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ORIGINAL PAPER

Artificial Intelligence-Enabled Electrocardiography Predicts Future Pacemaker Implantation and Adverse Cardiovascular Events

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Abstract
Medical advances prolonging life have led to more permanent pacemaker implants. When pacemaker implantation (PMI) is commonly caused by sick sinus syndrome or conduction disorders, predicting PMI is challenging, as patients often experience related symptoms. This study was designed to create a deep learning model (DLM) for predicting future PMI from ECG data and assess its ability to predict future cardiovascular events. In this study, a DLM was trained on a dataset of 158,471 ECGs from 42,903 academic medical center patients, with additional validation involving 25,640 medical center patients and 26,538 community hospital patients. Primary analysis focused on predicting PMI within 90 days, while all-cause mortality, cardiovascular disease (CVD) mortality, and the development of various cardiovascular conditions were addressed with secondary analysis. The study's raw ECG DLM achieved area under the curve (AUC) values of 0.870, 0.878, and 0.883 for PMI prediction within 30, 60, and 90 days, respectively, along with sensitivities exceeding 82.0% and specificities over 81.9% in the internal validation. Significant ECG features included the PR interval, corrected QT interval, heart rate, QRS duration, P-wave axis, T-wave axis, and QRS complex axis. The AI-predicted PMI group had higher risks of PMI after 90 days (hazard ratio [HR]: 7.49, 95% CI: 5.40-10.39), all-cause mortality (HR: 1.91, 95% CI: 1.74–2.10), CVD mortality (HR: 3.53, 95% CI: 2.73–4.57), and new-onset adverse cardiovascular events. External validation confirmed the model's accuracy. Through ECG analyses, our AI DLM can alert clinicians and patients to the possibility of future PMI and related mortality and cardiovascular risks, aiding in timely patient intervention.

Keywords Artificial intelligence · Electrocardiogram · Deep learning model · Pacemaker · Major adverse cardiovascular events

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Introduction

Permanent pacemaker therapy is most commonly indicated for high-degree atrioventricular block (AVB) and sinus node dysfunction patients [1]. These conditions are often associated with degeneration of the cardiac conduction system and changes in intercellular conduction, which can be caused by either cardiac or noncardiac disease. The use of pacemakers has shown a continuous increase, which can be attributed to increasing life expectancy and aging populations worldwide. The estimated number of patients undergoing pacemaker implantation has been consistently increasing, with an annual implant rate of approximately one million devices globally [2, 3]. Due to the prevalence of these conditions in older patients, the majority of patients requiring cardiac pacing are elderly, with more than 80% of pacemaker implants occurring in patients older than 65 years [4]. Permanent pacemaker implantation (PMI) not only enhances the survival rate but also significantly improves quality of life as evidenced by various studies conducted on patients receiving pacing therapy [5–13]. However, predicting the need for PMI is challenging because some patients may not exhibit clear symptoms until the condition has progressed to a severe stage, such as involving injuries from falling or even cardiac arrest. In addition, certain risk factors that increase the likelihood of PMI, such as hypertension and diabetes, can be present in individuals without any obvious signs of heart disease. This can make it difficult to identify those who would benefit from a PMI before they experience a cardiac event. As a result, there is a need for more accurate and reliable methods to predict the need for future PMI.

Artificial intelligence (AI) has emerged in the medical field and is being facilitated by technological advancements in machine learning [14, 15]. These advances include the use of structured data sources, which can be captured in a spreadsheet format, unstructured data sources, such as free text in electronic medical records (EMRs), and medical images, such as electrocardiograms (ECGs) and echocardiography. With the assistance of deep learning models (DLMs), AI systems can develop highly accurate clinical prediction models, which are categorized into two major groups: diagnostic prediction models and prognostic prediction models [16, 17]. AI is being increasingly utilized to address various health care challenges related to CVD. Some examples of this include the automated detection of cardiac arrhythmias from ambulatory ECGs, the early detection of aortic stenosis and acute myocardial infarction (AMI), and the prediction of future adverse cardiovascular events in patients receiving digoxin therapy [16, 18–20]. This study was designed to utilize DLM-assisted AI to analyze ECGs for the early detection of the need for PMI. Furthermore, since ECGs contain a wealth of physical information that can predict future CVD incidence, we hypothesized that this model could provide additional information on the likelihood of major adverse cardiovascular events (MACEs).

Methods

Data Source and Population

We conducted a study to develop and evaluate a DLM by retrospectively analyzing ECGs collected from two hospitals between January 1, 2010, and April 30, 2021. The two hospitals included an academic medical center in Neihu District (hospital A) and a community hospital in Zhongzheng District (hospital B). To ensure ethical compliance, the study was reviewed and approved by the Institutional Ethics Committee of the Tri-Service General Hospital (C202105049). Patients under 20 years of age were excluded from the study. Figure 1 shows the assignment of samples in this study. There were 85,820 patients with at least one ECG in hospital A. The 42,903 patients were included in the development cohort, which included 158,471 ECG records for DLM training. A total of 17,277 patients were assigned to the tuning cohort. A total of 64,462 ECGs were obtained to guide the training process and determine the optimal operating point for subsequent usage. Finally, 25,640 patients were assigned to an internal validation set, which included only the first ECGs that were used for the accuracy test and follow-up analysis. We also enrolled 26,538 patients in hospital B using the same inclusion criteria as those in the internal validation set for the external validation set to verify the extrapolation of the DLM.

