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Comparing machine learning algorithms for prediction of osteoporosis: A systematic review and meta-analysis study

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ABSTRACT

Introduction: Osteoporosis is a prevalent bone disease that affects millions of individuals worldwide. Early identification and prediction of osteoporosis can enable timely interventions and preventive measures. This study investigates the potential of machine learning algorithms to accurately predict osteoporosis.

Material and Methods: This study is a systematic review and meta-analysis conducted by searching in three databases. Our search encompassed databases such as Web of Science, PubMed, and Scopus. Pertinent information from the selected studies was independently extracted by two authors. The PRISMA guidelines were followed to ensure a rigorous review process. The PROBAST tool was utilized to assess the risk of bias in the included studies. Data analysis was performed using Stata (v.17.1).

Results: A total of 63 algorithms from 18 studies were evaluated. In terms of predicting osteoporosis, support vector machine (SVM) and random forest (RF) algorithms demonstrated the highest sensitivity. For SVM, the sensitivity and diagnostic odds ratio (DOR) were 83.0% (95% confidence interval (CI): 76.0-88.0) and 10.4 (95% CI: 6.0-18.2), respectively. Similarly, in the case of RF algorithm, the sensitivity and DOR were 81.0% (95% CI: 74.0-87.0) and 13.0 (95% CI: 7.7-21.2), respectively. The artificial neoural networks (ANN), RF, and K-nearest neighbors (KNN) algorithms exhibited the highest specificity values: ANN- specificity of 79.0% (95% CI: 71.0-85.0) and DOR of 12.0 (7.3-18.7); RF- specificity of 75.0% (95% CI: 62.0-84.0) and DOR of 13.0 (7.7-21.2); KNN- specificity of 75.0% (95% CI: 67.0-82.0) and DOR of 7.7(6.6-9.0).

Conclusion: Our study highlights the promising potential of machine learning algorithms for the accurate prediction of osteoporosis. ANN model and SVM, RF, and KNN algorithms have emerged as the most robust predictors. These findings demonstrate substantial potential for aiding early detection and intervention strategies against osteoporosis.

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INTRODUCTION

Osteoporosis, a common skeletal disorder, poses significant challenges for individuals affected by it. This condition is characterized by reduced bone density and deterioration of bone microarchitecture, resulting in increased vulnerability to fractures [1]. Osteoporosis predominantly affects older adults, particularly postmenopausal women [2], but can also occur in men and younger individuals [3]. One of the primary challenges of osteoporosis lies in its asymptomatic nature until a fracture occurs, leading to delayed diagnosis and treatment initiation [4]. Moreover, the progressive nature of the disease increases the risk of recurrent fractures and significant impairment in mobility and quality of life [5].

Osteoporosis presents numerous challenges for individuals affected by the condition. One of the primary problems is the increased risk of fractures,

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which can lead to pain, disability, and a significant decline in quality of life [5, 6]. Osteoporotic fractures, especially in the hip and spine, can result in prolonged hospitalization, surgical interventions, and long-term rehabilitation [7]. Another issue is the asymptomatic nature of osteoporosis until a fracture occurs, making it difficult to detect and intervene at an early stage [8]. Additionally, the progressive nature of the disease puts individuals at a higher risk of recurrent fractures [9], further exacerbating the physical and emotional burden [10]. Addressing these problems requires early detection and prediction of osteoporosis.

The early detection and prediction of osteoporosis play a crucial role in preventing debilitating fractures and implementing appropriate interventions [11]. Traditional approaches for osteoporosis prediction rely on risk assessment tools based on clinical factors and dual-energy X-ray absorptiometry (DXA) scans. However, emerging research suggests that machine learning techniques have the potential to improve the accuracy and efficiency of osteoporosis prediction by integrating diverse data sources [12]. These techniques can integrate various types of data, such as clinical, genetic, and imaging information, to improve the accuracy and efficiency of predicting osteoporosis risk.

