

Leveraging AI-ECG Technology for Early Notification and Tracking of AF Development (LATENT): Study Rationale and Design of a Randomized Controlled Trial

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Background: Atrial fibrillation (AF) is a progressive condition that is often undiagnosed until adverse events occur. Traditional risk scores provide limited value for predicting short-term latent AF. Artificial intelligence (AI)-enabled electrocardiogram (ECG) algorithms enable early risk stratification from sinus rhythm ECGs, however their clinical utility remains unvalidated in randomized controlled trials (RCTs).

Objective: To evaluate an AI-ECG-guided strategy for targeted ambulatory Holter monitoring to enhance the early detection of AF or pre-AF atrial findings (PAAFs, defined as premature atrial complexes [PACs] > 500 beats per 24 hours, consecutive short runs of PACs > 20 beats, or non-sustained AF or atrial flutter) compared with usual care.

Design: The LATENT trial is a prospective, open-label, two-arm RCT (NCT06847932) that will recruit 14,726 participants undergoing routine ECGs at a tertiary medical center in Taiwan. Participants will be randomized 1:1 to the intervention group (AI-ECG risk stratification) or control group (usual care). In the intervention group, high-risk individuals identified by the AI-ECG model will be invited to undergo up to 7 days of ambulatory Holter monitoring. In the control group, AI-ECG analysis will be retrospectively applied after study completion to identify those at high risk. The primary endpoint is newly detected AF or PAAFs within 90 days.

Summary: This trial will evaluate the clinical utility of an AI-ECG-guided risk stratification strategy combined with targeted ambulatory Holter monitoring for the early detection of AF or PAAFs in a real-world hospital setting. The findings will inform future strategies for integrating AI-ECG technology to support early AF detection and prevention.

Key Words: Artificial intelligence • Atrial fibrillation • Atrial premature complexes • Targeted Holter monitoring

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INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia and a major contributor to stroke, heart failure, and mortality.¹⁻³ Despite its clinical impact, AF is often paroxysmal or asymptomatic in its early stages, making timely diagnosis challenging.^{4,5} The initial diagnosis of AF frequently occurs only after a major adverse event.^{6,7} This emphasizes the need for early detection strategies to enable timely intervention and reduce the risk of adverse outcomes.

Several clinical risk scores have been proposed to es-

Abbreviations

AF	Atrial fibrillation
AFL	Atrial flutter
AI	Artificial intelligence
ECG	Electrocardiogram
EMR	Electronic medical record
ICD	International Classification of Diseases
NPV	Negative predictive value
ORs	Odds ratios
P ₁	Expected event rate
P ₂	Projected event rate
PAAFs	Pre-AF atrial findings
PACs	Premature atrial complexes
PPV	Positive predictive value
RCT	Randomized controlled trial
SR	Sinus rhythm

timate long-term AF risk.⁸⁻¹⁰ These models were primarily developed and validated to predict incident AF over 5-10 years. However, their applicability to short-term AF detection and the identification of candidates for extended Holter monitoring remains uncertain. This gap between long-term prediction and immediate clinical decision-making presents a significant challenge in AF screening strategies.

AF is now recognized as a progressive condition, preceded by a period of subclinical atrial electrical remodeling.^{2,11,12} Identifying early changes of electrical activity may offer an opportunity to detect latent AF before it clinically manifests. Frequent premature atrial complexes (PACs), consecutive short runs of PACs, and non-sustained AF or atrial flutter (AFL) have been associated with a high risk of developing AF.¹³⁻¹⁷ These pre-AF atrial findings (PAAFs) are clinically significant, as they may indicate that patients are either progressing toward clinical AF or already have subclinical disease. The proactive identification of early AF or PAAFs may provide a chance to alter the disease trajectory and potentially prevent irreversible atrial remodeling.

