10-Year Risk Prediction of Higher-Grade AV Block in Patients with First-Degree AV Block

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Abstract

Background: *First-degree atrioventricular (AV) block has traditionally been considered benign, but emerging evidence suggests it may indicate a risk of progression to higher-degree AV block. This study developed and externally validated a machine learning model to predict AV block progression using ECG-derived parameters.*

Methods: *A retrospective cohort study was conducted using 12-lead ECG data from Severance Hospital (development) and Yongin Severance Hospital (external validation). The model was trained with six ECG-derived parameters (RR interval, P duration, PR segment, PR interval, QRS duration, QT interval), along with age and sex, using a Random Forest algorithm.*

Results*: It achieved an AUROC of 0.823 (AUPRC 0.719) in internal validation and AUROC 0.808 (AUPRC 0.894) in external validation. SHAP analysis identified PR segment, QRS duration, and age as key predictors.*

Conclusion: *This model enables early risk stratification for AV block progression using widely available ECG parameters, supporting clinical decision-making.*

Introduction

First-degree atrioventricular (AV) block, defined by a PR interval >200 ms, has traditionally been viewed as a benign incidental finding[1, 2]. This notion is being challenged by emerging evidence that even benign first-degree AV blocks can progress to higher-grade AV blocks. Longitudinal studies show that a subset of patients with first-degree AV block will develop second-degree (Mobitz type I or II) or complete heart block over time[3, 4, 5]. Such progression is not only an electrocardiographic curiosity, but it carries important clinical consequences. Notably, prolonged PR interval has been associated with a markedly elevated risk of future pacemaker implantation (reflecting progression to symptomatic high-grade block) and increased risks of heart failure and all-cause mortality[2, 6, 7]. These observations underscore that first-degree AV block is not entirely benign in all patients, and they highlight the need to identify individuals at risk of advanced conduction block.

From a clinical management perspective, the ability to predict AV block progression offers several benefits. Patients identified as high-risk could avoid AV nodal-blocking medications, such as beta-blockers or non-dihydropyridine calcium channel blockers, that might exacerbate conduction delay and precipitate higher-grade block[8]. Likewise, early consideration of permanent pacemaker implantation before the onset of syncope or hemodynamic collapse may improve outcomes. For example, in older adults with chronic second-degree AV block (Mobitz I), prophylactic pacing was associated with better survival[9], suggesting that timely pacemaker therapy can avert the consequences of conduction failure. Additionally, identifying high-risk patients permits optimized monitoring strategies. Such patients can be followed more closely (with serial exams or ambulatory electrocardiogram monitoring) to detect progression early[5, 10], or even be considered for insertable loop recorders to capture intermittent high-grade AV block episodes that would be missed on routine visits[5]. In short, risk stratification in first-degree AV blocks could directly inform personalized management – avoiding harm from certain drugs, guiding earlier pacemaker intervention, and tailoring follow-up intensity.

Reliable risk stratification, however, remains challenging. Continuous ambulatory monitoring (e.g. Holter monitors or implantable loop recorders) can unmask intermittent episodes of Mobitz II or complete heart block[5], but routine long-term monitoring of every patient with first-degree AV block is impractical. Invasive electrophysiology (EP)

study is the gold standard for pinpointing the level of AV conduction delay; a prolonged His–ventricular (HV) interval indicates distal (infra-Hisian) disease and strongly predicts future high-grade AV block[11]. Indeed, an HV interval >70 ms on EP study denotes His–Purkinje system involvement and is associated with a high likelihood of progressing to complete heart block[11]. However, EP testing is costly and invasive, and its predictive specificity is limited – many patients with bundle branch block have HV >70 ms yet only a 1–2% per year incidence of progressing to complete AV block[12]. By contrast, the standard 12-lead electrocardiogram (ECG) is a ubiquitous, noninvasive tool that already provides useful prognostic clues. A single resting ECG showing PR interval prolongation or concomitant intraventricular conduction block (e.g. bifascicular block) has been linked to higher rates of subsequent high-grade AV block and pacemaker requirement[6, 12]. Given its wide availability and low cost, the 12-lead ECG system represents an attractive modality for baseline risk stratification in first-degree AV block. Yet it remains underutilized for this purpose.