Machine learning models have the potential to identify high-risk individuals earlier, enabling timely interventions and preventive measures to mitigate the progression of osteoporosis and reduce fracture risk [13, 14]. In this context, we present a systematic review and meta-analysis study aimed at evaluating the predictive capabilities of machine learning models in identifying individuals at risk of osteoporosis. Through synthesizing and analyzing existing literature, we aim to provide a comprehensive overview of the current state of research in this field and shed light on the potential clinical implications of machine learning-based osteoporosis prediction.

MATERIAL AND METHODS

In this study, we utilized the Preferred Reporting Information for systematic reviews and meta-analysis (PRISMA) checklist to select studies and report the results.

Data Sources and Search strategy

To conduct this study, we conducted searches in Web of Science, PubMed, and Scopus databases to identify relevant published papers until July 10, 2023. To retrieve the relevant study, we employed the following search strategy:

((“Machine learning” OR “artificial intelligence” OR “machine learning algorithms” OR “deep learning” OR “neural networks” OR “artificial neural network”) AND (“low bone density” OR “osteoporosis” OR “osteopenia”))

Eligibility criteria

This study included articles that specifically addressed the prediction of osteoporosis using machine learning techniques. The inclusion criteria considered articles published in English, centering on the use of machine learning for osteoporosis prediction, and reporting machine learning algorithms, sensitivity, specificity, and/or receiver operating characteristic curve (ROC). Exclusion criteria were applied to papers that did not primarily concentrate on the prediction of osteoporosis with machine learning. Additionally, letters to the editor, conference abstracts, book chapters, and books, were excluded from the study.

Study selection

Initially, abstracts of relevant articles were collected from three databases: Web of Science, PubMed, and Scopus. These study abstracts were then imported into EndNote 21. Afterward, any duplicate articles were removed. Two researchers reviewed the titles and abstracts to select the relevant articles based on the inclusion and exclusion criteria.

In instances of disagreement, the research team members resolved disagreements through discussions, arriving at the ultimate decision for each article. Ultimately, the full text of the articles was examined to extract essential data.

Data charting process and data items

For each study, the following information was extracted: authors name, year of publication, study aim, used database, machine learning algorithms used, sample size, as well as measures used for assessing algorithm performance such as specificity, sensitivity, accuracy, positive predictive value (PPV), negative predictive value (NPV), and receiver operating characteristic (ROC) curve. For case studies lacking details on positive and negative cases, we conducted manual calculations using recognized formulas based on statistics available in the manuscripts or provided by the authors. When required data were not presented in the manuscripts or abstracts, we contacted the authors for clarification. Our initial contact prioritized the corresponding author, followed by the first author, and then the last author. If attempts to contact the authors in this specified sequence were unsuccessful, the studies were excluded from the meta-analysis. Furthermore, manuscripts or abstracts without sufficient evaluation data after author contact were also excluded.

Critical appraisal of individual sources of studies

To critically appraise individual sources of studies, we utilized the prediction model risk of bias assessment tool (PROBAST). This tool facilitates the assessment of both the risk of bias (ROB) and the applicability of diagnostic and prognostic prediction model studies. The PROBAST tool consists of 20 signaling questions that are categorized into four domains: participants, predictors, outcome, and analysis. This accompanying document provides a comprehensive explanation and elaboration for each domain and signaling question's inclusion. It serves as a helpful resource for researchers, reviewers, readers, and guideline developers, aiding them in effectively employing the tool to evaluate both the risk of bias and applicability concerns within their assessments [15].

Statistical analysis

In this study, a meta-analysis was conducted using a 2x2 contingency table. The table was constructed to include values for true false positive (FP), positive (TP), false negative (FN), and true negative (TN). Meta-analysis for diagnostic tests was carried out when more than four studies reported algorithms for predicting osteoporosis. The models encompassed estimates of sensitivity, specificity, diagnostic odds ratio, positive likelihood, negative likelihood, and ROC. The 'metandi' and 'metadta' commands in Stata (versions 17.1 and 14.1) were used to model these values along with 95% confidence intervals (CIs).

RESULTS

After extracting 1564 papers from three databases, duplicate entries were excluded, resulting in a collection of 1196 unique studies. Subsequently, these studies underwent a meticulous review and evaluation based on pre-established criteria for inclusion and exclusion. After this comprehensive assessment, a final set of 17 articles was selected for inclusion in the research (Fig 1).