Data Collection

A 12-lead ECG was recorded at a 500-Hz frequency for a duration of ten seconds, and the raw ECG traces were used to train the DLMs. Besides the raw-data ECG tracings, additionally analyzed ECG data included various abnormalities and findings, comprising 31 diagnostic pattern classes and 8 continuous ECG measurements obtained from quantitative measurements and abnormal findings based on standard phrases in the Philips' system (PageWriter TC30 and TC50, Philips, Amsterdam, Netherlands). Specifically, the abnormal ECG patterns detected included: abnormal T wave, atrial fibrillation, atrial flutter, atrial premature complex, complete atrioventricular (AV) block, complete bundle branch blocks (including complete left bundle branch block and complete right bundle branch block), first-degree AV block, incomplete bundle branch blocks (including incomplete left bundle branch block and incomplete right bundle branch block), ischemia/infarction (indicating myocardial

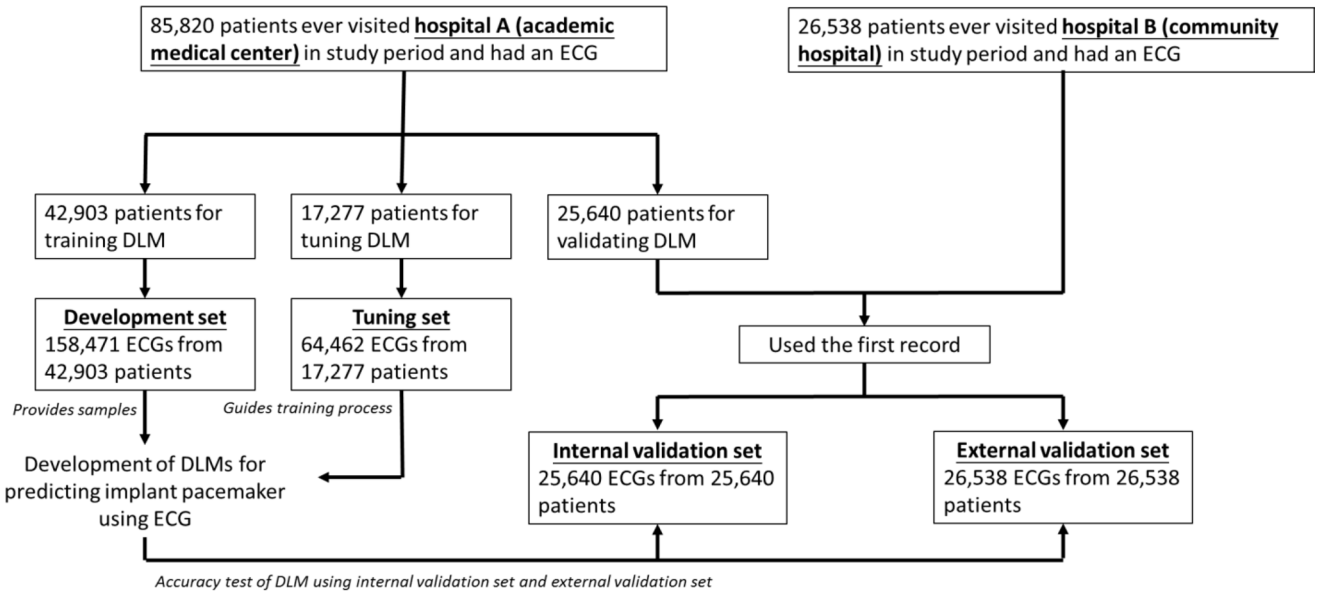

Fig. 1 Flowchart diagram of development, tuning, internal validation, external validation set generation and ECG labeling for pacemaker implantation. Schematic of the dataset creation and analysis strategy, which was devised to assure a robust and reliable dataset for training, validating, and testing the network; to prevent cross-contamination among the training, validation, and test datasets, each patient's data were exclusively used in one dataset; the Methods section provides detailed information on how each dataset was utilized; DLM, deep learning model; ECG, electrocardiogram

ischemia or infarction), junctional rhythm, left anterior fascicular block, left atrial enlargement, left axis deviation, left posterior fascicular block, left ventricular hypertrophy, low QRS voltage, pacemaker rhythm, prolonged QT interval, right atrial enlargement, right ventricular hypertrophy, second-degree AV block, sinus bradycardia, sinus pause, normal sinus rhythm, sinus tachycardia, supraventricular tachycardia, ventricular premature complex, ventricular tachycardia, and Wolff-Parkinson-White syndrome. These latter data were used to generate and train an extreme gradient boosting (XGB) model, as previously described [21]. They reflect a variety of cardiac conduction system abnormalities, arrhythmias, structural abnormalities, and other conditions. ECG measurements with missing data were imputed using multiple imputation methods [22]. The disease histories were based on the International Classification of Diseases, Ninth Revision and Tenth Revision (ICD-9 and ICD-10, respectively) as described previously [23]. The primary objective was to predict PMI 90 days after the index ECG. Patient status was defined by EMRs and updated by hospital staff. Nonimplant pacemaker data were censored at the patient's last known live hospital visit to limit bias from incomplete records. We also performed a secondary outcome analysis of all-cause mortality, CVD mortality and new-onset MACEs, such as AMI, stroke, coronary artery disease (CAD), atrial fibrillation (AF), and heart failure (HF). New-onset events were defined as records of corresponding ICD codes. Patients who met any of the above criteria before the index date of the ECG were excluded and defined as having a corresponding disease history.

