

A Nomogram Model for Rheumatoid Arthritis-Related Low Muscle Strength was Developed Based on the HALP Score Combined With Clinical Characteristics

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Background: Low muscle strength is a common but underrecognized complication of rheumatoid arthritis (RA), associated with functional disability, impaired mobility, reduced quality of life, and adverse health outcomes. This study aimed to identify factors associated with low muscle strength in RA patients and evaluate the incremental value of the hemoglobin, albumin, lymphocyte, and platelet (HALP) score for its identification.

Methods: This retrospective multicenter study included patients with RA who were hospitalized in the Departments of Nephrology, Rheumatology and Immunology at Jinhua Hospital of Traditional Chinese Medicine and Lanxi Hospital of Traditional Chinese Medicine between January 2022 and June 2026. Univariate and multivariate logistic regression analyses were performed to identify factors associated with low muscle strength. Multicollinearity among candidate variables was assessed using the variance inflation factor (VIF). To evaluate the incremental value of HALP beyond the clinical-variable selection process, the Clinical Base Model was initially established without including HALP. After the Clinical Base Model was finalized, HALP was added as a single additional variable to construct the nested Base + HALP Model. The incremental discriminative performance of the HALP score was evaluated by comparing changes in the area under the receiver operating characteristic curve (Δ AUC), integrated discrimination improvement (IDI), and net reclassification improvement (NRI). Decision curve analysis (DCA) was performed to assess the estimated net benefit of each model across a range of risk thresholds. Internal validation was conducted using bootstrap resampling, and sensitivity analysis was performed among patients aged ≥ 50 years using the same analytical procedures.

Results: A total of 220 patients with RA were included, of whom 81 (36.8%) had low muscle strength. Compared with patients without low muscle strength, those with low muscle strength were older, had lower body mass index (BMI) and HALP scores, higher erythrocyte sedimentation rate disease activity score (DAS28-ESR) values, and were more likely to be female. Multivariate logistic regression analysis identified age, sex, BMI, DAS28-ESR, current glucocorticoid (GC) use, and HALP score as independent factors associated with low muscle strength. The clinical base model demonstrated an apparent AUC of 0.784 (95% confidence interval (CI), 0.722–0.847). After the addition of the HALP score, the AUC increased to 0.829 (95% CI, 0.775–0.883), with a Δ AUC of 0.045 (DeLong test, $p = 0.020$). The Base + HALP model also demonstrated improved classification performance, with an NRI of 0.663 (95% CI, 0.402–0.924; $p = 0.001$) and an IDI of 0.072 (95% CI, 0.039–0.107; $p = 0.002$). After 1000-bootstrap internal validation, the AUCs of the clinical base and Base + HALP model were 0.766 (95% CI, 0.707–0.826) and 0.809 (95% CI, 0.757–0.863), respectively. Decision curve analysis demonstrated that the Base + HALP model provided a greater estimated net benefit than the clinical base model and the treat-all and treat-none strategies, particularly across threshold probabilities from approximately 10% to 60%.

Conclusions: The HALP score, age, sex, BMI, DAS28-ESR and current GC use were independently associated with low muscle strength in patients with RA. The Base + HALP Model demonstrated good discrimination, calibration and estimated net benefit. However, further independent external validation and prospective studies are still needed in the future to clarify the role of this model.

Keywords: HALP score; RA; low muscle strength; nomogram; identification model

Introduction

Rheumatoid arthritis (RA) is a chronic systemic autoimmune inflammatory disease that primarily affects the joints and surrounding soft tissues. Its pathogenesis involves genetic susceptibility, abnormal immune cell activation, and dysregulation of inflammatory factor networks, and it is often accompanied by functional impairment of the skeletal muscle system [1]. Sarcopenia is characterized by reductions in muscle mass, strength, and physical function, and is associated with increased risks of falls, fractures, disability, and death [2,3]. Patients with RA have a high risk of sarcopenia, with a reported prevalence exceeding 31% [4]. RA related sarcopenia not only increases the risks of falls, fractures and dysfunction, but also substantially affects patients' quality of life and long-term prognosis [5]. Previous studies have shown that RA patients with sarcopenia are generally older, have longer disease duration, and exhibit higher levels of inflammatory cytokines compared with those without sarcopenia [6]. These findings suggest that chronic systemic inflammation, increased disease activity, reduced physical activity, and impaired nutritional status may collectively contribute to the deterioration of skeletal muscle structure and function in patients with RA.

The underlying mechanisms are multifactorial. Within the inflammatory microenvironment of RA, elevated levels of pro-inflammatory cytokines (such as tumor necrosis factor- α , interleukin-1 β and interleukin-6) promote muscle atrophy by accelerating protein degradation and inhibiting muscle regeneration [7]. Malnutrition, particularly inadequate protein intake, adversely affects muscle protein synthesis, a key process involved in the pathogenesis of sarcopenia [8]. These interconnected inflammatory and nutritional disturbances underscore the need for composite biomarkers capable of simultaneously capturing both dimensions.

Recently, the hemoglobin, albumin, lymphocyte and platelet (HALP) score has been proposed as a simple, economical and reproducible composite assessment index [9]. The score integrates measurements of hemoglobin, albumin, lymphocytes and platelets levels, which may reflect nutritional status, immune function, and inflammatory activity to some extent [10]. Although the HALP score has demonstrated potential clinical utility in various diseases, its association with low muscle strength in patients with RA remains unclear. Previous studies have suggested that the HALP score is negatively correlated with the prevalence of low muscle mass and related mortality [11]. However, evidence remains limited regarding whether the HALP score can further improve the identification performance of low muscle strength.

According to the Asian Working Group for Sarcopenia (AWGS) 2025 consensus, the conceptual framework has shifted from sarcopenia to muscle health, and routine screening for low muscle strength using handgrip strength

assessment is recommended in patients with chronic conditions, including heart failure, chronic obstructive pulmonary disease, diabetes mellitus, and chronic kidney disease [12]. Given that RA shares similar chronic inflammatory and nutritional vulnerabilities, systematic screening for low muscle strength in this population is also warranted.