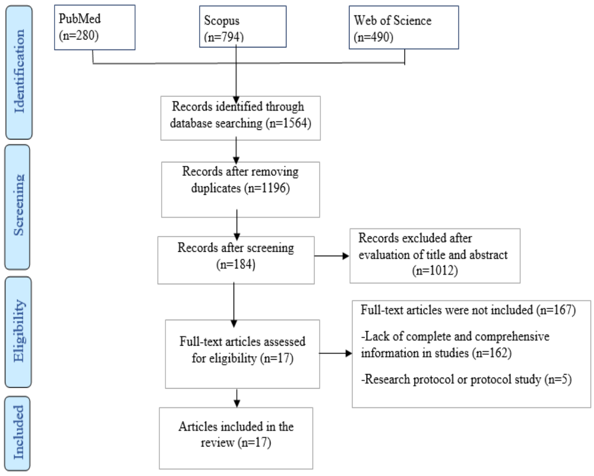

Fig 1: PRISMA diagram depicting the screening and inclusion process of studies

Characteristics of the included studies

Table 1 provides a thorough summary of the selected studies. A total of 63 algorithms from 17 distinct studies were evaluated. The majority of the studies were conducted in China (n=6) and Korea (n=5).

Table 1: Comprehensive examination of the chosen studies

Ref	Year	Country	Database name	Number of samples	Number of algorithms	Algorithm name
[16]	2009	Korea	Korea National Health and Nutrition Examination Surveys (KNHANES)	1792	7	KNN, random forest (RF), gradient boosting machine (GBM), SVM, ANN, decision tree (DT), and logistic regression (LR)
[17]	2010	Chaina	Medical records of participants at the Second Affiliated Hospital of Harbin Medical University and the Affiliated Hospital of the Medical School of Ningbo University.	1559	1	ANN
[18]	2013	Taiwan	The dataset in this study, which included SNPs, age, menopause, and BMI, was the same dataset used in a previous study by the first author of this paper [9]	295	3	Multilayer feedforward neural network (MFNN), Naive Bayes (NB), and LR
[19]	2013	Korea	Korea National Health and Nutrition Examination Surveys (KNHANES)	1674	4	SVM, RF, ANN, and LR
[20]	2013	Korea	Korea National Health and Nutrition Examination Surveys (KNHANES V-1)	1674	4	SVM, RF, ANN, and LR

Ref	Year	Country	Database name	Number of samples	Number of algorithms	Algorithm name
[21]	2016	China	Data collated from chain hospitals	119	2	ANN, LR
[22]	2019	Chaina	Data were collated from the electronic medical record systems of the Second Affiliated Hospital of Harbin Medical University and the Affiliated Hospital of the Medical School of Ningbo University.	1559	1	ANN
[14]	2020	Korea	Korea National Health and Nutrition Examination Surveys (KNHANES)	1792	7	LR, KNN, DT, RF, GBM, SVM, ANN
[23]	2021	Taiwan	Data were collected from individuals living in the community who took part in health checkup programs at a medical center in northern Taiwan from 2008 to 2018.	5982	5	ANN, SVM, RF, KNN, LR
[24]	2021	China	Data collection from Hospital of Chongqing Medical University	1419	4	Deep Belief Network (DBN), SVM ANN, and combinatorial heuristic method (Genetic Algorithm - Decision Tree (GA-DT))
[25]	2021	Korea	Data collated from Hallym University Sacred hospital	500	1	RF
[26]	2021	Greece	Data was collated from cases referred to a university hospital's specialized bone marrow imaging referral clinic.	213	3	Extreme gradient boosting (XGBoost), CatBoost and SVM
[27]	2022	India	Data collated from Abhilasha orthopedic hospital in Banashankari	80	4	DT, NB, SVM, KNN
[28]	2022	China	Data collated from the Second Affiliated Hospital of Wenzhou Medical University	172	5	Gaussian naïve Bayes (GNB), RF, LR, SVM, Gradient boosting machine (GBM), and XGBoost
[29]	2023	USA	Data for this secondary analysis was collected from patients participating in the Study of Women's Health Across the Nation (SWAN), who initially joined between 1996 and 1997 at seven designated research centers across the USA.	1,685	1	LR
[30]	2023	China	Data collated from department of Endocrinology at Cangzhou Central Hospital	433	9	XGBoost, LR, Light Gradient Boosting Machine (LightGBM), RF, Multilayer Perceptron (MLP), Gaussian Naive Bayes (Gaussian NB), Adaptive Boosting (AdaBoost), SVM, and KNN
[31]	2023	USA	Data collected from a tertiary care academic centre.	273	2	SVM, and RF