Implementation of the Deep Learning Model

The major architecture of the proposed survival DLM for the prediction of PMI and the detailed derivation and explanation process are summarized in Supplement Fig. 1. In brief, each ECG was recorded as a standard 12 leads consisting of 5000 number sequences, and a 5000×12 matrix was generated based on these sequences for the DLM. An input format of this architecture is a 4096×12 matrix [21]. We developed a DLM using the Cox proportional hazard model to conduct survival analysis, the model being commonly used for prospective studies with a follow-up period to observe event occurrence. The DLMs were trained with a batch size of 32 using an initial learning rate of 0.001 and an Adam optimizer with standard parameters ($\beta 1 = 0.9$ and $\beta 2 = 0.999$). The learning rate was decayed by a factor of 10 each time the loss of the validation cohort plateaued after an epoch. To prevent the networks from overfitting, early stopping was performed by saving the network after every epoch and choosing the saved DLMs with the lowest loss in the validation cohort. The only regularization method for avoiding overfitting was L2 regularization, for which the coefficient was 10^{-4} in this study.

Statistical Analysis

We provided descriptive statistics for the different sets, including means and standard deviations for continuous variables and counts and percentages for categorical variables. The performance of the DLMs was assessed using receiver operating characteristic (ROC) curves, and the area under the curve (AUC), sensitivity (Sens), specificity (Spec), positive predictive value (PPV), and negative predictive value (NPV) were reported. The optimal operating point was selected based on Youden's index in the training set. For the additionally collected ECG data, we employed an XGB model to rank the importance of variables and investigate the relationship between PMI and explainable features. Furthermore, we used multivariable Cox proportional hazard models to analyze the association between baseline characteristics and outcomes of interest. For the analysis of new-onset outcomes, we will analyze the population without a history of that disease. We reported hazard ratios (HRs) and 95% confidence intervals (95% CIs) for comparisons. All the statistical analyses were conducted using R (version 3.4.4; R Core Team, 2018), for which the significance level was set at $p < 0.05$.

Results

Table 1 displays the baseline characteristics of the patients in the four distinct sets: development, tuning, internal validation, and external validation. The internal validation set had a significantly greater proportion of older patients and comorbidities, such as diabetes, hypertension, hyperlipidemia, chronic kidney disease, stroke, CAD, AF, and chronic obstructive pulmonary disease but a lower proportion of male patients than did the other sets. Conversely, there were fewer instances of AMI in the internal validation set than in the other sets.

In Fig. 2, we present the performance of the DLM in predicting the PMI within 30, 60, and 90 days in both the internal and external validation sets. With respect to the internal validation set, the AUC for predicting PMI within 30 days was 0.870, with a Sens of 82.0%, a Spec of 81.9%, a PPV of 1.2%, and an NPV of 99.9%. The AUC values for predicting the PMI within 60 days and 90 days were similar (0.878 and 0.883, respectively). With respect to the external validation set, the AUC for detecting PMI within 30 days was 0.916, with a Sens of 85.3%, a Spec of 80.9%, a PPV of 1.2%, and an NPV of 100.0%. The AUCs for predicting the PMI within 60 and 90 days were 0.920 and 0.919, respectively. The results obtained from the external validation set were consistent with those of the internal validation set, providing evidence for the ability of the model to accurately predict future pacemaker implantation.

Figure 3 presents a detailed analysis of the importance of the 12 most important ECG features in relation to the PMI as assessed by the information gained from the XGB model. The R^2 values were 59.5% and 62.7% based on all the traditional ECG features in the internal and external validation sets, respectively. In the internal validation set, the top 7 ECG features that contributed to PMI were the PR interval, corrected QT interval, QRS duration, P wave axis, T wave axis, heart rate, and QRS complex axis. Similarly, in the external validation set, the top 7 ECG features that contributed to PMI were the PR interval, QRS duration, corrected

Table 1 Baseline characteristics

	Development	Tuning	Internal validation	External validation
Demography				
Gender (male)	86,043(54.3%)	34,584(53.7%)	57,699(52.4%)	50,380(53.1%)
Age (years)	63.8 ± 17.0	63.6 ± 17.1	66.4 ± 17.0	64.0 ± 17.0
Height (cm)	162.2 ± 9.1	162.4 ± 9.1	162.6 ± 9.0	162.2 ± 9.1
Weight (cm)	64.5 ± 13.9	64.5 ± 13.8	65.2 ± 14.0	64.3 ± 13.8
BMI (kg/m^2)	24.4 ± 4.3	24.4 ± 4.3	24.6 ± 4.3	24.4 ± 4.3
Primary outcome				
Implant pacemaker within 90 days	1171(0.9%)	482(0.9%)	833(0.9%)	612(0.8%)
Disease history				
Diabetes mellitus	50,412(31.8%)	19,984(31.0%)	44,224(40.1%)	30,386(32.0%)
Hypertension	18,460(11.7%)	7336(11.4%)	17,790(16.1%)	11,445(12.1%)
Hyperlipidemia	64,622(40.8%)	26,186(40.6%)	60,323(54.8%)	38,433(40.5%)
Chronic kidney disease	45,296(28.6%)	17,950(27.9%)	35,054(31.8%)	26,940(28.4%)
Acute myocardial infarction	9405(5.9%)	3762(5.8%)	6159(5.6%)	5559(5.9%)
Stroke	28,065(17.7%)	11,648(18.1%)	26,528(24.1%)	17,026(17.9%)
Coronary artery disease	51,361(32.4%)	20,503(31.8%)	45,129(41.0%)	30,581(32.2%)
Atrial fibrillation	13,335(8.4%)	5285(8.2%)	12,309(11.2%)	7521(7.9%)
Chronic obstructive pulmonary disease	31,497(19.9%)	12,511(19.4%)	35,212(32.0%)	18,729(19.7%)