Therefore, this study aimed to investigate factors associated with low muscle strength in patients with RA and to evaluate the incremental identification value of the HALP score. Furthermore, we constructed and internally validated a nomogram model integrating the HALP score with clinical characteristics.

Methods

Study Design

This retrospective multicenter study included patients with RA who were hospitalized in the Departments of Nephrology, Rheumatology and Immunology at Jinhua Hospital of Traditional Chinese Medicine and Lanxi Hospital of Traditional Chinese Medicine between January 2022 and June 2026. The study was approved by the Institutional Ethics Committees (approval no. 2026-048; approval no. LZY-LSL-202608). Because this retrospective study used anonymized routinely collected clinical data, the requirement for written informed consent was waived by the respective Ethics Committees. All procedures were performed in strict accordance with the Declaration of Helsinki. A total of 356 patients were initially enrolled, of whom 136 were excluded due to age, missing data, or comorbidities affecting muscle metabolism. Ultimately, 220 patients with RA were included in the analysis. The detailed patient screening process and reasons for exclusion are presented in Fig. 1.

The inclusion criteria were as follows: (1) age 18–80 years; (2) fulfilment of the 2010 American College of Rheumatology/European League against Rheumatism (ACR/EULAR) RA classification criteria [13]; (3) complete assessment data for muscle strength; and (4) complete blood routine and clinical characteristics data. The exclusion criteria were as follows: (1) concomitant systemic autoimmune or inflammatory rheumatic diseases, such as systemic lupus erythematosus, systemic sclerosis, spondyloarthritis, etc.; (2) neuromuscular diseases (such as muscular dystrophy, myasthenia gravis, motor neuron disease, etc.) that clearly affect skeletal muscle structure or function; (3) active malignant tumors; (4) diseases that may significantly affect serum albumin levels (such as severe liver failure, decompensated cirrhosis, nephrotic syndrome, etc.); (5) recent major trauma, major surgery, prolonged bed rest, or other conditions that may lead to acute muscle loss; and (6) obvious hematological diseases or recent blood transfusion that could substantially affect hemoglobin, lymphocyte, or platelet counts.

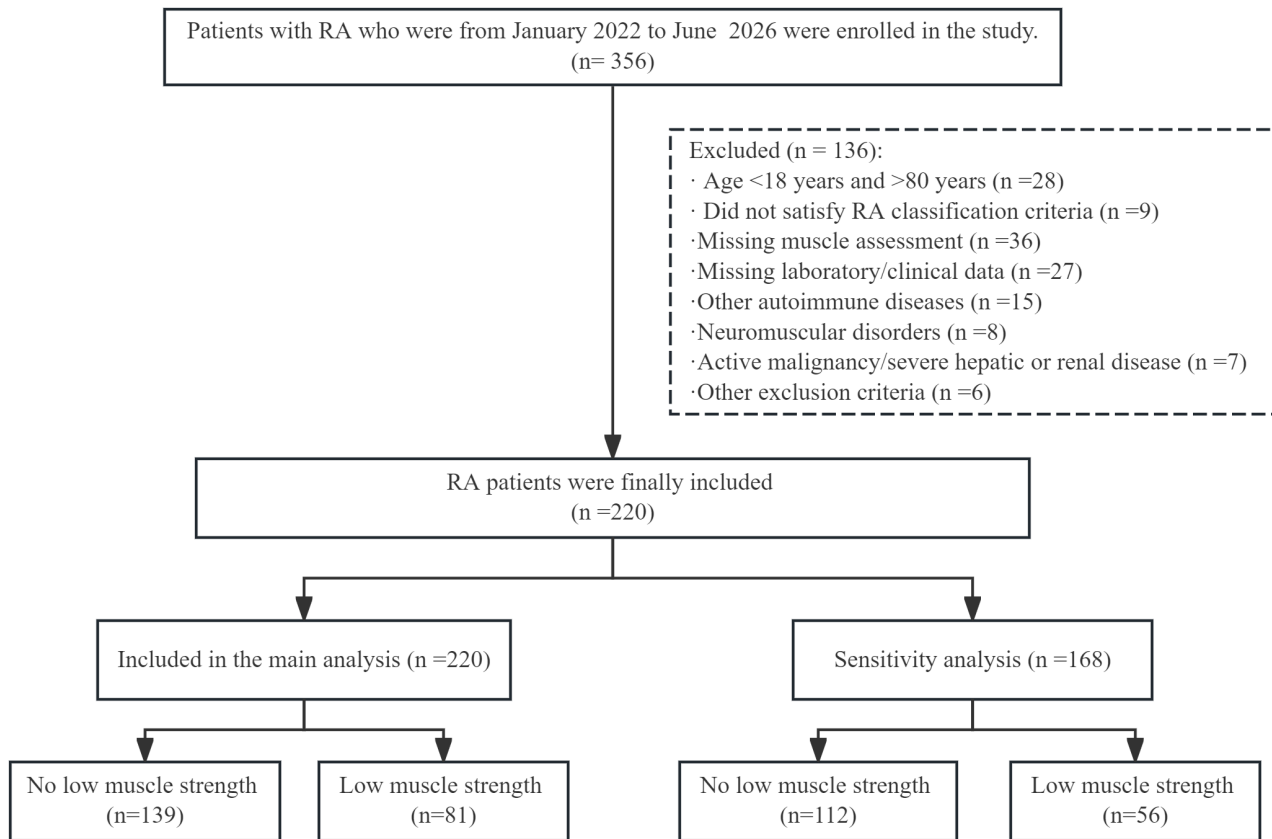


Fig. 1. Flow diagram of the study population. The figure was created by the authors using Microsoft PowerPoint 2019 (Microsoft Corporation, Redmond, WA, USA).

