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Review

Types of application of artificial intelligence in the diagnosis and prognosis of osteoporosis; a narrative review

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Abstract

Introduction: The rising impact of osteoporosis and fragility fractures highlights the need for advanced management strategies. Integrating digital health interventions, especially artificial intelligence (AI) algorithms, is essential. Osteoporosis, a major contributor to elderly disability, demands AI to minimize diagnostic errors. This review targets stakeholders interested in employing AI for osteoporosis management.

Methods: We examined 16 articles from PubMed, Google Scholar, and Medline (January 1, 2015, to January 1, 2023) using keywords like AI, osteoporosis, fragility fracture, and machine learning. After excluding redundancies, 15 articles were selected, covering five key aspects of osteoporosis management: Bone mineral densitometry (BMD) predictive variables (n=1), diagnosis, screening, and classification of osteoporosis (n=5), diagnosis and screening of fractures (n=4), fracture risk forecast (n=2), and automated image segmentation (n=3)

Results: Recent machine learning (ML) advances empower AI in assessing bone health beyond X-rays. Techniques, including AI-driven analysis with multi-detector computed tomography scans, extend beyond X-ray imaging. Convolutional neural networks (CNNs) excel in fracture diagnosis, surpassing medical professionals. Enhanced CNN performance is achieved through data augmentation and generative networks.

Conclusion: Initial ML applications in osteoporosis research focus on the macroscopic scale, leaving a gap in microscale exploration. Establishing a robust system for bone micro-damage initiation detection is crucial for future applications in bone micromechanics. Ongoing development is essential to assess effectiveness and affordability through controlled studies.

Keywords: Artificial intelligence, Osteoporosis, Fragility fracture, Bone density

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Introduction

Osteoporosis is a multifactorial disease that results in weakened, porous, and more easily fractured bones (1-3). Among the causes of osteoporosis, one can mention (a) defects in trabecular microarchitecture, (b) inherent characteristics of incomplete bone tissue, (c) incomplete repair of microdamage resulting from daily activities, and (d) excessive remodeling rate (4).

Osteoporotic fractures most commonly occur in the hip, proximal humerus, distal forearm, and vertebral column; however, other skeletal sites can also be affected (5). Osteoporosis is characterized by low bone mineral density (BMD). According to the World Health Organization (WHO) definition of osteoporosis, a BMD score of less than -2.5 (T-score) is required (6,7), with the gold standard for measuring BMD being dual-energy X-ray absorptiometry (DXA) (5). Computed tomography (CT) scanning is one of the methods used for diagnosing osteoporosis and its consequences, including vertebral and hip fractures (2). Despite the potential use of CT scans for osteoporosis screening, it is often overlooked in the National Health Service (NHS) due to the radiologists' primary focus, even though it could potentially be used for osteoporosis screening (2). Automated differentiation of osteoporotic fractures from non-osteoporotic vertebral anomalies and traumatic, grading the severity of vertebral fractures, and detecting mild vertebral fractures remains challenging (8). Currently, microscale assessments are only possible using high-resolution imaging techniques, which can be time-consuming in terms of image analysis (9).

The increasing burden of osteoporosis and fragility fractures necessitates an improvement in osteoporosis management within healthcare systems (10). Suboptimal osteoporosis management creates an appropriate setting for digital health interventions (10). The term "digital

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■ **Implication for health policy/practice/research/ medical education**

This review study aims to address concerns and inform stakeholders interested in employing artificial intelligence for osteoporosis management.

health" encompasses various tools, including support systems, clinical decision support, electronic health record (EHR) tools, educational tools, and new artificial intelligence (AI) algorithms (10) (Figure 1). This disease has costly impacts in all developed countries, and delayed osteoporosis diagnosis can lead to a worsened prognosis (7,11). Osteoporosis is a major cause of disability in older age, leading to a reduced quality of life and loss of independence (12). The use of AI is essential for minimizing diagnostic errors related to osteoporosis (11).

Artificial intelligence tools have found new applications in medical diagnosis (6), including the identification and classification of images and modeling fracture fragility, osteoporosis detection, and fracture-related patterns (5,6). Recent advancements in machine learning (ML) have enabled remarkable progress in complex data environments where human capacity is limited (1). Bone density measurement for osteoporosis screening using AI algorithms provides automatic population-based screening on a large scale. Preliminary investigations into biometric and body composition metrics, especially when these CT-based metrics are used in combination, offer promising tools for predicting osteoporotic complications (13). Several companies have developed software methods for the identification of vertebral fractures in CT datasets, bone fragility assessment, or osteoporosis detection using various approaches, including AI, image processing, concepts from biomechanical engineering, and computational modeling (Figure 2) (2).