Recent advances in artificial intelligence (AI) have enabled the development of electrocardiogram (ECG)-based algorithms capable of identifying patients at high risk of AF from sinus rhythm (SR) ECGs alone.¹⁸⁻²⁰ These tools are non-invasive, widely accessible, and independent of symptoms or clinician interpretation. By identifying individuals at high risk of AF, AI-ECG algorithms can guide clinical decisions for targeted monitoring, facilitat-

ing diagnostic evaluation at an earlier stage of atrial disease and identifying patients who warrant closer surveillance. However, the clinical benefits of such tools have not yet been validated in randomized controlled trials (RCTs).

Based on this concept, this study aims to evaluate whether AI-ECG-guided risk stratification can be used as a decision tool to allocate targeted ambulatory Holter monitoring and improve the detection of AF or PAAFs compared with usual care.

STUDY OBJECTIVE AND DESIGN

We have developed and validated a deep learning model, AI-ECG, that uses a 10-second, 12-lead SR ECG to detect latent AF, defined as either (1) pre-existing AF that has spontaneously reverted to SR, or (2) new-onset AF not yet clinically diagnosed. The AI-ECG model has demonstrated excellent performance, achieving an area under the receiver operating characteristic curve of 0.87 in both internal and external validation cohorts.²¹ At an optimal cutoff value of 0.994, which identified approximately 1.5% of the population as high risk, the model yielded a sensitivity of 29.2%, specificity of 98.4%, positive predictive value (PPV) of 4.0%, and negative predictive value (NPV) of 99.8%.

This prospective, single-center, open-label, parallel-group RCT is designed to evaluate whether the AI-ECG-guided screening strategy, combined with up to 7 days of ambulatory Holter monitoring, is superior to standard care in detecting newly diagnosed AF, AFL, or PAAFs, defined as > 500 PACs per 24 hours, consecutive short runs of PACs > 20 beats, or non-sustained AF/AFL.

The secondary objectives are to assess downstream antiarrhythmic treatment decisions, including the initiation of medication or catheter ablation, as well as the incidence of monitoring- and treatment-related adverse events, captured as observational outcomes during routine clinical follow-up rather than protocol-directed interventions.

The study protocol schema is demonstrated in Figure 1.