Machine learning algorithms and osteoporosis prediction

We present the results of six algorithms used for predicting osteoporosis: ANN, was recommended in 10 studies, encompassing a sample size of 17,570; LR was recommended in 11 studies, with a total sample size of 15,618; SVMs were recommended in 12 studies, involving a sample size of 15,504; RF algorithms were recommended in 9 studies, with a sample size of 12,618; KNN algorithms were recommended in six studies, with a sample size of 10,079; and DT algorithms were recommended in four studies, with a sample size of 5,083.

The results of this review reveal that SVM and RF algorithms exhibited the highest sensitivity, whereas the ANN model, RF, and KNN algorithms demonstrated the highest levels of specificity. Subsequently, detailed findings for each algorithm are described below.

ANN

The sensitivity and specificity were 76.0% (95% CI: 66.0-83.0) and 79.0% (95% CI: 71.0-85.0), respectively (Fig 2). The odds of obtaining positive results in the test outcomes for osteoporosis patients were 12.0 times higher (95% CI: 7.3-18.7) than in non-patients, and the likelihood of a positive test result was 3.6 times higher (95% CI: 2.7-4.8) (Table 2)

LR algorithm

The sensitivity and specificity were 76.0 (95% CI: 65.0-84.0) and 70.0 (95% CI: 63.0-77.0) respectively (Fig 2). The odds of obtaining positive results in the test outcomes for osteoporosis patients was 7.4 times (95% CI: 4.3-12.5) higher than in non-patients, also probable positivity in the test results was 2.6 times (95% CI: 2.0-3.2) (Table 2).

SVM algorithm

The sensitivity and specificity were 83.0% (95% CI: 76.0-88.0) and 69.0% (95% CI: 60.0-76.0), respectively (Fig 2). The odds of obtaining positive results in the test outcomes for osteoporosis patients were 10.4 times higher (95% CI: 6.0-18.2) than in non-patients, and the likelihood of a positive test result was 2.6 times higher (95% CI: 2.0-3.4) (Table 2).

RF algorithm

The sensitivity and specificity were 81.0 (95% CI: 74.0-87.0) and 75.0 (95% CI: 62.0-84.0) respectively (Fig 3). The odds of obtaining positive results in the test outcomes for osteoporosis patients was 13.0 times (95% CI: 7.7-21.2) higher than in non-patients, also probable positivity in the test results was 3.2 times (95% CI: 2.1-4.8) (Table 2).

KNN algorithm

The sensitivity and specificity were 72.0% (95% CI: 63.0-70.0) and 75.0% (95% CI: 67.0-82.0), respectively (Fig 3). The odds of obtaining positive results in the test outcomes for osteoporosis patients were 7.7 times higher (95% CI: 6.6-9.0) than in non-patients. Additionally, the likelihood of a positive test result was 2.8 times higher (95% CI: 2.3-3.5) (Table 2).

DT algorithm

The sensitivity and specificity were 67.0% (95% CI: 58.0-74.0) and 71.0% (95% CI: 62.0-79.0), respectively (Fig 3). The odds of obtaining positive results in the test outcomes for osteoporosis patients were 5.0 times higher (95% CI: 4.3-5.6) than in non-patients. Additionally, the likelihood of a positive test result was 2.3 times higher (95% CI: 2.0-2.7) (Table 2).

