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Original Article

Application of machine learning on health examination data for predicting the decrease of bone mineral density

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Abstract: Background: Timely identification and preventative strategies for diminished bone density can markedly enhance patients' quality of life and reduce economic burdens. This study intended to create machine learning algorithms that precisely forecast the probability of bone mineral density loss. Methods: The study comprised people aged 40 years and above who received health examinations at an affiliated institution from January 2022 to January 2024. Five machine learning algorithms were employed to forecast the risk of osteoporosis: k-nearest neighbor (KNN), random forest (RF), support vector machine (SVM), artificial neural network (ANN), and logistic regression (LR). The efficacy of these algorithms was assessed according to accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve (AUROC). Results: This study comprised 11,132 patients, of whom 3,568 exhibited diminished bone density. The original dataset comprised 17 variables, and after data screening, 13 variables were incorporated into the machine learning model. The AUROC scores for ANN, KNN, LR, RF, and SVM were 0.882, 0.906, 0.684, 0.918, and 0.896 for males, and 0.881, 0.843, 0.784, 0.922, and 0.872 for females, respectively. The accuracies of ANN, KNN, LR, RF, and SVM were 0.83, 0.86, 0.75, 0.88, and 0.82 for males, and 0.81, 0.77, 0.74, 0.85, and 0.79 for females. Conclusion: Herein, we created five machine learning algorithms to precisely predict bone density reduction. The RF model had superior performance in both male and female cohorts, attaining the highest AUROC. Implementing machine learning models in clinical implementation can improve the prevention, identification, and early intervention of bone density deterioration.

Keywords: Machine learning, osteoporosis, osteopenia, bone mineral density

Introduction

Osteoporosis is a systemic bone disorder frequently associated with ageing, characterized by low bone mass and deterioration of bone tissue, leading to increased bone fragility and susceptibility to fracture [1]. Besides advanced age, multiple factors contribute to the development of osteoporosis, including female sex (particularly postmenopausal status), genetic predisposition, nutritional deficiencies (such as low calcium and vitamin D intake), sedentary lifestyle, smoking, excessive alcohol consumption, and the use of certain medications [2, 3].

Approximately 50% of postmenopausal women and 20% of men over 50, globally, are afflicted with osteoporosis [4, 5]. In China, the prevalence of osteoporosis among people was almost 7%, with 22.5% in males aged 50 years and above, and 50.1% in women [6]. Another multicenter study indicated that the age-standardized prevalence of osteoporosis among those over 50 years old in China was 6.46% for males and 29.13% for women [7]. The accelerated ageing process has resulted in a rise in osteoporosis and osteoporotic fractures, presenting a substantial public health concern that impacts the medical and economic progress of nations globally [8, 9]. Consequently, the prevention, early detection, and efficient management of osteoporosis can enhance patients' quality of life and alleviate their financial burden.

The advancement of medical imaging has facilitated the development of various diagnostic methods for osteoporosis, such as dual-energy

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X-ray absorptiometry (DXA), quantitative CT, and quantitative ultrasound absorptiometry [10-12]. The definitive method for diagnosing osteoporosis is the assessment of bone mineral density (BMD) using DXA [13]. According to the recommendations of the World Health Organization, osteoporosis is diagnosed by calculating the BMD T-score [14]. Although DXA scans were expedient and efficient, they were impractical for widespread screening in the general population. This underscores the necessity for alternative, simple, and efficient instruments to evaluate the hazards associated with low bone mineral density and osteoporosis.

In recent years, research has increasingly focused on integrating multiple risk factors into predictive models rather than examining isolated variables. In recent years, research has increasingly focused on integrating multiple risk factors into predictive models rather than examining isolated variables [15]. In recent years, research has increasingly focused on integrating multiple risk factors into predictive models rather than examining isolated variables [16, 17]. Osteoporosis prediction models based on machine learning have been created utilizing several clinical and preclinical characteristics, such as computed tomography scans, radiographs, ultrasound signals, molecular and genetic biomarkers, daily routines, and educational background [18-20]. In contrast to current prediction techniques like OSTA, which depend on a limited set of linear risk factors, machine learning models can more adeptly incorporate intricate nonlinear relationships within extensive physical examination data in Beijing, hence enhancing prediction accuracy dramatically.