Ethics and informed consent

All authors materially contributed to the study de-

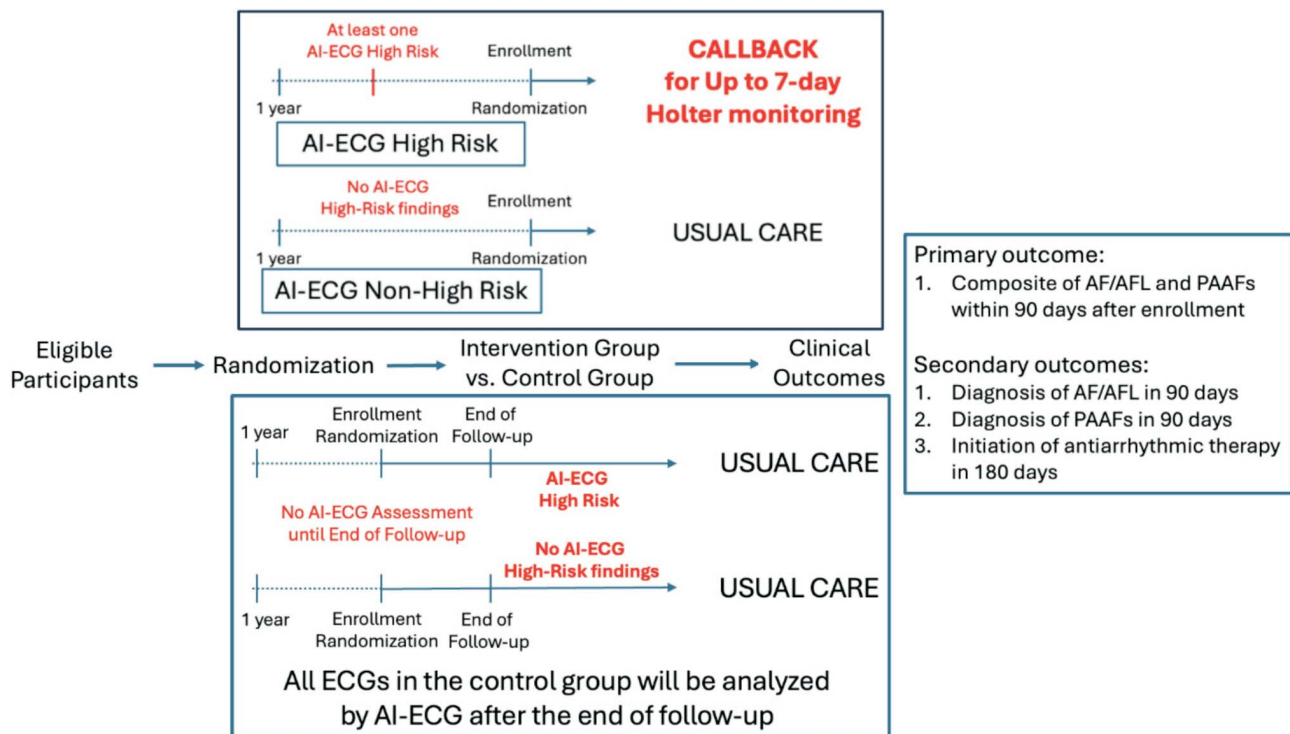


Figure 1. Protocol schema for LATENT Trial / Approximately 14,726 patients without a history of AF/AFL, ablation therapy for AF/AFL, CIED implantation, rhythm control therapy, and anticoagulant treatment will be enrolled and randomized to an AI-ECG-guided extended Holter monitoring strategy. The primary outcome is whether the AI-ECG-guided risk stratification combined with targeted ambulatory Holter monitoring can improve detection of AF or PAAFs compared with usual care. AF, atrial fibrillation; AFL, atrial flutter; AI, artificial intelligence; CIED, cardiac implantable electronic device; ECG, electrocardiogram; PAAFs, pre-AF atrial findings.

sign, manuscript drafting, and revision, and approved the final version. All participants will receive a comprehensive explanation of the study objectives, intervention, potential risks, and benefits. Written informed consent will be obtained after confirming the participants' understanding and voluntary agreement to participate.

This study was approved by the Institutional Review Board of Tri-Service General Hospital, Taipei, Taiwan (IRB No. A202205179) prior to initiation. The RCT will not involve the collection or storage of additional blood samples. Results and reports from the ambulatory Holter monitoring will be integrated into the electronic medical record (EMR) system of the hospital.

Inclusion and exclusion criteria

Eligible participants are adults aged 40 to 85 years who present to the outpatient clinics or are hospitalized at Tri-Service General Hospital, a tertiary academic medical center in Taipei, Taiwan. All participants are required to provide written informed consent and to have had at

least one 10-second, 12-lead SR ECG recorded within the preceding 12 months in our EMR system.

Patients with prior documentation of AF and AFL, identified through EMRs, International Classification of Diseases (ICD-9/10) diagnostic or procedural codes, or 12-lead ECG prior to enrollment will be excluded from the study. Individuals with a history of catheter ablation or surgical ablation for AF or AFL will also be excluded. Patients with any cardiac implantable electronic device, including permanent pacemakers, implantable cardioverter-defibrillators, cardiac resynchronization therapy devices, or leadless pacemakers, prior to enrollment will be excluded. In summary, exclusion is based on any of the following criteria: presence of relevant ICD-9/10 diagnostic or procedural codes; a documented history of device implantation in the EMR system; visits to a device follow-up clinic; ECG evidence of pacing rhythm; or radiology reports indicating the presence of pacemaker leads, defibrillator leads, leadless devices, or subcutaneous/extravascular components. The full list of codes used to

define these criteria is provided in Supplementary Table 1.

Patients with a prior or current history of treatment with class I or class III antiarrhythmic drugs or any oral anticoagulants, including vitamin K antagonists or non-vitamin K antagonist oral anticoagulants, will be excluded. These medications are commonly prescribed in patients with confirmed or strongly suspected AF or AFL, regardless of the original indication. The inclusion and exclusion criteria are summarized in Table 1.