Data Collection

Clinical data were retrospectively collected from the hospital electronic medical records. The examined variables included demographic characteristics (age, sex, body mass index (BMI), smoking history), comorbidities (hypertension, diabetes, chronic kidney disease), RA-specific characteristics (RA duration, rheumatoid factor (RF), current glucocorticoid (GC) use, erythrocyte sedimentation rate (ESR) disease activity score (DAS28-ESR)) and laboratory parameters (lymphocyte count, hemoglobin, platelet count, and albumin). All measurements were obtained from the initial laboratory tests and clinical assessments performed at admission. Serum albumin and other biochemical parameters were measured using an AU5800 automated biochemical analyzer (Beckman Coulter, Inc., Brea, CA, USA). ESR was measured using the standard Westergren method according to the manufacturer's instructions (Siemens Healthcare, Erlangen, Germany).

The DAS28-ESR was calculated using the following formula

$$\text{DAS28-ESR} = 0.56 \times \sqrt{\text{TJC28}} + 0.28 \times \sqrt{\text{SJC28}} + 0.70 \times \ln(\text{ESR}) + 0.014 \times \text{GH} \quad (1)$$

DAS28-ESR represents the disease activity score based on the assessment of 28 joints and erythrocyte sedimentation rate. TJC28 represents the number of tender joints among the 28 assessed joints. SJC28 represents the number of swollen joints among the 28 assessed joints. ESR represents erythrocyte sedimentation rate in mm/h; GH represents the patient's global health assessment, measured using a 100-mm visual analogue scale, where 0 mm indicates the best possible health status and 100 mm indicates the worst possible health status.

The HALP score was calculated using the following formula [14]:

$$\text{HALP} = \frac{\text{Hemoglobin(g/L)} \times \text{Albumin(g/L)} \times \text{Lymphocyte}(\times 10^9/\text{L})}{\text{Platelet}(\times 10^9/\text{L})} \quad (2)$$

Measurement and Assessment of Low Muscle Strength

Grip Strength Measurement

Grip strength was measured using a CAMRY EH101 electronic hand dynamometer (Zhongshan Camry Electronic Co., Ltd., Zhongshan, China), with a measurement range of 1–90 kg, a resolution of 0.1 kg, and a permissible measurement error of ± 0.5 kg according to the manu-

facturer's specifications. During testing, participants stood with their upper limbs relaxed alongside the body and exerted maximal force on the dynamometer until the reading stabilized. Each hand was measured twice, and the maximum value from the two trials was recorded for each hand. According to the handgrip-strength measurement approach recommended by the AWGS 2025 consensus, the highest value obtained from all measurements of both hands was used as the final grip-strength value for classifying low muscle strength.

Assessment of Low Muscle Strength

The primary outcome of this study was low muscle strength, a key component of the sarcopenia syndrome. Because the study population covered a broad age range (18–80 years) and grip strength varies substantially according to age and sex, age- and sex-specific CNHS P25 values were used as an operational population-referenced definition of relatively low grip strength in the primary analysis. The P25 threshold was not intended to replace established consensus diagnostic criteria for sarcopenia [15]. The specific cutoff values for each age group among men and women were as follows (Table 1).

Table 1. Age- and sex-specific 25th percentile cutoff values for handgrip strength based on the China National Health Survey.

P ₂₅	Male	Female
18–19 years	<33.5 kg	<20 kg
20–29 years	<37 kg	<21 kg
30–39 years	<37 kg	<22 kg
40–49 years	<36 kg	<22 kg
50–59 years	<32 kg	<19 kg
60–69 years	<28 kg	<17 kg
70–80 years	<22 kg	<14 kg

To assess the robustness of the findings using an alternative consensus-based definition, the AWGS 2025 thresholds [12] were applied in a sensitivity analysis among participants aged ≥50 years (Table 2).

Table 2. Age- and sex-specific handgrip strength cutoff values for low muscle strength according to the AWGS 2025 criteria.

Age group, years	Male	Female
50–64	<34 kg	<20 kg
≥65	<28 kg	<18 kg

Model Complexity and Events-Per-Variable Assessment

Model complexity was assessed using the events-per-variable (EPV) approach. Following univariate analysis,

eight candidate variables were entered into the multivariate logistic regression analysis, including age, BMI, HALP score, DAS28-ESR, sex, RF status, current glucocorticoid use, and RA disease duration. With 81 events of low muscle strength, the EPV was 10.1 (81/8), meeting the commonly used benchmark of approximately 10 events per candidate variable. After multivariate adjustment, six variables—age, sex, BMI, DAS28-ESR, current glucocorticoid use, and HALP score—remained independently associated with low muscle strength and were subsequently included in the final model construction.

Statistical Analysis

All analyses were performed using R software (version 4.3.0, R Foundation for Statistical Computing, Vienna, Austria). The Kolmogorov-Smirnov test was used to assess the distribution characteristics of continuous variables. Normally distributed continuous variables were presented as mean ± standard deviation, and comparisons between groups were performed using the independent sample *t*-test. Non-normally distributed variables were presented as median (interquartile range) [M (P₂₅, P₇₅)], and comparisons between groups were performed using the Mann-Whitney U test. Categorical variables were presented as number of cases (percentage) [n (%)], and comparisons between groups were performed using the χ^2 test or Fisher exact probability method.

Taking low muscle strength as the dependent variable, univariate logistic regression analysis was performed to screen candidate factors associated with low muscle strength, and the odds ratio (OR) and 95% confidence interval (95% CI) were calculated for each variable. Variables were selected for inclusion in the multivariable logistic regression model based on clinical relevance and a *p* value < 0.10 in the univariable analyses. The variance inflation factor (VIF) was used to assess multicollinearity among independent variables. A VIF ≥5 indicated the presence of multicollinearity, requiring model refitting after excluding or combining relevant variables. Variables that remained statistically significant after multivariate adjustment were considered independently associated with low muscle strength. The formula of the multivariate logistic regression model was as follows:

$$\log \text{it}(p) = \ln \frac{p}{1-p} = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_k X_k \quad (3)$$

Where *p* represents the probability of low muscle strength, β_0 represents the intercept, β_1 – β_k represent the regression coefficients of the independent variables, and X_1 – X_k represent the independent variables included in the model.

