Article

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A Retrospective Study on the Diagnostic Efficacy of Bone Turnover Markers Combined With Inflammatory Indicators in Elderly Patients With Chronic Kidney Disease for Osteoporosis

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Background: Elderly patients with chronic kidney disease (CKD) are at high risk for osteoporosis. Inflammation and abnormal bone metabolism are key underlying mechanisms, yet the diagnostic utility of combining their respective biomarkers remains unclear. This study aimed to evaluate the diagnostic efficacy of inflammatory and bone turnover markers for osteoporosis in elderly CKD patients.

Methods: This single-center retrospective cohort study included 194 elderly (≥60 years) patients with chronic kidney disease who underwent bone mineral density testing between March 2021 and March 2024. Patients were divided into osteoporosis and non-osteoporosis groups based on dual-energy X-ray absorptiometry (DXA) T-score. Inflammatory markers were collected within 24 hours of admission, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), neutrophil count, lymphocyte count, monocyte count, platelet count, platelet distribution width, erythrocyte distribution width, mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC). The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), and systemic immune-inflammation index (SII) were calculated. Bone turnover markers included serum type I procollagen N-terminal propeptide (P1NP), osteocalcin (OC), and type I collagen crosslinked C-terminal peptide (CTX). Univariate and multivariate logistic regression analyses were performed to identify independent factors influencing osteoporosis, and receiver operating characteristic (ROC) curves were used to evaluate the diagnostic efficacy of individual markers and combined models.

Results: Multivariate logistic regression showed that elevated ESR and SII levels among inflammation-related markers were independently associated with osteoporosis in elderly CKD patients; among bone turnover markers, P1NP, OC, and CTX levels were all independent predictors of osteoporosis (all $p < 0.05$). The comprehensive model combining ESR, SII, P1NP, OC, and CTX showed excellent discriminative performance, with an area under the ROC curve (AUC) of 0.86 (95% confidence interval (CI): 0.80–0.91), suggesting that the combined assessment of inflammatory and bone metabolism markers can significantly improve the accuracy of osteoporosis identification in elderly CKD patients.

Conclusion: In elderly CKD patients, both inflammatory status and abnormal bone turnover are closely associated with osteoporosis risk. Combining inflammatory markers such as ESR and SII with bone turnover markers such as P1NP, OC, and CTX can improve the screening efficacy for osteoporosis. Combined assessment of inflammatory and bone remodeling markers holds promise as an important supplementary tool for bone health management in patients with chronic kidney disease-mineral and bone disorder (CKD-MBD), providing a more reliable foundation for early intervention.

Keywords: chronic kidney disease; osteoporosis; inflammatory markers; bone turnover markers

Introduction

Chronic kidney disease (CKD) is a disease caused by persistent abnormalities in kidney structure or function (≥3 months). Its core diagnostic criteria are a decrease in glomerular filtration rate (GFR) or a clear abnormality in kidney injury markers [1]. With the aging population and the increasing burden of metabolic diseases, the global prevalence of CKD continues to rise, posing a serious public health challenge [2]. The pathological effects of CKD extend well beyond the kidneys themselves. Patients often experience multiple severe complications, such as cardiovascular events, metabolic disorders, and bone metabolic disorders (BKD), which significantly increase morbidity, hospital readmission rate, and overall mortality in this population [3,4]. Epidemiological data show that the incidence

of osteoporosis in CKD patients is much higher than that in the general population of the same age, especially in elderly CKD patients. This not only directly leads to a decline in quality of life and an increase in the need for long-term care, but also significantly increases the all-cause mortality rate [5]. Therefore, osteoporosis screening and differential diagnosis for elderly CKD patients have important public health and clinical significance. Traditionally, dual-energy X-ray absorptiometry (DXA) has been considered the gold standard for diagnosing osteoporosis. However, in the context of CKD, DXA only reflects bone mass and cannot fully reflect bone quality or remodeling. In addition, vascular calcification and spinal degenerative changes may interfere with DXA accuracy, thereby reducing its diagnostic efficacy in CKD patients [6]. Therefore, integrating biochemical markers to improve the early identification of osteoporosis and fracture risk in CKD patients has become a current research hotspot and clinical priority.