Methods

The potential applications of digital health interventions in the general management of osteoporosis have been investigated in this study. The purpose of this research is to address concerns and inform stakeholders about the use of AI in osteoporosis management.

A mini-review was conducted based on an examination of articles available in the PubMed, Google Scholar, and Medline databases from January 1, 2015, to January 1, 2023, using keywords such as AI (artificial intelligence), osteoporosis, fragility fracture, and machine learning. This review led to the identification of 16 articles for inclusion. Five articles were excluded due to their similarity in three different databases, resulting in a final selection of 11 articles for the study.

In this article, potential applications of digital technology in the general management of osteoporosis were examined using diverse signal and image resources such as echocardiography, magnetic resonance imaging (MRI), CT, and X-rays. Recent research indicates the use of AI for high-level prediction of osteoporosis and screening. Both deep learning and ML models have applications in osteoporosis. Here, we focus on the findings of the 15 selected articles. These articles cover the following five areas:

1. Bone mineral densitometry (BMD) predictive variables (n=1)
2. Diagnosis, screening, and classification of osteoporosis (n=5)
3. Diagnosis and screening of fractures (n=4)
4. Forecast of fracture risk (n=2)
5. Auto-division of various images (n=3)

The results from a study conducted by Smets et al in the domain of bone properties assessment (13 studies) aimed primarily at improving osteoporosis detection

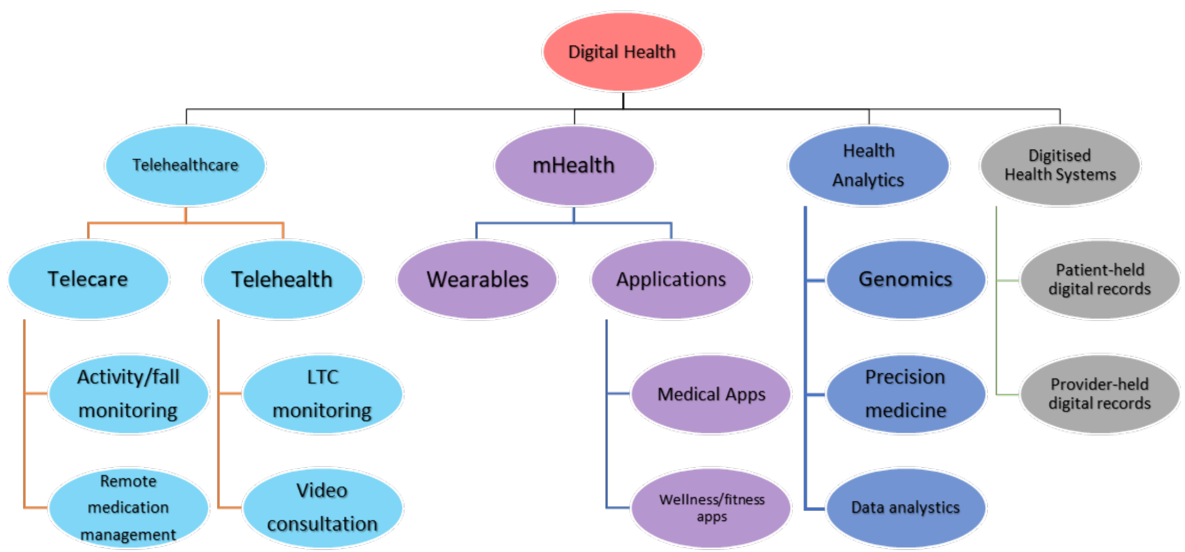

Figure 1. Sub-categories of digital health.

(1). Properties investigated in bone studies included load-bearing capabilities of the humerus, using finite element analysis and donor-specific parameters, micro-architectural parameters derived from simulations or data collected from human cadavers, vertebral and hip heights, and BMD for the lumbar spine and hip (1).

Smets et al also conducted a study related to osteoporosis classification, where thirty-four studies examined osteoporosis classification based on BMD at the lumbar spine, hip, lumbar, and hip, using data and image-based osteoporosis detection (1). Some studies identified osteoporosis based on opportunistic CT imaging, X-rays, or dental records. Other studies used patient-related data, bone biomarkers, or acoustic responses (1).