Randomization and blindness

Eligible participants will be randomly assigned weekly in a 1:1 ratio to the intervention or control group using simple randomization. The allocation sequence will be generated with the sample() function in R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria), without stratification or blocking. Randomization will be performed by an independent investigator not involved in enrollment or outcome assessment to ensure allocation concealment.

This study is an open-label RCT. Due to the nature of the intervention, participants will not be blinded to group allocation. However, all ECG and Holter recordings will be independently interpreted by board-certified electrophysiologists who are blinded to treatment assignment and AI-ECG risk stratification.

Intervention

In the intervention group, all 12-lead ECGs recorded within one year prior to enrollment will be analyzed by the AI-ECG model. Patients identified as high-risk, defined as having at least one high-risk ECG within the 12

months prior to enrollment, will be invited to undergo up to 7 days of ambulatory Holter monitoring. Patients without any high-risk ECGs will receive standard care, and all clinical decisions, including follow-up, examinations, and treatment, will be made by treating physicians. In the control group, patients' ECGs will not be analyzed by the AI-ECG model during the study period. After study completion, retrospective AI-ECG risk stratification will be performed in the control group for descriptive and subgroup analyses only, without informing any additional clinical intervention based on AI-ECG risk stratification. To assess potential verification bias, an age- and sex-matched subset of control patients will be invited to undergo up to 7 days of ambulatory Holter monitoring.

We have selected a cutoff value of 0.994 to define high-risk patients based on the model performance in internal validation, which achieved high specificity (> 98%) and NPV (~99.8%) while minimizing false positives. The modest PPV (~4%) reflects the low disease prevalence, but this threshold successfully identifies individuals at substantially higher risk, facilitating targeted ambulatory Holter monitoring and early arrhythmia detection.

Assessments

After randomization, baseline demographics, comorbidities, and medication history will be retrieved from the EMR system. Echocardiographic parameters obtained within one year prior to enrollment will also be collected. Risk factors associated with AF development will be assessed using two validated clinical scores: the C2HEST score (Coronary artery disease, Chronic obstructive

Table 1. Inclusion and exclusion criteria

Inclusion criteria

1. Age 40-85 years.
2. Able to provide informed consent.
3. At least one 12-lead sinus rhythm electrocardiogram recorded within the preceding 12 months.
4. Presenting to outpatient clinics or hospitalized at Tri-Service General Hospital, Taipei, Taiwan.

Exclusion criteria

1. History of atrial fibrillation or atrial flutter.
2. History of catheter or surgical ablation for atrial fibrillation or atrial flutter.
3. Presence of any cardiac implantable electronic device implantation, including permanent pacemaker, implantable cardioverter-defibrillator, cardiac resynchronization therapy device, or leadless pacemaker.
4. Prior or current use of any class I or class III antiarrhythmic drugs.
5. Prior or current use of any oral anticoagulants, including vitamin K antagonists or non-vitamin K antagonist oral anticoagulants.

tive pulmonary disease, Hypertension, Elderly, Systolic heart failure, Hyperthyroidism) and TWAF score (Age, Gender, Hypertension, Diabetes mellitus, Heart failure, Coronary artery disease, Chronic kidney disease, Chronic obstructive pulmonary disease, Stroke).^{8,10} All patient-level data will be extracted at the time of enrollment. Detailed definitions are provided in Supplementary Table 2.

The 7 days of continuous ambulatory Holter monitoring among high-risk patients in the intervention group will use the Rooti RX® patch device (Rooti Labs Inc., Taipei, Taiwan). This is a single-lead, chest-worn ECG patch that captures high-resolution signals at 250 Hz. The CE-marked algorithm of the device automatically detects candidate atrial arrhythmia episodes and has been validated to have the following diagnostic performance: sensitivity 95.2%, specificity 99.6%, PPV 75.8%, NPV 99.9%, and overall accuracy 99.6%.²² All auto-detected segments will be reviewed by certified technicians and confirmed by a board-certified electrophysiologist.