Against this backdrop, biochemical markers of bone turnover (BTMs) have gradually gained attention from researchers. As metabolites or enzymes released into the blood during bone formation and bone resorption, BTMs can serve as indicators of dynamic bone remodeling. They are easy to detect and respond sensitively to changes—often earlier than bone density—making them, in theory, an ideal tool for monitoring bone metabolism and assessing treatment response [7]. Commonly used formation markers include type I procollagen N-terminal propeptide (P1NP) and osteocalcin (OC), and resorption markers include type I collagen crosslinked C-terminal peptide (CTX) and N-terminal peptide (NTX) [8]. P1NP reflects the rate of new type I collagen synthesis and serves as a sensitive indicator of bone formation; CTX/NTX reflects type I collagen degradation products and suggests osteoclast-mediated bone resorption activity [9]. Numerous studies in the general elderly population have confirmed that BTMs are correlated with bone loss rate and fracture risk to varying degrees, and follow-up studies have shown their advantages for short-term risk dynamic monitoring [10,11]. The application of BTMs in CKD populations presents certain challenges. As renal function declines, some biomarkers excreted by the kidneys (such as some CTX fragments) may accumulate in the blood [11]. Therefore, rationally selecting a combination of indicators, such as combining inflammatory markers with formation/absorption biomarkers, to construct a more robust diagnostic/screening model is a reasonable direction for research.

The role of inflammation and immune status in bone metabolism disorders in CKD patients has been increasingly recognized in recent years. Chronic low-grade systemic inflammation is a common comorbidity of CKD. Inflammatory cytokines, such as interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α), can not only directly stimulate osteoclast differentiation and activation (by upregulating the nuclear factor κB receptor activator ligand RANKL and other pathways), promoting bone resorption, but also inhibit osteoblast function and activity, thus hindering bone formation [12,13]. Clinical observational studies have repeatedly confirmed that markers of systemic inflammation, such as high-sensitivity C-reactive protein (hs-CRP), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) , and the systemic immune-inflammatory index (SII), which integrates neutrophils, platelets, and lymphocytes, are significantly associated with increased osteoporosis and fracture risk in the general population and patients with various chronic diseases (including CKD) [14,15]. Inflammation and the inherent metabolic disorders of CKD, such as acidosis, active vitamin D deficiency, and secondary hyperparathyroidism, are intertwined and form a complex network that drives bone metabolism toward abnormality. Therefore, incorporating indicators reflecting systemic inflammatory load into the assessment system of bone health in CKD patients not only has a solid theoretical basis in terms of pathophysiological mechanisms but is also very likely to improve the ability to identify high-risk individuals in clinical practice and provide a new entry point for early intervention.

In summary, an effective and integrative screening strategy is needed for osteoporosis in the growing elderly CKD population. Therefore, this study aimed to evaluate the diagnostic value of combining routinely available inflammatory markers with bone turnover markers (P1NP, OC, CTX) for identifying osteoporosis in elderly CKD patients.

Methods

Patients

This study was a single-center retrospective cohort study that consecutively included elderly patients with CKD who were treated and underwent bone mineral density testing at Wenzhou Central Hospital between March 2021 and March 2024. All patients' clinical data were obtained from the electronic health record (EHR) system to ensure data completeness and continuity. Inclusion criteria included: (1) age $\geq$60 years; (2) clinical diagnosis meeting the Kidney Disease Improvement Global Organization (KDIGO) diagnostic criteria for CKD; (3) completion of DXA bone mineral density testing during hospitalization; (4) complete inflammatory markers, complete blood counts, and bone turnover biochemical indicators within 24 hours of admission; and (5) complete key demographic and clinical data. Exclusion criteria included: (1) other malignant diseases (such as malignant tumors, acute infections); (2) severe organic damage or major comorbidities that could independently and severely affect bone metabolism, inflammatory status, or life expectancy, including but not limited to decompensated cirrhosis, severe chronic heart failure, advanced chronic obstructive pulmonary disease, active autoimmune diseases requiring

high-dose immunosuppression, and major neurological disabilities; and (3) use of drugs that significantly affect bone metabolism during the study period, such as potent anti-resorption drugs, abnormal thyroid hormone therapy.

