.027	0.96 (0.92–0.99)
Platelets	0.00	0.00	0.53	0.600	1.00 (1.00–1.01)
Total protein	–0.05	0.03	–1.45	0.147	0.95 (0.90–1.02)
Albumin	–0.21	0.05	–4.52	<0.001	0.81 (0.74–0.89)
Urea	0.31	0.20	1.60	0.110	1.37 (0.93–2.01)
Creatinine	–0.03	0.02	–1.45	0.148	0.97 (0.94–1.01)
Uric acid	0.00	0.00	1.04	0.298	1.00 (1.00–1.01)
Triglycerides	0.33	0.37	0.88	0.378	1.38 (0.67–2.85)
Cholesterol, mmol/L	0.15	0.18	0.82	0.411	1.16 (0.82–1.64)
HDL-C, mmol/L	–0.57	0.77	–0.75	0.456	0.56 (0.13–2.54)
LDL-C, mmol/L	0.08	0.18	0.46	0.644	1.09 (0.76–1.56)
PNI	–0.19	0.04	–4.85	<0.001	0.83 (0.77–0.89)

Abbreviations: RA, rheumatoid arthritis; BMI, body mass index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; DAS28-CRP, Disease Activity Score 28 with CRP; DAS28-ESR, Disease Activity Score 28 with ESR; RF, rheumatoid factor; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PNI, prognostic nutritional index; SE, standard error; OR, odds ratio; CI, confidence interval.

Table 3. Multivariate logistic regression analysis of sarcopenia-associated risk factors.

Variable	β	SE	Z	p-value	OR (95% CI)
PNI	–0.13	0.05	–2.68	0.007	0.88 (0.80–0.97)
Age	0.07	0.03	2.53	0.011	1.07 (1.02–1.13)
BMI	–0.10	0.06	–1.83	0.067	0.90 (0.81–1.01)
RA duration	0.41	0.08	5.44	<0.001	1.50 (1.30–1.74)
CRP	0.05	0.02	2.33	0.020	1.06 (1.01–1.11)
Hemoglobin	–0.05	0.03	–1.60	0.110	0.95 (0.89–1.01)

factors. To minimise multicollinearity, PNI components such as serum albumin and lymphocyte count and other indicators, including white blood cell count, ESR levels, DAS28-ESR, and DAS28-CRP (VIF $\geq$10) were all excluded from the analysis. The final adjusted model included PNI, age, BMI, RA disease duration, CRP levels, and hemoglobin. As detailed in Table 3, after adjusting for confounders, decreased PNI (OR = 0.88, 95% CI: 0.80–0.97, p = 0.007), older age (OR = 1.07, 95% CI: 1.02–1.13, p = 0.011), longer RA duration (OR = 1.50, 95% CI: 1.30–1.74, $p <$ 0.001), and higher CRP (OR = 1.06, 95% CI: 1.01–1.11, p = 0.020) were identified as independent risk factors for sarcopenia. These observations indicated a 12% reduction in sarcopenia risk per 1-point increase in the PNI. However, BMI and hemoglobin were not significant predictors ($p > 0.05$).

Diagnostic Value of the Model for Sarcopenia

Using the predicted indicators, we developed a sarcopenia risk prediction model incorporating age, PNI, RA duration, and CRP. The model showed excellent discriminative performance, with an area under the curve (AUC) of 0.92 (95% CI: 0.87–0.97, $p < 0.001$). The Youden index showed an optimal cut-off value of 0.476, with a sensitivity of 95.1%, a specificity of 80.4%, a positive predictive value of 91.3%, and a negative predictive value of 88.2%. These findings suggest a stronger ability of the model to identify high-risk patients (Fig. 2).

Discussion

Analysing 178 RA patients, this study provides the first systematic evaluation of the association between PNI and sarcopenia in RA, and assesses their diagnostic significance. This study identified PNI as an independent risk factor for sarcopenia, and a model combining PNI with age, RA disease duration, and CRP revealed excellent discriminative performance (AUC = 0.92).