We propose a new approach to bridge this gap by leveraging standard 12-lead ECG-derived features to predict AV block progression. In this study, we develop and validate a predictive model that uses routine ECG measurements to identify patients with first-degree AV block who are at heightened risk of progressing to second- or third-degree AV block within 10 years. This ECG-based risk model, to our knowledge the first of its kind, could enable early intervention in high-risk individuals while sparing low-risk patients from unnecessary interventions. By focusing on a readily obtainable test, the 12-lead ECG, our work aims to provide clinicians with a practical tool for anticipating AV conduction deterioration and guiding proactive management of patients with apparently "benign" first-degree AV block.

Methods

Data source

This study was designed as a retrospective cohort study. The development cohort was derived from Severance Hospital, while the external validation cohort was obtained from Yongin Severance Hospital. For the Severance Hospital cohort, data were collected from all patients who underwent 12-lead electrocardiogram (ECG) recordings between November 1, 2005, and October 31, 2022. This cohort comprised 1,188,665 patients, contributing a total of 5,092,736 ECG recordings. For external validation, we utilized data from Yongin Severance Hospital, where all patients with 12-lead ECG recordings between January 1, 2012, and January 31, 2025, were included. This validation cohort consisted of 177,422 patients, with 446,600 ECG recordings collected during the study period.

The study was approved by the Institutional Review Board of Yonsei University Severance Hospital (No. 4-2022-1506), with a waiver of additional written consent owing to its retrospective design. To ensure patient privacy and compliance with data security protocols, all data used in this study were fully anonymized.

Study Design

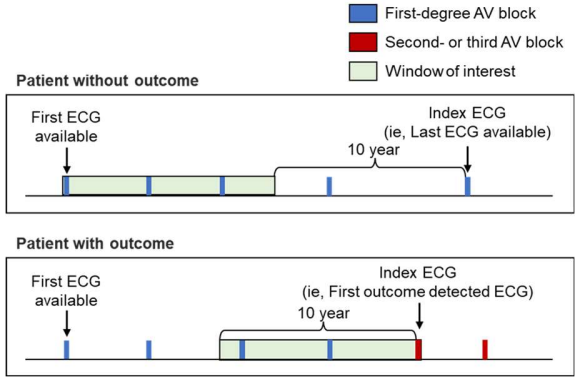

Figure 1. Schematic representation of the study design. The outcome was defined as the occurrence of a second- or third-degree AV block. For patients without the outcome, the index ECG was set as the latest available ECG. For those with the outcome, the index ECG was the first ECG recorded at the time of progression. A window of interest was defined based on the index ECG for data selection. ECG: electrocardiogram.

This study compared patients with first-degree AV block who progressed to second- or third-degree AV block within 10 years to those who did not. For patients who experienced progression, the first ECG confirming second- or third-degree AV block was designated as the index ECG. All prior first-degree AV block ECGs recorded within a 10-year window preceding the index ECG were included in the analysis. For patients without progression, the last available

ECG served as the index ECG, with the preceding 10 years of first-degree AV block ECGs defining the observation window.

Inclusion and exclusion criteria for study population

This study included adult patients with first-degree AV block and selected cases based on specific inclusion and exclusion criteria. Patients aged 20 years or older with documented first-degree AV block were included. ECGs from patients with atrial fibrillation or atrial flutter were excluded to avoid confounding effects. Recordings with missing P, Q, R, S, or T wave measurements were removed, as these were necessary for calculating P duration, PR interval, PR segment, QRS duration, and QT interval. Additionally, ECGs were excluded if they contained clinically implausible values, pre-existing pacemaker implantation, lead reversal, low signal quality, technical errors, or were misclassified as pediatric despite being from adult patients.

