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A diagnostic model for assessing the risk of osteoporosis in patients with rheumatoid arthritis based on bone turnover markers

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Abstract

Background The risk of developing osteoporosis (OP) is increased in patients with rheumatoid arthritis (RA), which is associated with poorer prognosis and higher mortality. Many patients with RA may experience bone loss early in the disease course. Therefore, timely assessment of the risk of OP in RA patients is essential.

Methods This is a retrospective study in which we collected information from 500 RA patients who underwent bone mineral density assessments at Longhua Hospital, Shanghai University of Traditional Chinese Medicine, from January 2018 to December 2022. Based on the data collection timeline, the first 70% of patients were assigned to the training set, while the remaining 30% were included in the validation set. The model was established using the training set and evaluated through plotting of the receiver operating characteristic curves, calibration curves, and clinical decision curves. Internal validation was performed by resampling the training set data 1,000 times using the bootstrap method, while internal hold-out validation was conducted using the validation dataset.

Results Ultimately, six variables were identified as independently associated with RA combined with OP (RA-OP): female sex, age, beta C-terminal cross-linked peptide (β-CTX), anti-cyclic citrullinated peptide antibody (ACPA), triglycerides (TG), and N-terminal propeptide of type I procollagen (PINP). The regression equation for the model is as follows: Logistic (RA-OP) = -8.703 + 0.946*female + 0.053*age + 0.004*β-CTX + 0.001*ACPA + 0.6*TG-0.008*PINP. The model demonstrated good discrimination (AUC = 0.819, 95% CI: 0.775–0.863) and calibration. In both internal and internal hold-out validation, the model also performed well, with AUC values of 0.814 (95% CI: 0.772–0.864) and 0.772 (95% CI: 0.697–0.847), respectively. Clinical decision curves indicated that the model outperformed both extreme curves, suggesting good clinical utility.

Conclusions Our model is user-friendly and has shown good predictive performance in both internal and internal hold-out validation, offering new insights for the early screening and treatment of OP risk in RA patients.

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Keywords Rheumatoid arthritis, Osteoporosis, Clinical prediction models, Bone turnover markers, Risk factors

Introduction

Rheumatoid arthritis (RA) is a systemic, autoimmune disease of unknown etiology with erosive, symmetric polyarthritis as the main clinical manifestations [1]. The fundamental pathological changes involve the development of synovitis, leading to progressive destruction of articular cartilage and bone erosion. This process ultimately results in joint deformities, disabilities, and a range of extra-articular manifestations [2]. Osteoporosis (OP), a disease characterized by decreased bone mass, destruction of bone microarchitecture, and increased risk of fracture, is one of the most common complications of RA, affecting approximately 30% patients with RA [3]. The underlying mechanisms of OP in individuals with RA remain poorly understood. However, it is noted that they are twice as likely to develop osteoporosis compared to the general population of the same age and gender [4]. The most significant consequence of OP is the occurrence of fragility fractures, which are among the leading causes of disability and mortality in elderly patients. However, patients with RA exhibit a 1.3-fold increased risk of femoral fractures and a 2.4-fold increased risk of spinal fractures [5]. It is estimated that by 2050, the medical costs associated with common fragility fractures in China (including vertebral, hip, and wrist fractures) will reach approximately $24 billion [6]. Research suggests that bone loss or osteoporosis frequently occurs early in the course of RA [7]. Due to the overlapping clinical symptoms of RA and OP, the diagnosis of osteoporosis is often overlooked, resulting in missed opportunities for early detection and prevention. This can lead to poorer prognosis and higher mortality rates [8]. Therefore, it is crucial for clinicians to focus on how to identify trends in bone loss in RA patients during the early stages of the disease, before significant changes in bone mineral density (BMD) occur, and to implement timely interventions. Changes in bone turnover markers (BTMs) often precede the onset of systemic osteoporosis and local joint deformities [9]. Therefore, it is significant to clarify the alterations in BTMs during the progression of RA to prevent and delay the onset of OP.

Clinical prediction models (CPMs) refer to the use of baseline patient information to assess the probability of an individual currently having a particular disease or experiencing a specific outcome in the future [10]. Owing to the advantages of predictive models in the early identification of complications associated with RA, there has been rapid advancement in predictive models for RA-related cardiovascular diseases and interstitial lung disease in recent years [11]. However, there is a relative lack of models specifically designed to predict the occurrence of OP in RA patients. Furthermore, existing tools for assessing OP risk in the general population do not account for the impact of chronic inflammation associated with RA on BMD [12–14], often leading to an underestimation of OP risk. Therefore, the development of OP risk assessment models specifically tailored for RA patients is of paramount importance.