Additionally, Smets et al, study on bone fracture detection (32 studies) covered the diagnosis of various bone fractures, including vertebral fractures (11 cases), hip fractures (17 cases), and the detection of other fractures, such as arm or wrist fractures (10 cases). Convolutional neural network (CNN) was the most commonly used model (1). The findings suggested that hospital-related variables, such as scanner model, were better predictors of fractures compared to patient characteristics or their images (1). Twelve studies compared the performance of ML models against human experts, with ML outperforming human experts significantly in four of these studies (1). Some studies did not report significant improvements with data augmentation, while larger datasets and data augmentation had positive effects on hip fracture detection (1).

The results from study by Smets et al, in the domain of risk prediction (14 studies) encompass various types of risks examined in these studies. These include predicting the risk of osteoporotic fractures, falls, bone loss, or related diseases in osteoporotic patients over time (1). Within these studies, a risk-clustering model was created to categorize patient subgroups at risk. Subgroups of osteoporotic patients and their risk of developing associated diseases were also investigated. Predicting osteoporotic risk through supervised learning was the most commonly studied aspect (12 studies) (1). Risk prediction included the following parameters: risk of bone density loss over ten years, an event in six months, an event in one-year, vertebral fractures in eight months, hip fractures in 4, 5, or 10 years, vertebral or hip fractures in 7.5 years, major osteoporotic fractures (arm, wrist, spine, or hip) in 4.5–10 years, and various fracture locations in years 1 and 2 (1). Since unsupervised learning's objective is not to predict a predefined outcome, no performance metrics were reported. Nonetheless, interesting features such as adherence to treatment responses that could improve osteoporosis treatment were identified (1).

In Ferizi et al, study on automated image segmentation, seven studies were examined. These studies explicitly utilized image analysis, where AI models, often referred to as tissue analysis, were employed to identify patterns in images and discover fundamental relationships between groups (6). The reviewed studies utilized various techniques to assess bone health that extended beyond X-ray imaging, including acoustic bone assessment, dental X-ray for predicting jaw osteonecrosis, BMD analysis, and MRI for image diagnosis and classification. The deep learning models' ability to search for intricate patterns can aid in image classification (6).

In the study by Ferizi et al on-risk prediction, an assessment tool for fracture risk (FRAX) was investigated. The model included 12 risk factors, such as age, gender, weight, height, smoking, prior fractures, alcohol consumption, parental fracture history, glucocorticoid use, rheumatoid arthritis, and secondary osteoporosis as inputs (6). The 10-year probability of fracture was considered as the output. Criticisms were made regarding the model's description limitations and its assumptions, as most parameters are input independently without

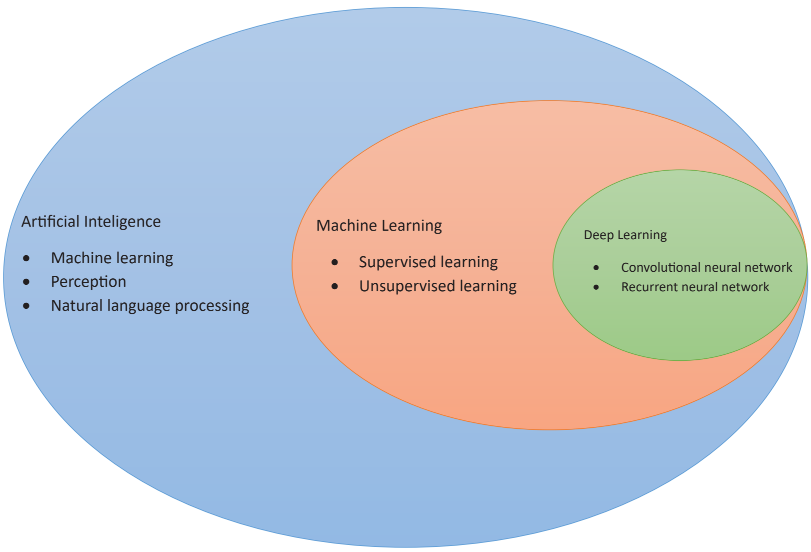

Figure 2. Hierarchical classification with examples of artificial intelligence, machine learning, and deep learning.

accounting for their strong interdependencies. Deep learning models can also be useful for large datasets, such as "big data" (6).