Table 2: Algorithms employed in the prediction of osteoporosis

Algorithms	Algorithm's frequency in studies	Sensitivity (95%CI)	Specificity (95%CI)	DOR	Positive likelihood ratio	Negative likelihood ratio	I^2
ANN	10	76.0 (66.0-83.0)	79.0 (71.0-85.0)	12.0 (7.3-18.7)	3.6 (2.7-4.8)	3.3 (2.4-4.5)	95.0
LR	11	76.0 (65.0-84.0)	70.0 (63.0-77.0)	7.4 (4.3-12.5)	2.6 (2.0-3.2)	2.9 (2.0-4.2)	93.3
SVM	12	83.0 (76.0-88.0)	69.0 (60.0-76.0)	10.4 (6.0-18.2)	2.6 (2.0-3.4)	4.0 (2.8-5.6)	87.5
RF	9	81.0 (74.0-87.0)	75.0 (62.0-84.0)	13.0 (7.7-21.2)	3.2 (2.1-4.8)	4.0 (2.9-5.4)	93.2
KNN	6	72.0 (63.0-70.0)	75.0 (67.0-82.0)	7.7 (6.6-9.0)	2.8 (2.3-3.5)	2.7 (2.2-3.3)	0.67
DT	4	67.0 (58.0-74.0)	71.0 (62.0-79.0)	5.0 (4.3-5.6)	2.3 (2.0-2.7)	2.1 (2.0-2.5)	0.2