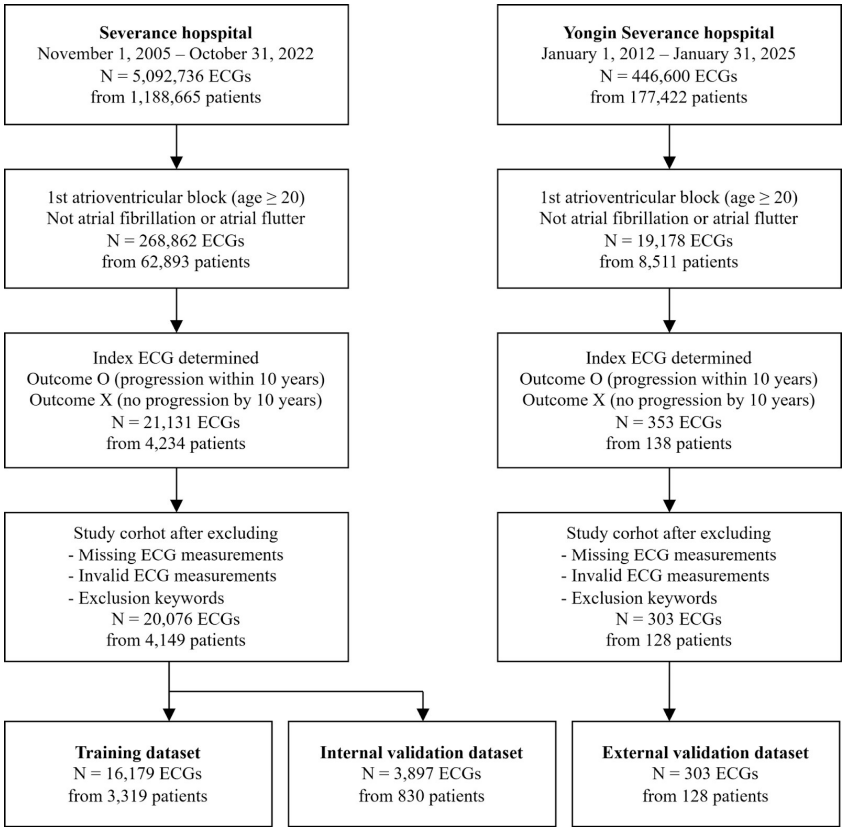

Figure 2. Patient selection flowchart.

After applying these criteria, 268,862 ECGs from 62,893 patients in the Severance Hospital cohort met the initial selection criteria. Based on progression status within 10 years, 4,234 patients with 21,131 ECGs were identified for further analysis. Following the exclusion of invalid or incomplete ECGs, 20,076 ECGs from 4,149 patients were retained. These were randomly split 8:2 into a training dataset and an internal validation dataset. For external validation, the same initial criteria were applied to Yongin Severance Hospital, resulting in 19,178 ECGs from 8,511 patients. After excluding invalid and incomplete ECGs, 303 ECGs from 128 patients remained in the final external validation dataset.

Feature extraction and data processing

All ECG parameters were extracted from the GE MUSE 12-lead ECG system, including patient age, sex, RR interval, and automated measurements of P, Q, R, S, and T waves. Using these wave measurements, P duration, PR interval, PR segment, QRS duration, and QT interval were calculated. All calculations were standardized to milliseconds (ms) to ensure consistency across records. These extracted and derived features, total 8 features, were used as input variables.

These eight variables were chosen because they represent the core time-domain intervals that the AHA/ACCF/HRS electrocardiography standardization statement designates as mandatory automated outputs for any digital 12-lead ECG; moreover, their normal limits vary systematically with both age and sex, making age and sex necessary covariates[13,14]. Therefore, this minimal yet guideline-concordant feature set captures the entire atrial–ventricular–ventricular conduction sequence while respecting events-per-variable constraints for modelling.

