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RESEARCH

Artificial Intelligence-Enabled Electrocardiography Identifies Osteoporosis and has Prognostic Value

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Abstract

Background: Osteoporosis, a common disease leading to weakened bones and increased fracture risk, often goes undiagnosed until a fracture occurs. Dual-energy X-ray absorptiometry (DXA) is the current gold standard for bone mineral density (BMD) measurement, but it has limitations. Recent studies reported Artificial Intelligence (AI)-enabled Electrocardiography (ECG) for disease screening. We hypothesized that AI ECG could serve as a screening tool for osteoporosis. Objective: This study aimed to develop a deep learning model (DLM) to identify osteoporosis using EKG features and to assess its performance and clinical implications. Methods: We conducted a retrospective study involving 25,401 patients who underwent 44,732 EKGs with DXA-measured BMD at two hospitals. The area under the receiver operating characteristic curve (AUC) was used for evaluation. Additionally, our DLM was tested for predicting mortality using Kaplan-Meier survival analysis and the Cox proportional hazards model. Results: The DLM achieved an AUC of 0.741 in internal validation and 0.868 in external validation for detecting osteoporosis. Furthermore, the negative predictive value for osteoporosis was 93.7% in the internal set and 85.8% in the external set. The DLM-detected osteoporosis group exhibited a higher risk of all-cause mortality with a hazard ratio (HR) of 2.06 (95% CI: 1.23–3.45) in the internal validation set, and similar results were observed in the external validation set (HR: 1.87, 95% CI: 1.21–2.89). Conclusion: Our DLM, utilizing EKG for osteoporosis identification, demonstrated impressive results. It has the potential to serve as a cost-effective and practical screening tool for early osteoporosis detection, with significant prognostic implications.

Keywords Deep learning model · Artificial intelligence · Electrocardiography · Osteoporosis · Osteopenia

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Introduction

Osteoporosis is a prevalent condition that diminishes bone strength, rendering them fragile and susceptible to fractures, especially in areas like the spine, hip, wrist, humerus, and pelvis [1].

Osteoporotic fractures contribute significantly to disability, with hip fractures specifically linked to a 20% higher mortality rate within the first year following the fracture [2, 3]. It develops slowly over several years and is often only diagnosed when a fall or sudden impact causes bone fracture. Unfortunately, despite the availability of densitometry, osteoporosis often remains undiagnosed until a fracture occur [4].

Dual-energy x-ray absorptiometry (DXA) is considered the gold standard for diagnosing osteoporosis, as per the World Health Organization (WHO) classification. T scores falling between 1 and 2.5 Standard Deviations (SDs) below the reference population's average are categorized as osteopenia. Measurements falling 2.5 SDs or more below the young adult mean are classified as osteoporosis [5]. Despite being effective, DXA has limitations and drawbacks, including the requirement for specialized equipment and potential radiation exposure. [6, 7]. A DXA scan typically lasts 10–20 min. In certain cases, patients might be unable to undergo hip and spine DXA scans due to mobility issues. BMD measurement may not be valid in some situations due to skeletal structural abnormalities. Increasing awareness about osteoporosis could be an effective way to prevent related fractures. [8].

Deep-learning techniques (DLMs) have undergone rapid advancements in recent years, offering a novel approach to disease diagnosis. Initially trained to detect ECG changes like arrhythmia, dyskalemias, and acute myocardial infarction, DLMs have consistently delivered reliable results. [9–12]. Moreover, leveraging the connected database, DLMs have demonstrated significant advancements in screening, with wide-ranging applications including cardiac contractile dysfunction, aortic stenosis recognition, atrial fibrillation (Af) prediction, age or sex estimation through ECG, localization of angiography-verified coronary artery disease, pneumothorax detection, and aortic dissection – all posing challenges for physicians. [13–20]. These findings underscore the vital role of AI in categorizing ECGs for medical purposes. Emerging evidence suggests that cardiovascular health and bone density are interlinked, with conditions like osteoporosis often coexisting with cardiovascular disease (CVD) [21]. This relationship is partly due to shared risk factors such as age, gender, and lifestyle, as well as common pathophysiological pathways, including endothelial dysfunction and atherosclerosis. Given this interconnection, the electrical activity of the heart, as captured by an ECG, might reflect subtle systemic changes that also affect bone density. We postulated that AI application could identify osteoporosis in EKGs. Our study aimed to train a DLM to differentiate between osteoporosis, osteopenia, and normal bone mineral density (BMD) using a 12-lead ECG. Utilizing AI could assist clinicians in osteoporosis screening, potentially streamlining diagnosis and optimizing management.

Method

Data Source and Population

The study protocol received approval from the institutional ethics committee of the Tri-Service General Hospital (C202105049). Patient consent was waived due to retrospective data collection. Our study involved the retrospective development and assessment of a DLM, both internally and externally. EKGs were sourced from two hospitals, an academic medical center (Hospital A) and a community hospital (Hospital B), spanning from January 1, 2010, to April 30, 2021. Patients below 20 years of age were excluded.

Figure 1 depicts the sample allocation. We retrospectively acquired patients with both BMD data and at least one 12-lead EKG within a 7-day window. Hospital A contributed 21,060 patients, with 10,522 assigned to the development set. Among them, 17,898 EKGs were used for DLM training. Additionally, 4,184 patients formed the tuning set, providing 7,061 EKGs for guiding training and establishing an optimal operational point. Finally, an internal validation set included 6,324 patients. Patient allocation was determined chronologically for the development, tuning, and internal validation sets. Hospital B contributed 4,341 patients, following the same inclusion criteria for external validation testing.