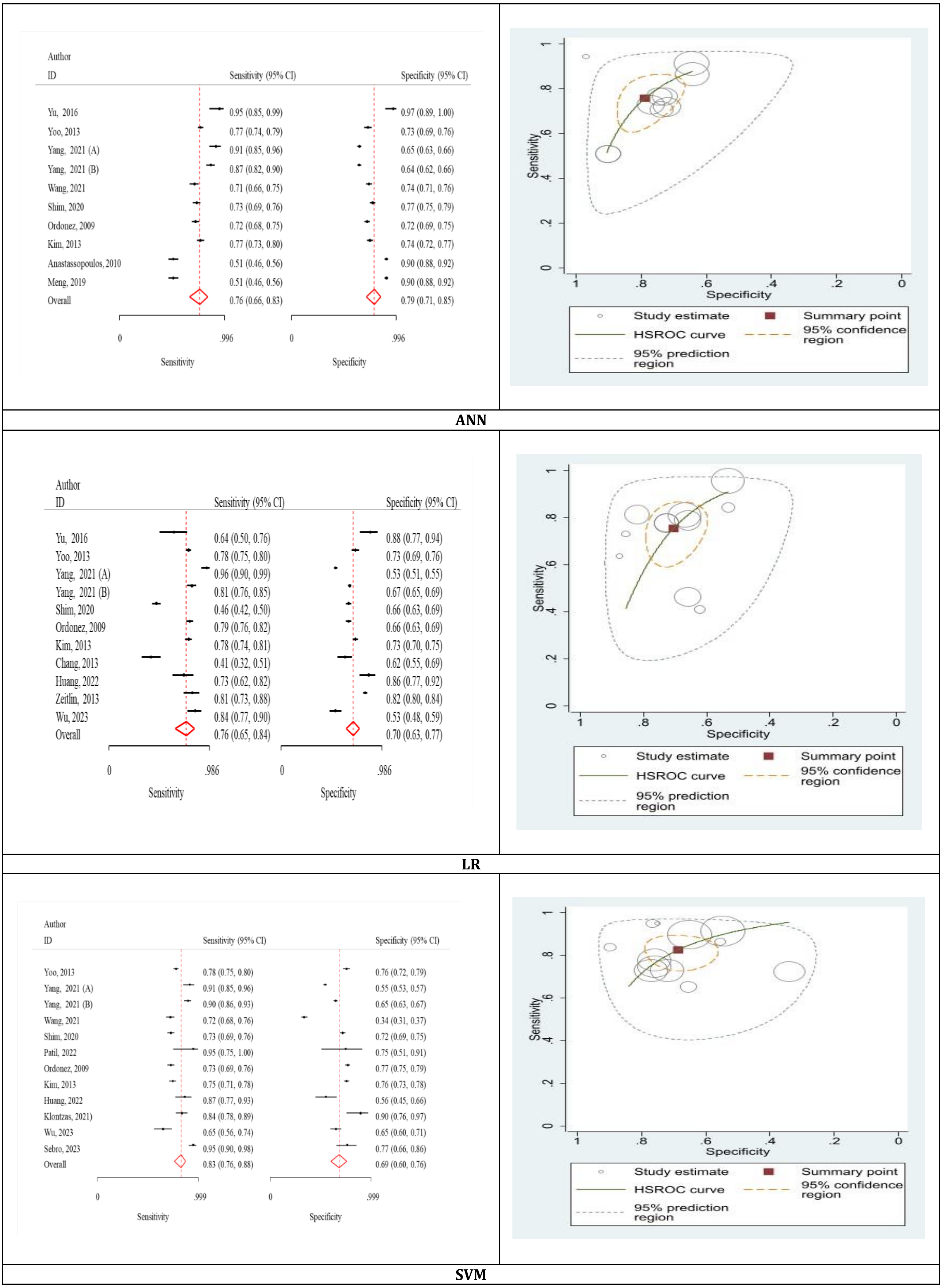

Fig 2: Sensitivity and specificity and ROC curves comparing different machine learning algorithms