Machine learning model training

The predictive model was developed using the Severance Hospital cohort as the development cohort. Patients selected according to the study design criteria were randomly split into an 8:2 ratio, forming the training dataset (16,179 ECGs from 3,319 patients) and internal validation dataset (3,897 ECGs from 830 patients). Model training was conducted using five commonly applied algorithms: Random Forest, Logistic regression, Support vector machine (SVM), XGBoost, and LightGBM. Hyperparameters were tuned with fivefold cross-validation on the training dataset. The model with the highest area under the receiver operating characteristic curve (AUROC) during cross-validation was selected as the optimal model.

Performance evaluation and model explainability

To evaluate model performance, we assessed AUROC and area under the precision-recall curve (AUPRC) using both the internal validation set and the external validation set. Additionally, we calculated accuracy, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and F1-score, based on the Youden index derived during model training. Furthermore, feature importance was analyzed using SHapley Additive exPlanations (SHAP) analysis to quantify the contribution of each feature to model predictions and assess its impact on classification performance.

Statistical analysis

To assess the statistical significance of patient characteristics, appropriate statistical tests were conducted. For sex, a binary categorical variable, statistical significance was evaluated using the chi-square test. For continuous variables, normality was assessed using the Shapiro-Wilk test. Depending on normality, independent t-tests were performed to compare differences between groups. All analyses, including statistical testing, machine learning model development, and performance evaluation, were conducted in a Python environment.

Results

Patient baseline characteristics

For the development dataset (Severance Hospital), a total of 4,149 patients with 20,076 ECG recordings were included in the final analysis. Patients who progressed to second- or third-degree AV block were significantly older (mean age: 67.9 years vs. 60.3 years, $p < 0.001$) and had a higher proportion of males (69.1%, $p = 0.011$) compared to those without progression (Table 1). Among ECG parameters, RR interval and P duration were significantly shorter in the progression group ($p < 0.001$), whereas PR segment, PR interval, QRS duration, and QT interval were significantly longer in patients who experienced progression (all $p < 0.001$).

Table 1. Patients baseline characteristics: Severance Hospital

	Overall (n = 20,076)	Progression (n = 6,627)	Non-progression (n = 13,449)	P-value
Age (years)	62.8 (13.1)	67.9 (14.2)	60.3 (11.8)	<0.001
Sex				0.011
Male	14,113 (70.3%)	4,581 (69.1%)	9,532 (70.9%)	
Female	5,963 (29.7%)	2,046 (30.9%)	3,917 (29.1%)	
RR interval (ms)	946.5 (182.4)	922.4 (204.8)	958.3 (168.9)	<0.001
P duration (ms)	117.7 (20.8)	112.5 (23.5)	120.2 (18.7)	<0.001
PR segment (ms)	123.3 (39.7)	144.5 (47.8)	112.9 (30.0)	<0.001
PR interval (ms)	241.0 (35.5)	257.0 (44.7)	233.1 (26.6)	<0.001
QRS duration (ms)	108.9 (23.3)	113.9 (27.1)	106.5 (20.7)	<0.001
QT interval (ms)	429.3 (47.2)	434.2 (56.4)	426.9 (41.7)	<0.001

Note: Two sample t-test: mean (SD), Chi-squared: n (%)

A similar comparison in the external validation dataset (Yongin Severance Hospital) demonstrated consistent findings (Table 2). Patients in the progression group were older (mean age: 72.3 years vs. 61.7 years, $p < 0.001$) and predominantly male (77.2%, $p = 0.001$). Significant differences were observed in PR segment and PR interval ($p < 0.001$), aligning with the findings from the development dataset, while differences in other ECG parameters were not statistically significant.