In this study, we employed five machine learning models, namely logistic regression (LR, benchmark interpretable model), K-nearest neighbor (KNN, based on similarity), support vector machine (SVM, skilled in high-dimensional nonlinearity), random forest (RF, ensemble decision tree anti overfitting), and artificial neural network (ANN, powerful feature learning), to thoroughly assess the efficacy of various algorithms in predicting bone density within the Beijing population. Machine learning-based automated prediction tools, such as the RF model in this study, can be effortlessly incorporated into the routine physical examination process of Beijing community hospitals, efficiently identifying high-risk individuals without requiring supplementary DXA scans, thereby facilitating early intervention, and mitigating the burden of osteoporosis in Beijing's ageing population.

Materials and methods

Data acquisition

This study received clearance from the ethics council of the authors' institution (The Second Hospital of Shandong University, approval number was KYLL2024981).

We examined and evaluated the data of community inhabitants aged 40 years and older who underwent health examinations at The Second Hospital of Shandong University from 2022 to 2024.

Inclusion criteria were as follows: 1) All participants underwent pertinent medical history assessments and physical examinations, which included vital signs, height, weight, and the acquisition of hematological and biochemical test findings. DXA (GE Healthcare, Madison, WI, USA) was employed to assess bone density; 2) Reduced bone density denotes a clinically significant decline in bone density relative to the average BMD of healthy young adults of the same gender and ethnicity, with a T-score of ≤-1.0 standard deviation (SD). The T-score indicates the standard deviation of bone density relative to healthy young individuals of the same sex and ethnicity. The T-score values were classified as follows: osteoporosis (≤-2.5), osteopenia (-2.5< score <-1), or normal (score ≥-1).

The exclusion criteria were as follows: 1) patients who underwent anti-osteoporosis therapy for diagnosed osteoporosis or bone loss; 2) a history of metabolic bone disorders or chronic conditions affecting calcium absorption, history of malignant tumors, administration of medications known to influence bone metabolism, and/or confirmed pregnancy; 3) a history of fractures or previous surgical interventions for fractures; 4) a history of lumbar spine surgery; 5) incomplete data; and 6) extreme outliers. A total of 11,132 people were enrolled in the study.

Feature data preprocessing

The subsequent data were gathered: age, weight, diabetes, hypertension, albumin, hemoglobin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine (Cr), urea nitrogen, uric acid (UA), total cholesterol (TC), triglycerides (TG), high-density lipoprotein cholesterol (HDL-C), alkaline phosphatase (ALP), low-density lipoprotein cholesterol (LDL-C), and Hemoglobin (Hb). Features deemed statistically significant for inclusion in the final machine learning model were identified by chi-squared tests, t-tests, or non-parametric testing. Age is an established independent risk factor for diminished bone density, with its mode of action encompassing various elements, including reduced osteoblast function, heightened osteoclast activity, and changes in hormone levels [21]. The mechanical stress induced by weight gain can promote bone development. Epidemiological studies indicate a positive link between BMI and bone density, where a higher BMI serves as a protective factor for bone density [22]. An elevated sugar environment can directly impede osteoblasts proliferation and induce their apoptosis, while intensifying oxidative stress and inflammatory responses via the buildup of advanced glycation end products (AGEs), resulting in the degradation of bone microstructure [23].