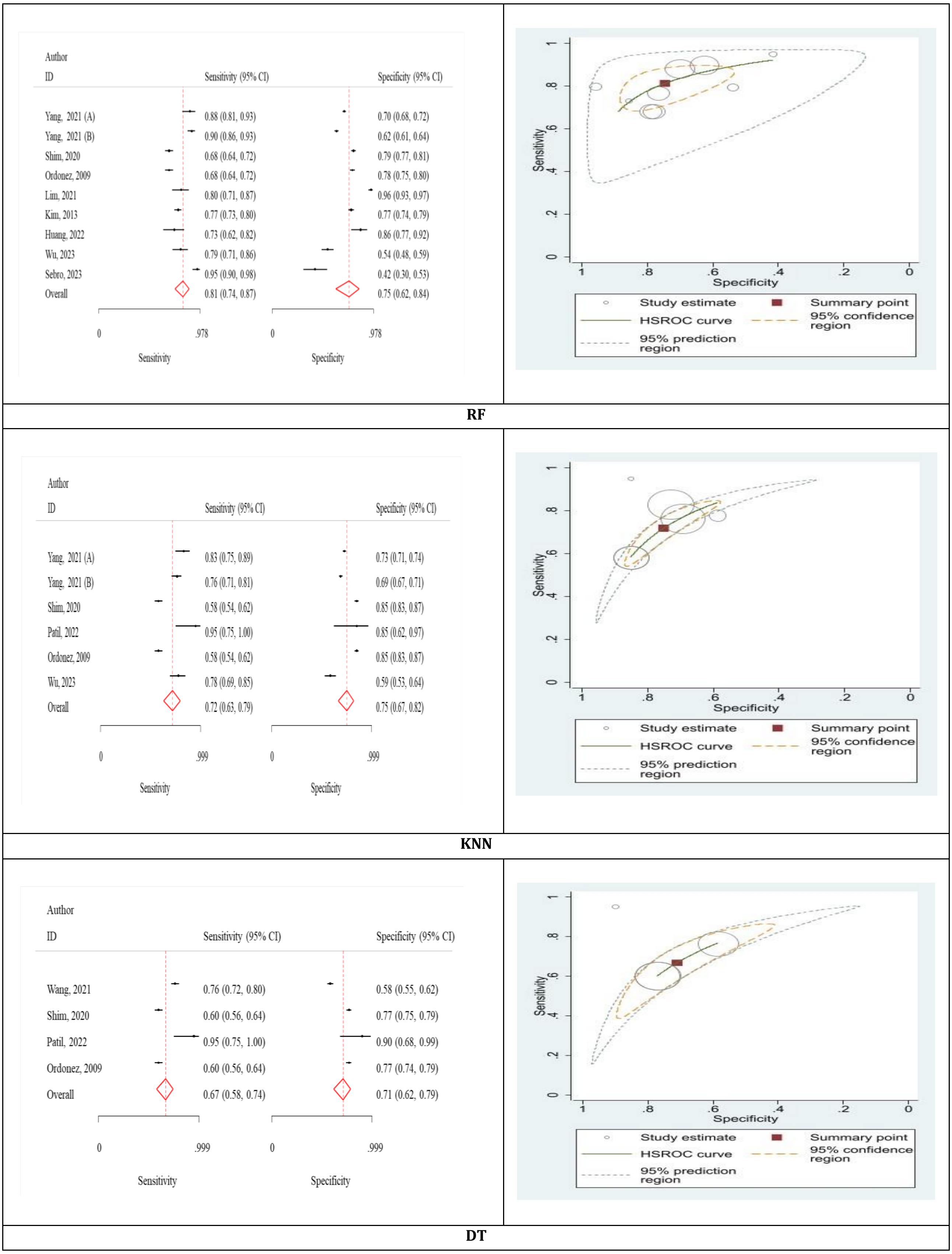

Fig 3: Comparison of various machine learning algorithms using Sensitivity and Specificity along with ROC curves.

DISCUSSION

To our current understanding, this study is the inaugural instance of a meta-analytic methodology employed in the field of machine learning research, encompassing numerous studies with thousands of participants, and centering on predicting machine learning algorithms' performance in osteoporosis. This study stands out as a groundbreaking endeavor in the realm of meta-analytic approaches applied to machine learning research. Thorough examination encompasses numerous studies with thousands of participants, providing insights into the effectiveness of different machine learning algorithms for predicting osteoporosis. The findings from this review indicate that SVM and RF algorithms exhibited the highest sensitivity. On the other hand, the ANN model, RF, and KNN algorithms demonstrated the highest specificity values.

As it mentioned a significant finding of this study is the elevated performance of the SVM and RF algorithms in terms of sensitivity. Various studies [32, 33] have shown that SVM and RF algorithms are very effective in predicting osteoporosis. This observation resonates with previous research demonstrating the prowess of these algorithms in capturing intricate patterns within datasets [34]. The capacity of SVM and RF algorithms to detect even subtle variations within data suggests their suitability for identifying individuals at risk of osteoporosis at an early stage [32]. This aspect of the findings underscores the importance of these algorithms as potential tools in clinical settings, enabling healthcare practitioners to intervene promptly and implement preventive measures to mitigate the progression of osteoporosis.

The elevated sensitivity observed in these algorithms could be attributed to their underlying mechanisms. SVM works by finding the optimal hyperplane that maximally separates different classes in the dataset. This capability enables SVM to accurately discriminate between healthy individuals and those at risk of osteoporosis, even when the differences are subtle [35]. On the other hand, RF employs an ensemble of decision trees to make predictions [36]. By combining the outputs of multiple trees, RF can capture complex interactions among variables and make robust predictions, which proves beneficial in identifying early signs of osteoporosis. As it mentioned a significant finding of this study is the elevated performance of the SVM and RF algorithms in terms of sensitivity. This observation resonates with previous research demonstrating the prowess of these algorithms in capturing intricate patterns within datasets.

This aspect of the findings underscores the importance of these algorithms as potential tools in clinical settings. The ability of SVM and RF algorithms to identify individuals at risk with high sensitivity suggests their potential application in real-world clinical settings. Javaid et al. [37], mentioned that healthcare practitioners can leverage these algorithms to accurately identify those who need closer monitoring or preventive measures. This proactive approach could lead to improved patient outcomes, reduced healthcare costs, and an overall enhancement in the management of osteoporosis.