Table 2. Patients baseline characteristics: Yongin Severance Hospital

	Overall (n = 303)	Progression (n = 197)	Non-progression (n = 106)	P-value
Age (years)	68.6 (13.3)	72.3 (13.0)	61.7 (10.7)	<0.001
Sex				0.001
Male	213 (70.3%)	152 (77.2%)	61 (57.5%)	
Female	90 (29.7%)	45 (22.8%)	45 (42.5%)	
RR interval (ms)	944.4 (229.9)	933.8 (255.2)	964.1 (172.8)	0.222
P duration (ms)	111.4 (24.1)	111.6 (24.9)	111.0 (22.7)	0.836
PR segment (ms)	150.0 (55.8)	162.5 (59.4)	126.9 (39.0)	<0.001
PR interval (ms)	261.4 (52.9)	274.1 (56.8)	237.9 (33.9)	<0.001
QRS duration (ms)	106.5 (25.8)	105.7 (25.9)	108.0 (25.6)	0.452
QT interval (ms)	427.3 (44.5)	428.5 (49.5)	425.2 (33.2)	0.489

Note: Two sample t-test: mean (SD), Chi-squared: n (%)

Performance of candidate classification models

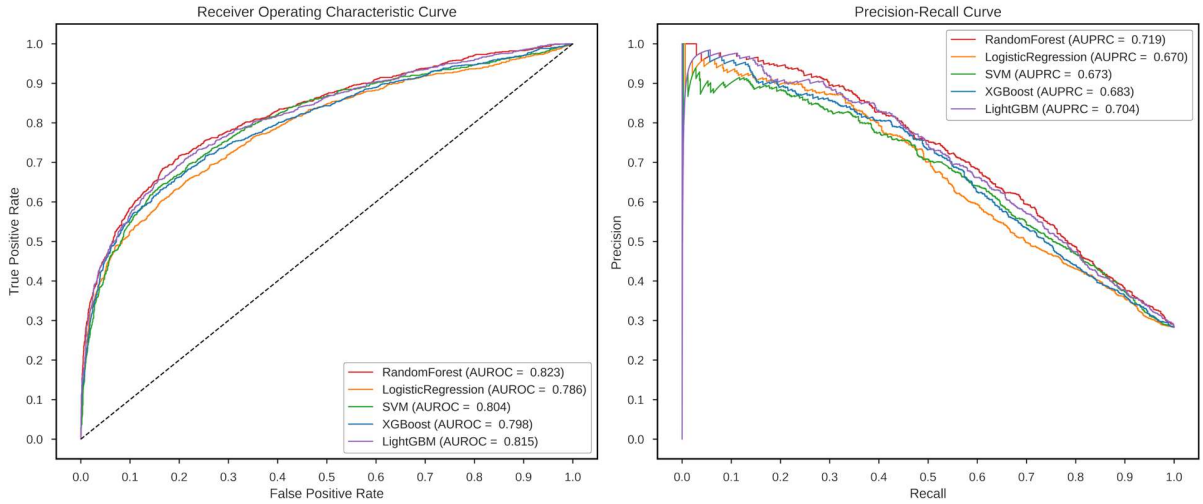

Figure 3. Discrimination of five candidate models on the internal validation dataset. Receiver operating characteristic (ROC, left) and precision–recall (PRC, right) curves generated from the Severance Hospital internal validation set. Curves are colour-coded as follows: red, random Forest; orange, logistic regression; green, support vector machine; teal, XGBoost; blue, LightGBM. The in-plot legends list the corresponding area under the ROC curve (AUROC) and area under the PRC curve (AUPRC) for each model.

The predictive ability of five classification algorithms was compared on the internal validation set (Figure 3). The Random Forest achieved the best discrimination, with an AUROC of 0.823 and an AUPRC of 0.719. Logistic regression, SVM, XGBoost and LightGBM showed lower performance, with AUROC values between 0.786 and 0.815 and AUPRC values between 0.670 and 0.704. Owing to this consistently higher performance, the Random Forest was selected for further evaluation.