Observation Variables

Bone mineral density (BMD) data (measured in g/cm2) were obtained using a DXA scanner (Lunar Prodigy Series; GE Healthcare, Madison, WI, USA). BMD values were retrospectively retrieved from the hospital's electronic medical system. Participants were categorized based on WHO T-score classification [22], defining osteoporosis as a T-score below −2.5, osteopenia as a T-score of −1 to −2.5, and healthy as a T-score above −1. Scans were conducted on the same day for each participant, with experienced radiologists confirming and evaluating the reports. If the patient has two or more sets of bone density test data during this period, the values from the closest examination will be selected.

Disease histories were determined using the International Classification of Diseases, Ninth Revision and Tenth

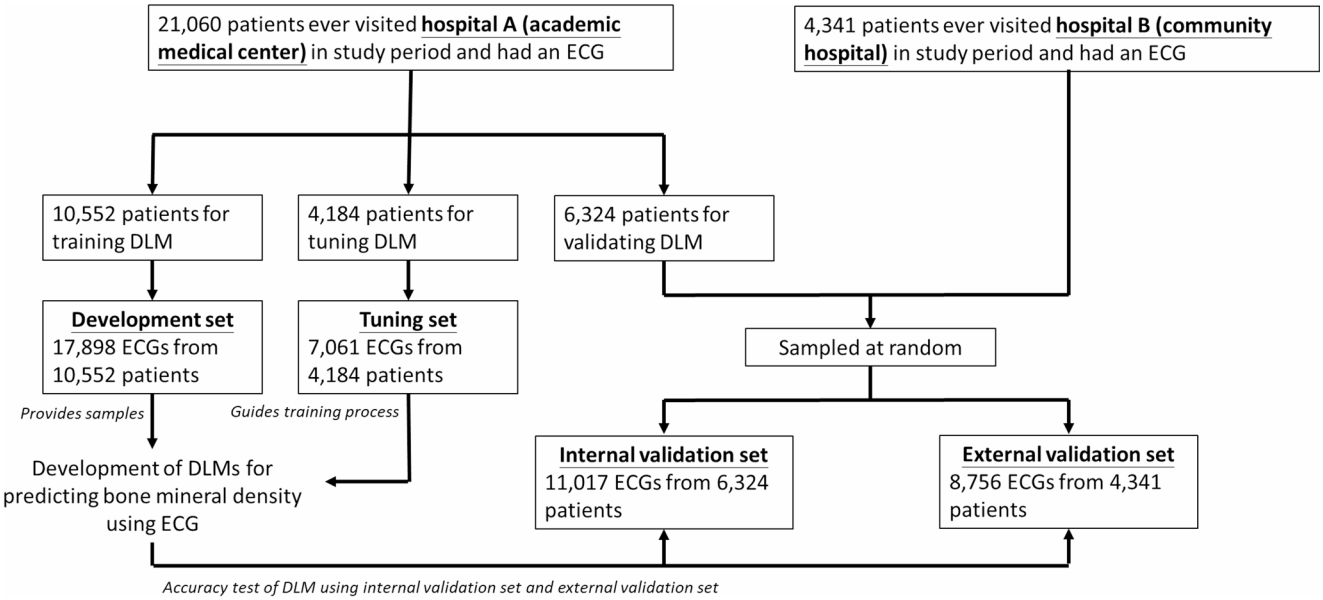


Fig. 1 Development, tuning, internal validation, and external validation sets generation and ECG labelling of bone mineral density. Schematic of the data set creation and analysis strategy, which was devised to assure a robust and reliable data set for training, validating, and testing of the network. Once a patient's data were placed in one of the data sets, that individual's data were used only in that set, avoiding 'cross-contamination' among the training, validation, and test data sets. The details of the flow chart and how each of the data sets was used are described in the Methods

Revision (ICD-9 and ICD-10, respectively), as described previously [23]. The primary aim was to predict the categories of healthy, osteopenia, and osteoporosis. Additionally, a secondary analysis focused on all-cause mortality. Survival time for mortality was calculated with respect to the ECG record date, and only patients with follow-up hospital visits were included. Mortality events were recorded through electronic medical records. Data for living visits were censored at the patient's last known alive hospital encounter to minimize bias from incomplete records. Patients with any of the mentioned criteria prior to the EKG index date were excluded and classified as having a corresponding disease history.

The Implementation of the Deep Learning Model

The ECGs were captured digitally, sampling at 500 Hz for each lead, using a Philips 12-lead ECG machine (PH080A, Philips Medical Systems, 3000 Minuteman Road, Andover, MA 01810 USA). The ECG-DLM was constructed based on the ECG12Net architecture, previously developed [11]. A new DLM was built using EKG raw data, adhering to the same architecture. Training of the DLM employed an ECG development set with three categories: healthy, osteopenia, and osteoporosis. The standard input format for ECG12Net consists of numeric sequences of length 1024. An oversampling approach was implemented to ensure accurate osteoporosis detection. To address the black box nature of DLMs [24], we incorporated established ECG features into the DLM. These included eight quantitative ECG measures and 31 widely recognized diagnostic pattern classes. The eight ECG measurements comprised heart rate, PR interval, QRS duration, QT interval, corrected QT interval, P wave axis, RS wave axis, and T wave axis. The 31 clinical diagnosis patterns were extracted from structured findings statements using standard key phrases within the Philips system. These patterns included abnormalities like T wave abnormalities, atrial fibrillation, atrial flutter, atrial premature complexes, complete AV block, complete left bundle branch block, complete right bundle branch block, and various others. For improved transparency in DLM prediction, we employed an XGBoost (XGB) classifier using the mentioned variables. The final XGB classifier retained features that significantly enhanced predictability. This approach enhances our understanding of DLM prediction.