For the remaining patients, physicians can arrange 24-hour, 7-day, or 14-day Holter monitoring based on their clinical judgment. The 24-hour Holter systems used in the study will include Philips and GE Holter systems. All recordings will be interpreted by two electrophysiologists. In cases of disagreement, final interpretations will be determined by consensus. Otherwise, all 12-lead ECG reports in the study will be reviewed and verified by cardiologists. An electrophysiologist will be consulted in cases of diagnostic uncertainty. All Holter and ECG interpretations will be performed independently and blinded to study group and AI-ECG risk stratification.

The primary outcome, latent AF, is a composite endpoint comprising events occurring within 90 days after enrollment:

(1) Newly diagnosed AF/AFL

- A new AF/AFL diagnosis code identified through the EMR system, or
- Sustained AF/AFL documented on a 10-second, 12-lead ECG, or
- An AF/AFL episode lasting ≥ 30 seconds detected by continuous Holter monitoring.

(2) Newly detected pre-AF atrial findings, PAAFs (any one of the criteria below).¹⁴⁻¹⁷

- Frequent PACs: > 500 PACs in 24 hours on continuous Holter monitoring.

- Burst PACs: > 20 consecutive PACs in a single run, detected on continuous Holter monitoring or 12-lead ECG.
- Non-sustained AF/AFL: episodes < 30 seconds documented by continuous Holter monitoring or 12-lead ECG.

The secondary outcomes include:

- (1) Newly diagnosed AF/AFL within 90 days after enrollment.
- (2) Newly detected PAAFs within 90 days after enrollment.
- (3) Initiation of antiarrhythmic therapy (including antiarrhythmic medications or catheter ablation) within 180 days after enrollment.

Treatment decisions, including the initiation of medications or catheter ablation, will be made at the discretion of the treating physicians based on current guidelines, individual clinical assessment and patient preference. Antiarrhythmic medications may include first prescriptions of beta-blockers, non-dihydropyridine calcium channel blockers, and class Ia, Ic, and III antiarrhythmic agents.

Monitoring-related adverse events will be evaluated when the ambulatory Holter monitoring device is returned. Patients will self-report adverse events using a standardized questionnaire (Supplementary Table 3). The questionnaire includes local erythema, itching, contact dermatitis, blistering, skin peeling, sleep disturbance, interference with daily activities, and other events.

We will report the adverse events associated with antiarrhythmic medications throughout the study period, including bradycardia, hypotension, worsening heart failure, bronchospasm, QT prolongation, proarrhythmia, conduction abnormalities, liver dysfunction, thyroid dysfunction, and others. Only the events leading to emergency department visit, hospitalization or discontinuation of treatment will be reported. Detailed definitions are provided in Supplementary Table 4.

Sample size estimation

Based on our model performance with a cutoff value of 0.994 indicating high risk, a PPV of 4.0%, NPV of 99.8%, and high-risk prevalence of approximately 1.5% were used to estimate the sample size. For the control group, the expected event rate (P_1) was conservatively estimated at 0.2% (0.002) based on retrospective data from our hospital population. This estimate reflects the

expected short-term detection of new-onset AF under usual care within the prespecified follow-up window, in the absence of systematic rhythm monitoring. For the intervention group, the projected event rate (P_2) was 0.52%, based on the PPV of the model (4.0%), an assumed Holter response rate of 67% (defined as the proportion of high-risk patients expected to return for the 7-day Holter monitoring), and diagnostic yield from ambulatory Holter monitoring (30%). The sample size was estimated based on a two-sided α of 0.05, 90% power, and a 1:1 allocation ratio. Consequently, a total of 7,363 participants per group (14,726 in total) are required to detect a statistically significant absolute risk difference of 0.32% ($P_2 = 0.52\%$ vs. $P_1 = 0.2\%$).

Statistical analysis plan

Continuous variables will be summarized as mean $\pm$ standard deviation or median with interquartile range, and compared using the Student's t-test or Mann-Whitney U test, depending on distribution. Categorical variables will be presented as frequencies and percentages, and compared using the chi-square test or Fisher's exact test, as appropriate. All statistical tests will be two-tailed with a significance level of 0.05.

