Application of Machine Learning on Health Examination Data for Predicting the Decrease of Bone Mineral Density

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ABSTRACT

Background: *Early detection and preventive measures for reduced bone density can greatly improve patients' quality of life and reduce economic burdens. This study aimed to develop machine learning algorithms that can accurately predict the risk of bone mineral density loss.* ***Methods:*** *The study included participants aged 40 years and older who underwent health evaluations at an affiliated institution from January 2022 to January 2024. Five machine learning algorithms were used to predict the risk of osteoporosis: k-nearest neighbor (KNN), random forest (RF), support vector machine (SVM), artificial neural network (ANN), and logistic regression (LR). The performances were evaluated based on accuracy, sensitivity, specificity, and area under the receiver operating characteristic curve (AUROC).* ***Results:*** *This study included 11132 patients, of whom 3568 had decreased bone density. The initial dataset contains 17 variables. After the data screening, 13 variables were included in the machine learning model. The AUROC for ANN, KNN, LR, RF, and SVM were 0.882, 0.906, 0.684, 0.918, 0.896 for males and 0.881, 0.843, 0.784, 0.922, 0.872 for females, respectively. The accuracies of ANN, KNN, LR, RF, and SVM were 0.83, 0.86, 0.75, 0.88, 0.82 for males, and 0.81, 0.77, 0.74, 0.85, 0.79 for females.* ***Conclusion:*** *In this study, we developed five machine learning models to accurately predict bone density reduction. The RF model performed best in both male and female populations, with the highest AUROC. Application of machine learning models in clinical settings can help improve the prevention, detection, and early treatment of bone density reduction.*

Key Words: *Machine Learning, KNN, RF, SVM, ANN, LR, Osteoporosis, Osteopenia, Bone Mineral Density*

INTRODUCTION

Osteoporosis is a systemic bone disease that commonly occurs with aging and is characterized by low bone mass and fragile bone structure, which increases the risk of fractures.[1] Approximately 50% of postmenopausal women and 20% of men over 50 worldwide were affected by osteoporosis.[2,3] In China, the prevalence of osteoporosis in adults is approximately 7%, 22.5% in males aged 50 years and above, and 50.1%.[4] Another multicenter study revealed that the age-standardized prevalence of osteoporosis in men and women aged > 50 years in China was 6.46% and 29.13%, respectively.[5] Acceleration of the aging process has led to an increase in the incidence of osteoporosis and osteoporotic fractures. These conditions now pose a significant public health problem, impacting the medical and economic development of countries worldwide.[6,7] Therefore, preventing osteoporosis or detecting it early, along with effectively managing it, can improve patients' quality of life and reduce their financial burden.

With the rapid evolution of imaging technology, an increasing number of techniques for diagnosing osteoporosis have been introduced, such as dual-energy X-ray absorptiometry, quantitative CT, and quantitative ultrasound absorptiometry.[8-10] The gold standard for the diagnosis of osteoporosis is measurement of bone mineral density (BMD) using dual-energy X-ray absorptiometry (DXA).[11] According to the recommendations of the World Health Organization working group, osteoporosis was diagnosed by calculating the BMD T-score.[12] Although Dual-energy X-ray Absorptiometry (DXA) scans are both convenient and rapid, they are not feasible for universal screening across the general population. Consequently, there is a need for alternative, straightforward, and effective tools to evaluate the risks of low bone mineral density and osteoporosis.

Current research on osteopenia and osteoporosis has identified multiple risk factors, including age, sex, and lifestyle, which are closely related to the development of osteopenia and osteoporosis.[13,14] Researchers have been shifting their attention from solely studying risk factors of osteoporosis to enhancing screening models, and researchers have established the Asian Osteoporosis Self-Assessment Tool (OSTA) model for postmenopausal Asian women, which is simple and convenient to use.[15] In recent years, the use of machine learning in medicine has become increasingly widespread, particularly for predicting disease risk, because it can automatically build analytical models and make decisions with minimal human involvement.[16,17] Currently, machine learning-based osteoporosis prediction models have been established using clinical or preclinical features such as computed tomography images, radiographs, ultrasound signals, molecular and genetic biomarkers, daily habits, and education.[18-20] Earlier research had concentrated on predicting osteoporosis. This study aimed to employ machine learning technology to achieve four main objectives: early detection of a decrease in bone mineral density (BMD), enhanced risk prediction of bone density loss across genders, timely prevention of osteoporosis, and promotion of personalized clinical interventions.