Grouped according to DXA bone mineral density T-scores: lumbar spine or femoral neck T-scores. A T-score $\leq$–2.5 was defined as the osteoporosis group; a T-score $>$–2.5 was defined as the non-osteoporosis group. Ultimately, a total of 194 eligible elderly CKD patients were included and divided into two groups based on the presence of osteoporosis for subsequent analysis. This study followed the principles of the Declaration of Helsinki, and the research protocol was approved by the hospital's ethics committee (ethics approval number: L2025-12-010). The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study, which involved the analysis of anonymized historical clinical data and posed minimal risk to participants. All data were used for research purposes while protecting patient privacy.

Collection of Biomarkers

Venous blood was drawn within 24 hours of admission for testing. Inflammatory markers included C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR), measured by immunoscattering and automated ESR, respectively. Complete blood count parameters included neutrophil count, lymphocyte count, monocyte count, platelet count, platelet distribution width (PDW), erythrocyte distribution width (RDW), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), measured using a fully automated hematology analyzer (Sysmex, Chuo-ku, Japan). Derived inflammatory markers were calculated based on these baseline parameters, including: NLR, PLR, lymphocyte-to-monocyte ratio (LMR), and SII, calculated as: SII = Platelet count $\times$ Neutrophil count / Lymphocyte count.

Bone metabolism parameters were measured in fasting morning venous blood samples and analyzed using electrochemiluminescence immunoassay. Measurements were performed using the SAVANT 8000 analyzer (Tianjin Huaketai Biotechnology Co., Ltd, Tianjin, China), and the parameters included: P1NP, OC, and type I collagen cross-linked C-terminal peptide.

Data Processing and Analysis

All statistical analyses were conducted in accordance with SPSS 2 4.0 (IBM Corp., Armonk, NY, USA). The results were completed using R 4.2.2 (R Foundation for Statistical Computing, Vienna, Austria). First, the normality of continuous variables was assessed using the Kolmogorov–Smirnov test. Variables conforming to a normal distribution were expressed as mean $\pm$ standard deviation ($\bar{x} \pm$ SD), and differences between groups were compared using an independent samples *t*-test. Variables not conforming to a normal distribution were expressed as median and interquartile range [M(Q_1, Q_3)], and the Mann–Whitney U test was used. Categorical variables were expressed as numbers of cases and percentages, and the χ^2 test was used. To explore the associated factors of osteoporosis in elderly CKD patients, univariate logistic regression was first performed. Variables with $p < 0.05$ in the univariate analysis were further included in a multivariate logistic regression model to identify independent factors influencing osteoporosis. Results were reported as odds ratio (OR) and 95% confidence interval (95% CI).

Receiver operating characteristic (ROC) curves were used to analyze the diagnostic performance of individual indicators and the combined model, with the area under the curve (AUC) assessing discriminative ability. To evaluate the agreement between the model's predicted probabilities and observed outcomes, a bootstrap method (1000 samples) was used to construct calibration curves. Clinical utility was evaluated using decision curve analysis (DCA), with net benefit used to measure its clinical value across a range of threshold probabilities. All statistical tests were two-tailed, and a $p < 0.05$ was considered statistically significant.

Results

Baseline Data

This study ultimately included 194 patients, of whom 138 (71.13%) were non-osteoporosis patients and 56 (28.87%) were osteoporosis patients. There were no statistically significant differences between the two groups in terms of age, BMI, CRP, Lymphocytes, Monocytes, Platelets, PDW, MCH, MCHC, smoking history, or sex ($p > 0.05$). However, regarding inflammation and bone metabolism markers, the osteoporosis group had significantly higher levels of ESR, Neutrophils, Lymphocytes, NLR, PLR, and SII than the non-osteoporosis group, while the osteoporosis group had significantly lower levels of CTX, P1NP, and OC. Detailed baseline characteristics are shown in Table 1.

Univariate and Multivariate Logistic Regression Analysis

To avoid multicollinearity, neutrophils (N), lymphocytes (L), platelets (P), and monocytes (M), which are used to derive NLR, PLR, and SII, were excluded from the regression model, and only the derived indices were included.