Furthermore, the correlation between hypertension and decreased bone density may come from the same pathophysiological foundation, encompassing activation of the renin-angiotensin system, disturbances in calcium metabolism disorders, and chronic inflammation. Angiotensin II can directly enhance osteoclast activity and result in negative calcium balance by elevating urine calcium excretion [24]. Clinical investigations have identified a positive association between diastolic blood pressure and ALP levels in hypertensive patients, suggesting that elevated ALP, as a marker of bone production, may indicate compensatory activity of bone metabolism [25]. ALT and AST levels in NAFLD patients are negatively correlated with bone mineral density, and this association is independent of such confounding factors as obesity and diabetes [26]. The elevation of ALP may mostly originate from the liver, necessitating evaluation with bone specific ALP. A study including postmenopausal women identified a positive link between serum ALP and bone density, while in male hypertensive patients, the positive correlation between ALP and diastolic blood pressure may indicate a compensatory increase of bone metabolism [25, 27]. Recently, the correlation between abnormal lipid metabolism and decreased bone density has garnered a significant research hotspot in recent years. Increased TC and LDL-C are believed to indirectly influence bone metabolism by facilitating atherosclerosis and inflammatory responses. The protective effect of high-density lipoprotein cholesterol (HDL-C) on bone density has been confirmed by multiple studies. HDL-C can enhance bone microcirculation via anti-inflammatory, antioxidant mechanisms, and the stimulation of endothelial nitric oxide generation, and may also directly promote osteoblast proliferation [22]. Ultimately, renal function indicators (creatinine, urea nitrogen, uric acid) directly influence bone density control by impacting calcium and phosphorus metabolism and acid-base equilibrium. A decline in creatinine levels typically indicates a reduction in muscle mass, which is directly associated with bone density. Consequently, low creatinine may indirectly signify an elevated risk of diminished bone density [28]. Increased urea nitrogen indicates renal impairment, perhaps resulting in secondary hyperparathyroidism and promote bone resorption [29]. Finally, hemoglobin (Hb), as a marker of anemia and nutritional status, is closely associated with bone density. Under anemia, tissue hypoxia can stimulate osteoclast activity and suppresses osteoblast function, while aberrant iron metabolism may damage bone tissue through oxidative stress mechanisms [30].

Model development and validation

The dataset was randomly partitioned into a training set (80%) and a testing set (20%). The training set was used to generate the predictive models and adjust the parameters, whereas the testing set was employed to assess the performance of the constructed model. PyCharm software was used to implement machine learning methods and develop prediction models for bone density reduction, encompassing five models: artificial neural network (ANN), k-nearest neighbors (KNN), logistic regression (LR), random forest (RF), and support vector machine (SVM). The performance of the models

Table 1. Baseline characteristics of the study population

	Male (n=5793, 52.0%)	Female (n=5339, 48.0%)
Age (y)	54.91±10.12	55.58±10.01
Weight	77.53±11.63	63.08±9.42
Hypertension (n, %)	3253 (56.2)	2039 (38.2)
Diabetes (n, %)	918 (15.8)	490 (9.2)
ALT (U/L)	25.27±17.67	19.67±17.72
AST (U/L)	21.19±9.78	19.88±14.91
Alb (g/L)	46.78±2.50	45.74±2.33
ALP (U/L)	70.92±18.23	72.52±20.96
GGT (U/L)	36.90±40.23	21.05±18.01
Cr (μmol/L)	73.57±11.83	56.32±8.71
UA (μmol/L)	362.46±80.04	282.66±65.33
BUN (mmol/L)	5.07±1.20	4.60±1.14
TC (mmol/L)	5.05±1.04	5.40±1.01
TG (mmol/L)	1.72±1.97	1.35±1.00
HDL-C (mmol/L)	1.20±0.24	1.37±0.27
LDL-C (mmol/L)	2.84±0.83	2.96±0.86
Hb (g/L)	153.17±10.92	132.11±12.25
Decreased bone density (n, %)	1610 (27.8)	1958 (36.7)

Decreased bone density referred to osteopenia or osteoporosis. *p*-values were calculated with two-tailed T tests for continuous variables, and two-tailed Z tests for binary variables.

was thoroughly evaluated by plotting the Receiver Operating Characteristic (ROC) curve for the participants. To evaluate the effectiveness of different machine learning models, essential measures including the Area Under the ROC Curve (AUROC), sensitivity, specificity, and accuracy were computed. Sensitivity, also known as the true positive rate (TPR), denotes the ratio of individuals accurately identified as possessing the condition. Specificity, or the true negative rate (TNR), represents the percentage of individuals correctly identified as healthy. The false-positive rate, denoted as 1-specificity, is the percentage of individuals erroneously classified as having the disease. Accuracy was defined as the total percentage of subjects accurately classified as either healthy or diseased [31].