Osteoporosis is characterized by low BMD. In the study by de Cos Juez et al, the impact of 38 variables on BMD was examined, and the least relevant variable was excluded using a genetic algorithm for variable selection. This study was conducted on 200 postmenopausal women (7). The method involved using 38 variables as input, with BMD as the output variable. The important variables considered in this study, as determined by the genetic algorithm, included body mass index, carbohydrates, cholesterol, calcium intake, fat, folate, vitamin D, weekly physical activity, the number of pregnancies of the patient, and sun exposure. Therefore, only 10 variables out of the original set of 38 variables were necessary (7). All of these variables were used as input neurons for a multilayer perceptron neural network model, with the output variable being the BMD of the patients. A design of experiments approach was used to optimize the multilayer perceptron neural network model. The model's topology included an input layer, a hidden layer, and an output layer (7). Moreover, in the study by Engelke et al, multiple scans obtained in three days, with and without a phantom, were conducted for detecting vertebral fractures using BMD. In this 10-year study involving 199 subjects, the height values of L1-L4 vertebrae obtained from CT data were used directly for predicting incidental vertebral fractures (30 cases) (8). AI algorithms are used as the standard for distinguishing between fractures resulting from osteoporosis and traumatic fractures (8).

The study by Engelke et al comprised two parts. The first part involved the analysis of data related to hip and wrist fractures, DXA BMD, as well as the use of antiresorptive medications in individuals aged 65 and older. The institute for clinical evaluative sciences extracted data from the Ontario Health Insurance Plan (OHIP) database, the national ambulatory care reporting system (NACRS), and the Ontario drug benefit (ODB) database. The data was analyzed to examine the trends in DXA BMD utilization from 1992 to 2005 and identify areas in need of improvement (8). The second part involved a systematic review and analysis of data, which included 8 systematic reviews and/or meta-analyses, 34 randomized controlled trials, and 63 observational studies (8). A wide range of technologies for automated vertebral fracture detection has been developed and successfully validated (8). Most of them are based on AI algorithms. Automatic differentiation between traumatic vertebral fractures and osteoporotic, severity grading of vertebral fractures, and the detection of mild vertebral fractures remain challenging (8).

In the study conducted by Buccino et al, the goal was to illuminate the microstructural complexity of bones using high-resolution and phase-contrast synchrotron X-ray imaging with automatic detection of fine bone features provided by a neural network. The aim of such scenarios is to assist less experienced surgeons or clinical physicians in the diagnosis process. Samples of trabecular bone obtained from the healthy femoral head and femoral head with osteoporosis (FH) were studied, and they were subjected to temporary micro-compression inside a synchrotron for the assessment of the initiation and progression of microdamage under test (9).

The findings of Gupta et al in the field of fracture risk assessment using online tools are as follows; fracture risk assessment tools, such as the online tool FRAX, are prominent in the realm of digital health specifically tailored for osteoporosis (10). These tools calculate the 10-year risk of fractures for individuals benefiting from osteoporosis treatment. Physicians often prefer manually inputting clinical data and interpreting the outputs in clinical practice, limiting the effectiveness of FRAX due to human factors such as acceptability and usability (10). QFracture is an online alternative to FRAX. This method aims to help patients understand their risk graphically by reporting adverse outcomes with an "unhappy" face and favorable outcomes with a "happy" face using 100-face networks. Another advantage of this method is its automatic fracture calculation without the need for manual input (10).

Study results in the area of fracture risk assessment and identifying individuals at risk using AI and ML are as follows: Computer-based algorithms or predictive algorithms using various input datasets help physicians calculate 5 or 10-year fracture risk based on known risk factors. The use of AI through ML for identifying individuals at high fracture risk and "high fall risk" from obtained data is typically feasible (10). There is no standardized gold standard for fracture assessment, but combined and composite data can be used, such as using QFracture alongside fracture risk assessment tools (FRAX) in conjunction with BMD, Garvan in conjunction with BMD, or administrative health data accessible in this method. The input data can be automatically integrated into EHRs, providing risk assessment at the point of care and ideally functioning as a screening tool for a broader population (10). In the United States, an EHR-based fall risk prediction model has been successfully developed using advanced ML algorithms, which accurately identifies falls that occur 30 and 30-60 days after calculation, with a success rate of 58.01% and 54.93%. However, the results suggest better performance of the model for short-term fall prediction (10).

According to study by Huang et al, ML can be used to predict T-scores and vertebral bone density using HU (Hounsfield unit) analysis of CT images. This study involved 70 cases and 198 lumbar vertebral T-scores for QCT and HU values for conventional CT (11). Using a logistic regression algorithm, a 92.5% accuracy in distinguishing osteoporotic from non-osteoporotic spine was achieved. ML models enabled the prediction of

T-scores and osteoporotic vertebral bones solely based on HU values from a standard CT, assisting spine surgeons in more accurately identifying osteoporotic vertebral bones before surgery (11).