Univariate logistic regression analysis showed that ESR, NLR, SII, P1NP, OC, and CTX were significantly associated with osteoporosis status in elderly patients with CKD (all $p < 0.05$). All statistically significant indicators from the univariate analysis were then included in the multivariate logistic regression model for correction. The results showed that ESR (OR = 1.06, 95% CI: 1.02~1.11, p = 0.004), P1NP (OR = 0.94, 95% CI: 0.92~0.97, $p < 0.001$), OC (OR = 0.91, 95% CI: 0.84~0.98, p = 0.017), CTX (OR

Table 1. Baseline characteristics of participants.

Variables	Non-osteoporosis group (n = 138)	Osteoporosis group (n = 56)	Statistic	*p*
Age (years)	60.94 ± 8.39	60.21 ± 8.03	t = 0.55	0.583
BMI (kg/m^2)	24.88 ± 3.76	24.08 ± 4.09	t = 1.31	0.192
CRP (mg/L)	4.68 ± 2.15	4.72 ± 2.32	t = –0.11	0.914
ESR (mm/h)	21.38 ± 10.74	25.40 ± 9.08	t = –2.47	0.014
Neutrophils (10^9/L)	4.69 ± 1.92	5.73 ± 2.04	t = –3.36	<0.001
Lymphocyte (10^9/L)	1.81 ± 0.61	1.74 ± 0.57	t = 0.77	0.444
Monocytes (10^9/L)	0.53 ± 0.14	0.54 ± 0.12	t = –0.86	0.392
Platelets (10^9/L)	223.84 ± 68.45	235.15 ± 57.25	t = –1.09	0.277
PDW (%)	16.77 ± 4.73	16.81 ± 4.92	t = –0.05	0.961
MCH (pg)	28.79 ± 3.58	28.94 ± 3.68	t = –0.27	0.788
MCHC (g/L)	313.94 ± 36.47	324.40 ± 39.13	t = –1.77	0.078
CTX (ng/L)	501.09 ± 83.18	427.39 ± 96.54	t = 5.33	<0.001
P1NP (μg/L)	48.90 (34.89, 67.52)	34.55 (22.04, 42.21)	Z = –4.77	<0.001
OC (μg/L)	15.59 (11.84, 20.87)	13.27 (9.10, 17.81)	Z = –2.93	0.003
NLR	2.69 (1.65, 3.90)	3.12 (2.44, 4.96)	Z = –2.23	0.026
PLR	119.90 (90.30, 168.46)	147.78 (118.97, 189.10)	Z = –3.14	0.002
SII	550.22 (342.37, 782.86)	758.69 (458.35, 1077.74)	Z = –2.73	0.006
Smoking, n (%)			χ^2 = 0.16	0.690
Yes	50 (36.23)	22 (39.29)		
No	88 (63.77)	34 (60.71)		
Sex, n (%)			χ^2 = 0.46	0.496
Male	36 (26.09)	12 (21.43)		
Female	102 (73.91)	44 (78.57)		

BMI, Body Mass Index; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PDW, platelet distribution width; MCH, mean corpuscular hemoglobin; MCHC, mean corpuscular hemoglobin concentration; CTX, C-terminal peptide; P1NP, type I procollagen N-terminal propeptide; OC, osteocalcin; NLR, neutrophil-to-lymphocyte ratio; PLR, platelet-to-lymphocyte rati; SII, systemic immune-inflammatory index.

= 0.99, 95% CI: 0.98~0.99, $p < 0.001$) and SII (OR = 1.01, 95% CI: 1.01~1.01, $p = 0.002$) were independent risk factors for osteoporosis. Elevated levels of the inflammatory markers ESR and SII were associated with an increased risk of osteoporosis, while elevated levels of the bone turnover markers P1NP, OC, and CTX were associated with a decreased risk of osteoporosis. Detailed results are shown in Table 2.

Evaluation of Model Diagnostic Efficacy

To evaluate the diagnostic value of combined indicators, a predictive model was constructed including ESR, P1NP skewness, OC skewness, CTX, and SII. The model achieved an area under the ROC curve (AUC) of 0.86 (95% CI: 0.80–0.91) for differentiating osteoporosis from non-osteoporosis, indicating good discriminative ability (Fig. 1).