Model performance evaluation

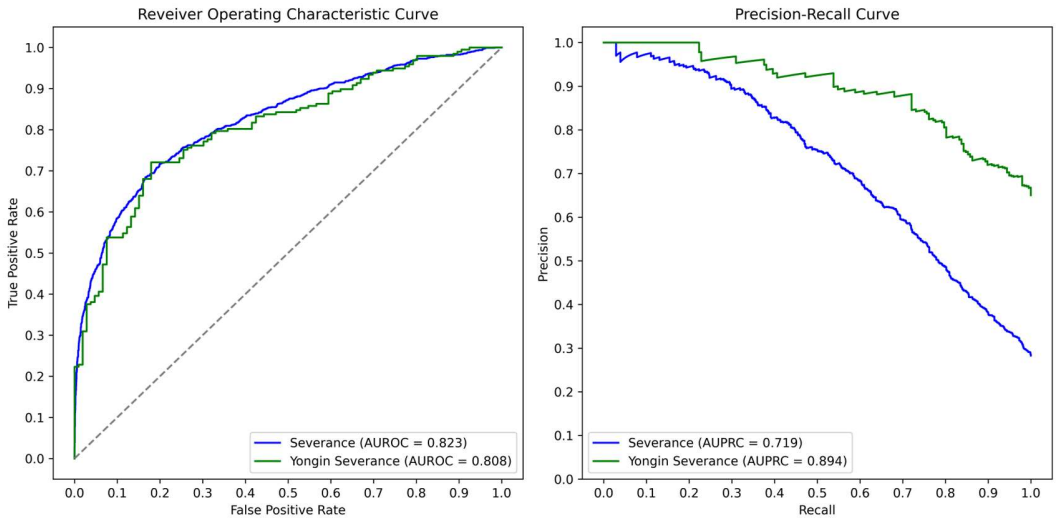

Figure 4. Performance evaluation of the Random Forest model. Receiver operating characteristic (ROC) and precision-recall (PRC) curves for model performance assessment in the internal validation dataset (Severance Hospital, blue) and external validation dataset (Yongin Severance Hospital, green). (Left) ROC curve with AUROC values for each dataset. (Right) PRC curve with AUPRC values for each dataset.

Table 3. Model performance in internal and external validation datasets

	AUROC	AUPRC	Accuracy	Sensitivity	Specificity	PPV	NPV	F1 score
Severance Hospital	0.823	0.719	0.790	0.656	0.844	0.624	0.862	0.640
Yongin Severance Hospital	0.808	0.894	0.740	0.721	0.774	0.855	0.600	0.739

Note: Model performance metrics for the two datasets. Accuracy, sensitivity, specificity, PPV, NPV, and F1-score were calculated based on the Youden index threshold, 0.396.

The model trained on the training dataset was evaluated on both the internal validation dataset and the external validation dataset to assess its predictive performance (Figure 3, Table 3). In the internal validation dataset, the model achieved an AUROC of 0.823 and an AUPRC of 0.719. Performance metrics at the optimal threshold determined by the Youden index, which was 0.396, were as follows: accuracy, 0.790; sensitivity, 0.656; specificity, 0.844; PPV, 0.624; NPV, 0.862; and F1-score, 0.640. In the external validation dataset, the model demonstrated robust generalizability, with an AUROC of 0.808 and an AUPRC of 0.894. At the Youden index threshold, the model achieved an accuracy of 0.740, sensitivity of 0.721, specificity of 0.774, PPV of 0.855, NPV of 0.600, and F1-score of 0.739.

Calibration curves showed acceptable agreement between predicted and observed 10-year risk. The Brier score was 0.138 in the internal validation set and 0.193 in the external set, indicating moderate calibration that was preserved when the model was applied to data from an independent hospital.

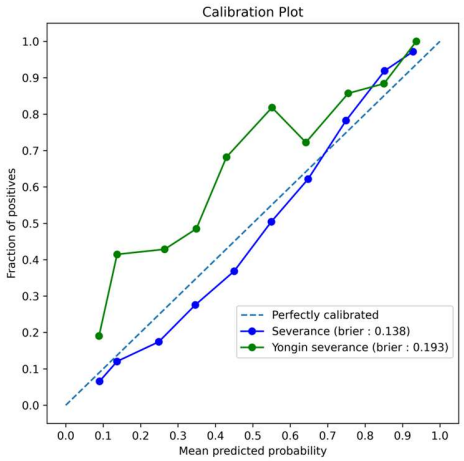

Figure 5. Calibration of the Random Forest model. Calibration plot comparing predicted and observed 10-year risk of progression. The dashed diagonal represents perfect calibration. Blue circles show the internal validation dataset (Brier score 0.138), and green circles show the external validation dataset (Brier score 0.193).