In summary, this study aims to establish and validate a reliable and user-friendly osteoporosis diagnostic model based on BTMs in RA patients, alongside their laboratory tests and clinical information. This model is anticipated to play a significant role in the early clinical detection of osteoporosis in individuals with RA.

Methods

Study design

This retrospective study gathered medical record information from patients diagnosed with RA according to the 1987 American College of Rheumatology (ACR) classification criteria [15] or the 2010 ACR /European League Against Rheumatism classification criteria [16]. The data was collected from Longhua Hospital, Shanghai University of Traditional Chinese Medicine, over the period from January 2018 to December 2022.

We collected data from the hospital's electronic medical record system regarding RA patients during a single visit, including: (1) general Information: patient gender, age, and duration of RA; (2) Laboratory Indicators: rheumatoid factor (RF), anti-cyclic citrullinated peptide antibody (ACPA), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), N-terminal propeptide of type I procollagen (PINP), beta C-terminal cross-linked peptide (β-CTX), osteocalcin (OC), 25-hydroxy vitamin D (25[OH]D), high-density lipoprotein cholesterol (HDL-C), low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), total cholesterol (TC); (3) bone density assessment: BMD of the lumbar spine or femur measured by dual-energy X-ray absorptiometry (DEXA).

The following exclusion criteria will be applied: (1) patients with incomplete data regarding the required information; (2) patients with comorbid autoimmune diseases, such as ankylosing spondylitis, systemic lupus erythematosus, and Sjögren's syndrome; (3) patients with comorbid endocrine disorders, including hyperthyroidism, hypothyroidism, Cushing's syndrome, and hypogonadism; (4) patients who have been using medications that affect bone metabolism for an extended period, such as glucocorticoids, estrogens, and androgens (cumulative duration exceeds two years).

Statistical analysis

SPSS statistics v25.0 (IBM Corp, Los Angeles, CA, USA) and R statistical software (version 4.1.3; http://www.Rproject.org/) were used to analyse the data. For normally distributed continuous variables, data are expressed as mean ± standard deviation ($\bar{x} \pm s$), while non-normally distributed data are presented as median (M, P25, P75). Continuous variables that met the conditions of normal distribution and homogeneity of variance were analyzed using an independent samples t-test; otherwise, the Mann Whitney U test was applied. Categorical data are expressed as percentages, and comparisons were made using the Chi-square test. Statistical tests were two-tailed, and P values < 0.05 were considered statistically significant.

Methods for model development and validation

According to the 1994 osteoporosis diagnostic criteria [17], patients were divided into the RA group and the RA combined with OP (RA-OP) group. Based on the data collection timeline, the first 70% of patients were assigned to the training set, while the remaining 30% were included in the validation set. Univariate analysis was conducted in the training set, and statistically significant variables ($P < 0.05$) identified by comparing the RA and RA-OP groups were considered potential predictive factors. Subsequently, we employed stepwise logistic regression (backward selection, with an inclusion criterion of 0.05 and an exclusion criterion of 0.1) and LASSO logistic regression (selecting the number of variables corresponding to the minimum binomial deviance) to further filter these important variables and establish the final model. During the logistic regression analysis, none of the variables were standardized or normalized.

The nomogram function from the rms package in R was utilized to construct a nomogram for predicting the probability of RA-OP, facilitating the clinical application of the model. The receiver operating characteristic (ROC) curve was plotted using the ggplot function from the ggplot2 package in R, and the area under the curve (AUC) along with the 95% confidence interval was calculated to quantify the discriminative ability of the model. Calibration plots were generated using the calibrate function from the rms package to assess the degree of agreement between predicted risks and actual event occurrences; closer proximity of the model calibration curve to the reference line indicates better calibration performance. Clinical decision analysis (DCA) was performed using the rmda package in R to determine the clinical utility of the model by quantifying net benefits at various threshold probabilities.

Internal validation was conducted through resampling of the training set data using the Bootstrap method, with 1,000 iterations. ROC curves were plotted based on the resampled data to evaluate the model's discriminative ability during internal validation, and calibration curves were also drawn to assess calibration performance. Internal hold-out validation of the model was performed using data from the validation set.

Results

General information

From January 2018 to December 2022, a total of 1,497 rheumatoid arthritis (RA) patients were assessed, with 997 excluded (Figure S1). Ultimately, 500 patients were included in the study, among whom 184 patients had concurrent osteoporosis (OP), accounting for 36.8% of the total cohort. Among all patients, 130 (26%) were male and 370 (74%) were female, resulting in a male-to-female ratio of 1:2.8. In the RA-OP group, there were 34 (18.5%) males and 150 (81.5%) females, yielding a male-to-female ratio of 1:4.4. In contrast, the pure RA group comprised 96 (30.4%) males and 220 (69.6%) females, with a male-to-female ratio of 1:2.3.