Model Calibration Evaluation

Internal validation using the Bootstrap method (Fig. 2) showed that calibration curves exhibited a good agreement between the model's predicted probabilities and the observed probabilities. The bias-corrected curve nearly approximates the ideal reference line (diagonal), indicating high predictive accuracy and low risk of overfitting.

Discussion

With changes in the social living environment and the intensification of population aging, the population of elderly patients with CKD is steadily increasing. The associated bone metabolism abnormalities and osteoporosis have emerged as important clinical challenges, affecting patients' quality of life while increasing fracture risk and healthcare burden [16]. This study selected elderly CKD patients as the research subjects and systematically explored the diagnostic value of inflammatory markers and BTMs for osteoporosis through retrospective analysis. The results revealed that the increase of inflammatory markers ESR and SII, as well as the decrease of bone turnover markers P1NP, OC and CTX, were independently associated with osteoporosis. The combined diagnostic model constructed from these indicators showed good discrimination ability (AUC = 0.86), calibration and clinical utility. The above findings provide new evidence and insights for early identification of osteoporosis risk by integrating inflammatory and bone metabolism markers in the elderly CKD, and also highlight the need to further explore the complex pathophysiological mechanism underlying chronic kidney disease-mineral and bone disorder (CKD-MBD).

Table 2. Results of logistic regression analysis.

Variables	Single factor					Multiple factors				
	β	SE	Z	p	OR (95% CI)	β	SE	Z	p	OR (95% CI)
Smoking										
0					1.00 (Reference)					
1	–0.13	0.33	–0.40	0.690	0.88 (0.46~1.66)					
Sex										
0					1.00 (Reference)					
1	0.17	0.32	0.54	0.588	1.19 (0.64~2.21)					
Age	–0.01	0.02	–0.55	0.581	0.99 (0.95~1.03)					
BMI	–0.05	0.04	–1.30	0.192	0.95 (0.87~1.03)					
CRP	0.01	0.07	0.11	0.913	1.01 (0.87~1.16)					
ESR	0.04	0.02	2.41	0.016	1.04 (1.01~1.07)	0.06	0.02	2.87	0.004	1.06 (1.02~1.11)
PDW	0.00	0.03	0.05	0.960	1.00 (0.94~1.07)					
MCH	0.01	0.04	0.27	0.786	1.01 (0.93~1.10)					
MCHC	0.01	0.00	1.75	0.079	1.01 (1.00~1.02)					
P1NP	–0.04	0.01	–4.28	<0.001	0.96 (0.94~0.98)	–0.06	0.01	–4.66	<0.001	0.94 (0.92~0.97)
OC	–0.09	0.03	–3.02	0.003	0.91 (0.86~0.97)	–0.10	0.04	–2.40	0.017	0.91 (0.84~0.98)
CTX	–0.01	0.00	–4.72	<0.001	0.99 (0.99~0.99)	–0.01	0.00	–4.52	<0.001	0.99 (0.98~0.99)
NLR	0.16	0.07	2.07	0.038	1.17 (1.01~1.35)	–0.33	0.21	–1.58	0.115	0.72 (0.47~1.08)
PLR	0.00	0.00	0.44	0.660	1.00 (1.00~1.00)					
SII	0.01	0.00	2.43	0.015	1.01 (1.01~1.01)	0.01	0.00	3.05	0.002	1.01 (1.01~1.01)

OR, odds ratio; CI, confidence interval.