Feature importance

Feature importance was analyzed using SHAP to interpret the contributions of individual variables to the model's predictions (Figure 4). Among the eight features included in the model, the top five most influential features were age, PR segment, QRS duration, RR interval, and PR interval, in descending order of importance. Higher age, PR segment, QRS duration, and PR interval values were associated with an increased likelihood of disease progression. In contrast, shorter RR intervals, indicative of higher heart rates or underlying autonomic imbalance, were associated with an increased risk of progression.

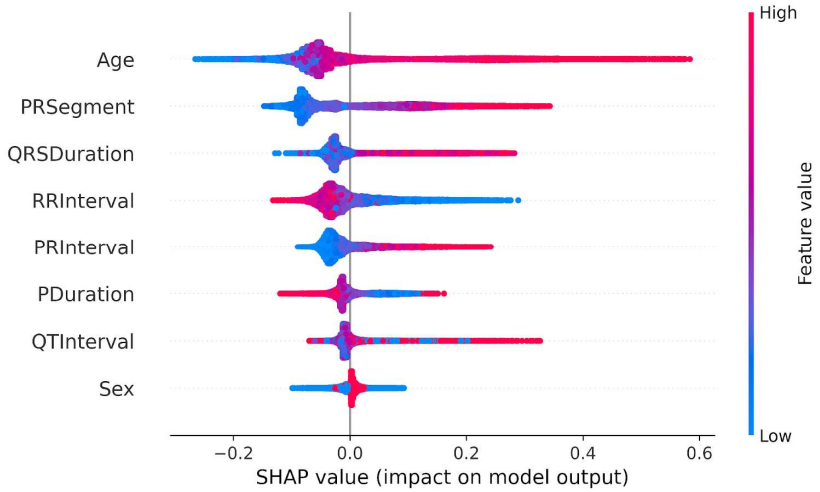

Figure 6. SHAP summary plot for feature importance. SHAP summary plot displaying the impact of all eight features on the model's predictions. Features are ranked on the y-axis by their influence, with more impactful features appearing higher. The x-axis represents SHAP values, indicating the magnitude and direction of each feature's effect on the model output. Color intensity transitions from blue to red, reflecting lower to higher feature values.

Discussion and Conclusions

In this study, we developed and externally validated a predictive model to identify patients with first-degree AV block at risk of progressing to second- or third-degree AV block within 10 years. Using only readily available ECG parameters along with age and sex, our model achieved strong discriminatory performance (internal validation: AUROC 0.823, AUPRC 0.719, brier score 0.138; external validation: AUROC 0.808, AUPRC 0.894, brier score

0.193), highlighting the clinical relevance and generalizability of simple ECG-based predictors for identifying high-risk patients.

Our model's interpretability aligns closely with established clinical and electrophysiological knowledge, as demonstrated by the SHAP analysis, which identified key ECG parameters robustly predicting AV block progression. In accordance with prior studies suggesting that a prolonged QRS duration reflects distal conduction delay and an extended PR interval indicates AV nodal dysfunction, our findings reinforce the notion that these parameters are significant risk markers[15]. The observed association between prolonged PR and QRS intervals and higher progression risk suggests an underlying conduction system pathology extending beyond the AV node, likely involving the His-Purkinje system. Notably, while the PR interval has traditionally been considered the key parameter in AV block progression, our model identified the PR segment as a particularly influential predictor. Furthermore, our study revealed an inverse relationship between RR interval and AV block progression, indicating that a faster heart rate is associated with a heightened risk. This finding may reflect underlying autonomic or structural cardiac changes that accelerate conduction system disease progression[16]. Additionally, while first-degree AV block is often considered benign in middle-aged individuals, its presence in older adults may serve as a marker of subclinical cardiac disease, a notion supported by our SHAP analysis[15]. This aligns with prior studies suggesting that age itself is a key factor in conduction system deterioration, necessitating closer monitoring in elderly patients.