The median age of all patients was 64 years (interquartile range [IQR] 57–70), with RA-OP patients having a median age of 66 years (IQR 62–71) and pure RA patients having a median age of 63 years (IQR 52–70). The median RA duration for all patients was 9 years (IQR 4–15), with RA-OP patients having a disease duration of 9 years (IQR 4–19) and RA patients without OP having a disease duration of 9 years (IQR 4–13).

Comparison of training and validation set data

There were no statistically significant differences ($P > 0.05$) between the training ($n = 350$) and validation ($n = 150$) sets regarding general information, laboratory tests, and the number of patients with concurrent OP (Table 1). This indicates that the patient data in both sets exhibited good consistency, suggesting that the validation set data can be utilized for Internal hold-out validation.

Model development in the training set

In the training set, univariate analysis of the RA group and the RA-OP group identified eight potential predictive factors, namely: female sex, age, β-CTX, OC, PINP, ACPA, TG, and HDL-C (Table 2).

Stepwise logistic regression further narrowed down the selection to six variables for model establishment (Table 3). The regression equation for the model is as follows: Logistic(RA-OP) = -8.703 + 0.946*female + 0.053*age + 0.004*β-CTX + 0.001*ACPA + 0.6*TG-0.008*PINP. A nomogram for predicting the probability of RA-OP was constructed to facilitate the clinical application of the model (Fig. 1). We plotted the ROC curve (Fig. 2A) and calculated the AUC to be 0.8192 (95% CI: 0.7752–0.8633), indicating that the model demonstrates good discriminative

Table 1 Comparison of training and validation set data

Variables	Training set (*n* = 350)	Validation set (*n* = 150)	*P*
OP (%)	124 (35.4%)	60 (40%)	0.331
Female (%)	258 (73.7%)	112 (74.7%)	0.824
Age (years)	64 (57, 70)	64 (57, 71)	0.750
RA duration (years)	9 (4, 16)	9 (4, 14)	0.795
25 (OH)D (nmol/L)	38.9 (28.6, 52.7)	40.9 (26.5, 55.1)	0.447
β-CTX (pg/mL)	273 (190, 339)	290 (200, 340)	0.402
OC (ng/mL)	13.3 (9.9, 18.8)	13.2 (9.1, 18.5)	0.79
PINP (ng/mL)	43.2 (32.4, 55.1)	41.9 (32.5, 55.6)	0.946
ACPA (U/mL)	249 (44, 514)	318 (35, 676)	0.645
RF (IU/mL)	70.1 (14.5, 288.5)	68.5 (14.2, 211.3)	0.863
ESR (mm/h)	44.5 (25.3, 66.0)	41.0 (24.0, 65.0)	0.584
CRP (mg/L)	9.55 (1.35, 26.45)	9.80 (2.07, 23.14)	0.605
TG (mmol/L)	4.40 (3.77, 5.06)	4.48 (3.96, 5.08)	0.482
TC (mmol/L)	1.04 (0.80, 1.44)	1.10 (0.85, 1.56)	0.213
HDL-C (mmol/L)	1.20 (0.97, 1.49)	1.19 (0.94, 1.43)	0.409
LDL-C (mmol/L)	2.60 (2.04, 3.37)	2.73 (2.04, 3.44)	0.502

25(OH)D: 25-hydroxy vitamin D; ACPA: anti-cyclic citrullinated peptide antibody; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; OC: osteocalcin; OP: osteoporosis; PINP: N-terminal propeptide of type I procollagen; RF: rheumatoid factor; TC: total cholesterol; TG: triglycerides; β-CTX: beta C-terminal cross-linked peptide