The primary and secondary outcomes will be analyzed based on the intention-to-treat principle, in which all randomized participants will be included in the analysis according to their originally assigned groups, regardless of adherence to the assigned intervention.

Clinical outcomes will be analyzed using logistic regression models to estimate crude odds ratios (ORs) with 95% confidence intervals. If significant baseline imbalances between groups are detected, inverse-probability-of-treatment weighting will be used to estimate adjusted ORs in sensitivity analyses.

Safety outcomes, including monitoring-related adverse events, antiarrhythmic medication-related adverse events and procedural complications will be summarized descriptively. Between-group comparisons for categorical safety outcomes will be performed using the same analytical principles as those used for the efficacy outcomes.

Pre-specified subgroup analyses will be performed to assess the effect of assignment to the AI-guided screening strategy in the AI-defined high-risk subgroup. In addition, subgroup analyses will be conducted to assess

whether the effects of the intervention differ across clinically relevant categories: sex (male vs. female), age (40-64 vs. 65-85 years), C₂HES₂ score (≥ 4 vs. < 4), TWAF score (≥ 10 vs. < 10), and CHA₂DS₂-VA score (≥ 2 vs. < 2). Logistic regression models including interaction terms between treatment and subgroup variables will be used to evaluate effect modification. A p value < 0.05 for the interaction term will be considered statistically significant.

All analyses will be performed using R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria).

DISCUSSION

The significance of the present RCT is to demonstrate that an AI-ECG-guided screening strategy, when combined with ambulatory Holter monitoring, can significantly improve the diagnostic yield of new-onset AF/AFL and PAAFs in a hospital-based setting. This strategy relies solely on a 10-second, 12-lead SR ECG without requiring additional clinical or demographic information. It offers a simple and feasible approach to identify individuals with previously unrecognized AF or at elevated risk for atrial disease, thereby enabling efficient and targeted screening in routine clinical workflows.

Prior studies have demonstrated that AI-ECG-derived risk scores are associated with subsequent incident AF.^{19,23} Building on this foundation, the present study extends the application of AI-ECG from risk prediction to clinical implementation by integrating AI-guided risk stratification with targeted ambulatory Holter monitoring in a randomized controlled design. To our knowledge, this is the first RCT to investigate whether AI-ECG can be used to guide monitoring strategies.

The natural course of AF development frequently involves subclinical atrial arrhythmias or paroxysmal episodes in its early stages.^{12,24} Relying solely on sustained AF or AFL as diagnostic endpoints may underestimate the true burden of atrial electrical instability in at-risk populations. Current evidence suggests that these subclinical atrial arrhythmias are strong predictors of incident AF and carry meaningful prognostic relevance comparable to early-stage AF.^{25,26} A daily PAC burden > 500 beats or short atrial tachyarrhythmia runs (> 20 beats) has been consistently associated with increased suscep-

tibility to AF.^{17,27} From a screening perspective, incorporating PAAFs allows for the identification of individuals with atrial electrical dysfunction and may broaden the pool of patients eligible for intensified surveillance.

Current guidelines emphasize the importance of the early identification of individuals at high risk of AF to facilitate risk modification.^{2,28,29} Although early rhythm control after a confirmed AF diagnosis has been shown to improve cardiovascular outcomes, the present trial addresses an earlier step in the care pathway by supporting timely risk stratification and diagnostic evaluation that may precede therapeutic decision-making.³⁰⁻³² With respect to the secondary objectives, we will report observational findings reflecting real-world clinical responses following early arrhythmia detection. Downstream treatment decisions should be interpreted as reflections of routine clinical judgment after identifying arrhythmia rather than as protocol-driven or endpoint-defining interventions.

We adopted a hospital-based setting for this trial due to several important considerations. Compared with the general population, patients in a hospital setting, whether inpatient or outpatient, tend to have more comorbidities associated with increased AF risk.³³⁻³⁵ Moreover, once AF is diagnosed, hospital-based populations have been shown to have higher rates of stroke, cardiovascular events, and all-cause mortality compared with those identified through community-based screening.^{36,37} Starting with a high-risk population allows a clearer demonstration of the clinical utility and predictive value of the AI-ECG-guided screening strategy in a setting where undiagnosed AF and pre-AF states are more prevalent.