The Clinical Base Model was established using a clinically informed, HALP-independent variable-selection strategy. Conventional clinical candidate variables were

initially identified based on clinical relevance and evidence from previous studies. HALP was excluded from all stages of Clinical Base Model development. After the Clinical Base Model was established and finalized, HALP was added as a single additional variable to construct the nested Base + HALP Model.

Model discrimination was assessed using the area under the receiver operating characteristic curve (AUC), and the change in AUC (Δ AUC) was calculated. Accuracy, sensitivity, and specificity for each model were derived from the receiver operating characteristic (ROC) curve based on the predicted probabilities. The primary cutoff value was defined as the predicted probability corresponding to the maximum Youden index. The incremental value of the HALP score in improving model identification performance was quantified using the integrated discrimination improvement (IDI) and net reclassification improvement (NRI). Additionally, decision curve analysis (DCA) was performed to evaluate the estimated net benefit of each model across a range of risk thresholds. Internal validation was conducted using 1000 bootstrap resamples to assess model calibration through calibration curves and model discrimination through the optimism-corrected C-statistic. Optimism-corrected AUCs were obtained from the bootstrap validation procedure, with 95% CIs defined by the 2.5th and 97.5th percentiles of the bootstrap distribution of the optimism-corrected AUC.

To assess the robustness of the findings using an alternative definition of low muscle strength, a sensitivity analysis was performed among participants aged ≥ 50 years according to the AWGS 2025 criteria. Low muscle strength was redefined based on the AWGS 2025 thresholds. Univariable logistic regression analysis was first performed, and variables with $p < 0.10$ were entered into the multivariable model, with ORs and 95% CIs reported. For the model-performance sensitivity analysis, the same fixed variable sets as those used in the primary analysis were retained: age, sex, BMI, DAS28-ESR, and current glucocorticoid use for the Clinical Base Model, with HALP additionally included in the Base + HALP Model. The models were refitted in the subgroup, and their discrimination, calibration, and decision-curve performance were reassessed.

Results

Baseline Data

A total of 220 patients with RA were enrolled in this study, including 81 (36.8%) patients with low muscle strength. Compared with patients without low muscle strength, those with low muscle strength were significantly older [68.00 (60.00, 73.00) vs. 62.00 (57.00, 69.00) years, $p < 0.001$], had lower BMI (22.36 ± 3.54 vs. 23.81 ± 3.44 kg/m², $p = 0.004$), and exhibited lower HALP scores [26.61 (23.49, 34.89) vs. 37.18 (27.68, 43.40), $p < 0.001$]. Additionally, patients with low muscle strength had higher

disease activity, as assessed by DAS28-ESR (4.22 ± 0.61 vs. 3.85 ± 0.60 , $p < 0.001$), were more likely to be female (79.01% vs. 62.59%, $p = 0.011$), and had a higher prevalence of rheumatoid factor positivity (79.01% vs. 65.47%, $p = 0.034$). Furthermore, current GC use (49.38% vs. 23.74%, $p < 0.001$) and RA duration ≥ 10 years (38.27% vs. 18.71%, $p = 0.001$) were more common among patients with low muscle strength. No statistically significant differences were observed between the two groups in terms of smoking status, hypertension, diabetes, or chronic kidney disease (all $p > 0.05$) (Table 3).

Logistic Regression Analysis of Factors Associated With Low Muscle Strength in Patients With RA

Univariate logistic regression analysis identified age, BMI, HALP score, DAS28-ESR, sex, rheumatoid factor positivity, current GC use, and RA duration as factors associated with low muscle strength (all $p < 0.1$) (Table 4). These variables were subsequently entered into the multivariate logistic regression model. Multivariate analysis revealed that age (OR 1.06, 95% CI 1.02–1.10, $p = 0.004$), female sex (OR 3.14, 95% CI 1.45–7.21, $p = 0.005$), DAS28 ESR (OR 2.51, 95% CI 1.38–4.76, $p = 0.003$), and current GC use (OR 2.55, 95% CI 1.24–5.31, $p = 0.011$) were independently associated with low muscle strength. In contrast, BMI (OR 0.87, 95% CI 0.78–0.96, $p = 0.009$) and HALP score (OR 0.93, 95% CI 0.89–0.96, $p < 0.001$) were negatively associated with low muscle strength. No significant multicollinearity was detected among the variables. Rheumatoid factor positivity and RA duration ≥ 10 years were not significantly associated with low muscle strength in the multivariate model.

Incremental Identification Value of the HALP Score

When the Clinical Base Model was established independently without HALP, age, sex, BMI, DAS28-ESR, and current glucocorticoid use remained significantly associated with low muscle strength, whereas RF status and RA disease duration were not statistically significant. The HALP score was subsequently added to the clinical base model to construct the extended model (Base + HALP Model). As shown in Table 5, incorporation of the HALP score into the clinical base model improved discrimination and reclassification performance. At the model-specific maximum-Youden index cutoffs, the Base + HALP model demonstrated higher sensitivity than the Clinical Base Model (0.864 vs. 0.642), whereas accuracy (0.718 vs. 0.755) and specificity (0.633 vs. 0.820) were lower. Thus, threshold-dependent classification metrics did not improve consistently despite the improvement in overall discrimination.

The apparent AUCs of the clinical base model and base + HALP model were 0.784 (95% CI, 0.722–0.847) and 0.829 (95% CI, 0.775–0.883), respectively. The addition of the HALP score resulted in a significant increase in the AUC of 0.045, as confirmed by DeLong's test ($p = 0.020$).

Table 3. Baseline characteristics of patients with RA stratified by low muscle strength status.