Statistical analysis

Continuous data were described using the mean and standard deviation, whilst categorical variables were presented as frequencies and percentages. The disparities between continuous variables were evaluated using either the t-test or non-parametric test, while the distinctions among categorical variables were examined using the chi-square test. All statistical analyses were conducted using SPSS software (version 29.0). The machine learning models were developed and evaluated in the PyCharm environment. *p*-values were computed using the nonparametric method for comparing two ROC curves as provided by DeLong et al. Statistical significance was set at $P<0.05$.

Results

Demographic information of the research population

Among the 11,132 participants in the study, 5,793 were male and 5,339 were female, with average ages of 54.91± 10.12 for males and 55.58± 10.01 for females. Reduced bone density was noted in 1,610 males and 1,958 females. The remaining findings are displayed in **Table 1**.

Results of data screening

We compared the candidate features between the normal and reduced bone density groups using the chi-square test or t-test, as presented in **Tables 2** and **3**. Selected indicators ($P<0.05$) were incorporated into the machine learning model. The conclusive markers for male inclusion in the model were age, weight, hypertension, diabetes, ALT, AST, ALB, ALP, Cr, UA, TG, HDL-C, and Hb. The parameters for female inclusion in the model included age, weight, hypertension, diabetes, ALT, ALP, UA, BUN, TC, TG, HDL-C, LDL-C, and Hb.

Results of machine learning

Table 4 presents the AUROC, sensitivity, specificity, and accuracy of the five machine learning models. The ROC curves for these models are depicted in **Figures 1** and **2**. This study identified substantial disparities in the principles and efficacy of the five algorithms: Logistic regression (LR), based on linear decision boundaries,

Table 2. Comparison of the features between male participants with normal bone density and decreased bone density

	Normal Bone Density (n=4184, 72.2%)	Decreased Bone Density (n=1610, 27.8%)	*P*-value
Age (y)	53.55±9.27	58.44±11.33	<0.0001
Weight	79.15±11.32	73.34±10.53	<0.0001
Hypertension (n, %)	2314 (55.31)	939 (58.32)	0.038
Diabetes (n, %)	605 (15.06)	351 (17.89)	0.008
ALT (U/L)	26.27±19.12	22.66±12.81	<0.0001
AST (U/L)	21.42±10.46	20.60±7.69	0.004
Alb (g/L)	46.91±2.45	46.46±2.62	<0.0001
ALP (U/L)	69.76±17.61	73.93±19.42	<0.0001
GGT (U/L)	37.86±42.17	34.38±34.55	0.003
Cr (μmol/L)	74.00±11.55	72.47±12.54	<0.0001
UA (μmol/L)	366.78±79.53	351.32±80.34	<0.0001
BUN (mmol/L)	5.08±1.19	5.03±1.24	0.167
TC (mmol/L)	5.06±1.05	5.03±1.02	0.302
TG (mmol/L)	1.78±2.10	1.59±1.58	0.0012
HDL-C (mmol/L)	1.20±0.24	1.23±0.26	<0.0001
LDL-C (mmol/L)	2.83±0.83	2.85±0.84	0.58
Hb (g/L)	153.76±10.59	151.62±11.61	<0.0001

Decreased bone density referred to osteopenia or osteoporosis. *p*-values were calculated with two-tailed *T* tests for continuous variables, and two-tailed *Z* tests for binary variables.

Table 3. Comparison of the features between female participants with normal bone density and decreased bone density

	Normal Bone Density (n=3382, 63.32%)	Decreased Bone Density (n=1959, 36.68%)	*P*-value
Age (y)	52.49±8.78	60.93±9.74	<0.0001
Weight	64.58±9.61	60.50±8.48	<0.0001
Hypertension (n, %)	1112 (32.88)	928 (47.37)	<0.0001
Diabetes (n, %)	248 (7.33)	242 (12.35)	<0.0001
ALT (U/L)	20.33±20.96	18.52±9.72	<0.0001
AST (U/L)	20.03±18.20	19.62±5.81	0.326
Alb (g/L)	45.76±2.32	45.72±2.34	0.561
ALP (U/L)	69.35±19.68	77.99±21.93	<0.0001
GGT (U/L)	21.38±19.94	20.47±14.06	0.074
Cr (μmol/L)	56.15±8.44	56.62±9.15	0.062
UA (μmol/L)	284.40±65.68	279.64±64.65	0.010
BUN (mmol/L)	4.47±1.09	4.81±1.19	<0.0001
TC (mmol/L)	5.22±0.99	5.43±1.02	<0.0001
TG (mmol/L)	1.33±0.97	1.39±1.05	0.045
HDL-C (mmol/L)	1.35±0.26	1.40±0.27	<0.0001
LDL-C (mmol/L)	2.91±0.83	3.04±0.88	<0.0001
Hb (g/L)	131.50±13.16	133.16±10.40	<0.0001