METHODS

Data Acquisition

We reviewed and analyzed the data of community residents aged 40 years and above who participated in health examinations at the author's institution from 2022 to 2024. Conduct relevant medical history and physical examinations of all participants, including vital signs, height, weight, and collection of all hematological and biochemical test results. DXA (GE Healthcare, Madison, WI, USA) was used to evaluate bone density. The t-score represents the standard deviation of bone density compared with healthy young adults of the same sex and race. The t-score results were interpreted as osteoporosis (≤ -2.5), osteoporosis (-2.5< score<-1), or normal (score ≥ -1).

Exclusion criteria were as follows: 1. patients who had received anti-osteoporosis treatment due to known osteoporosis or bone loss, 2. History of metabolic bone disease or chronic diseases related to calcium absorption, history of malignant tumors, use of drugs known to affect bone metabolism, and/or positive pregnancy; 3. history of fractures or previous surgical treatment for fractures; 4. History of lumbar spine surgery, 5. data missing, 6. extreme outliers, 11132 participants were ultimately included in the study.

Ethics Statement

This study was approved by the ethics committee of the authors' institution (approval number KYLL2024981).

Feature Data Preprocessing

The following data were collected: 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), and low-density lipoprotein cholesterol (LDL-C). Statistically significant features for input into the final machine learning model were selected using chi-squared tests, t-tests, or non-parametric tests.

Model Development and Validation

The dataset was randomly divided into a training set (80%) and a testing set (20%). The training set was used to train the predictive models and adjust the parameters, whereas the testing set was used to test the performance of the developed model. We used PyCharm software to apply machine learning algorithms to build predictive models for bone density reduction, including the following five machine learning models: artificial neural network (ANN), k-nearest neighbors (KNN), logistic regression (LR), Random Forest (RF), and support vector machine (SVM). The performance of the model was comprehensively assessed by plotting the Receiver Operating Characteristic (ROC) curve for the subjects involved. To compare the efficacy of various machine learning models, key metrics such as the Area Under the ROC Curve (AUROC), sensitivity, specificity, and accuracy were calculated. Sensitivity, also known as the true positive rate (TPR), refers to the proportion of participants correctly identified as having a disease. Specificity, or the true negative rate (TNR), denotes the proportion of participants who are accurately recognized as healthy. The false-positive rate, represented as 1-specificity, was the proportion of participants incorrectly identified as having the disease. Accuracy was defined as the overall proportion of participants correctly classified as either healthy or diseased. [21].

Statistical Analysis

Continuous variables are described using mean and standard deviation, whereas categorical variables are presented as frequencies and percentages. The differences between continuous variables were evaluated using either the t-test or a non-parametric test, while the differences among categorical variables were assessed using the chi-square test. All statistical analyses were performed using the SPSS software (version 29.0). The development and performance evaluation of the machine learning models were performed in the PyCharm environment. Statistical significance was set at P<0.05.

RESULTS

Demographic Information of Research Population

Among the 11132 participants in the study, there were 5793 males and 5339 females, with an average age of 54.91 ± 10.12 for males and 55.58 ± 10.01 for females. There were 1610 males and 1958 females with decreased bone density. The

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 is referred to as osteopenia or osteoporosis. P-values were calculated with two-tailed T tests for continuous variables, and two-tailed Z tests for binary variables other results are presented in **Table 1**.

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Results of Data Screening

We compared the candidate features between the normal and decreased bone density groups using the chi-square test or t-test, as shown in **Table 2**. Selected indicators ($p<0.05$) were included in the machine-learning model. The final indicators for male inclusion in the model were Age, Weight, Hypertension, Diabetes, ALT, AST, ALB, ALP, Cr, UA, TG, HDL-C, and Hb levels. The indicators for female inclusion in the model were Age, Weight, Hypertension, Diabetes, ALT, ALP, UA, BUN, TC, TG, HDL-C, LDL-C, and Hb levels.