Variables	No low muscle strength (n = 139)	Low muscle strength (n = 81)	Statistic	p
Age, years	62.00 (57.00, 69.00)	68.00 (60.00, 73.00)	Z = -3.53	<0.001
BMI, kg/m ²	23.81 ± 3.44	22.36 ± 3.54	t = 2.96	0.004
HALP	37.18 (27.68, 43.40)	26.61 (23.49, 34.89)	Z = 4.59	<0.001
DAS28-ESR	3.85 ± 0.60	4.22 ± 0.61	t = -4.30	<0.001
Sex, n (%)			$\chi^2 = 6.41$	0.011
Male	52 (37.41%)	17 (20.99%)		
Female	87 (62.59%)	64 (79.01%)		
RF, n (%)			$\chi^2 = 4.51$	0.034
Negative	48 (34.53%)	17 (20.99%)		
Positive	91 (65.47%)	64 (79.01%)		
Smoking, n (%)			$\chi^2 = 0.26$	0.607
No	117 (84.17%)	66 (81.48%)		
Yes	22 (15.83%)	15 (18.52%)		
Hypertension, n (%)			$\chi^2 = 0.51$	0.474
No	79 (56.83%)	42 (51.85%)		
Yes	60 (43.17%)	39 (48.15%)		
Diabetes, n (%)			$\chi^2 = 0.55$	0.458
No	117 (84.17%)	65 (80.25%)		
Yes	22 (15.83%)	16 (19.75%)		
CKD, n (%)			$\chi^2 = 1.00$	0.319
No	129 (92.81%)	72 (88.89%)		
Yes	10 (7.19%)	9 (11.11%)		
Current GC use, n (%)			$\chi^2 = 15.18$	<0.001
No	106 (76.26%)	41 (50.62%)		
Yes	33 (23.74%)	40 (49.38%)		
RA duration, n (%)			$\chi^2 = 10.21$	0.001
<10 years	113 (81.29%)	50 (61.73%)		
≥10 years	26 (18.71%)	31 (38.27%)		

RA, rheumatoid arthritis; BMI, body mass index; HALP, hemoglobin, albumin, lymphocyte, and platelet; DAS28-ESR, ESR disease activity score; RF, rheumatoid factor; CKD, chronic kidney disease; GC, glucocorticoid.

After bootstrap correction, the AUCs were 0.766 (95% CI, 0.707–0.826) for the clinical base model and 0.809 (95% CI, 0.757–0.863) for the base + HALP model, indicating that the extended model maintained better discrimination during internal validation. Furthermore, the addition of the HALP score improved risk reclassification, with an NRI of 0.663 (95% CI, 0.402–0.924; $p = 0.001$) and an IDI of 0.072 (95% CI, 0.039–0.107; $p = 0.002$). These findings indicate that the HALP score provides incremental identification value beyond the clinical base model.

Nomogram Model Construction and Evaluation

Using the fixed variables from the Clinical Base Model (age, sex, BMI, DAS28-ESR, and current GC use) together with HALP, a nomogram corresponding to the Base + HALP Model was constructed (Fig. 2A). The nomogram was used to estimate the probability of low muscle strength.

ROC curve analysis showed an apparent AUC of 0.829 (95% CI, 0.775–0.883) for the Base + HALP model and 0.784 (95% CI, 0.722–0.847) for the Clinical Base Model (Fig. 2B). The ROC curve of the Base + HALP model was generally positioned above that of the clinical base model, indicating improved discrimination between patients with and without low muscle strength after incorporation of the HALP score.

The calibration plot showed that both the apparent and bias-corrected calibration curves of the Base + HALP model were generally close to the ideal reference line, indicating good agreement between the predicted and observed probabilities (Fig. 2C). The Hosmer-Lemeshow test showed no statistically significant evidence of poor calibration ($p = 0.274$), further supporting the model's calibration performance.

Decision curve analysis demonstrated that the Base + HALP model generally provided greater net benefit than the clinical base model across a broad range of threshold probabilities and outperformed the “treat-all” and “treat-none” strategies (Fig. 2D). In particular, across threshold probabilities of approximately 10%–60%, the Base + HALP model showed a greater estimated net benefit.

Sensitivity Analysis

To assess the robustness of the findings using an alternative definition of low muscle strength, we conducted a sensitivity analysis among patients aged ≥50 years according to the AWGS 2025 criteria. Among the 168 patients included in this subgroup analysis, 56 (33.3%) met the AWGS 2025 definition of low muscle strength (Table 6).

In the sensitivity analysis using the AWGS 2025 definition, age, female sex, BMI, DAS28-ESR, and HALP score remained independently associated with low muscle strength. In particular, a higher HALP score remained inversely associated with low muscle strength (adjusted OR 0.91, 95% CI 0.87–0.95; $p < 0.001$). RF status, current glucocorticoid use, and RA duration were not statistically significant after multivariate adjustment. Overall, the direction of the major associations was broadly consistent with the primary analysis, although not all factors retained statistical significance in the smaller subgroup (Table 7).

A nomogram specific to the ≥50-year subgroup was constructed using the same model variables (Supplementary Fig. 1A). As shown in Supplementary Fig. 1, among patients with RA aged ≥50 years, the Base + HALP model incorporating age, sex, BMI, DAS28-ESR,

Table 4. Logistic regression analysis of candidate factors associated with low muscle strength in RA patients.