Statistical analysis

We detailed the set characteristics using means, standard deviations, patient counts, and percentages. DLM performance was assessed through the receiver operating characteristic (ROC) curve for osteopenia and osteoporosis. We presented the area under the curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The operating point was determined by maximizing Youden's index within the tuning set. Furthermore, we employed multivariable Cox proportional hazard models to examine the link between baseline characteristics

and the outcomes of interest. We employed hazard ratios (HRs) along with 95% confidence intervals (95% CIs) for comparisons. Statistical analysis was performed using the R software environment version 3.4.4. A significance level of $p<0.05$ was maintained throughout the analysis.

Results

Table 1 displays patient characteristics across the development, tuning, internal validation, and external validation cohorts. Notably, significant disparities were observed in the external validation set compared to the other three sets. In the external validation set, patients were predominantly elderly and female (67.9% women, average age 65.65 ± 14.70 years), with a higher prevalence of chronic histories and comorbidities like AMI, stroke, CAD, HF, AF, DM, CKD, and hyperlipidemia. In the development set, 3,384 patients (18.9%) had osteoporosis, 5,007 (28%) had osteopenia, and 9,507 (53.1%) had normal BMD. A similar patient distribution was seen in the tuning and internal validation sets (53%/29%/18% in the tuning set; 54.4%, 27.3%, 18.3% in the internal validation set). In contrast, the external validation set showed 1,993 patients (22.8%) with osteoporosis, 3,078 (35.2%) with osteopenia, and 3,685 (42.1%) with normal BMD. The external validation set also exhibited a lower mean T score of −1.10 ± 1.67. Patient sources varied, with fewer ECG examinations originating from health check centers in the external validation set compared to the other groups.

Due to the significant difference in the prevalence of osteoporosis between males and females, we provided a table presenting the distribution of osteoporosis, osteopenia, and normal bone density stratified by sex in Supplementary Table 1. Males are more likely to have normal bone density and less likely to develop osteoporosis. In contrast, females have a higher risk of osteoporosis and consistently show a lower proportion of normal bone density across all datasets.

Figure 2 illustrates a comparison between actual bone density status (osteopenia, osteoporosis, normal) and ECG predictions in both the internal validation and external validation sets. ROC curves were generated, presenting sensitivities, specificities, PPVs, and NPVs. The AUCs for detecting osteopenia, low bone density (osteopenia, osteoporosis), and osteoporosis were 0.746, 0.709, and 0.741, respectively, in the internal validation set. In the external validation set, the AUCs for detecting osteopenia, low bone density (osteopenia, osteoporosis), and osteoporosis were 0.709, 0.793, and 0.868, respectively. The DLM exhibited osteoporosis detection through EKGs with a sensitivity of 79.4%, specificity of 80.4%, positive predictive value of 51.7%, and negative predictive value of 93.7% in the internal validation cohort. In the external validation cohort, the DLM displayed sensitivity of 75.5%, specificity of 68.3%, positive predictive value of 52.3%, and negative predictive value of 85.8%.

In Fig. 3, the cumulative percentage of all-cause mortality throughout the follow-up period is depicted. For DLM-predicted osteopenia patients versus DLM-predicted normal bone density patients, a noticeable year-to-year increase in

Table 1 Patient characteristics across the development, tuning, internal validation, and external validation cohorts

	Development set	Tuning set	Internal validation set	External validation set
Gender				
female	10,702(60.1%)	4330(61.6%)	6449(58.9%)	5947(67.9%)
male	7113(39.9%)	2695(38.4%)	4499(41.1%)	2809(32.1%)
Age	60.39 ± 15.96	60.44 ± 16.19	60.09 ± 15.86	65.65 ± 14.70
Height	159.64 ± 9.00	159.30 ± 8.47	159.85 ± 8.94	159.69 ± 8.36
Weight	61.16 ± 12.53	61.26 ± 12.58	61.59 ± 12.51	62.50 ± 12.72
BMI	24.06 ± 3.96	24.16 ± 4.00	24.19 ± 3.92	24.53 ± 4.18
BMD				
Normal	9507(53.1%)	3742(53.0%)	5990(54.4%)	3685(42.1%)
Osteopenia	5007(28.0%)	2045(29.0%)	3009(27.3%)	3078(35.2%)
Osteoporosis	3384(18.9%)	1274(18.0%)	2018(18.3%)	1993(22.8%)
BMD-T-score	−0.73 ± 1.77	−0.73 ± 1.73	−0.68 ± 1.80	−1.10 ± 1.67
AMI	185(1.0%)	47(0.7%)	136(1.2%)	171(2.0%)
STK	1777(10.0%)	712(10.1%)	1099(10.0%)	1515(17.3%)
CAD	3183(17.9%)	1183(16.8%)	2013(18.4%)	3058(34.9%)
Afib	681(3.8%)	302(4.3%)	496(4.5%)	685(7.8%)
HF	1065(6.0%)	449(6.4%)	597(5.5%)	1156(13.2%)
DM	3213(18.0%)	1255(17.9%)	1960(17.9%)	2759(31.5%)
HTN	1065(6.0%)	416(5.9%)	594(5.4%)	941(10.7%)
CKD	2263(12.7%)	970(13.8%)	1391(12.7%)	1724(19.7%)
HLP	5721(32.1%)	2128(30.3%)	3572(32.6%)	4731(54.0%)
COPD	2375(13.3%)	901(12.8%)	1317(12.0%)	2441(27.9%)