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 is referred to as 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±10.97	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 is referred to as osteopenia or osteoporosis. *P-values* were calculated with two-tailed *T* tests for continuous variables, and two-tailed *Z* tests for binary variables

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Results of Machine Learning

The AUROC, sensitivity, specificity, and accuracy of the five machine-learning models are presented in **Table 4**. The receiver operating characteristic (ROC) curves of the five machine learning models are illustrated in **Figures 1** and **2**. Among these models, the Random Forest (RF) model demonstrated superior performance across both male and female populations.

Table 4. Different machine learning models for the 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)	0.926	0.839	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 a weight set at 0.6. *p*-values were calculated with the nonparametric method to compare two ROC curves proposed by DeLong et al.

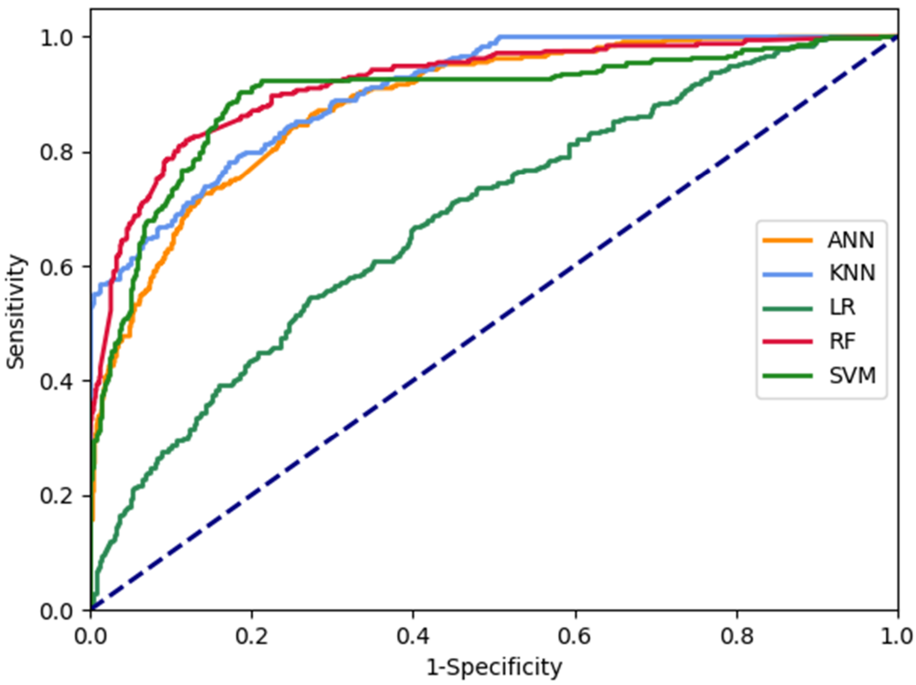

Figure 1. The Receiver operating characteristic(ROC) curves of five machine learning models for the prediction of decreased bone density in males. ANN: Artificial neural network; SVM: Support vector machine; RF: Random Forest; KNN: K-nearest neighbors; LoR: Logistic regression.