Decreased bone density referred to osteopenia or osteoporosis. *p*-values were calculated with two-tailed *T* tests for continuous variables, and two-tailed *Z* tests for binary variables.

provided robust interpretability but exhibited constrained nonlinear fitting capability (lowest AUROC: male 0.684, female 0.784). K-nearest neighbors (KNN) relied on sample similarity voting, exhibiting robust local pattern recognition (male AUROC 0.906, female AUROC reaches 0.843) but is sensitive to computational resources and feature scaling. Support vector machines (SVM) addressed nonlinearity through kernel functions, demonstrating strong performance (AUROC 0.896/0.872), while necessitating intricate parameter tuning. Artificial neural networks (ANN) leveraged multilayer nonlinear mapping for feature learning (AUROC 0.882/0.881) but required extensive datasets and exhibited a lack of interpretability. Random forest (RF) model surpassed others by amalgamating decision trees and enhancing feature interactions, attaining the highest AUROC (0.918/0.923) due to its adeptness in managing high-dimensional features and anti-overfitting characteristics, especially in identifying synergies such as age and bone metabolism markers. Among them, the RF model exhibited enhanced performance in both the male and female subgroups.

Discussion

Herein, five distinct machine learning algorithms, ANN, SVM, RF, KNN, and LR, were employed to assess bone density loss in adults aged 40 years and older. The definitive markers for male inclusion in the model were age, weight, hypertension, diabetes, ALT, AST, ALB, ALP, Cr, UA, TG, HDL-C, and Hb levels. The parame-

Table 4. Different machine learning models for prediction of osteoporosis in men and women

Model	AUROC (95% CI)	Sensitivity	Specificity	Accuracy	*P*-value
Men					
ANN	0.882 (0.864-0.902)	0.881	0.849	0.83	ref
KNN	0.906 (0.889-0.926)	0.887	0.988	0.86	0.0656
LR	0.684 (0.657-0.724)	0.716	0.744	0.75	<0.0001
RF	0.918 (0.944-0.942)	0.897	0.890	0.88	0.0081
SVM	0.896 (0.870-0.916)	0.887	0.821	0.82	0.2438
Female					
ANN	0.881 (0.862-0.900)	0.885	0.822	0.81	ref
KNN	0.843 (0.818-0.867)	0.888	0.856	0.77	0.0012
LR	0.784 (0.756-0.813)	0.814	0.807	0.74	<0.0001
RF	0.923 (0.908-0.940)	0.901	0.825	0.85	0.0004
SVM	0.872 (0.853-0.890)	0.903	0.788	0.79	0.2678

ANN: Artificial neural network; KNN: K-nearest neighbors; LR: Logistic regression; RF: Random Forest; SVM: Support vector machine; AUROC: Area under the receiver operating characteristic curve; CI: Confidence interval; ROC curve: receiver operating characteristic curve. Sensitivity and specificity were based on cutoff values calculated by the weighted Youden index with weight set at 0.6. *p*-values were calculated with the nonparametric method to compare two ROC curves proposed by DeLong et al.