Abbreviations BMI, body mass index

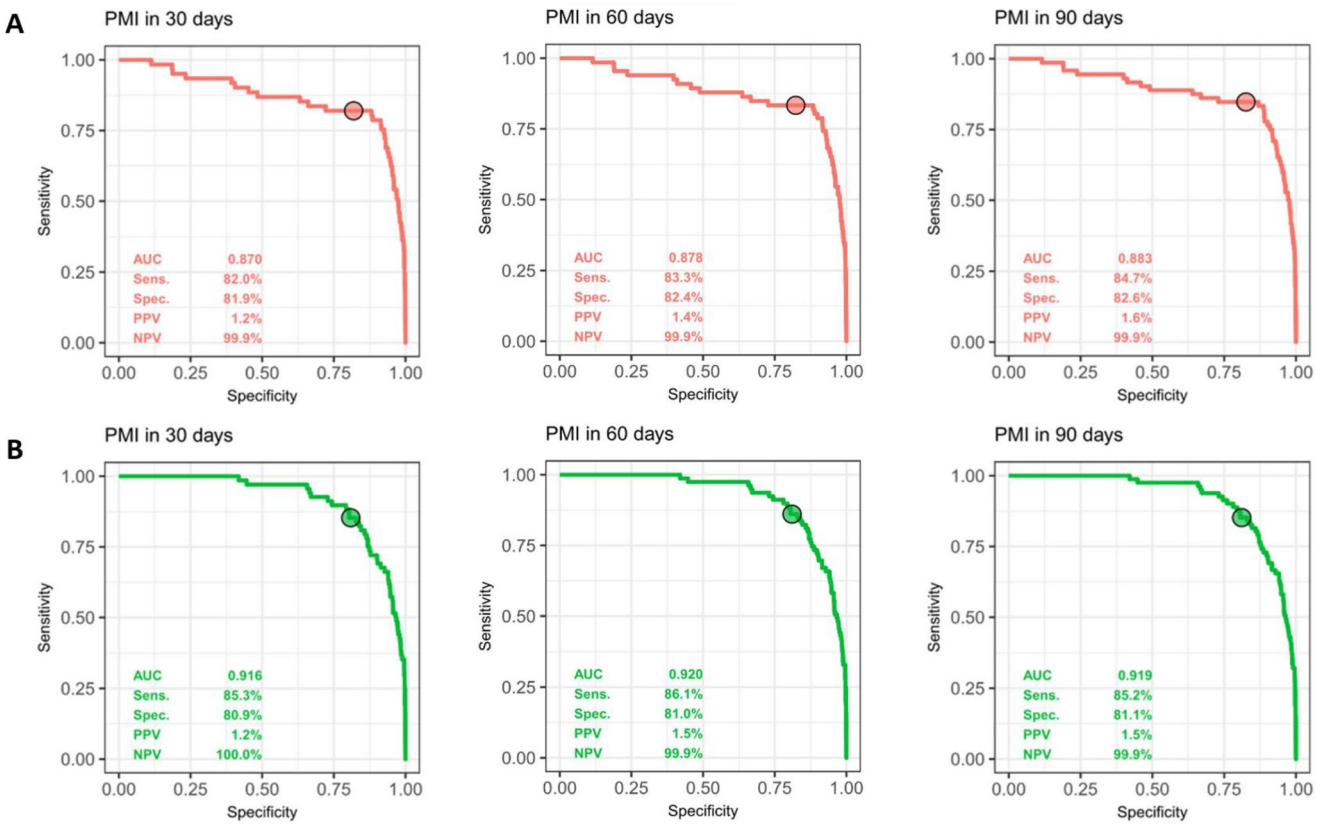

Fig. 2 Summarizes the performance of our DLM model in predicting pacemaker implantation (PMI) within 30, 60, and 90 days in both the internal (**A**) and external validation sets (**B**). We used receiver operating characteristic (ROC) curves to evaluate the DLM's predictive power based on the ECG data; the operating point was selected based on the maximum Youden's index in the tuning set and is denoted by a circle mark on the ROC curve; we calculated the area under the curve (AUC), sensitivity (Sens.), specificity (Spec.), positive predictive value (PPV), and negative predictive value (NPV) based on this operating point; DLM, deep learning model

QT interval, P wave axis, heart rate, T wave axis, and QRS complex axis. Additionally, we performed an analysis of the risk of future pacemaker implantation associated with Afib and bundle branch block (BBB), and the results are shown in Supplemental Tables 1 and 2.

Figure 4 demonstrates the prognostic value of the AI-predicted PMI (PACE group) in the internal and external validation groups after adjustments for sex and age. Patients in the PACE group had a significantly greater risk than those without an AI-predicted PMI (the no-PACE group). In the internal validation set, the PACE cohort had an HR of 7.49 (95% CI: 5.40-10.39) for PMI after 90 days, an HR of 1.91 (95% CI: 1.74–2.10) for all-cause mortality, and an HR of 3.53 (95% CI: 2.73–4.57) for CVD mortality. The external validation set showed similar findings to the internal validation set, with an HR of 8.40 (95% CI: 6.30-11.19) for PMI after 90 days, an HR of 1.77 (95% CI: 1.61–1.94) for all-cause mortality, and an HR of 4.14 (95% CI: 3.23–5.31) for CVD mortality, indicating the robustness of the model's predictive performance. Furthermore, patients in the PACE group had a greater incidence of new-onset MACEs, such as AMI, stroke, CAD, AF, and HF, than did those in the non-PACE group in both validation sets (Fig. 5).