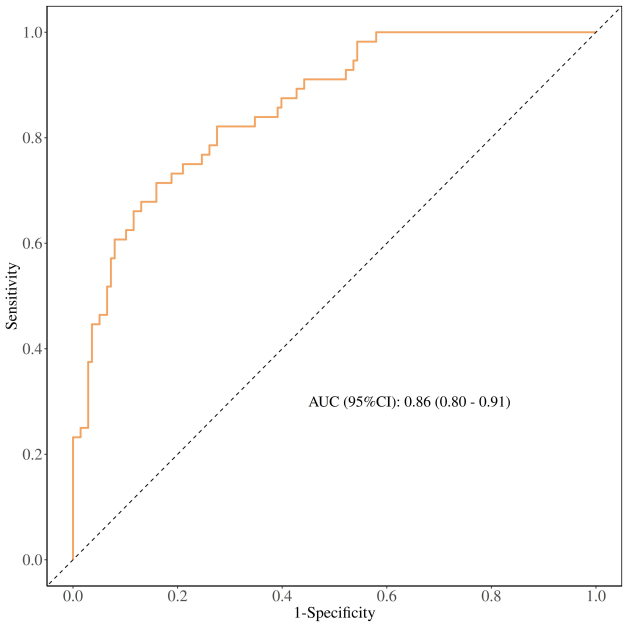

Fig. 1. Receiver operating characteristic (ROC) curve of the combined diagnostic model. The model incorporates ESR, SII, P1NP, OC, and CTX for discriminating osteoporosis in elderly chronic kidney disease (CKD) patients (n = 194). The area under the curve (AUC) is 0.86 (95% CI: 0.80–0.91). The diagonal grey line represents the reference of no discrimination (AUC = 0.50).

Chronic inflammation has been widely recognized as a key contributor to osteoporosis, and the results of this study clearly extend this association to the elderly CKD population. ESR and SII remained independently correlated with bone loss in multivariate analysis, which strongly suggests that systemic inflammatory burden serves as a critical link between CKD and osteoporosis. CKD itself can be regarded as a persistent microinflammatory state, which is caused by a variety of factors such as the accumulation of uremic toxins and enhanced oxidative stress [17,18]. This state promotes the increase of pro-inflammatory cytokines (such as IL-1β, IL-6, TNF-α), which, on the one hand, directly stimulate osteoclast activity and enhance bone resorption by activating the RANKL/RANK/OPG system; on the other hand, they inhibit the differentiation and function of osteoblasts, thereby simultaneously aggravating bone resorption and inhibiting bone formation [19]. ESR, as a classic indicator reflecting changes in acute phase proteins (such as fibrinogen), serves as an indirect indicator of chronic inflammatory burden [20]. In contrast, the SII integrates three key blood cell parameters—neutrophils, platelets, and lymphocytes—to provide a more comprehensive assessment of the balance between pro-inflammatory and anti-inflammatory immune states. This study observed the independent predictive value of the SII, which aligns with the emerging trend of using composite inflammatory markers in chronic disease assessment, and provides strong clinical evidence for understanding the mechanisms underlying increased bone fragility in CKD patients.

This study showed that elevated levels of P1NP, OC, and CTX are associated with a reduced risk of osteoporosis, a finding that seems to contradict the classic theory that “high bone turnover leads to bone loss”. However,