Table 2 Univariate analysis of RA and RA-OP in the training set

Variables	RA (*n* = 226)	RA-OP (*n* = 124)	*P*
Female (%)	154 (68.1%)	104 (83.9%)	0.001
Age (years)	62 (51, 69)	68 (63, 71)	<0.001
RA duration (years)	9 (4, 14)	10 (4, 20)	0.071
25 (OH)D (nmol/L)	37.9 (26.3, 52.5)	41.3 (30.0, 52.7)	0.418
β-CTX (pg/mL)	245 (180, 320)	318 (248, 373)	<0.001
OC (ng/mL)	14.3 (11.3, 19.2)	11.0 (7.9, 17.2)	<0.001
PINP (ng/mL)	44.6 (34.5, 57.1)	37.5 (25.8, 52.6)	0.001
ACPA (U/mL)	164 (25, 373)	388 (142, 1246)	<0.001
RF (IU/mL)	69 (12, 312)	71 (20, 220)	0.796
ESR (mm/h)	44 (24, 65)	45 (29, 73)	0.388
CRP (mg/L)	8.46 (1.35, 26.30)	10.75 (1.32, 27.73)	0.322
TG (mmol/L)	4.13 (3.55, 4.84)	4.76 (4.36, 5.30)	<0.001
TC (mmol/L)	1.06 (0.84, 1.47)	1.02 (0.74, 1.43)	0.171
HDL-C (mmol/L)	1.12 (0.93, 1.42)	1.27 (1.05, 1.56)	<0.001
LDL-C (mmol/L)	2.54 (2.03, 3.15)	2.79 (2.06, 3.50)	0.072

25(OH)D:25-hydroxy vitamin D; ACPA: anti-cyclic citrullinated peptide antibody; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; OC: osteocalcin; PINP: N-terminal propeptide of type I procollagen; RF: rheumatoid factor; TC: total cholesterol; TG: triglycerides; β-CTX: beta C-terminal cross-linked peptide

performance. Additionally, a calibration plot was generated (Fig. 2B) to evaluate the consistency between the predicted risks and the actual occurrence of events. The calibration curve of the model was found to be closely aligned with the reference line, indicating good calibration.

LASSO logistic regression (Figure S2) incorporated all eight potential predictive factors (Table S1), resulting in a model with an AUC of 0.8189 (95% CI: 0.7748–0.8631). Although this model included two additional predictive factors, OC and HDL-C, compared to the model constructed using stepwise logistic regression, there was no significant enhancement in predictive performance (Figure S3A). Therefore, this study adopted the model derived from stepwise regression as the final model. To assess the incremental value of the predictive factors in the final model, we established the simplest model, which included only age and gender, yielding an AUC of 0.715 (95% CI: 0.662, 0.768). Subsequently, we incrementally added predictive factors to the simplest model, resulting in a gradual increase in the AUC values as more factors were incorporated (Figure S3B). When a cutoff value of 0.390 is applied for the diagnosis of OP, the final model achieves a maximum Youden index of 0.52. At this threshold, the model demonstrates a sensitivity of 73.4%, specificity of 78.8%, positive predictive value of 67.0%, and negative predictive value of 83.4%.

Internal and internal hold-out validation of the final model

Internal validation of the model was performed using the Bootstrap method, involving 1,000 resampling iterations of the training set data. The ROC curve after internal validation was plotted (Fig. 3A), revealing an adjusted AUC of 0.814 (95% CI: 0.772–0.864), indicating that the model demonstrated good discriminative ability during the internal validation period. The calibration curve indicated that the predictive accuracy during the internal validation period was satisfactory (Fig. 3B).

Internal hold-out validation of the model was conducted using the validation set data, and the ROC curve after Internal hold-out validation was plotted (Figure S4A). The AUC was found to be 0.772 (95% CI: 0.697–0.847), indicating that the model exhibited acceptable discriminative ability during the Internal hold-out validation. Furthermore, the calibration curve demonstrated that the model showed reasonable predictive accuracy during the Internal hold-out validation stage (Figure S4B).

DCA in the training and validation sets

Clinical decision curves for the model were plotted for both the training and validation set data. This analysis quantifies the net benefit of the model at different threshold probabilities, thereby determining the clinical utility of the model. Both the training and validation set curves for the model demonstrate superior performance compared to the two extreme lines (Figure S5A and S5B), suggesting a favorable overall benefit for the population.

Table 3 Stepwise logistic regression analysis of RA and RA-OP in the training set

Variables	B score	Wald score	*P*	OR	OR(95% CI)	
					Lower	Upper
Female	0.946	8.297	0.004	2.575	1.353	4.901
Age	0.053	17.314	<0.001	1.054	1.028	1.081
β-CTX	0.004	13.292	<0.001	1.004	1.002	1.006
ACPA	0.001	19.319	<0.001	1.001	1.001	1.002
TG	0.600	16.603	<0.001	1.821	1.365	2.430
PINP	-0.008	4.028	0.045	0.992	0.984	0.999
Constant	-8.703	53.071	<0.001	/	/	/

ACPA: anti-cyclic citrullinated peptide antibody; PINP: N-terminal propeptide of type I procollagen; TG: triglycerides; β-CTX: beta C-terminal cross-linked peptide