BMI: body mass index; BMD: Bone Mineral Density; AMI: acute myocardial infarction; STK: stroke; CAD: coronary artery disease; Afib: atrial fibrillation; HF: heart failure; DM: diabetes mellitus; HTN: hypertension; CKD: chronic kidney disease; HLP: hyperlipidemia; COPD: chronic obstructive pulmonary disease

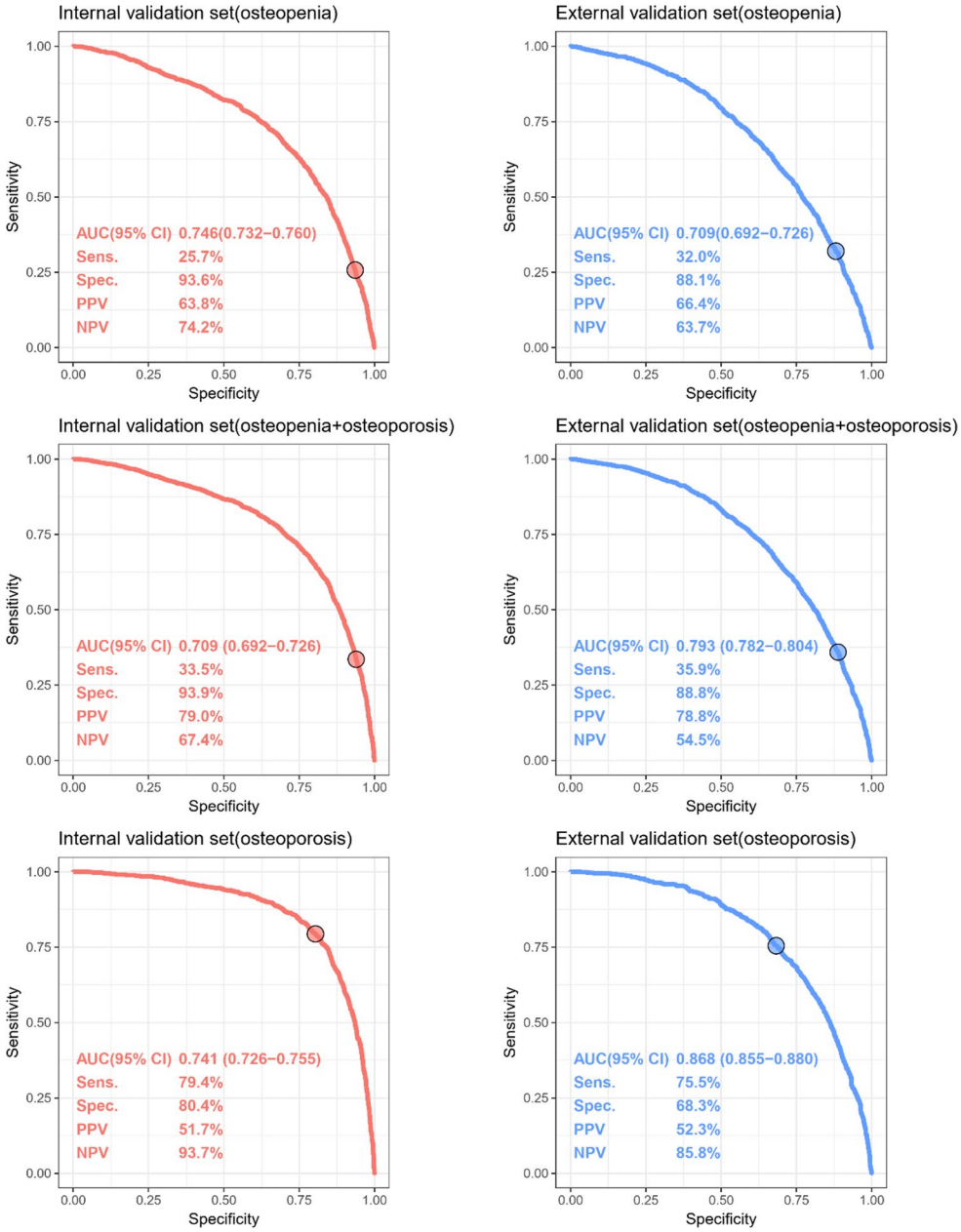


Fig. 2 The ROC curve illustrates the DLM's predictions using ECG data for the detection of Osteopenia and Osteoporosis. The operating point was determined by maximizing Yunden's index within the tuning set, denoted by a circle mark. The corresponding metrics, including area under the ROC curve (AUC), sensitivity (Sens.), specificity (Spec.), positive predictive value (PPV), and negative predictive value (NPV), were calculated based on this selected operating point