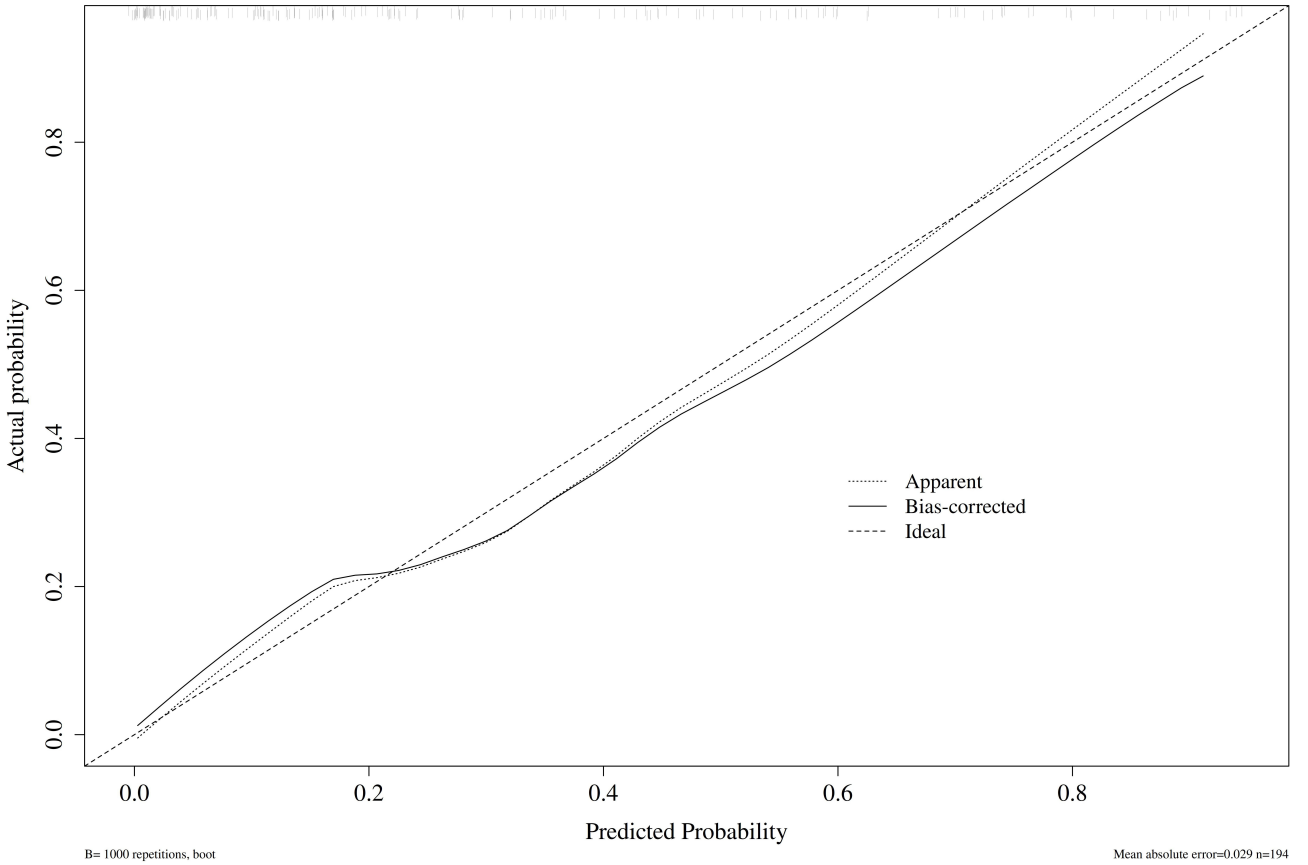

Fig. 2. Calibration curve of the combined diagnostic model. The curve depicts the agreement between the predicted probability of osteoporosis and the observed outcomes.

this highlights the complexity of diagnosing and predicting osteoporosis in the CKD population. Studies have shown that, unlike ordinary primary osteoporosis, which is mainly caused by relatively hyperactive bone resorption, in the CKD population, due to the combined effects of secondary hyperparathyroidism, uremic toxin accumulation, chronic inflammation, diabetes, and other factors, the skeleton often exhibits a "low turnover" state, that is, both bone formation and bone resorption activities are inhibited, with akinetic osteopathy being the most typical and common [21]. Therefore, it is preliminarily speculated that under this low bone turnover state, the serum levels of P1NP and OC, which reflect osteoblast activity, and CTX, which reflects osteoclast activity, are likely to remain in a low range. It is noteworthy that in the multivariate model of this study, CTX remained an independent predictor for osteoporosis (OR = 0.99, 95% CI: 0.98–0.99, $p < 0.001$). This result may suggest that in the specific group of elderly CKD patients, the serum level of CTX is affected by the clearance impairment caused by renal insufficiency, and the simple linear association between CTX and bone mineral density or osteoporosis status is weakened; or after adjusting for inflammatory factors such as ESR and SII and other bone metabolism markers, the predictive information carried by CTX has been covered by other variables. This highlights the limitations of interpreting a single bone turnover marker in the complex context of CKD-MBD. In Baik's study, the levels of P1NP, OC and CTX in osteoporotic patients were also significantly lower than those in the non-osteoporotic group, which is similar to our study results [22]. Regarding the inflammatory indices, it is notable that while NLR showed a significant association with osteoporosis in univariate analysis, it did not retain independent significance in the multivariate model. This may be attributed to collinearity with SII, which remained a robust independent predictor. The SII might capture a broader spectrum of systemic inflammatory and pro-thrombotic states relevant to bone metabolism in CKD by integrating neutrophil, platelet, and lymphocyte counts, thereby accounting for its greater explanatory power compared with other correlated markers.

