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Prediction model for the new onset of atrial fibrillation combining features of 24-hour Holter electrocardiogram with 12-lead electrocardiogram

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ABSTRACT

Background: Several factors that predict new-onset atrial fibrillation (AF) have been investigated using the 24-hour Holter electrocardiogram (ECG) and 12-lead ECG; however, these have been based on each test independently. The aim of this study was to combine findings from the two tests to create a comprehensive, easy-to-use score and to examine its validity.

Methods and Results: A total of 502 patients underwent 24-hour Holter ECG and 12-lead ECG were followed up for 6.2 ± 3.5 years, and 66 patients developed new-onset AF. Multivariate Cox regression analyses revealed that total number of supraventricular extrasystoles (SVEs) ≥ 100 beats/day and SVE's longest run ≥ 3 beats on 24-hour Holter ECG and PR interval ≥ 185 ms, amplitude ratio of P wave (aVR/V1) < 1.0 and amplitude of RV5 + SV1 ≥ 2.2 mV on 12-lead ECG were significant independent predictors for developing AF (all $p < 0.01$). Using these cut-off points, the PAAFS (acronym for risk factors) score was constructed by adding one point for each parameter if the patient met each of the criteria. The area under the curve (AUC) of the PAAFS score was 0.80, compared to the AUCs of 24-hour Holter ECG-only factors (0.73) and 12-lead ECG-only factors (0.72), indicating an improvement in score. The annual incidence of AF for each PAAFS score were 0.0%, 0.2%, 0.7%, 1.9%, 5.6%, and 11.1%/year for scores 0 to 5, respectively.

Conclusion: The PAAFS score, which combines findings from 24-hour Holter ECG and 12-lead ECG, was superior to 24-hour Holter ECG and 12-lead ECG alone in predictive accuracy for new-onset AF.

1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia in the elderly, and its incidence increases with age [1,2]. AF is also associated with an increased risk of stroke, heart failure, and death; however, appropriate anticoagulation can reduce the risk of stroke by about 60% [1,2,3]. AF is difficult to diagnose because it can be asymptomatic or only paroxysmal, and it is often not diagnosed until complications occur [4]. For this reason, many studies have investigated factors that predict the new-onset AF.

First, supraventricular extrasystole (SVE) of pulmonary venous origin has been reported to precede the onset of AF [5], and studies using 24-hour Holter ECG have considered frequent or sequential SVE to be risk factors for AF [6]. Also, predictors on 12-lead electrocardiograms (ECGs) have been reported to include the P-wave duration [7], P-wave dispersion [8,9], P-wave amplitude in leads aVR and V1 [8,10], and findings of left ventricular hypertrophy [11].

However, no study has combined both findings to stratify the risk of new-onset AF. We hypothesized that 24-hour Holter ECG detects its trigger and 12-lead ECG detects the substrate of AF, and that the combination of both tests may have improved the prediction accuracy of AF. This study aimed to investigate data on the morphologies of SVE (AF trigger) from 24-hour Holter ECG and the P wave and QRS wave (AF substrate) from 12-lead ECG to identify useful predictors of new-onset AF, and combine those findings to create a comprehensive, easy-to-use score and examine its validity.

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2. Methods

2.1. Study design and study population

The study protocol complied with the Declaration of Helsinki of 1975 and the study was approved by the Ethics Committee of Kyoto Prefectural University of Medicine (KPUM). We included 1794 patients aged ≥ 20 years who visited the KPUM hospital between January 2008 and December 2014 for a diagnosis of symptoms such as palpitations, dizziness, and syncope, and for whom 24-hour Holter ECG was performed. Patients with no 12-lead ECG within 12 months before or after the 24-hour Holter ECG, patients with a history of AF, and patients with less than one year of follow-up were excluded from the study. Additionally, patients after pacemaker or implantable cardioverter-defibrillator implantation at baseline, and patients on Class I/III/IV (bepridil) antiarrhythmic drugs at baseline were also excluded from the study. If multiple 24-hour Holter ECGs were performed in the same patient, the first data were included in the analysis and the second and following data were excluded. Finally, 502 patients were included in the analysis (Fig. 1). Medical records of the KPUM hospital were comprehensively referenced to record demographic data, cardiovascular risk factors, medications, 12-lead ECG, 24-hour Holter ECG, and subsequent onset of AF events. Medical records, emergency visit records, and all available ECGs were reviewed for the onset of AF.