Discussion

This DLM-enabled AI ECG analysis model accurately predicted future PMI, all-cause mortality, and CVD mortality. Additionally, this AI prediction model provided additional information on new-onset MACEs. Patients in the PACE group had a higher risk of pacemaker implantation after 90 days, all-cause mortality, CVD mortality, and new-onset MACEs, such as AMI, stroke, CAD, AF, and HF.

The incidence of PMI increases with age, and it is estimated that approximately 70–80% of all permanent pacemakers are implanted in patients aged 65 or older. Previous surveys have identified high-degree AVB and sick sinus syndrome as the leading indications for PMI [2]. Both the increasing incidence and declining mortality rates of PMI have contributed to its growing prevalence [24]. However, predicting the need for PMI in a patient can be challenging. A previous study has shown that male patients with AF

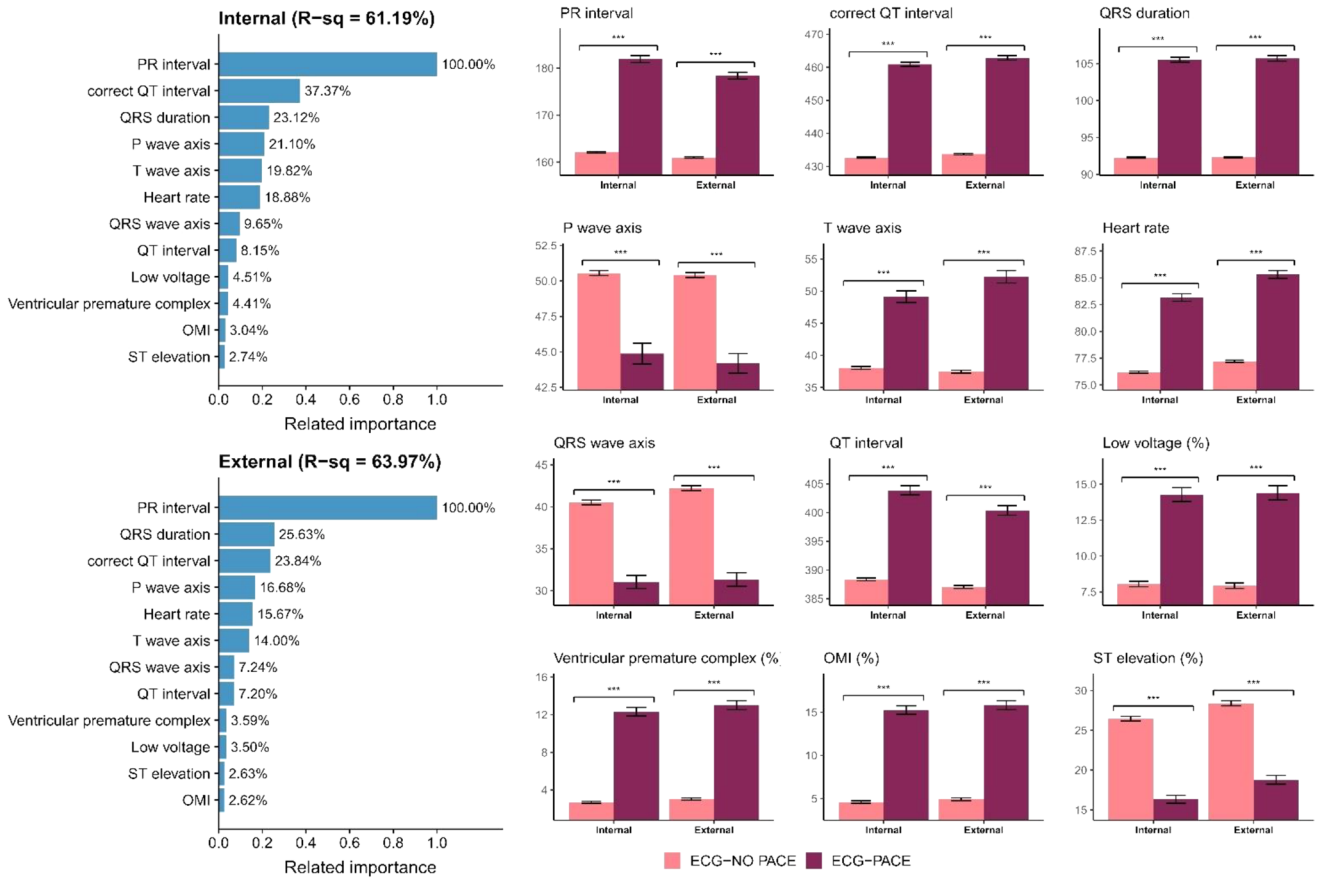

Fig. 3 Relationship between the selected ECG features and the predicted PMI. The importance of each ECG feature was determined based on the information gained from the XGB model, and the R-squared (R-sq) value represents the coefficient of determination for using these selected ECG features to predict the PMI; the AI-ECG signals were classified into PACE or non-PACE groups based on previously established operating points according to the receiver operating characteristic (ROC) curve analysis; the analysis was conducted in both the internal and external validation sets, with a significant difference observed between the two groups (*** $p < 0.001$; PMI, pacemaker implantation; XGB, extreme gradient boosting; AI, artificial intelligence; ECG, electrocardiogram; PACE, AI-predicted PMI)

who are above the age of 60 years and have congenital heart disease, or early HF, or a history of syncope, valvular heart disease, hypertension, ischemic heart disease or diabetes are at a higher risk of requiring PMI [25]. A study conducted in Finland has shown that risk factors associated with AV block include advanced age, male sex, a history of myocardial infarction, congestive HF, higher systolic blood pressure (greater than 120 mmHg), and elevated fasting glucose levels (greater than 100 mg/dL) [26]. A separate study revealed that the presence of distal conduction disease, along with the absence of historical factors that predispose or precipitate the condition, age older than 65 years, and a prolonged PR interval (collectively referred to as the DROP score), may serve as predictors of PMI in patients with unexplained syncope [27]. Additional studies have demonstrated that specific ECG parameters, including an abnormal QRS axis, prolonged QRS duration, prolonged QTc interval, and the presence of AF, may serve as indicators of the need for PMI or the risk of severe adverse events [28, 29].