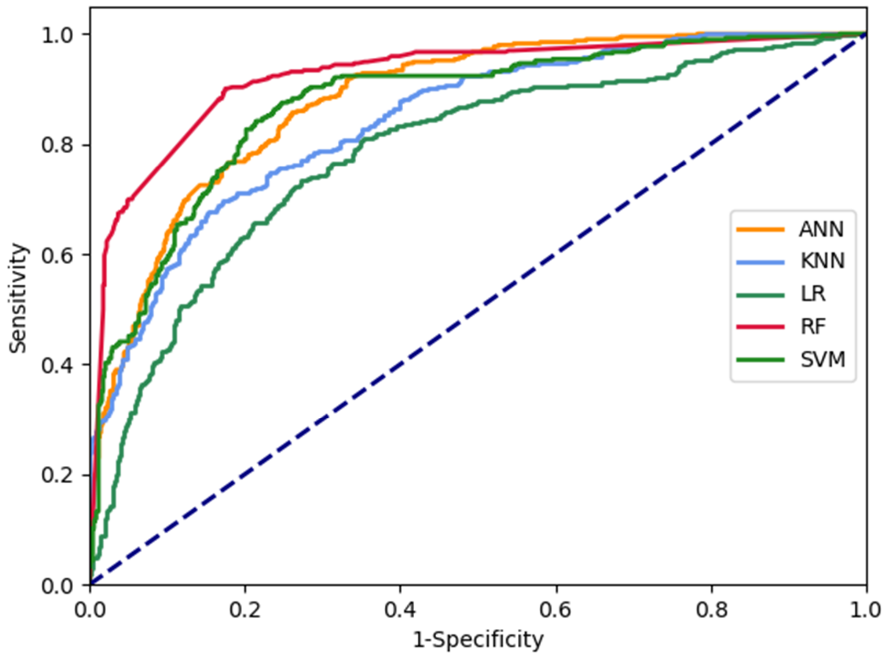

Figure 2. The Receiver operating characteristic(ROC) curves of five machine learning models for the prediction of decreased bone density in females. ANN: Artificial neural network; SVM: Support vector machine; RF: Random Forest; KNN: K-nearest neighbors; LoR: Logistic regression.

DISCUSSION

In this study, five different machine learning algorithms were used, namely ANN, SVM, RF, KNN, and LR, to screen for bone density reduction in individuals aged 40 years and above. The final indicators for male inclusion in the model were Age, Weight, Hypertension, Diabetes, ALT, AST, ALB, ALP, Cr, UA, TG, HDL-C, and Hb levels. The indicators 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 (RF) model demonstrated superior performance across both male and female populations.

Osteoporosis is a chronic condition characterized by decreased bone mass and deterioration of the bone tissue, resulting in a heightened risk of fractures. This disease significantly threatens patient health, particularly due to fractures that can severely impair mobility and diminish the quality of life. Moreover, osteoporosis places a substantial economic burden on healthcare systems, encompassing both the costs of treatment and the associated losses in productivity. Recent studies have identified various risk factors for osteoporosis, including age, sex, and lifestyle choices, which are intricately linked to disease progression. Studies have demonstrated that the identification of these risk factors lays the groundwork for developing personalized treatment strategies.[22] To better identify osteoporosis risk, researchers have established 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 known for high sensitivity but low specificity.[15,23,24,25] By improving the accuracy of osteoporosis risk predictions using machine learning techniques, researchers can enhance clinical decision-making and patient management. This required the ability to predict the risk of osteoporosis but did not require causal inference of the impact of input variables on this risk.[26]

Previous research has predominantly focused on developing machine learning models for osteoporosis prediction. Yang et al. published a study in 2023 targeting the population aged 45 and above in Hong Kong, China. Gradient Boosting Machine (GBM), Support Vector Machine (SVM), Naive Bayes (NB), and Logistic Regression (LR) models were used to predict osteoporosis using the POST tool. The models achieved an optimal Area Under the Receiver Operating Characteristic Curve (AUROC) of 0.858, with a sensitivity of 0.83, and specificity of 0.83.[20] A study by Kim et al. in 2013 involved 1,674 postmenopausal Korean women using an SVM model for osteoporosis prediction, yielding an optimal AUROC of 0.827, sensitivity of 0.78, and specificity of 0.76.[27] In another study published 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) demonstrated superior performance, achieving an Area Under the Receiver Operating Characteristic Curve (AUROC) of 0.743, sensitivity of 0.72, and specificity of 0.77.[28] In a separate 2019 study by Meng et al., the research focused on the demographics of women aged 20 years and above, where an ANN model was developed that attained an AUROC of 0.829, sensitivity of 0.51, and specificity of 0.90.[29] The study by Wen Yu Ou Yang et al. involved participants aged 50 years and older, including both men and women. This study used ANN, Support Vector Machine (SVM), Random Forest (RF), k-nearest neighbors (KNN), and Logistic Regression (LoR) models to predict the risk of osteoporosis. The findings revealed that for males, the ANN, SVM, RF, and LoR models, and for females, the ANN, SVM, and RF models significantly outperformed the Osteoporosis Self-assessment Tool for Asia (OSTA) model.[30] Compared with previous studies, this research focuses on the reduction in bone density, and the findings indicate that machine learning algorithms offer significant advantages in predicting bone density reduction. The SVM, RF, KNN, LightGBM, and XGBoost models demonstrated robust predictive performance in males. The RF, LightGBM, and XGBoost models showed strong predictive capabilities for females.