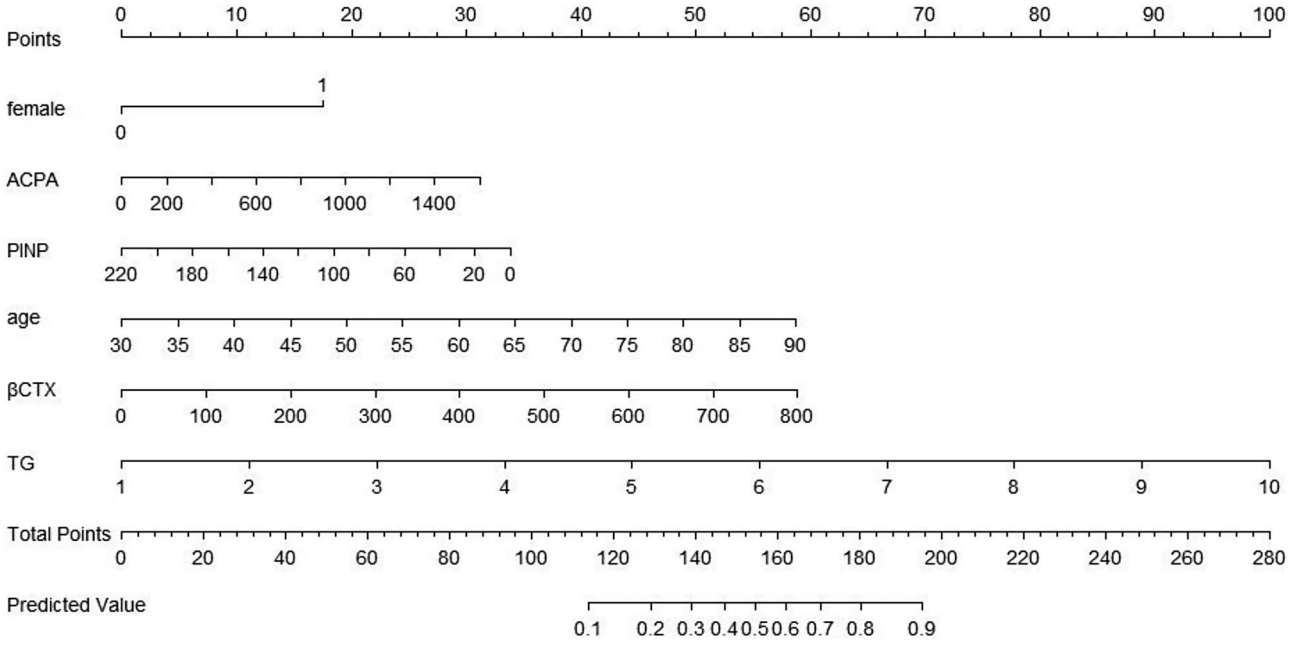

Fig. 1 Nomogram for Predicting the Probability of OP in RA Patients. Scores are assigned to each predictor based on their respective values, and the total score is calculated by summing all individual scores. Finally, the corresponding probability of developing osteoporosis is determined based on the total score

Discussion

As the medical paradigm evolves from empirical medicine to evidence-based medicine and then to precision medicine, the rapid advancements in the acquisition, storage, and analytical prediction of medical data have made the vision of personalized healthcare increasingly attainable [18]. CPMs not only provide high-quality evidence for evidence-based medicine but also serve as valuable tools for the implementation of precision medicine. Even in conditions with complex pathological mechanisms, such as RA, CPMs offer advantages in the early detection of complications and the prediction of drug responses [11]. With the advent of the precision medicine era, the application of CPMs in areas such as medical decision-making, patient prognostic management, and public health resource allocation has become more widespread, underscoring their growing importance [19].

RA and OP are both common conditions that are closely related. Due to the increased risk of OP in RA patients, they are twice as likely to experience osteoporotic fractures compared to the general population, which is associated with a higher mortality rate [20]. In addition to the general risk factors for OP found in the population, such as being female, older age, smoking, alcohol consumption, malnutrition, corticosteroid use, history of fractures, and low body mass index (BMI), there are specific risk factors associated with RA-OP. These include a longer duration of RA, higher disease activity, and positivity for ACPA [8]. Currently, there are several models established based on these risk factors for predicting OP in patients with RA.