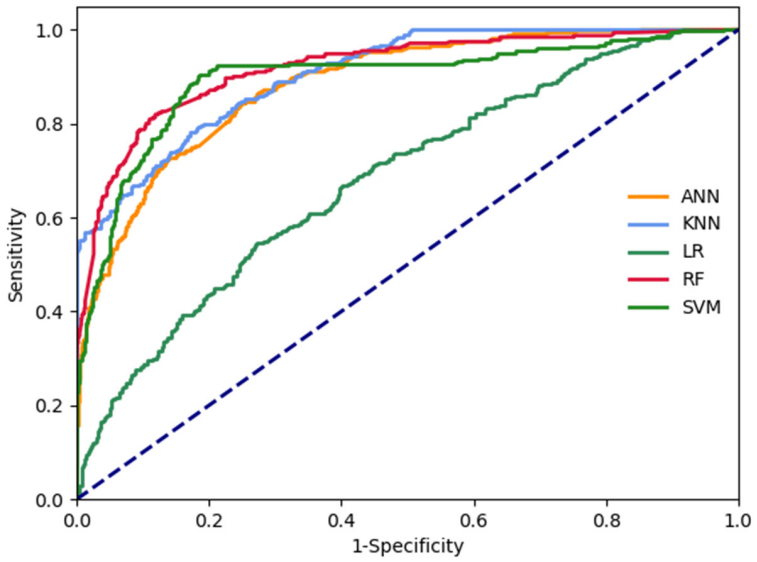

Figure 1. The Receiver operating characteristic (ROC) curves of five machine learning models for prediction of Decreased bone density in males. ANN: Artificial neural network; SVM: Support vector machine; RF: Random Forest; KNN: K-nearest neighbors; LoR: Logistic regression.

ters for female inclusion in the model were age, weight, hypertension, diabetes, ALT, ALP, UA, BUN, TC, TG, HDL-C, LDL-C, and Hb levels. The random forest (RF) model exhibited enhanced performance in both male and female cohorts. The primary conclusion is that the RF model based on routine health check data demonstrates superior predictive accuracy in both male and female cohorts, markedly exceeding the performance of other comparative models (such as logistic regression) and conventional screening tools (such as OSTA). This underscores the significance of developing gender differentiation models and suggests that efficient risk assessment of bone density reduction can be accomplished using routine physical examination data. This outcome offers robust tool support for executing cost-effective and efficient early screening for bone density deterioration in clinical practice.

Osteoporosis is a persistent disorder marked by diminished bone mass and the degradation of bone structure, resulting in an increased risk of fractures. This condition represents a substantial risk to patient health, especially because fractures can greatly hinder movement and reduce quality of life. Furthermore, osteoporosis exerts a significant economic burden on healthcare systems, encompassing both treatment costs and related productivity losses. Recent studies have discovered various risk factors for osteoporosis, including age, sex, and lifestyle choices, all of which

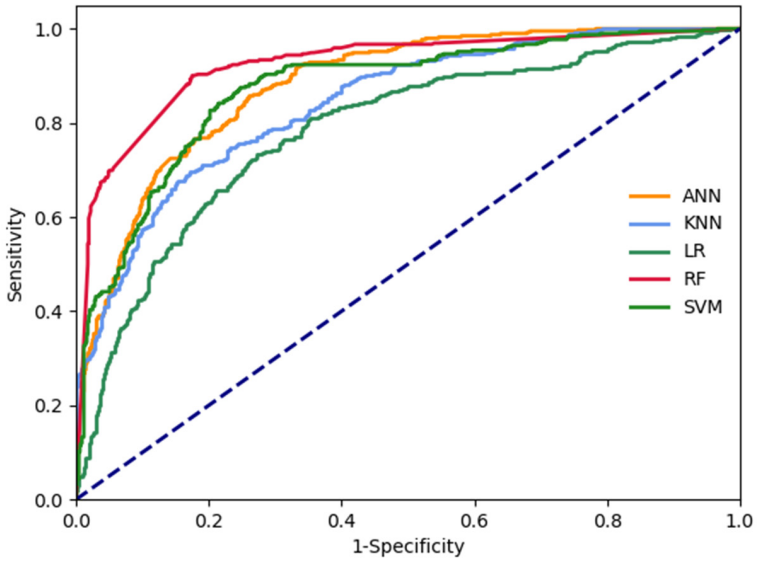

Figure 2. The Receiver operating characteristic (ROC) curves of five machine learning models for prediction of Decreased bone density in females. ANN: Artificial neural network; SVM: Support vector machine; RF: Random Forest; KNN: K-nearest neighbors; LoR: Logistic regression.