First-degree AV block has traditionally been regarded as a benign finding, particularly in the absence of structural heart disease[17]. However, emerging evidence suggests that first-degree AV block may not always be clinically innocuous, as a proportion of patients experience progression to second- or third-degree AV block over time[3-6,18]. This progression is associated with adverse outcomes including syncope, heart failure, and sudden cardiac death, particularly when left unrecognized or unmanaged[6,17,19]. Yet, despite these clinical concerns, only few studies have quantified the long-term risk of such progression that could guide early clinical decision-making[20]. Importantly, existing guidelines recommend permanent pacemaker implantation only in the presence of a clear causal relationship between symptoms and conduction abnormality, leaving a substantial gap in the management of patients who may be asymptomatic but at increased risk of disease progression[17]. The lack of well-defined markers to differentiate truly benign conduction delay from early-stage conduction system disease underscores the need for improved risk stratification[20]. Our study addresses this unmet clinical need by providing long-term (10-year) prognostic evidence in patients with first-degree AV block, using widely available electrocardiographic parameters to predict progression to more advanced AV block. By identifying individuals at elevated risk, the proposed model may inform tailored follow-up strategies and contribute to more proactive management approaches in clinical practice.

Our study has several strengths. To the best of our knowledge, it is the first to apply machine learning methods to predict the 10-year risk of progression from first-degree to higher-grade AV block, while providing formal model explainability. The longitudinal design, with a follow-up period of up to ten years, allowed us to capture the incidence of late-onset high-grade AV blocks that might have been missed in shorter studies. We used rigorous definitions for outcomes and relied on uniformly curated digital ECG data, which enhances the reliability of our findings. Another strength is the use of SHAP for model interpretation, as mentioned above, which addresses the oft-cited “black box” criticism of machine learning in clinical settings. By demonstrating that our model’s predictions can be explained in terms of known conduction system pathology, we make the tool more transparent and clinically credible. Finally, the model’s performance metrics suggest it has practical utility in distinguishing high-risk patients from low-risk ones, which is the fundamental requirement for any risk stratification tool in practice.

However, we also recognize important limitations. First, as a retrospective study, prospective validation is necessary to confirm the model’s predictive value in real-world clinical settings. Second, the external validation set was modest, consisting of 303 ECGs from 128 patients (Figure 1), which broadens the confidence intervals around the performance estimates and underscores the need for larger validation samples. Third, although the model relies on ECG-derived parameters that are automatically generated by most digital systems, subtle differences in acquisition algorithms, filter settings, or calibration across ECG vendors could shift measured values and thereby affect model generalizability; cross-platform standardization or local recalibration may therefore be required before clinical deployment. Finally, while our model was validated in an external cohort, both datasets were derived from Korean tertiary hospitals, limiting ethnic and geographic diversity. Future studies should evaluate the model’s performance in multiethnic populations to assess its broader applicability.

In conclusion, we have developed a robust and interpretable model for predicting the progression of first-degree AV block to more advanced AV block. The model's ability to identify high-risk individuals can support clinicians in making earlier, proactive decisions. For patients flagged as high risk, clinicians may consider closer cardiac monitoring or timely referral for electrophysiological evaluation. In some cases, this could prompt earlier consideration of pacemaker implantation before a potentially life-threatening complete heart block occurs, thereby improving patient safety. By integrating such a prediction tool into clinical practice, healthcare providers could personalize management for patients with first-degree AV block, focusing attention and resources on those most likely to benefit from early intervention. This approach has the potential to reduce the morbidity associated with sudden advanced AV block and to guide optimal timing of therapy, ultimately improving outcomes in individuals with conduction system disease.

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