Feature selection is a critical concept in machine learning owing to its substantial impact on model performance. In this study, rather than incorporating all potential indicators into the machine-learning model, statistical methods were employed to screen the data. This approach aims to eliminate superfluous indicators, thereby optimizing the model performance and enhancing the accuracy of machine learning predictions. The indicators selected for inclusion in the male model were Age, Weight, Hypertension, Diabetes, ALT, AST, ALB, ALP, Cr, UA, TG, HDL-C, and Hb. For the female, Age, Weight, Hypertension, Diabetes, ALT, ALP, UA, BUN, TC, TG, HDL-C, LDL-C, and Hb were included in the model. The indicators identified through screening have been demonstrated in prior studies to correlate with reduced bone density or the presence of osteoporosis. Numerous studies have indicated that the prevalence of osteoporosis and osteopenia with advancing age is markedly higher in women than in men. Chiu et al. identified that individuals classified as underweight possess a greater risk of developing osteoporosis relative to those with normal weight, with underweight status being an independent risk factor for osteoporosis.[31] Additionally, studies have established a connection between aberrant serum albumin levels and abnormal bone density as well as osteoporosis. ALT and AST are crucial biomarkers for liver function, with elevated levels indicating liver dysfunction.[32] Importantly, research over the last decade has revealed that the skeletal joint system functions not only as a mechanical load-bearing structure, but also as a significant endocrine organ. Cytokines secreted by the skeletal system exert regulatory control over numerous organs throughout the body, including the liver.[33] Although there is currently no definitive research establishing a direct relationship between BMD and liver enzyme levels, the aforementioned findings may provide insights into this potential connection. ALP is an enzyme that is widely distributed across various organs, including the liver, bile ducts, kidneys, and bones. However, it has a primary association with osteoblast activity in bone metabolism, where it plays a significant role in osteoid formation and bone mineralization.[34] Creatinine is often used as a marker of muscle mass, and in elderly individuals with normal kidney function, low serum creatinine levels are independently associated with reduced bone density.[35] Yan et al. conducted a study that demonstrated a protective role of uric acid in postmenopausal women; however, they found that uric acid did not increase the risk of osteoporosis in men.[36] Lian et al. identified TC and LDL-C as risk factors for osteoporosis, whereas HDL-C and weight were protective factors for osteoporosis.[37]

Limitations

This study enhances the features integrated into the machine learning model. However, this study had several limitations, such as the sample size and potential bias stemming from data collection at a single center. These factors may affect the generalizability of the findings, particularly their applicability across diverse populations and clinical settings. Future studies should aim to increase the sample size and conduct multicenter studies to improve the external validity of the results. Furthermore, although this study provides preliminary insights into the risk factors for osteoporosis, additional longitudinal studies are needed to validate the consistency and effectiveness of various predictive models.

CONCLUSION

In summary, our study showed that the SVM, RF, KNN, LightGBM, and XGBoost models were effective in predicting osteoporosis risk in males, whereas the RF, LightGBM, and XGBoost models were effective in predicting osteoporosis risk in women. These models offer a cost-effective prescreening tool that can help clinicians implement early prevention strategies for osteoporosis and osteoporotic fractures.

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CONFLICT OF INTEREST

Bohan Li, Hui Yuan, Xiaoqian Kong, Yan Shi, and Yixin Li declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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