all-cause mortality was observed. DLM-predicted osteopenia patients exhibited elevated all-cause mortality rates, both in the internal validation set (gender and age adjusted hazard ratio (HR): 1.56, 95% CI: 1.05–2.31; Top left of Fig. 3) and the external validation set (gender and age adjusted HR: 1.89, 95% CI: 1.37–2.61; Bottom left of Fig. 3). Similarly, for DLM-predicted osteoporosis patients versus DLM-predicted normal bone density patients, there was an evident rise in year-to-year all-cause mortality. The DLM-detected osteoporosis group exhibited a heightened risk of all-cause mortality in the internal validation set (hazard ratio (HR): 2.06, 95% CI: 1.23–3.45). Comparable outcomes were evident in the external validation set ([HR: 1.87, 95% CI: 1.21–2.89]). In the top right of Fig. 3, the all-cause mortality incidence was 6.6% at 2 years and 20.1% at 8 years in the DLM-predicted osteoporosis group within the internal validation set. These figures were notably higher than the DLM-predicted normal bone density group (1.3% and 5%), with an adjusted HR of 2.06 (95% CI: 1.23–3.45). A similar pattern was evident in the bottom right of Fig. 3, validated in the external validation set with an adjusted HR of 1.87 (95% CI: 1.21–2.89). And we provided a table presenting the distribution of baseline comorbidities between deceased and surviving patients in the supplementary Table 2.

Figure 4 illustrates our utilization of an XGBoost model to visualize the specific ECG region utilized by the

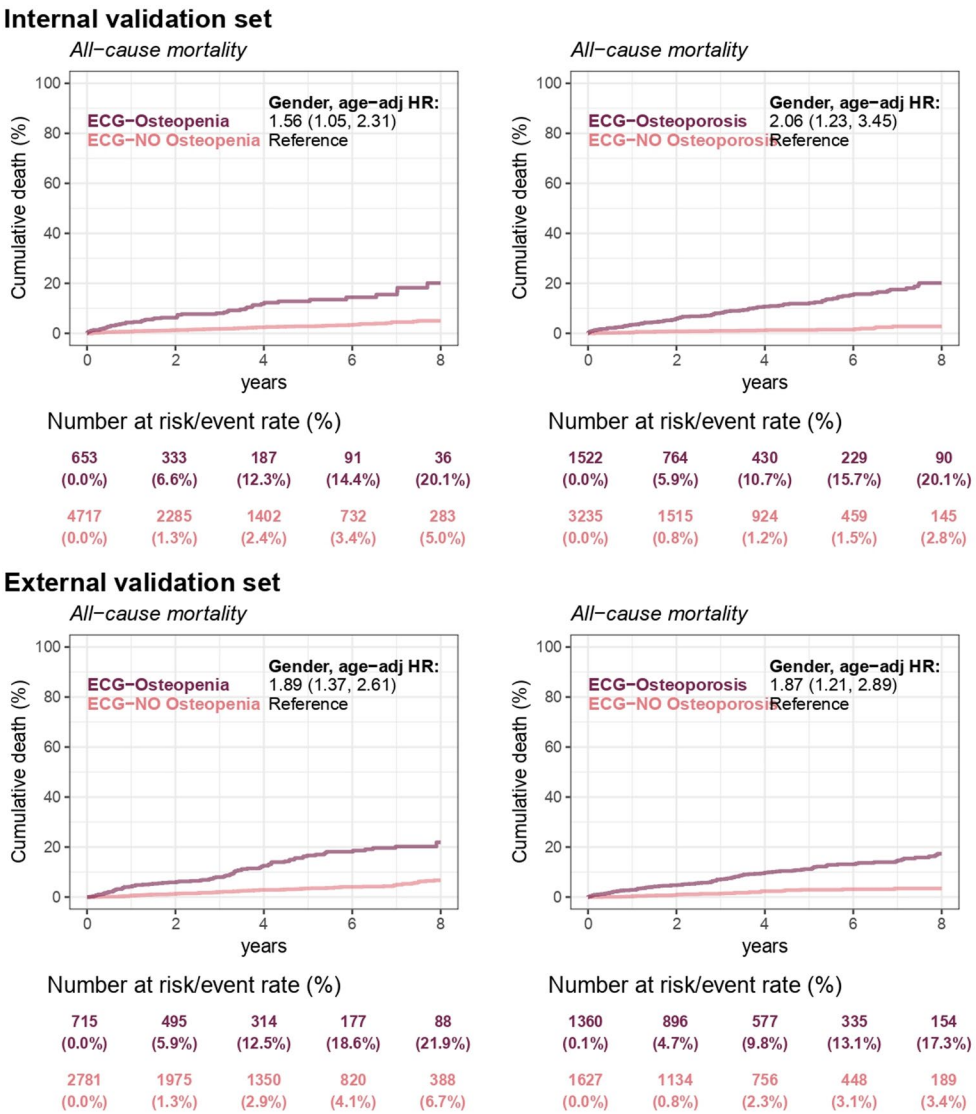


Fig. 3 The long-term incidence of developing mortality events is categorized based on whether DLM predicted osteopenia or DLM predicted osteoporosis. The analyses are performed in both the internal and external validation sets. The table presents the at-risk population and cumulative risk for specific time intervals in each risk stratification. The top left and bottom left figures depict DLM-predicted osteopenia patients compared to DLM-predicted normal bone density patients. The top right and bottom right figures illustrate DLM-predicted osteoporosis patients versus DLM-predicted normal bone density patients

algorithm for osteoporosis identification. The R-squares achieved were comparable to those when using all ECG features (49.35%/43.49% in the internal/external validation sets). We selected the ECG features most closely associated with osteoporosis. Among the most vital ECG features contributing to the DLM's ability to detect osteoporosis, the hierarchy was as follows: corrected QT interval, heart rate, T wave axis, QRS duration, P wave axis, and PR interval. Notably, the corrected QT interval, heart rate, T wave axis, QRS duration, PR interval, and QT interval exhibited higher values in the DLM-predicted osteoporosis group, while QRS wave axis and P wave axis displayed lower values.