Our AI-ECG approach offers several potential clinical applications. The AI-ECG-guided strategy enables identification of high-risk individuals using a 12-lead SR ECG, thereby facilitating targeted recommendations for extended ambulatory Holter monitoring. By improving the efficiency of rhythm surveillance, this approach supports more focused diagnostic evaluation of AF and PAAFs in clinical practice and provides a potential framework for future strategies aimed at improving AF-related clinical outcomes. Furthermore, this validated approach provides a foundation for expanding into community-based screening programs for broader, efficient population-level AF detection.

Several limitations should be acknowledged. First, the trial has been designed to evaluate diagnostic yield

within a prespecified follow-up period and is not designed to assess hard clinical outcomes. Accordingly, outcomes such as stroke, hospitalization, and mortality are beyond the scope of the primary analysis. Extended follow-up is planned to explore longer-term outcomes, including newly diagnosed AF/AFL, stroke, and all-cause mortality. In addition, a cost-effectiveness analysis is planned to assess the economic implications of the AI-ECG-guided screening strategy compared with usual care. Although simple randomization without stratification may carry the risk of baseline imbalance in a single-center trial, the large planned sample size and prespecified adjusted analyses are expected to mitigate this concern.

CONCLUSION

This RCT will evaluate the use of AI-ECG-guided targeted ambulatory Holter monitoring to enhance diagnostic yield while informing more efficient resource utilization for rhythm surveillance, thereby providing a screening framework for identifying individuals at increased risk of, or in the early stage of, AF.

DECLARATION OF CONFLICT OF INTEREST

All the authors declare no conflict of interest.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1. Exclusion criteria diagnosis codes and procedure codes

1. Atrial fibrillation/atrial flutter diagnosis codes:
ICD-9-CM: 427.31/427.32
ICD-10-CM: I48, I48.0, I48.1, I48.11, I48.19, I48.2, I48.20, I48.21, I48.3, I48.4, I48.91, I48.92
2. Atrial fibrillation/atrial flutter ablation:
NHI code: 33139B, 33140B, 33091B
ICD-9-CM Procedure: 37.34
ICD-10-PCS: 02583ZZ
3. Cardiac implantable electronic device related diagnosis codes:
ICD-9-CM: V45.01, V45.02, V53.31
ICD-10-CM: Z95.0, Z95.810
4. Cardiac implantable electronic device procedure codes
NHI code: 68012B, 68041B
ICD-9-CM Procedure: 37.80, 37.83, 37.85
ICD-10-PCS: 0JH604Z, 0JH605Z, 0JH606Z, 0JH607Z, 0JH632Z, 0JH638Z, 0JH639Z

CM, Clinical Modification; ICD, International Classification of Diseases; NHI, Taiwan National Health Insurance; PCS, Procedure Coding System.

NHI codes correspond to Taiwan's National Health Insurance procedural billing codes.