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Age, years	1.05 (1.02–1.08)	0.001	1.06 (1.02–1.10)	0.004
BMI, kg/m ²	0.88 (0.80–0.96)	0.004	0.87 (0.78–0.96)	0.009
HALP	0.93 (0.90–0.96)	<0.001	0.93 (0.89–0.96)	<0.001
DAS28-ESR	2.75 (1.70–4.60)	<0.001	2.51 (1.38–4.76)	0.003
Sex				
Male	1.00 (Reference)		1.00 (Reference)	
Female	2.25 (1.21–4.34)	0.012	3.14 (1.45–7.21)	0.005
RF				
Negative	1.00 (Reference)		1.00 (Reference)	
Positive	1.99 (1.06–3.84)	0.035	1.74 (0.82–3.77)	0.153
Smoking				
No	1.00 (Reference)			
Yes	1.21 (0.58–2.47)	0.607		
Hypertension				
No	1.00 (Reference)			
Yes	1.22 (0.70–2.12)	0.474		
Diabetes				
No	1.00 (Reference)			
Yes	1.31 (0.63–2.66)	0.458		
CKD				
No	1.00 (Reference)			
Yes	1.61 (0.61–4.18)	0.322		
Current GC use				
No	1.00 (Reference)		1.00 (Reference)	
Yes	3.13 (1.75–5.67)	<0.001	2.55 (1.24–5.31)	0.011
RA duration				
<10 years	1.00 (Reference)		1.00 (Reference)	
≥10 years	2.69 (1.46–5.04)	0.002	1.40 (0.62–3.12)	0.412

OR, odds ratio; 95% CI, 95% confidence interval.

Table 5. Incremental identification value of incorporating the HALP score into the clinical base model for identifying low muscle strength in RA patients.

Metric	Clinical base model	Base + HALP model
Accuracy	0.755	0.718
Sensitivity	0.642	0.864
Specificity	0.820	0.633
Apparent AUC (95% CI)	0.784 (0.722–0.847)	0.829 (0.775–0.883)
Corrected AUC (Bootstrap)	0.766 (0.707–0.826)	0.809 (0.757–0.863)
ΔAUC, DeLong <i>p</i>	Reference	0.045 (<i>p</i> = 0.020)
NRI (95% CI), <i>p</i>	Reference	0.663 (0.402–0.924), <i>p</i> = 0.001
IDI (95% CI), <i>p</i>	Reference	0.072 (0.039–0.107), <i>p</i> = 0.002

AUC, area under the receiver operating characteristic curve; NRI, net reclassification improvement; IDI, integrated discrimination improvement.

current GC use, and HALP score was used to estimate the probability of low muscle strength (**Supplementary Fig. 1A**).

ROC curve analysis showed an apparent AUC of 0.848 (95% CI, 0.790–0.906) for the Base + HALP model and 0.789 (95% CI, 0.718–0.860) for the Clinical Base Model (**Supplementary Fig. 1B**). After bootstrap internal

validation, the optimism-corrected AUCs were 0.822 (95% CI, 0.768–0.880) and 0.764 (95% CI, 0.697–0.837), respectively. The ROC curve of the extended model was generally positioned above that of the base model, indicating that incorporation of the HALP score improved discrimination between patients with and without low muscle strength in this age-specific subgroup.

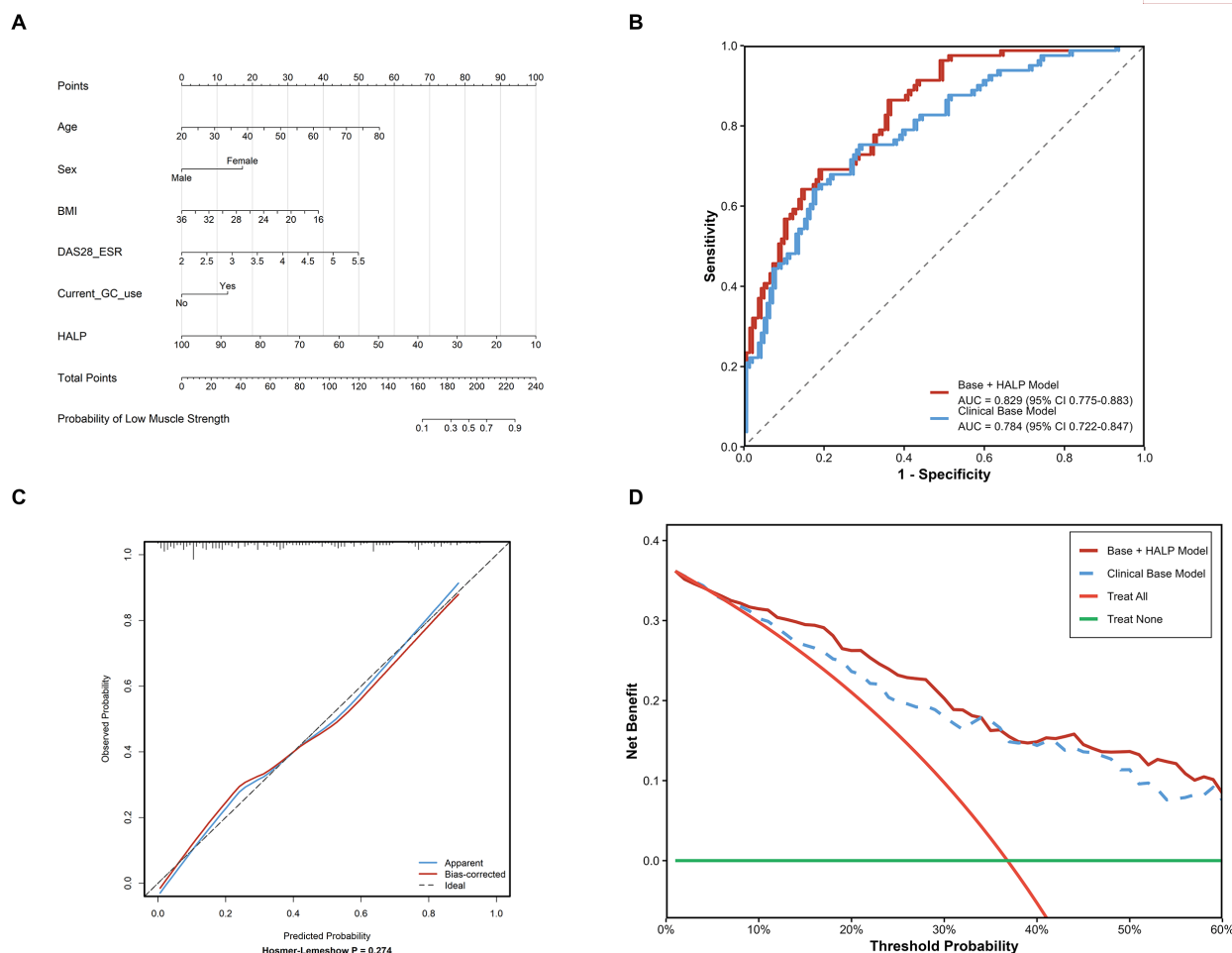


Fig. 2. Model performance and estimated net benefit of the Base + HALP model incorporating the HALP score. (A) Nomogram for estimating the probability of low muscle strength. (B) ROC curve analysis. (C) Calibration curve of the Base + HALP Model. (D) DCA for evaluating estimated net benefit. ROC, receiver operating characteristic; DCA, decision curve analysis.