We then proceeded to validate our findings using patients who had not undergone DXA examination for BMD in Fig. 5. The prediction of long-term development of all-cause mortality in patients stratified by the DLM, adjusted for age and sex, is presented in Fig. 5. The incidence of all-cause mortality was 7.0% at 2 years and 17.1% at 8 years for DLM-predicted osteopenia patients, compared to 1.4% at 2 years and 4.6% at 8 years for DLM-predicted normal BMD patients. This marked difference was observed with an adjusted hazard ratio (HR) of 2.56 (95% CI: 2.45–2.67). Similarly, the incidence of all-cause mortality was 7.7% at 2 years and 14.9% at 8 years for DLM-predicted osteoporosis patients, compared to 1.6% at 2 years and 5.0% at 8 years for DLM-predicted normal BMD patients. This discrepancy was significant with an adjusted HR of 2.52 (95% CI: 2.42–2.62).

Discussion

Our study developed a DLM using EKG to predict BMD status (low BMD, osteopenia, osteoporosis). The AUCs for osteoporosis detection were 0.741 in internal validation and 0.868 in external validation. The DLM demonstrated robust

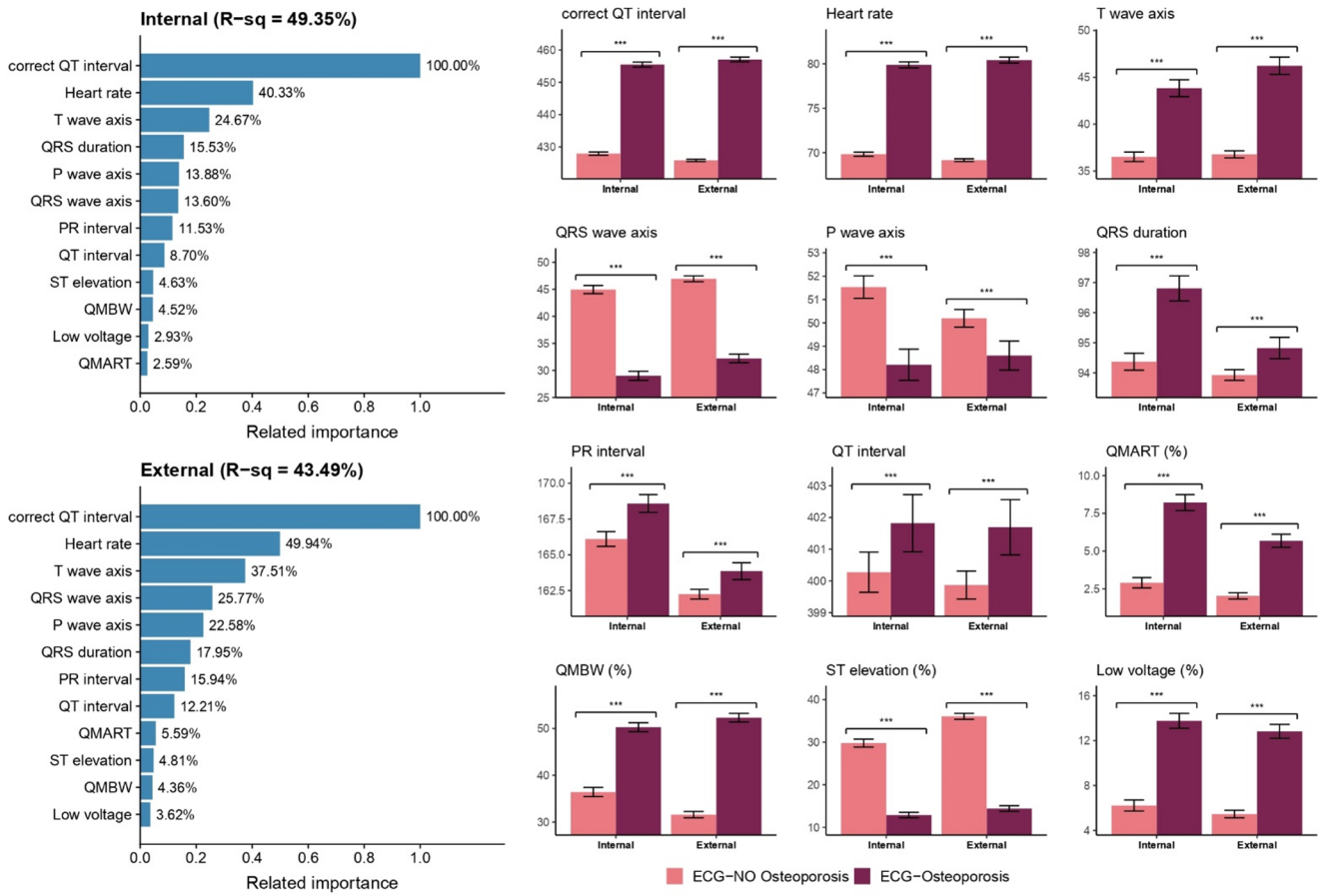
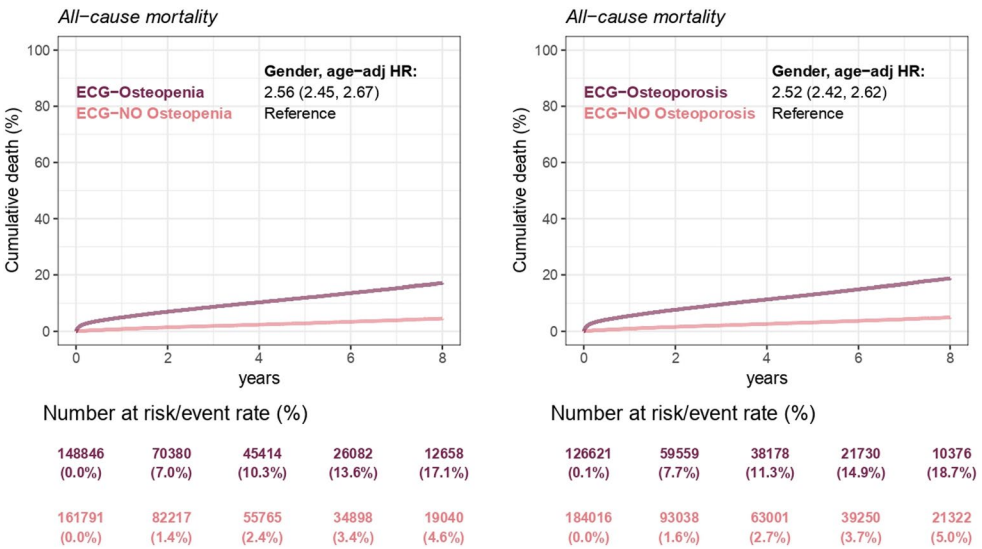