Multivariate regression analysis revealed a significant negative association between PNI and sarcopenia, with each 1-point increase in PNI reducing sarcopenia risk by 12%. This finding is consistent with previous evidence supporting the significance of PNI in sarcopenia risk assessment (Cheng et al, 2025). Because PNI incorporates serum albumin and lymphocyte count, it reflects both nutritional status and systemic inflammation (Wang et al, 2024). Low PNI usually indicates protein-energy malnutrition and an impaired lymphocyte-mediated immune response, conditions that promote muscle protein catabolism and inhibit protein

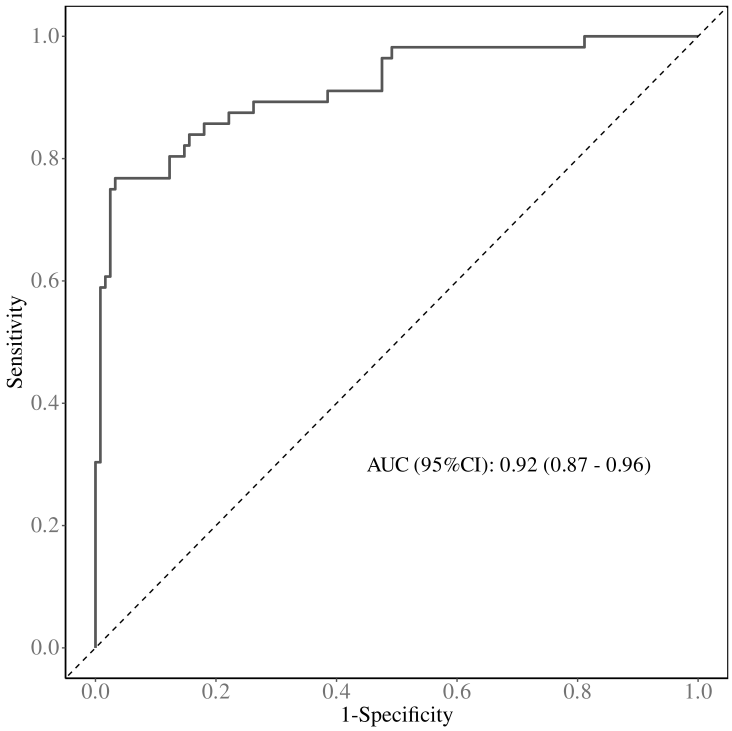

Fig. 2. ROC curve analysis and diagnostic performance of the model. ROC, receiver operating characteristic; AUC, area under the curve.

synthesis, thereby accelerating the onset and progression of sarcopenia (Lozada-Mellado et al, 2024; Öz et al, 2024; Torii et al, 2023). Mechanistically, the negative association between PNI and sarcopenia likely reflects the hypermetabolic and inflammatory characteristics of RA.

Pro-inflammatory cytokines promote muscle protein degradation via the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) signalling pathway; hypoalbuminemia indicates a hepatic shift towards acute-phase protein synthesis (e.g., CRP) rather than nutritional proteins; and lymphopenia reflects immune dysregulation that may further exacerbate muscle inflammation. Therefore, chronic inflammation is central to sarcopenia pathogenesis. In this study, patients with sarcopenia showed increased CRP, ESR, and DAS28 values alongside reduced PNI. Similarly, previous studies have shown that inflammatory mediators in RA directly activate muscle atrophy-related signalling pathways, while hypoalbuminemia reduces muscle repair capacity, creating a vicious cycle of inflammation and nutritional imbalance (Brance et al, 2021; Lozada-Mellado et al, 2024; Nakayama et al, 2024).

Epidemiological evidence further supports this association. In a large cohort (n = 8058), individuals in the highest PNI quartile had a 52% lower risk of sarcopenia compared to those in the lowest quartile (Cheng et al, 2025). Additionally, low PNI has also been correlated with higher RA disease activity (DAS28), suggesting that nutritional deficits and chronic inflammation may synergistically promote the onset and progression of sarcopenia (Öz et al, 2024). Moreover, some studies claim that nutritional interventions such as ω-3 fatty acid supplementation or

a Mediterranean-style diet can support muscle function by reducing inflammatory responses, although randomised controlled trials in RA populations remain limited (Fernández-Lázaro et al, 2024; Wunderle et al, 2024).

This study underscores the limitations of traditional nutritional indicators in evaluating sarcopenia. Multivariate regression analysis showed that BMI and hemoglobin were not independent predictors, suggesting that single parameters may not accurately reflect true muscle status in chronic inflammatory diseases. Specifically, BMI can be misleading: RA often involves muscle loss accompanied by compensatory fat gain, which may keep BMI stable or even elevated (Doubek et al, 2022). In our study, although BMI was slightly lower in the sarcopenia group, its predictive value disappeared after adjustment for confounders, confirming its limited utility for assessing muscle mass during chronic inflammation. Hemoglobin, while related to anaemia, was likewise not an independent predictor, likely because its effects are captured by PNI or overlap with inflammatory markers. Moreover, a previous study reporting lower prealbumin levels in sarcopenia and a stronger association between PNI and hemoglobin further supports the notion that PNI, as a composite measure, is more stable and predictive than single nutritional indicators (Pénichoux et al, 2023).