Recently, numerous studies have investigated the predictors of permanent PMI in patients who have undergone transcatheter aortic valve replacement (TAVR), which easily causes left bundle branch block (LBBB) due to injury to the conduction system during valve deployment. Multiple meta-analyses have demonstrated that certain ECG features, including first-degree atrioventricular (AV) block, preexisting right bundle branch block (RBBB), left anterior fascicular block (LAFB), AF, and wider baseline QRS duration, can predict future PMI after TAVR [30–34]. In a Chinese study, the author identified new-onset LBBB and T-wave elevation in lead I as the primary independent predictors of PMI in patients undergoing TAVR [35]. Several researchers have employed machine learning (ML) models to forecast future PMIs. One unpublished study utilized a gradient boosting ML model to predict the requirement for PMI within 30 days. The study revealed that RBBB was an important predictive parameter on ECG [36]. A recent study showed that an ML-based approach could effectively

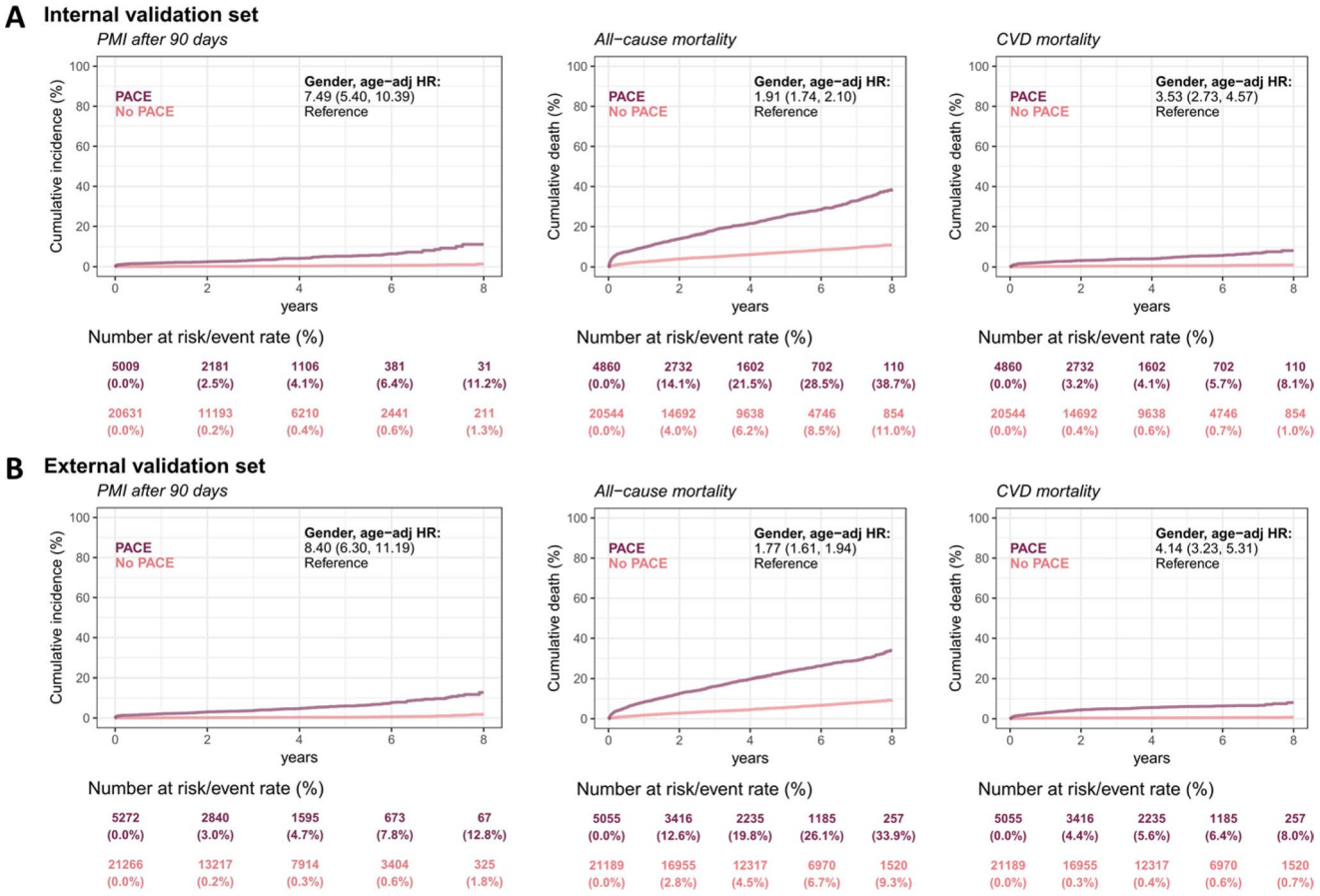

Fig. 4 Long-term PMI after 90 days, all-cause mortality, and CVD mortality in patients in the PACE group and non–PACE group stratified by AI-ECG prediction. CVD, cardiovascular disease; PACE, AI-predicted PMI