Kvien et al. [21] developed a clinical algorithm to identify RA women at high risk for OP, incorporating predictors such as age, BMI, disease activity score, current corticosteroid use, and history of previous non-vertebral

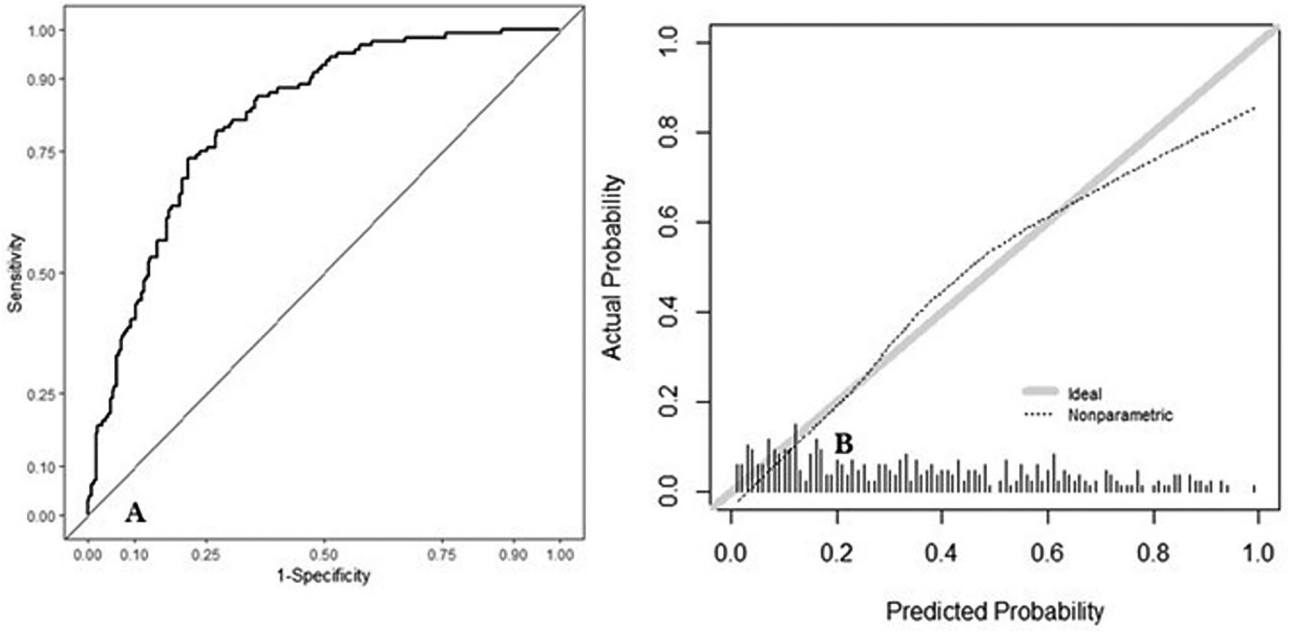

Fig. 2 ROC Curve (**A**) and Calibration Curve (**B**) of the Model. (**A**) The ROC curve of the model shows an AUC of 0.819 (95% CI: 0.775–0.863), indicating good discriminative ability. (**B**) The calibration curve of the model features the diagonal line representing the reference line, which indicates the actual occurrence of OP in RA patients, while the black dashed line represents the model's predictions