are strongly associated with the progression of the disease. Research indicates that identifying these risk variables is essential for formulating personalized treatment strategies [32]. Nonetheless, there remains an imperative necessity to create early risk assessment tools that are more precise, accessible, and appropriate for extensive groups. Consequently to better assess osteoporosis risk, researchers had developed various screening tools, including the Simple Calculated Osteoporosis Risk Estimation (SCORE), Osteoporosis Risk Assessment Instrument (ORAI), Osteoporotic Self-assessment Tool (OST/OSTA), Osteoporosis Index of Risk (OSIRIS), and others that were known for their high sensitivity but low specificity [15, 33-35]. Despite their simplicity and user-friendliness, these technologies frequently lack adequate specificity. This work proposes a machine learning based prediction model, particularly the RF model, which employs regular medical examination data to achieve high-precision risk stratification, offering a viable option to address the limitations of current tools. This work employs machine learning technology to enhance the precision of osteoporosis risk prediction, facilitating to optimize clinical decision-making and patient treatment by researchers. This approach emphasizes forecasting the risk of osteoporosis without requiring causal inference of the influence of input variables [36].

Prior studies predominantly concentrated on the creation of machine learning models for osteoporosis prediction. In a 2023 study, Yang et al. focused on individuals aged 45 and older in Hong Kong, China, employing Gradient Boosting Machine (GBM), Support Vector Machine (SVM), Naive Bayes (NB), and Logistic Regression (LR) models to forecast osteoporosis with the Preclinical Osteoporosis Screening Tool (POST). The models attained an ideal AUROC of 0.858, with a sensitivity of 0.83 and specificity of 0.83 [20]. A study by Kim et al. in 2013 examined 1,674 postmenopausal Korean women, employing an SVM model for osteoporosis prediction, achieving an ideal AUROC of 0.827, with a sensitivity of 0.78 and specificity of 0.76 [37]. In another study by Shim et al. in 2020, a cohort of 1,792 postmenopausal women was evaluated using five different machine learning models. Among these, the Artificial Neural Network (ANN) exhibited exceptional performance, attaining an AUROC of 0.743, sensitivity of 0.72, and specificity of 0.77 [38]. In a separate 2019 study by Meng et al., examining women aged 20 years and older, an ANN model was developed that attained an AUROC of 0.829, with a sensitivity of 0.51 and specificity of 0.90 [39]. Meanwhile, Wen Yu Ou Yang et al. included participants aged 50 years and above, comprising both genders. This study employed ANN, SVM, RF, k-nearest neighbors (KNN), and Logistic Regression (LoR) models to forecast the risk of osteoporosis. The results indicated that for males, the ANN, SVM, RF, and LoR models, and for females, the ANN, SVM, and RF models, greatly surpassed the Osteoporosis Self-assessment Tool for Asia (OSTA) model [40]. Compared with previous studies, this study presents significant advantages over prior research by concentrating on early prediction of bone density reduction, encompassing osteoporosis and bone loss, rather than solely diag-

nosing established osteoporosis, aligning with the clinical necessity for proactive intervention. Our RF model demonstrated exceptional prediction accuracy on an independent test set, effectively balancing and specificity. Incorporating both genders (n=11,132, aged ≥40 years) from the community population in the study enhances gender applicability and universality. It is crucial that the model relies solely on routine health examination data (vital signs, medical history, and blood biomarkers), hence obviating the necessity for specialized imaging and enabling implementation in basic healthcare environments. In terms of methodology, feature selection was optimized by prescreening via statistical testing ($P<0.05$), and the stability and interpretability of the model were improved by removing unnecessary variables.