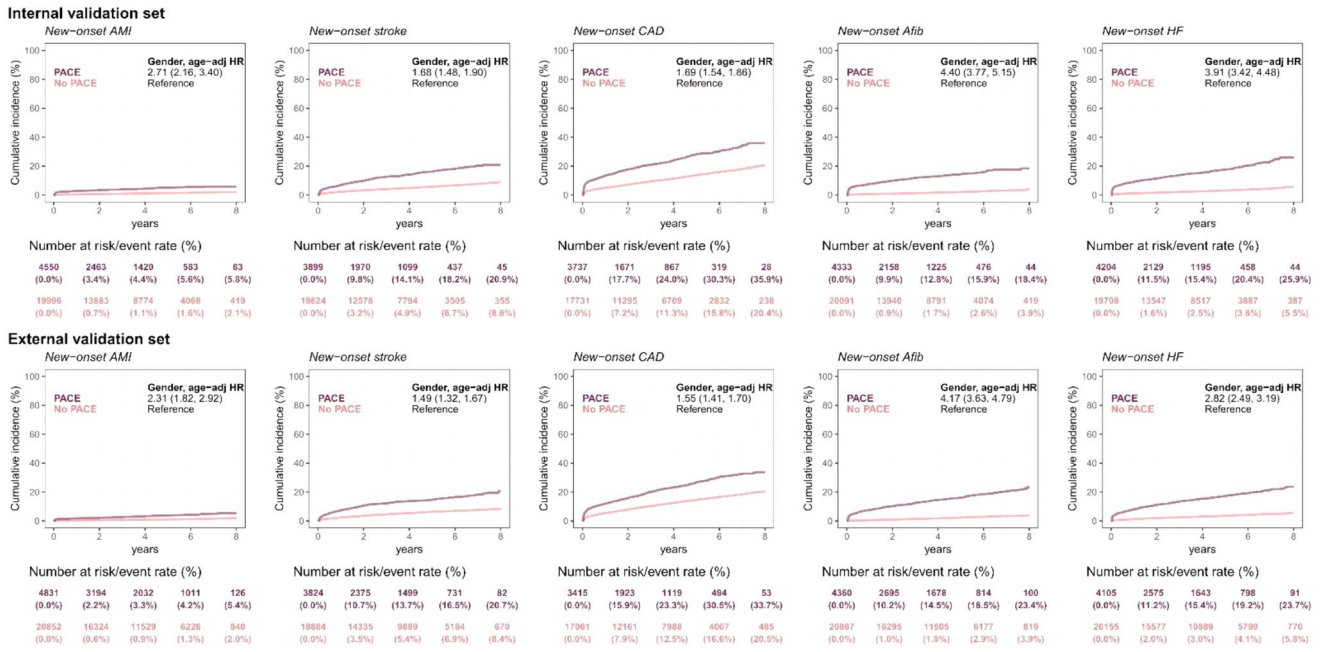

Fig. 5 Long-term incidence of new-onset AMI, stroke, CAD, AF, and HF in patients stratified by AI-ECG prediction and in the PACE and non–PACE groups. AMI, acute myocardial infarction; CAD, coronary artery disease; AF, atrial fibrillation; HF, heart failure; PACE, AI-predicted PMI

predict the need for PMI after TAVR [37]. The study examined data from 557 patients who underwent TAVR and were in sinus rhythm. Of these patients, 95 (17.1%) required PMI due to complete AV block (71 patients, 75%), pathological pauses and asystole (6 patients, 6%), or other symptomatic bradycardias (18 patients, 19%). The AI model used in the study utilized a random forest algorithm and accurately predicted which patients would require PMI. Several factors, including the delta QRS complex, delta PR, baseline QRS interval, baseline RBBB, and baseline PR interval, were strongly associated with the need for PMI after TAVR. These findings suggest that ML can be an effective tool for predicting the need for PMI after TAVR, thereby helping health care providers make more informed decisions about patient care.

However, it is more difficult to predict the PMI in the general population. Our data analysis demonstrated that our AI system has a high level of accuracy in predicting PMI within 30, 60, and 90 days in both the internal and external validation sets, with a sensitivity exceeding 82% and specificity exceeding 80%. The external validation set produced similar results to the internal validation set, with all the AUC values for predicting the PMI within 30, 60, and 90 days exceeding 0.85. This indicates that the AI model is effective at accurately predicting the PMI after its development and tuning. Despite the relatively low PPV, which ranged from 1 to 2% due to the low incidence of PMI among patients who received ECGs in both hospitals, the NPV was found to be extremely high. This finding indicates that patients in the non-PACE group had a very low risk of PMI. Over a follow-up period of up to 8 years, patients in the PACE group exhibited a significantly greater incidence of PMI, with 11.2% of patients experiencing the condition compared to only 1.3% of patients in the non-PACE group.