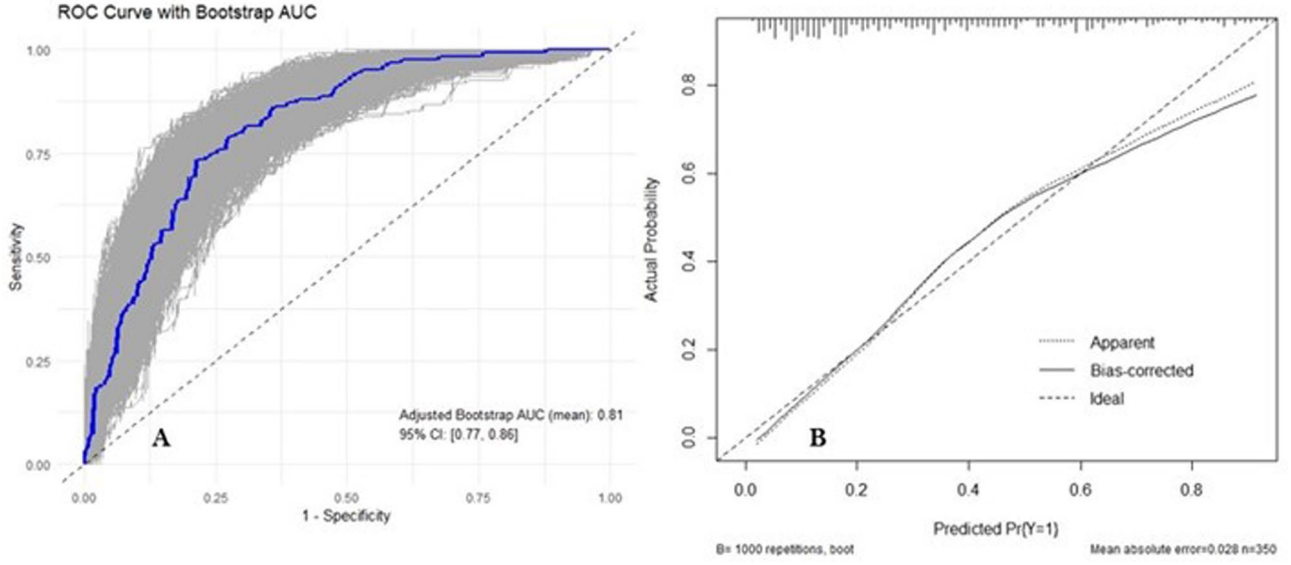

Fig. 3 ROC curve (**A**) and calibration curve (**B**) of the model in internal validation. (**A**) The ROC curve of the model during internal validation, where the gray solid lines represent the ROC curves from each resampling, and the blue solid line indicates the average level after adjusting for overestimation from 1,000 resampling iterations, yielding an AUC of 0.814 (95% CI: 0.772–0.864). (**B**) The calibration curve of the model during internal validation features the diagonal line representing the actual occurrence of OP in RA patients, the black dashed line representing the model's calibration curve, and the solid black line representing the calibration curve after internal validation

fractures. The sensitivity of the model across various measurement sites was approximately 50–60%, with specificity ranging from 80 to 90%. However, this model has not undergone validation, is limited to female patients, and involves a relatively complex calculation, making it less convenient for clinical use [22]. A simpler risk scoring tool based on age and BMI was designed to screen for RA-OP patients; however, it exhibited low specificity [23]. Additionally, Yan et al. [24] explored the correlation between the 7-joint ultrasound score (US7) and RA-OP, establishing a predictive model with good performance. Nevertheless, the limited availability of

US7 may restrict its clinical applicability. Compared to previous studies, our research benefits from a larger sample size and demonstrates good predictive performance in both internal and internal hold-out validation. Furthermore, our predictive factors can be easily obtained in clinical practice, enhancing the convenience of using the model.

The chronic inflammatory environment in RA presents multifaceted challenges to bone health, BTMs hold particular significance [25]. BTMs provide dynamic insights into the balance between bone formation and resorption, revealing the complex processes that regulate bone metabolism [26, 27]. In this context, the exploration of BTMs has become crucial for deciphering the intricate relationship between RA and OP [28]. Our study indicates that β-CTX (OR = 1.004, $P < 0.001$) serves as an independent risk factor for OP in RA patients, while PINP (OR = 0.992, $P = 0.045$) is identified as a protective factor (Table 3). Compared to healthy individuals, RA is associated with increased bone resorption and impaired bone formation [29]. The Wnt signaling pathway is a key regulatory molecular pathway for BTMs and plays a central role in maintaining bone homeostasis [30]. In RA patients, serum levels of the Wnt pathway inhibitor dickkopf-1 (DKK1), induced by tumour necrosis factor, are elevated [31, 32]. Given that the Wnt pathway is involved in the production of osteoprotegerin, the upregulation of DKK1 is thought to contribute to increased bone resorption [33]. Furthermore, the chronic inflammatory environment in RA directly suppresses bone formation [34, 35]. Consequently, under RA conditions, there is an increase in bone resorption coupled with a decrease in bone formation, leading to an imbalance in bone metabolism and a reduction in BMD.

Our model, like previous models, includes age (OR = 1.054, $P < 0.001$, Table 3) as a predictive factor, highlighting the need for heightened vigilance regarding the occurrence of OP in elderly RA patients [21, 23, 24]. Our study indicates that being female (OR = 2.575, $P = 0.004$, Table 3) is a risk factor for RA-OP. Female are not only a susceptible population for RA but also for OP; therefore, preventive measures for OP should be prioritized early for female RA patients. Age and female sex are also recognized risk factors for OP in the general population. Due to the limitations of our study, we were unable to include BMD information from an age- and sex-matched general population. Future research could investigate the relationships between age and sex among healthy individuals, OP patients, RA patients, and RA-OP patients to explore the deeper connections among these groups. Our study also identifies ACPA (OR = 1.001, $P < 0.001$, Table 3) as an independent predictive factor for RA-OP, which is consistent with previous research [24]. ACPA are the most relevant autoimmune antibodies associated with RA and can enhance bone resorption by directly recognizing the surface of osteoclast precursor cells, leading to osteoclast differentiation [36]. This makes ACPA a unique risk factor for OP in RA patients. The duration of the RA ($P = 0.134$, Table 2) did not show statistically significant differences in the univariate analysis between the two groups, which contradicts previous studies [24]. This may be attributed to the fact that our case data primarily came from hospitalized patients, who generally have a longer disease duration, and the retrospective nature of the analysis may have introduced various biases in the recorded disease duration.