The findings of the study by Kong and Shin in the realm of osteoporosis screening, bone fracture detection and predicting the risk of hip and vertebral fractures are as follows (14): Shim et al examined the performance of seven ML models for accurate osteoporosis classification, identifying ANN as one of the most precise methods (15). Yamamoto et al increased the performance of CNN networks significantly by incorporating additional clinical variables in the analysis of hip radiographs (16). Chung et al demonstrated that by using deep learning techniques, bone density of lumbar vertebrae could be estimated from non-contrast abdominal CT scans (17). They also observed a strong correlation between the estimated BMD from CT and BMD obtained through DXA, particularly in complex types of arm bone fractures (17).

Chung and colleagues displayed better performance by CNN in detecting humerus fractures compared to physicians and orthopedic surgeons (17). Mutasa and colleagues reached different results in the realm of hip fractures, where CNN's precision and F1 score were similar to the performance of radiologists in fracture detection. Visualization with color maps indicated that learning based on the target lesion is appropriate. According to findings of the study by Mutasa et al, generative adversarial networks, and data augmentation techniques, digitally reconstructed radiographs demonstrated improved performance compared to unaugmented data (18).

Su and colleagues investigated the classification of a high-risk group for hip fractures using a classical ML approach with CART, showing a similar discriminative power to FRAX ≥3%. According to the study by Almog, the development of a short-term fracture prediction model using natural language processing (NLP) methods suggests the potential use of unique patient medical history data over time to predict fracture risk (19). Muehlematter et al demonstrated that bone tissue analysis, coupled with ML, may accurately identify patients at risk of vertebral fractures on CT scans and enhance fracture risk prediction (20).

In the study by Poole, patients routinely use CT scans for diagnosis and screening purposes. However, due to radiologists primarily focusing on the main scan, skeletal abnormalities often go unnoticed. More than half a million CT scans performed annually in the national health service (NHS) have the potential for osteoporosis screening (21). Several companies have developed software-based methods for bone density assessment, fragility, and identifying vertebral fractures using various techniques, including image processing, computational modeling, AI, and concepts of biomechanical engineering (21).

Conclusion

- AI tools have found new applications in medical diagnostics. These applications include image recognition and classification, modeling fragility fractures, osteoporosis diagnosis, and fracture-related patterns.
- Recent advances in ML have enabled significant progress in the field of AI to create remarkable developments in complex data environments where human capacity is limited to handle high-dimensional relationships.
- Deep learning, by surpassing the capabilities of medical professionals in the analysis of medical images, represents a new frontier in healthcare systems.
- Designed CNNs are capable of automatic detection of cracks and microfractures at various levels of compression with high accuracy. To detect at a microscopic scale, CNNs are employed with the aim of combining the spatial visualization of microcrack propagation mechanisms.
- AI tools, such as AI-based imaging, have advanced in obtaining graphic images, including DXA, MRI, multi-detector computed tomography, and image analysis.

Study recommendations

Digital health and AI interventions in various domains of diagnosis, screening, and care have proven beneficial for patients with osteoporosis. However, initial efforts to harness the power of ML algorithms such as neural networks are still limited to a macro scale, while a noticeable gap exists in their application at a micro scale, where bone damage initiates. This approach paves the way for the application of ML studies in micro bone mechanics.

Strongly controlled studies are still necessary to assess the effectiveness and cost-effectiveness of these technologies. If the significant value of AI-assisted CT-based screening is ultimately confirmed in future research, this approach could be considered for widespread CT-based screening.

While recent advances have had successful applications in osteoporosis research, their development is ongoing, and as a result, further studies on AI applications are needed.

Authors' contribution

Conceptualization: Sara Moslehi and Zahra Sadat Mahmoodian.
Data curation: Sara Moslehi and Zahra Sadat Mahmoodian.
Formal analysis: Sara Moslehi and Zahra Sadat Mahmoodian.
Funding acquisition: Sasan Zandi Esfahan.
Investigation: Sara Moslehi and Zahra Sadat Mahmoodian.
Methodology: Sara Moslehi and Zahra Sadat Mahmoodian.
Project administration: Sara Moslehi.
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Software: Sasan Zandi Esfahan.
Supervision: Sara Moslehi.
Validation: Sasan Zandi Esfahan.
Visualization: Sara Moslehi.

Writing–original draft: Sara Moslehi and Zahra Sadat Mahmoodian.
Writing–review & editing: Zahra Sadat Mahmoodian.

Conflicts of interest

The authors declare that they have no competing interests.

Ethical issues

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

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