Our XGB model revealed that the PR interval, corrected QT interval, QRS duration, P wave axis, T wave axis, ventricular rate, and QRS axis were the most significant features for predicting pacemaker implantation. These findings demonstrated the importance of not only the duration of ECG parameters, such as the PR interval, QT interval, QRS duration, and ventricular rate (RR interval) but also the vectors of atrial depolarization, ventricular depolarization, and ventricular repolarization, which are indicated by the P wave, QRS complex, and T wave axis, respectively. These findings suggest that abnormalities in the duration and orientation of these ECG parameters can serve as indicators of bradycardia and may be useful in predicting the need for pacemaker implantation. Various studies have demonstrated the utility of ECG parameters such as the PR interval or QRS duration in predicting future pacemaker implantation and all-cause mortality [31, 32, 34, 38]. These intervals are commonly used to diagnose conduction abnormalities such as AVB and sinus node dysfunction, which are known risk factors for bradycardia and subsequent PMI. However, the association between ECG axes and bradycardia has not been fully explored in previous research. The ECG axes refer to the direction and magnitude of the electrical activity of the heart and can be represented as the frontal plane (i.e., the coronal plane) or the horizontal plane (i.e., the transverse plane). The normal range for the P-wave axis is 0 to + 75 degrees, but several pathological conditions, such as atrial cardiomyopathy or fibrosis in the area of Bachmann's bundle with intra-atrial conduction block, can result in an abnormal P-wave axis [39, 40]. An abnormal P-wave axis has been linked to mortality, AF, and stroke [41–45]. Various QRS axis abnormalities, including RBBB, LBBB, LAFB, and Left Posterior Fascicular Block, are associated with conduction disturbances. In cases of advanced conduction disturbance, such as high-degree or complete AV block, PMI becomes necessary. Previous studies have demonstrated that conduction system disease, such as new-onset BBB disease, may be predictive of PMI after aortic valve surgery [46, 47]. However, no previous research has reported whether baseline conduction disorders or the QRS axis can be used to predict future PMI in the general population; however, our current study shows that the QRS axis can be used to predict future PMI. An abnormal T-wave axis can be caused by several pathological factors, such as obesity and hypertension. One study revealed that an abnormal T-wave axis shift is independently associated with metabolic syndrome [48]. Additionally, T-wave axis orientation has been linked to an increased risk of coronary artery disease and heart failure [49]. Another study showed that an abnormal T-wave axis may be predictive of death from arrhythmia as well as all-cause mortality and nonarrhythmic cardiac death [50].

Despite the limited amount of research on the relationship between the ECG axis or bradycardia and PMI, our study has provided valuable insights into the potential use of abnormal P-waves, QRS complexes, and T-wave axes as predictors of PMI. These findings have important implications for clinical practice, as they suggest that health care providers should consider assessing the ECG axis as part of routine screening for patients with suspected bradycardia or other cardiac conditions. By incorporating ECG axis assessment into routine screening, health care providers may be able to identify patients at increased risk of developing bradycardia and undergoing subsequent PMI. Early identification of patients at increased risk of developing bradycardia and undergoing subsequent PMI can enable health care providers to initiate appropriate interventions. These interventions may include adjusting medication regimens, controlling comorbidities, and monitoring for the prompt detection of conditions that may require PMI. By implementing these measures, health care providers can effectively manage their

patients' conditions, leading to improved long-term health outcomes. In addition, our study revealed that the AI not only accurately predicts the likelihood of a patient needing PMI but also correlates closely with patient prognosis, including CVD mortality and MACEs. This finding aligns with previous research indicating that ECG abnormalities help identify patients at high risk of sudden cardiac death [51]; more recently, AI systems have been used to predict mortality via various ECG parameters via deep neural networks [52, 53].

While our study demonstrated the predictive ability of the DLM for PMI and adverse cardiovascular outcomes, it is important to acknowledge the limitations associated with such "black box" models. The lack of transparency and explainability inherent to DLMs, including our model, raises ethical concerns regarding their use in clinical decision-making [54, 55]. Although techniques like heat maps and XGB models may provide some insight into the model's decision-making process, they may not fully address the issues of transparency and explainability [56]. Furthermore, our study primarily focused on the predictive performance of the DLM using raw ECG data, but it is possible that classical machine learning models incorporating a more comprehensive set of discrete ECG measures and advanced signal processing techniques could have achieved comparable or even superior predictive ability. The fact that seven out of the eight discrete ECG measures analyzed in our study contributed significantly to PMI prediction suggests that a more rigorous approach to feature extraction and incorporation of advanced ECG measures may have enhanced the performance of traditional machine learning models. It is essential to acknowledge these limitations and continue exploring avenues to improve the transparency, explainability, and ethical considerations of DLMs while also recognizing the potential value of traditional machine learning approaches in conjunction with advanced signal processing techniques. Our findings demonstrated that patients in the PACE group, in addition to requiring a pacemaker device, had high overall mortality and CVD mortality rates, suggesting that they constitute a high-risk patient population. Additionally, this AI model can detect the early onset of new MACEs, such as AMI, stroke, CAD, AF, and HF, providing a critical aspect of monitoring the occurrence of these events in these patients. These findings underscore the importance of utilizing ECGs and other diagnostic tools to accurately identify patients who may be at risk for PMI and to take appropriate measures to monitor and manage their condition over time. By doing so, health care providers can improve patient outcomes and reduce the likelihood of serious cardiac events.

Conclusion

Our AI system, utilizing a DLM, is capable of analyzing patients' ECGs and providing early warnings to clinicians and patients regarding the likelihood of future PMI, all-cause mortality, and new-onset MACEs. This noninvasive tool can be particularly valuable in identifying asymptomatic patients who may benefit from timely interventions, such as medication adjustments or lifestyle modifications, before the patient becomes more symptomatic. By providing early warnings and personalized risk assessments, our AI system can help to optimize clinical decision-making and improve patient outcomes.

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Data Availability No datasets were generated or analysed during the current study.

Declarations

Ethics Approval and Consent to Participate The Tri-Service General Hospital, Taipei, Taiwan, conducted the ethical review of this study (IRB No. C202105049). The institutional review board agreed to waive individual consent since the data were collected retrospectively and analyzed on intranet.

Competing Interests The authors declare no competing interests.

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