Feature selection is a fundamental concept in machine learning because of its substantial influence on model performance. In this instance, statistical approaches were employed to filter the data rather than integrating all possible signs into the machine learning model. This methodology seeks to eradicate superfluous indications, hence optimizing model performance and augmenting the precision of machine learning predictions. This study identified that, age, low weight, hypertension, diabetes and specific blood indicators (such as ALT, ALP, creatinine) are significant predictors of decreased bone mineral density. Reduced body weight may influence bone remodeling by diminishing bone mechanical load [41] on the bones, but hypertension and diabetes may impair the bone microenvironment through persistent inflammation [42]. The inverse relationship between HDL-C and bone density in males requires additional validation and may be affected by unmeasured confounding variables. The indicators chosen for inclusion in the male model comprised age, weight, hypertension, diabetes, ALT, AST, ALB, ALP, Cr, UA, TG, HDL-C, and Hb. The chosen indicators for the female model included age, weight, hypertension, diabetes, ALT, ALP, UA, BUN, TC, TG, HDL-C, LDL-C, and Hb. These signs found through screening have been demonstrated in previous research to correspond with diminished bone density or the presence of osteoporosis. Multiple studies have demonstrated that the incidence of osteoporosis and osteopenia markedly escalates with advancing age, especially in women relative to males. Chiu et al. discovered that individuals classified as underweight faced an elevated chance of developing osteoporosis compared to those with normal weight, with underweight status acting as an independent risk factor for the condition [43]. Moreover, research has demonstrated a correlation between aberrant serum albumin levels and reduced bone density, as well as osteoporosis. ALT and AST are essential indicators for liver function, with increased levels signifying liver disease [44]. Our data systematically indicates, for the first time in a prediction model the correlation between traditional liver function metrics and the likelihood of decreased bone density decline. Research conducted over the past decade has demonstrated that the skeletal system serves not only as a mechanical load-bearing structure but also as a crucial endocrine organ. Cytokines released by the skeletal system modulate multiple organs throughout the body, including the liver [45]. While definitive research demonstrating a direct relationship between BMD and liver enzymes levels is lacking, the above described data may provide insights into this possible association. ALP is an enzyme extensively found in multiple organs, including the liver, bile ducts, kidneys, and bones. Its principal relationship pertains to osteoblast activity in bone metabolism, where it significantly contributes to osteoid production and bone mineralization. This robustly substantiates its biological validity as a predictor [46]. Creatinine serves as an indicator of muscle mass, and in elderly persons with normal kidney function, diminished serum creatinine levels were independently linked to decreased bone density [47]. Yan et al. conducted a study illustrating the preventive effect of uric acid in postmenopausal women; however, they determined that uric acid did not increase the risk of osteoporosis in men [48]. Lian et al. identified TC and LDL-C as risk factors for osteoporosis, whereas HDL-C and weight were determined to be protective factors [49]. In summary, our feature screening validated traditional risk factors, but more significantly, highlighted the utility of readily accessible blood biochemical markers (especially liver function, blood lipids, and kidney function related indicators) in developing a predictive model for bone density decline during routine physical examinations, while underscoring the gender specificity of the impact of these fac-

tors. The RF model's robust feature interaction capability allows it to identify intricate interactions, such as potential synergistic effects between age and ALP, weight and HDL-C, which may contribute significantly to its superior performance.

Limitations

Nonetheless, our study possesses certain limitations, including a relatively modest sample size of 11,132 cases and the possibility for bias stemming from data collection conducted exclusively at a single center. These characteristics may influence the generalizability of study findings, particularly in their applicability across diverse populations and clinical environments. The absence of external dataset validation and multi center research support necessitates additional testing of the model's stability and efficacy through larger scale longitudinal studies. This work has preliminarily identified risk factors for osteoporosis; however, further longitudinal investigations are necessary to confirm the reliability and efficacy of different predictive models. The identified limitations indicate that the existing research findings primarily offer a conceptual framework for a potential screening tool concept and preliminary validation, necessitating further assessment of its clinical translational value needs to be evaluated in a more rigorous prospective, multicenter environment.

Conclusion

In summary, our investigation indicated that the RF models were successful in predicting osteoporosis risk in both males and females. This approach provides a cost-efficient prescreening instrument that aids physicians in executing early prevention strategies for osteoporosis and osteoporotic fractures.

Disclosure of conflict of interest

Bohan Li, Dongjin Wu, Xiaoqian Kong, Yan Shi, Chunzheng Gao and Yixin Li declare that this research was performed without any commercial or financial relationships that could be construed as a potential conflict of interest.

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