Conversely, the study also brings attention to the high specificity values demonstrated by the ANN model, RF, and KNN algorithms. This facet of the findings emphasizes the accuracy of these algorithms in correctly identifying individuals without osteoporosis, further establishing their utility in the clinical context. The ability of these algorithms to minimize false positives can significantly contribute to reducing unnecessary interventions or treatments for individuals who are not at risk, thereby optimizing medical resources and patient care strategies. The success of these algorithms in achieving high specificity can be attributed to their unique characteristics and underlying mechanisms. Yu et al. [21], pointed out that ANNs are adept at learning complex patterns and relationships within data through interconnected layers of neurons. This ability enables them to identify subtle patterns that may indicate the absence of osteoporosis, leading to accurate predictions of negative cases.

Similarly, RF harnesses the power of ensemble learning by combining multiple decision trees, which collectively make robust predictions [38]. This ensemble approach enhances RF's ability to correctly classify negative cases by mitigating the impact of noisy data or outlier influences. KNN relies on proximity-based classification, identifying the class of a data point based on the classes of its neighboring data points [39]. This local decision-making process contributes to KNN's high specificity, as it can effectively discriminate between different classes within the dataset.

Furthermore, the article's emphasis on sample studies, such as Shim et al. [39], and Thawnashom et al. [40], underlines the consistency of the findings across different datasets. This not only adds credibility to the results but also indicates the generalizability of ANN, RF, and KNN algorithms' high specificity in diverse scenarios, reinforcing their potential as valuable tools in clinical applications. In clinical practice, high specificity holds immense value. Accurately identifying individuals without osteoporosis reduces unnecessary stress, interventions, and treatments for those who do not require them. This is particularly relevant in the context of osteoporosis, where overdiagnosis and overtreatment can have negative consequences. The precision offered by ANN, RF, and KNN algorithms can contribute to more targeted and efficient healthcare strategies, ultimately leading to improved patient experiences and outcomes.

In essence, this study offers a comprehensive overview of the predictive capacities of various machine learning algorithms in the domain of osteoporosis. The identification of algorithms that excel in sensitivity and specificity aspects underscores their potential for aiding clinicians in making informed decisions and improving patient outcomes. As the first of its kind to undertake a meta-analysis on this subject, this study not only expands our understanding of the intersection of machine learning and osteoporosis but also sets a precedent for future research endeavors seeking to harness the power of data-driven approaches in medical prediction and diagnosis.

Study limitation

This review was subject to two limitations. Firstly, it exclusively incorporated studies that had been published in the English language, thus disregarding any research available in other languages. For a more encompassing perspective, forthcoming studies should contemplate the incorporation of articles published in languages other than English. Secondly, the quest for pertinent studies was restricted to just three scientific databases: Scopus, PubMed, and Web of Science. To achieve more thorough outcomes, upcoming research should broaden their search scope to encompass a wider array of databases.

CONCLUSION

In summary, our comprehensive review and meta-analysis shed light on the remarkable potential of machine learning algorithms in predicting osteoporosis. Specifically, ANN and SVM, RF, and KNN algorithms have notably emerged as preeminent predictors, showcasing their robustness. The amalgamation of diverse studies presents a compelling case for the efficacy of these algorithms in proficiently recognizing individuals at risk of osteoporosis.

This significant advancement not only offers the potential for early interventions and enhanced results for patients but also marks the beginning of a new era characterized by personalized and targeted approaches for managing this incapacitating condition. Utilizing the potential of machine learning, healthcare professionals have the opportunity to transform the diagnosis and treatment of osteoporosis, leading to a fundamental change that may ease the impact of the disease and provide a more optimistic outlook for those facing it. The results of this meta-analysis establish a solid groundwork for future research, emphasizing the importance of incorporating machine learning methods into regular clinical procedures. This integration has the potential to equip healthcare providers worldwide with powerful tools to efficiently address osteoporosis.

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AUTHOR'S CONTRIBUTION

KM and NN: Conceived the study design; KM, EM, and NN: Conducted title/abstract and full-text screening; KM and NN: Performed the data extraction; KM and NN: wrote the manuscript.

All authors contributed to the drafting the manuscript, read and approved the final manuscript.

CONFLICTS OF INTEREST

The authors declare no conflicts of interest regarding the publication of this study.

ETHICAL APPROVAL

Not Applicable.

FINANCIAL DISCLOSURE

No financial interests related to the material of this manuscript have been declared.

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