In summary, the diagnostic platform developed in this study demonstrated good diagnostic efficacy. In the complex clinical environment of CKD, where numerous factors are involved, the diagnostic ability of a single indicator is often limited and unstable. In contrast, the combined model integrating ESR, SII, P1NP, OC, and CTX achieved an area under the curve (AUC) of 0.86, showcasing excellent discriminative ability. This likely reflects the model's ability to simultaneously capture the two core pathophysiological processes driving bone loss

in CKD patients—systemic inflammatory activation and abnormal bone turnover dynamics—thus providing more comprehensive and robust pathological information than a single-dimensional approach. The model's calibration curve shows a good agreement between its predicted probability and the observed incidence, indicating high predictive accuracy and low risk of overfitting. More importantly, decision curve analysis confirms that, across a wide range of threshold probabilities, the net clinical benefit of applying this model to guide clinical decision-making consistently outperforms that of simple strategies of "all-in" or "no-intervention".

We also recognize several limitations in this study. First, as a single-center retrospective study conducted in a hospitalized cohort, all 194 included patients were inpatients, which may introduce selection bias and limit the generalizability of our findings to community-dwelling elderly CKD patients with relatively stable conditions. Future multicenter, prospective studies with larger sample sizes are needed to externally validate the combined model and confirm its applicability across broader clinical settings. Second, the retrospective design limited comprehensive control over potential confounding factors. This study relied on the T-score of DXA as the gold standard for diagnosing osteoporosis, but in patients with moderate to severe CKD, ectopic calcification of blood vessels and soft tissues may interfere with DXA measurements. This potential misclassification bias could have affected the accuracy of group allocation and, consequently, the observed associations between biomarkers and osteoporosis status. Future studies that incorporate imaging techniques such as quantitative CT, which can better distinguish cortical bone from cancellous bone and reduce calcification interference, as reference standards, will strengthen future analyses. Third, this study did not conduct in-depth subgroup analysis according to CKD stages. As is well known, from CKD stages 3 to 5, mineral metabolism disorder, the degree of inflammation, and the state of bone turnover change significantly. Future studies with larger sample sizes are needed to explore whether the diagnostic efficacy of this model is stable at different stages of renal function. Fourth, several potential confounding factors, such as nutritional status (e.g., vitamin D levels, protein intake), physical activity, and the severity of comorbid metabolic diseases (e.g., diabetes), were not fully addressed due to the retrospective nature of the data. The absence of these variables may have influenced the observed associations. Future prospective studies should incorporate these factors to improve the validity of the conclusions.

Therefore, this combined model warrants further independent validation through multicenter, prospective, large-sample cohort studies. Future efforts could also focus on translating the model into a user-friendly risk scoring tool for clinical practice, as well as conducting long-term follow-up studies to dynamically monitor changes in inflammatory markers and bone turnover biomarkers. Such studies help clarify their association with the rate of bone mineral density decline and incidence of new fractures, thereby assessing their predictive ability for long-term skeletal prognosis.

Conclusion

This study has demonstrated that systemic inflammation and abnormal bone turnover status together constitute an important biological basis for osteoporosis risk in elderly patients with CKD. Combining readily available inflammatory markers (ESR, SII) with bone turnover markers (P1NP, OC, CTX) allows for the construction of a diagnostic model with good identification efficacy, accurate prediction, and potential clinical application value. These results not only deepen our understanding of the complexity of CKD-MBD but also suggest that adopting a strategy that integrates multidimensional information in clinical practice may be an effective way to overcome the limitations of current single-method approaches and achieve early identification and risk stratification management of osteoporosis in elderly CKD patients. Despite the inherent limitations of retrospective studies, this study provides valuable preliminary evidence and clear direction for further research on precision bone health management in this high-risk group.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

YCC and QW designed the research study. XWC, XZX, and SPL performed the research. ZMJ and YYG analyzed the data. QW drafted the article. All authors contributed to 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 was approved by the Ethics Committee of Wenzhou Central Hospital (approval number: L2025-12-010), and all procedures followed the principles of the Declaration of Helsinki. The requirement for informed consent was waived by the ethics committee due to the retrospective nature of the study, which involved the analysis of anonymized historical clinical data and posed minimal risk to participants. All data were used for research purposes while protecting patient privacy.

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Conflict of Interest

The authors declare no conflict of interest.

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