Fig. 4 The connection between the most significant ECG features and DLM-predicted osteoporosis: The relevance of these features is determined by the information gain of the XGBoost model, and the coefficient of determination (R-squared, R-sq) represents how well the selected ECG features predict ECG in log-scale. These analyses are carried out in both the internal and external validation sets

Fig. 5 The long-term occurrence of mortality events, categorized by ECG-predicted osteopenia or ECG-predicted osteoporosis in patients who have not undergone DXA examination. These analyses are conducted in both the internal and external validation sets. The table provides information about the population at risk and the cumulative risk for specific time intervals within each risk category



prediction performance, achieving a sensitivity for osteoporosis of 79.4% in the internal validation set and 75.5% in the external validation set. Furthermore, it showcased a high NPV for osteoporosis, reaching 93.7% in the internal validation set and 85.8% in the external validation set. We also examined mortality among DLM-predicted osteoporosis patients, observing increased year-to-year risk. However, as shown in Supplementary Table 2, the baseline distribution of comorbidities differs significantly between deceased and surviving patients. The observed association between osteoporosis and mortality risk could also be influenced by other underlying factors. Factors such as older age, lower BMI, and a higher prevalence of conditions like CAD, HF, DM, and CKD were more common in the deceased group. However, these factors are also associated with osteoporosis, making it challenging to disentangle their individual contributions to mortality risk. The DLM showed promising results in osteoporosis prediction, aiding clinicians in efficient screening, diagnostics, and management. Integration into health systems could enhance risk awareness for healthcare providers.

In the past, osteoporosis and cardiovascular disease (CVD) were seen as distinct chronic conditions. However, emerging evidence suggests a direct link between these health issues. Epidemiological studies have revealed a negative association between bone mineral density and vascular calcification [21]. For instance, higher bone speed of sound has been connected with lower arterial compliance, indicating that better bone health corresponds to improved vascular health [25]. Ongoing research strengthens the notion of a direct connection between CVD and osteoporosis, suggesting potential causality and diverse pathophysiological mechanisms for these debilitating chronic conditions. [21]. Arterial calcification involves arterial osteoblast and osteoclast-like cells [26]. Additionally, calcified plaque contains cellular and molecular elements implicated in bone formation, including Serum lipids [27, 28], oxidized lipid [29], low-density lipoprotein [30], and high-density lipoprotein [31]. This suggests a shared mechanism for both CVD and osteoporosis. Reduced peripheral blood flow could hinder bone cell function [32, 33]. Nitric oxide, which maintains vascular tone through continuous low-level release, also contributes to the osteogenic pathway [21]. Based on existing literature, multiple pathophysiological mechanisms could underlie the connection between CVD and osteoporosis, with vascular dysfunction playing a pivotal role. Improved vascular health is associated with better bone health. The ECG changes indicative of patients with low bone density might be detected using the DLM.

Our study attempted to explore the relationship between bone density and ECG parameters. We employed an XGBoost model to enhance predictability by visualizing ECG features. The R-squares for the internal validation set were 49.35%, and for the external validation set, they were 43.49%. These figures suggest that the known ECG features explained 49.35% and 43.49% of the variation in the internal and external validation sets, respectively. This indicates the presence of additional features in the ECG extracted by the DLM. The algorithm's focus encompassed factors such as prolonged corrected QT interval, elevated heart rate, higher T wave axis, lower QRS wave axis, lower P wave axis, prolonged QRS duration, and extended PR interval. Importantly, while human experts can't diagnose osteoporosis through ECG, AI-enabled ECG unveils the relationship between ECG and low BMD. This study provides new medical insights into ECG patterns and their connection with osteoporosis.

The accuracy of our DLM for detecting osteopenia was observed to decrease in the external analysis, a trend that has also been observed in previous AI studies. For instance, a Mayo Clinic DLM designed for left ventricular dysfunction (LVD) exhibited a lower AUC of 0.82 (down from 0.93) in external analysis conducted in Russia [14, 34]. This change might be due to variations in patient demographics. Gender imbalances, older age, and a higher prevalence of chronic diseases have been linked to decreased AUC values. [35]. Inconsistent disease severity between the two validation sets was also considered a factor contributing to the reduction in AUC [36]. The decrease in AUC observed in our study's external analysis might be due to a higher prevalence of osteoporosis, older patients, and a greater occurrence of chronic history and comorbidities.