Dyslipidemia in patients with RA has been well established, although results vary among different studies [37, 38]. Some research has also shown that TG, TC, and HDL-C are negatively correlated with overall bone mineral density in the general population [39]. However, there are few studies exploring the association between lipid levels and the risk of developing OP in RA patients. Our study indicates that, compared to RA patients without OP, those with RA-OP have higher levels of TG and HDL-C (Table 1). Further logistic regression analysis revealed that TG (OR = 1.821, $P < 0.001$, Table 3) is an independent risk factor for OP in RA patients. In contrast, Zeng et al. [40] reported that RA-OP patients had higher levels of TC and HDL-C, with HDL-C identified as an independent predictor of RA-OP, while TG did not show statistically significant differences between the two groups. This discrepancy may be attributed to differences in age distribution and the relatively small sample size of the patients included in the two studies. Interestingly, HDL-C is considered a protective factor for cardiovascular disease (CVD) but also a risk factor for OP [40], and both CVD and OP are common complications in RA patients [11]. In this context, investigating lipid levels is crucial for managing the complexities of RA and elucidating its intricate mechanisms.

It is noteworthy that the prevalence of OP varies across different studies on RA. A recent global meta-analysis indicated that the prevalence of OP in RA patients is 27.6% [3]. In our retrospective cohort, however, the prevalence reached as high as 36.8%. This discrepancy may be partially attributed to the older age of the patients included in our study. Similar situations have been observed in other related studies conducted in China; however, these studies recruited patients with a relatively younger average age [24, 40]. We cannot yet conclude that Chinese patients with RA are more prone to developing OP. To obtain accurate and reliable epidemiological data and to develop better strategies for the prevention and treatment of RA-OP, it is essential to conduct multicenter prospective cohort studies on RA in China.

Every study has its limitations, and this research is no exception. To ensure the authenticity and reliability of the

data in this retrospective study, we prioritized relatively objective indicators such as patient age, sex, and laboratory tests. Other important but more subjective indicators, such as current or recent steroid use, disease activity scores, smoking history, and alcohol consumption, were not included in the study. Additionally, clinicians tend to recommend bone mineral density assessments for older patients with a longer disease duration, which may have resulted in missing bone density information for relatively younger RA patients.

Conclusion

In summary, we have developed a user-friendly diagnostic model for assessing the risk of OP in patients with RA, which demonstrated good predictive performance in both internal and Internal hold-out validation. This model may provide new insights for the early screening of OP risk in RA patients. We look forward to advancements in CPMs in the future, which could usher us in a new era where the selection of optimal treatment strategies is based on precise pre-treatment predictions.

Abbreviations

25(OH)D	25-hydroxy vitamin D
ACPA	Anti-cyclic citrullinated peptide antibody
AUC	Area under the curve
BMD	Bone mineral density
BMI	Body mass index
BTMs	Bone turnover markers
CPMs	Clinical prediction models
CRP	C-reactive protein
CVD	Cardiovascular disease
DCA	Clinical decision analysis
ESR	Erythrocyte sedimentation rate
HDL-C	High-density lipoprotein cholesterol
LDL-C	Low-density lipoprotein cholesterol
OC	Osteocalcin
OP	Osteoporosis
PINP	N-terminal propeptide of type I procollagen
RA	Rheumatoid arthritis
RA-OP	Rheumatoid arthritis combined with osteoporosis
RF	Rheumatoid factor
TC	Total cholesterol
TG	Triglycerides

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13075-025-03544-5.

Supplementary Material 1

Acknowledgements

Not applicable.

Author contributions

YBS and YZY: Data collection, data analysis, and the drafting of the initial manuscript. YXY, ZHX and HZ: Data collection and study design. NL, HX and YJZ: Revision of the initial draft. QS, YJW and QQL: supervision. All authors had access to the data, and reviewed and approved the final manuscript before submission.

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Data availability

The data underlying this article cannot be shared publicly due to the privacy of the individuals who participated in the study but are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Medical Ethics Committee of Longhua Hospital, Shanghai University of Traditional Chinese Medicine (Approval No. 2022LCSY108), and written informed consent was obtained from all participants.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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