The calibration plot showed that both the apparent and bias-corrected calibration curves of the Base + HALP model were generally close to the ideal reference line, indicating good agreement between the predicted and observed probabilities (**Supplementary Fig. 1C**). The Hosmer–Lemeshow test did not indicate a statistically significant lack of fit ($p = 0.768$), further supporting the good calibration performance of the model among patients aged ≥ 50 years.

Decision curve analysis demonstrated that the Base + HALP model generally yielded a greater net benefit than the clinical base model across a broad range of threshold probabilities and outperformed the “treat-all” and “treat-none” strategies (**Supplementary Fig. 1D**). In particular, across threshold probabilities of approximately 10%–60%, the Base + HALP model consistently provided a higher estimated net benefit. These findings suggest that adding the HALP score to the clinical base model increased the estimated net benefit across the evaluated threshold range among patients with RA aged ≥ 50 years.

Discussion

The results of this study showed that the HALP score, age, sex, BMI, DAS28-ESR, and current GC use were independently associated with low muscle strength in patients with RA. Based on clinically relevant variables, we constructed a nomogram identification model, which demonstrated an AUC of 0.784. After adding the HALP score to this model, the AUC increased to 0.829, and the difference in discrimination between the two models was statistically significant ($p = 0.020$). These findings suggest that, beyond conventional clinical factors, the HALP score provides incremental identification value for low muscle strength in patients with RA.

Age was independently associated with low muscle strength in this study, consistent with the well-established age-related decline in skeletal muscle function. The prevalence of sarcopenia increases with advancing age among patients with RA. A study of patients with RA aged over 65 years demonstrated that the risk of sarcopenia signifi-

Table 6. Baseline characteristics of patients with RA aged ≥ 50 years stratified by low muscle strength status.

Variables	No low muscle strength (n = 112)	Low muscle strength (n = 56)	Statistic	<i>p</i>
Age, years	64.05 $\pm$ 7.58	67.12 $\pm$ 8.48	$t = -2.29$	0.024
BMI, kg/m ²	23.77 $\pm$ 3.48	22.39 $\pm$ 3.67	$t = 2.34$	0.021
HALP	36.39 $\pm$ 10.05	29.09 $\pm$ 7.80	$t = 5.18$	<0.001
DAS28-ESR	3.83 $\pm$ 0.58	4.28 $\pm$ 0.59	$t = -4.72$	<0.001
Sex, n (%)			$\chi^2 = 4.42$	0.035
Male	42 (37.50%)	12 (21.43%)		
Female	70 (62.50%)	44 (78.57%)		
RF, n (%)			$\chi^2 = 5.20$	0.023
Negative	39 (34.82%)	10 (17.86%)		
Positive	73 (65.18%)	46 (82.14%)		
Smoking, n (%)			$\chi^2 = 0.20$	0.656
No	95 (84.82%)	46 (82.14%)		
Yes	17 (15.18%)	10 (17.86%)		
Hypertension, n (%)			$\chi^2 = 0.05$	0.826
No	62 (55.36%)	30 (53.57%)		
Yes	50 (44.64%)	26 (46.43%)		
Diabetes, n (%)			$\chi^2 = 0.73$	0.393
No	94 (83.93%)	44 (78.57%)		
Yes	18 (16.07%)	12 (21.43%)		
CKD, n (%)			$\chi^2 = 1.32$	0.251
No	104 (92.86%)	49 (87.50%)		
Yes	8 (7.14%)	7 (12.50%)		
Current GC use, n (%)			$\chi^2 = 7.86$	0.005
No	84 (75.00%)	30 (53.57%)		
Yes	28 (25.00%)	26 (46.43%)		
RA duration, n (%)			$\chi^2 = 8.40$	0.004
<10 years	88 (78.57%)	32 (57.14%)		
≥ 10 years	24 (21.43%)	24 (42.86%)		

cantly increased with each additional year of age [16]. Sex also plays an important role in the development of sarcopenia. Although RA predominantly affects females, female patients may be more susceptible to muscle mass loss due to postmenopausal hormone changes and lower baseline muscle mass [17]. Therefore, age and sex should be considered fundamental variables for low muscle strength screening.

The relationship between BMI and sarcopenia is complex. In this study, BMI was associated with low muscle strength, consistent with previous studies suggesting that lower BMI may be associated with a higher risk of muscle impairment in patients with RA. A Thai cross-sectional study showed that the risk of sarcopenia increased by 46% for each 1-unit decrease in BMI [18]. It is worth noting that some patients with RA may still have sarcopenic obesity, characterized by reduced muscle mass accompanied by in-

creased fat mass, despite having a normal or even high BMI. This phenomenon also explains why relying on BMI alone may underestimate sarcopenia risk [19]. Therefore, BMI should be regarded as a readily available screening variable rather than a substitute for direct assessment of muscle mass, muscle strength, or physical performance.

DAS28-ESR is a commonly used tool for assessing RA disease activity. A previous study have reported an association between higher disease activity and myopenia or muscle impairment in patients with RA [20], and the findings of this study also showed that DAS28-ESR was associated with low muscle strength in patients with RA. This may be attributable to the role of persistent or elevated inflammatory activity in the development and progression of low muscle strength. Therefore, effective control of RA disease activity may be relevant to the preservation of muscle health, although the present retrospective analysis cannot establish whether improved disease control prevents subsequent deterioration in muscle strength.