Low BMD not only increases the risk of fractures but also serves as an independent risk factor for mortality [37]. This connection may arise from the interplay of BMD and overall health status. In women, each standard deviation decrease in bone mass was linked to a 1.2- to 1.3-fold higher risk of death from coronary artery disease or other forms of atherosclerosis [38]. The lowest quartile of bone mass correlated with a 2-fold rise in the risk of CVD-related death compared to the highest quartile [39]. A population-based prospective study in Göteborg revealed that low bone mass independently predicted mortality [40]. Additionally, low BMD emerged as a risk factor for patients with critical illnesses [41]. These findings imply that low BMD might act as an indicator of overall health or functional aging.

An ECG-based study discovered that positive patients without LVD had a four-fold greater risk of developing future LVD compared to those with negative screens [14]. A similar outcome emerged in an ECG-based dyskalemia study, which provided additional insights into all-cause mortality and hospitalizations [42]. Additionally, the ECG-predicted age gap from chronological age served as a predictor of mortality risk [43]. These studies validated the

utility of AI-ECG in predicting mortality risk. In our study, using medical record data, we assessed the mortality risk in patients with osteoporosis. The DLM model identified a heightened mortality risk in individuals predicted with osteoporosis by the DLM, with a hazard ratio of 2.06 (95% CI: 1.23–3.45), a finding also confirmed in the external validation set. Hence, our model not only predicts osteoporosis but also evaluates mortality risk.

Based on the current evidence, there exists a strong correlation between quantitative ultrasound parameters and BMD [44]. Ultrasound densitometry has been highlighted as a viable tool for osteoporosis screening within communities. It offers affordability, avoids ionizing radiation exposure, and is user-friendly. Among various sites, the forearm exhibits the highest reliability and diagnostic agreement with DXA. Ultrasound densitometer sensitivity for agreeing with DXA-diagnosed low BMD (osteopenia + osteoporosis) was 88.9% (56/63), specificity was 81.4% (35/43), and NPV was 83.3% (35/42). [45]. Our study showcases a similar NPV and sensitivity for predicting DXA-diagnosed osteoporosis while encompassing a substantial number of patients for both internal and external validation. We present an economical and convenient screening approach that doesn't necessitate additional equipment. Furthermore, previous research has demonstrated EKG's utility in screening for conditions like Af and LVD, opening the door to simultaneous screenings. The DLM serves as a tool to aid physicians in assessing the risk of osteoporosis.

Several limitations warrant consideration. Firstly, our study's retrospective design necessitates prospective validation to establish its efficacy. The inclusion of patients from various clinical indications could introduce selection bias. Consequently, generalizing our conclusions requires caution. Secondly, our patient cohort was derived exclusively from two Taiwanese hospitals (one academic medical center for development and internal validation; one community hospital for external validation). As ECG characteristics can differ across races [46], results should be validated in diverse racial and geographical contexts. Thirdly, the algorithm exhibited relatively low positive predictive value (PPV). However, physicians can identify high-risk osteoporosis patients using the model's sensitivity and negative predictive value, thereby facilitating appropriate further investigation. Additionally, we analyzed mortality events categorized based on whether DLM predicted osteopenia or DLM predicted osteoporosis; however, significant underlying differences between the two groups (deceased and surviving patients), including age, BMI, and comorbidities, should be taken into account when interpreting the results. Lastly, the opacity of existing DLMs poses methodological limitations. Although we employed an XGBoost model to analyze osteoporosis-related EKG features, the underlying reasons for the prominence of specific EKG patterns remain unclear. The R-squared values were 49.35% for the internal validation set and 43.49% for the external validation set, indicating that a substantial portion of variability remains unexplained. Further research or more sophisticated models may be necessary to enhance interpretability. At present, human experts still lack the capability to diagnose osteoporosis based solely on EKG findings. For the DLM to gain transparency, future studies must delve into the correlation and interpretability of EKG features in relation to osteoporosis.

Conclusion

We devised a novel approach using a DLM trained on a sizable collection of EKGs corroborated by DXA to detect osteoporosis. This innovative strategy offers a practical, accessible, and cost-effective means for aiding physicians in promptly recognizing individuals at risk of osteoporosis. The integration of AI-powered EKG assessment could introduce substantial prognostic value for osteoporosis and function as a screening tool, enhancing quality of life and mitigating mortality risk.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s10916-025-02333-6.

Author Contributions W.H.F contributed to the conception of this research idea, study design and supporting all stages of this paper. S.C.H drafted the manuscript. D.J.T contributed to data analysis and prepared figures. C.L and C.C.L contributed to DLM design and software. C.S.L contributed to the conception of this research idea. C.H.W contributed to Project Manager. All authors reviewed this manuscript and approved the final version of the manuscript.

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Data Availability The corresponding author is willing and ready to provide the de-identified datasets used and/or analyzed during the current study upon reasonable request.

Declarations

Ethics approval and consent to participate All methods were carried out in accordance with relevant guidelines and regulations. The need for informed consent was waived by the Ethics Committee/Institutional Review Board of the institutional ethics committee of the Tri-Service General Hospital (C202105049).

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Competing Interests The authors declare no competing interests.

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