The multivariate regression model identified additional independent risk factors beyond PNI: older age, longer disease duration, and higher CRP. Longer disease duration is linked to persistent inflammatory damage and reduced physical activity, accelerating muscle loss (Nakayama et al, 2024). Age-related decline in muscle mass, accompanied by inflammation, significantly increases disease risk (Cano-García et al, 2023). Consistent with previous studies. CRP independently predicted sarcopenia in our model, and its level correlates with pro-inflammatory cytokines, highlighting the central role of chronic inflammation in sarcopenia pathogenesis (Brance et al, 2021; Lozada-Mellado et al, 2024).

This study further substantiates the diagnostic application of PNI. ROC analysis showed that a model combining PNI with age, BMI, RA disease duration, and CRP achieved an AUC of 0.92, indicating excellent discriminatory ability and supporting its reliability as a tool for assessing sarcopenia risk in RA patients. This result outperforms previous single-parameter approaches; for example, PNI alone in predicting RA disease activity yielded an AUC of only about 0.66 (Öz et al, 2024). The improvement here can be attributed to the synergistic contributions of multiple factors: PNI reflects nutritional and inflammatory status; age captures age-related muscle decline; BMI relates to obesity-associated inflammation; RA duration indicates chronic disease burden; and CRP indicates systemic inflammation. This integrative approach addresses the multifactorial pathophysiology of sarcopenia in RA, where immune-mediated muscle catabolism interacts with hypoalbuminemia to accelerate muscle loss.

Although PNI is not a definitive diagnostic tool like Dual-energy X-ray Absorptiometry (DXA), its simplicity—using routine laboratory parameters (albumin and lymphocyte counts)—offers substantial practical value in resource-limited settings, especially for rapid screening of high-risk patients in primary care, thereby enabling early intervention (Utsumi et al, 2024).

Despite several promising findings, we acknowledge certain limitations to this study. Its single-centre, retrospective design and limited sample size may affect the broader applicability and generalizability of the findings. Additionally, several known confounding factors that influence muscle metabolism and nutritional status were not captured, including physical activity, dietary patterns, and medication history. Physical activity and nutritional status are crucial for maintaining muscle mass and function, and medications, particularly glucocorticoids, are closely associated with muscle wasting. Excluding these variables may reduce the accuracy of the results and also limit the depth of causal inferences.

Furthermore, lifestyle factors, particularly physical activity, may influence the PNI and potentially confound its association with sarcopenia. To improve the accuracy of PNI as a predictive tool for sarcopenia, future studies should incorporate these variables and analytically adjust for them. Additionally, using muscle imaging techniques and profiling inflammatory cytokines would further elucidate the biological mechanisms linking PNI to sarcopenia. Such approaches would also guide the development of early intervention strategies for those with low PNI, including individualised nutritional support and anti-inflammatory therapies, to enhance the prevention and management of sarcopenia.

Conclusion

This study identified lower PNI as an independent predictor of sarcopenia in RA patients. As a simple, cost-effective composite reflecting nutritional (albumin) and inflammatory (lymphocyte) status, PNI—combined with age, disease duration, and CRP—can help identify individuals at high risk. In clinical practice, PNI may facilitate early identification of RA patients at risk of sarcopenia and provide timely preventive measures. However, the single-centre, retrospective design and limited sample size limit the generalizability of our findings, warranting future validation. Prospective, multicentre investigations should explore whether early nutritional or anti-inflammatory interventions mitigate the clinical burden of sarcopenia among patients with low PNI.

Key Points

- Low PNI serves as an independent risk factor for sarcopenia in RA patients.
- Each 1-point increase in PNI reduces sarcopenia risk by 12% in RA patients.
- Out of the total 178 RA patients, 31.5% developed sarcopenia, with older age, longer RA duration, and higher CRP being observed as associated risk factors.
- A model combining PNI, age, RA duration, and CRP achieved an AUC of 0.92 for sarcopenia diagnosis.
- PNI's simplicity and cost-effectiveness make it an ideal tool for early sarcopenia screening in RA patients.

Availability of Data and Materials

The data and materials in the current study are available from the corresponding author on reasonable request.

Author Contributions

XWS, YFW and LH designed the study. XWS conducted the literature search. YFW acquired the data. XWS wrote the article and performed data analysis. LH revised the article. All authors contributed to the important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study protocol was approved by the Medical Ethics Review Committee of Affiliated Jinhua Hospital, Zhejiang University School of Medicine (Approval No. 20252300101). Because the study involved anonymised retrospective data, the requirement for informed consent was waived by the Medical Ethics Review Committee of Affiliated Jinhua Hospital, Zhejiang University School of Medicine. All procedures strictly adhered to the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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