In addition, there is a close relationship between glucocorticoid use and sarcopenia [21,22]. Glucocorticoids may contribute to muscle atrophy by inhibiting muscle protein synthesis, promoting protein degradation, and affecting glucose and lipid metabolism. Previous studies have further demonstrated that an average glucocorticoid dose ≥ 3.25 mg/day over one year is an independent risk factor for sarcopenia development in patients with RA [23]. In the present study, current GC use was independently associated with low muscle strength. This finding suggests that, despite the well-established anti-inflammatory effects of glucocorticoids, current GC use may have an adverse impact on muscle homeostasis in patients with RA, potentially counteracting their anti-inflammatory benefits with regard to skeletal muscle preservation.

In this study, the AUC increased to 0.829 (95%CI: 0.775–0.883) after the addition of the HALP score, with a Δ AUC of 0.045, indicating the incremental identification value of the HALP score. The HALP score comprises hemoglobin, albumin, lymphocyte count and platelet count, which may reflect nutritional status, inflammatory activity, and immune function to some extent [10]. Previous studies have shown that a lower HALP score is associated with an increased prevalence of low muscle mass and a higher risk of related mortality, suggesting its potential association with poor muscle status in patients with RA [11]. The results of this study further support an independent inverse association between the HALP score and low muscle strength in patients with RA. The underlying mechanism may be related to the close relationship between enhanced inflammatory response, oxidative stress, and sarcopenia [24]. Nutritional deficiency can impair muscle protein synthesis, while chronic inflammation may accelerate the decline of muscle mass and function by promoting protein catabolism, inducing oxidative stress, and affecting muscle cell function [25]. Thus, malnutrition and chronic inflammation may act

Table 7. Univariate and multivariate logistic regression analyses of factors associated with low muscle strength among patients aged ≥ 50 years according to the AWGS 2025 definition.

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	<i>p</i> -value	OR (95% CI)	<i>p</i> -value
Age, years	1.05 (1.01–1.10)	0.023	1.06 (1.00–1.13)	0.044
BMI, kg/m ²	0.89 (0.80–0.98)	0.021	0.86 (0.76–0.97)	0.020
HALP	0.92 (0.88–0.95)	<0.001	0.91 (0.87–0.95)	<0.001
DAS28-ESR	3.91 (2.14–7.59)	<0.001	4.27 (2.02–9.89)	<0.001
Sex				
Male	1.00 (Reference)		1.00 (Reference)	
Female	2.20 (1.07–4.78)	0.038	2.99 (1.18–8.34)	0.027
RF				
Negative	1.00 (Reference)		1.00 (Reference)	
Positive	2.46 (1.15–5.64)	0.025	1.85 (0.74–4.91)	0.198
Smoking				
No	1.00 (Reference)			
Yes	1.21 (0.50–2.82)	0.656		
Hypertension				
No	1.00 (Reference)			
Yes	1.07 (0.56–2.05)	0.826		
Diabetes				
No	1.00 (Reference)			
Yes	1.42 (0.62–3.19)	0.394		
CKD				
No	1.00 (Reference)			
Yes	1.86 (0.62–5.46)	0.257		
Current GC use				
No	1.00 (Reference)		1.00 (Reference)	
Yes	2.60 (1.32–5.15)	0.006	1.84 (0.78–4.38)	0.163
RA duration				
<10 years	1.00 (Reference)		1.00 (Reference)	
≥ 10 years	2.75 (1.37–5.55)	0.004	1.30 (0.50–3.33)	0.587

synergistically to promote the onset and progression of sarcopenia. As a composite index reflecting both nutritional and inflammatory status, the HALP score may provide an important basis for understanding this pathophysiological mechanism.

This study has several limitations that warrant consideration. First, its retrospective design precludes the establishment of temporal relationships and causal inferences between the HALP score and low muscle strength. Second, although this study was conducted across two centers, the relatively modest sample size may limit the external generalizability of the findings. Third, muscle strength was assessed solely by handgrip dynamometry without concurrent evaluation of muscle mass or physical performance, preventing a formal diagnosis of sarcopenia according to current consensus criteria. Fourth, several potential confounders—including objective physical activity levels, dietary intake, vitamin D status, alcohol consumption, and detailed glucocorticoid dosage and duration—were not comprehensively captured in the retrospective dataset. Finally, the nomogram model requires external validation in indepen-

dent multi-center prospective cohorts to confirm its stability and clinical utility. Future research should focus on large-scale, prospective, multi-center studies to externally validate these findings and investigate the longitudinal trajectories of HALP score changes in relation to the incidence, progression, and prognostic outcomes of sarcopenia in patients with RA.

Conclusions

In conclusion, age, sex, BMI, DAS28-ESR, current glucocorticoid use, and HALP score were independently associated with low muscle strength in patients with RA. Adding HALP to the clinical base model improved discrimination and reclassification performance within the present internally validated dataset. Because HALP is derived from routinely available laboratory measurements, it may provide additional information for identifying patients who may benefit from further muscle-strength assessment. However, independent external validation and prospective evaluation are required before the model can be considered for routine clinical risk stratification or decision-making.

Availability of Data and Materials

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

Author Contributions

XYX, JL, YD, DC and BX contributed to the study design. XYX and YD conducted the literature search. JL and YD acquired the data. XYX, JL and DC drafted the article. JL and XYX performed data analysis. YD and BX have been involved in revising it critically for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

The study was approved by the Ethics Committee of Jinhua Hospital of Traditional Chinese Medicine (approval no. 2026-048) and the Ethics Committee of Lanxi Hospital of Traditional Chinese Medicine (approval no. LZY-LSL-202608). Because this retrospective study used anonymized routinely collected clinical data, the requirement for written informed consent was waived by the respective Ethics Committees. All procedures were conducted in accordance with the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.24976/Discover.Med.202638213.256>.

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