Supplementary Table 2. Patient baseline characteristics

Patient characteristics	Definition or supplementary note
1. Demographics	
Source	Inpatient department or outpatient department
Gender	Male or female, biological sex
Age	Years old
2. Comorbidities	
Diabetes mellitus	ICD-9 (250.x) and ICD-10 (E10-E14)
Hypertension	ICD-9 (401.x to 404.x) and ICD-10 (I10 to I16)
Coronary artery disease	ICD-9 (410 to 414) and ICD-10 (I20 to I25)
Peripheral arterial disease	ICD-9 (440.2x, 443.9) and ICD-10 (I70.x, I73.9, I74.x)
Heart failure	ICD-9 (428.x, 398.91, 402.x1, 404.x1, 404.x3) and ICD-10 (I50.x, I11.0, I13.0, I13.2)
Valvular heart disease	ICD-9 (394 to 397, 424.0 to 424.3) and ICD-10 (I05 to I08, I34 to I39)
Stroke/TIA/thromboembolism	ICD-9 (430 to 438, V12.54) and ICD-10 (I60 to I69, G45.x, Z86.73, H34.1)
Chronic kidney disease	ICD-9 (585.x) and ICD-10 (N18.x)
Chronic obstructive pulmonary disease	ICD-9 (491.x, 492.x, 496) and ICD-10 (J44.x)
Obstructive sleep apnea	ICD-9 (780.57, 327.23) and ICD-10 (G47.3)
Thyroid disease	ICD-9 (240 to 246) and ICD-10 (E00 to E07)
3. Medical history	
Beta-blockers	Extract from EMR system
Non-dihydropyridine CCB	Extract from EMR system
ACEi or ARB	Extract from EMR system
SGLT2i	Extract from EMR system
Statin	Extract from EMR system
4. Echocardiographic parameters	
LA diameter	By PLAX view (2D or M-mode); mm
LVEF	By PLAX view M-mode by Teichholz Formula; or AP4 view by Simpson's method; %
RVSP	TR jet velocity from CW Doppler in AP4 view, estimated RAP based on IVC diameter; calculated by Modified Bernoulli equation; mmHg

ACEi, angiotensin-converting enzyme inhibitors; AP4, apical four chamber; ARB, angiotensin II receptor blockers; CCB, calcium channel blocker; CW, continuous-wave; EMR, electronic medical record; ICD, International Classification of Disease; IVC, inferior vena cava; LA, left atrium; LVEF, left ventricular ejection fraction; PLAX, parasternal long axis view; RAP, right atrial pressure; RVSP, right ventricular systolic pressure; SGLT2i, sodium-glucose cotransporter-2 inhibitors; TIA, transient ischemic attack; TR, tricuspid regurgitation.

Supplementary Table 3. Monitoring-related adverse events questionnaire

Record date:

Medical record number:

Patient name:

- | | | |
|---|------------------------------|-----------------------------|
| 1. Is there any localized erythema (redness of the skin)? | ☐ Yes | ☐ No |
| 2. Is there any localized itching? | ☐ Yes | ☐ No |
| 3. Has contact dermatitis occurred? | ☐ Yes | ☐ No |
| 4. Are there any blisters present? | ☐ Yes | ☐ No |
| 5. Is there any skin peeling? | ☐ Yes | ☐ No |
| 6. Has sleep been disturbed? | ☐ Yes | ☐ No |
| 7. Has daily activity been affected? | ☐ Yes | ☐ No |
| 8. Are there any other discomforts or adverse events? | ☐ Yes | ☐ No |

Supplementary Table 4. Antiarrhythmic medications related adverse events

Category	Events reported (emergency department visit, hospitalization, or drug discontinuation)
Bradycardia	Sinus bradycardia or junctional rhythm ≤ 50 bpm, or symptomatic bradycardia
Hypotension	Systolic BP < 90 mmHg, or ≥ 20 mmHg drop from baseline with symptoms
Worsening heart failure	New-onset or exacerbated of heart failure signs or symptoms
Bronchospasm	Acute respiratory compromise attributable to the AAD
QT prolongation/TdP	QTc > 500 ms, QTc prolongation > 60 ms from baseline, or documented TdP episode
Proarrhythmia	New-onset sustained or non-sustained VT, VF, or atrial flutter with 1:1 conduction
Conduction abnormalities	New Mobitz Type II AVB, complete AVB, or new bundle branch block
Liver dysfunction	ALT/AST $> 3 \times$ ULN or total bilirubin $> 2 \times$ ULN
Thyroid dysfunction	New-onset hypothyroidism or hyperthyroidism link to AAD
Other intolerant AEs	Unspecified AAD-related adverse events leading to emergency department visit, hospitalization, or drug discontinuation

AAD, antiarrhythmic drug; AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; AVB, atrioventricular block; bpm, beats per minute; BP, blood pressure; QTc, corrected QT interval; TdP, Torsades de Pointes; ULN, upper limit of normal; VF, ventricular fibrillation; VT, ventricular tachycardia.