2.2. Data analysis

Heart rate, SVE and ventricular extrasystole (VES) counts were recorded by Two-channel Holter ECG recorder (FM-960; Fukuda Denshi Co, Ltd, Tokyo, Japan) with CM5 and NASA leads and automatically analyzed using a Holter ECG analyzer (SCM-8000; Fukuda Denshi Co, Ltd, Tokyo, Japan). The 12-lead ECG (FCP-8700; Fukuda Denshi Co, Ltd, Tokyo, Japan) was recorded at rest with a standard gain of 0.1 mV/mm and a recording speed of 25 mm/s. The absolute values of P-wave amplitudes of leads aVR and V1, the amplitude ratio of the P wave (aVR/V1), the mean and maximum P-wave durations, P-wave terminal force in lead V1 (PWTF), and the amplitude of RV5 + SV1 were obtained by the following definitions using a 12-lead ECG analyzer (MBF-1000; Fukuda Denshi Co, Ltd, Tokyo, Japan). When the P wave showed biphasic characteristics, its amplitude was defined as the absolute difference between the peak of the positive component and the bottom of the negative component, and the duration was measured, including the backward component. If the P-wave amplitude was<0.01 mV and the P-wave duration was difficult to measure, it was excluded from the analysis. The PWTF was calculated by multiplying the P-wave duration by the amplitude of the negative component of the V1 lead.

The CHADS2 (congestive heart failure, hypertension, age ≥ 75 years, type 2 diabetes, and previous stroke/transient ischemic attack [doubled]) score, CHA2DS2-VASc (congestive heart failure, hypertension, age ≥ 75 years [doubled], type 2 diabetes, previous stroke/transient ischemic attack [doubled], vascular disease, age 65 to 75 years, and sex category) score, and CHARGE-AF (0.508 × age (5 years) + 0.248 × height (10 cm) + 0.115 × weight (15 kg) + 0.197 × systolic blood pressure (20 mmHg) − 0.101 × diastolic blood pressure (10 mmHg) + 0.359 × current smoker + 0.349 × antihypertensive medication + 0.237 × type 2 diabetes + 0.701 × congestive heart failure + 0.496 × myocardial infarction) score were calculated based on the data obtained [12]. The follow-up period was calculated from the date of the 24-hour Holter ECG to the last follow-up date or the date of onset of AF. The primary endpoint was defined as new-onset AF.

2.3. Statistical analysis

Continuous variables were presented as the mean ± standard deviation. Categorical variables are presented as frequencies (percentages). Statistical significance was assessed using Student's *t*-test or the Man–Whitney *U* test for continuous variables and the chi-square statistics for categorical variables. P-values of < 0.05 were considered statistically significant. Receiver operating characteristic (ROC) curves for the detection of new-onset AF patients were used to calculate the area under the curve (AUC) and cut-off values for continuous variables were calculated based on max Youden's index. Cox regression models were used to calculate hazard ratios (HR) and 95% confidence intervals (CI) for the new-onset AF. The selection of variables for the multivariate Cox regression model was performed using the stepwise method involving variables with p-values of < 0.05 in the univariate analysis. JMP version 16.2.0 (SAS, Tokyo, Japan) was used for the statistical analysis.

2.4. The PAAFS score

Using five cut-off points that were independent risk factors in the abovementioned multivariate analyses, a PAAFS (acronym for risk factors) score was constructed by adding one point if the patient met each of the criteria (PR interval ≥ 185 ms, amplitude ratio of P wave (aVR/V1) < 1.0, amplitude of RV5 + SV1 ≥ 2.2 mV, frequent SVEs, and SVE's longest run ≥ 3 beats).

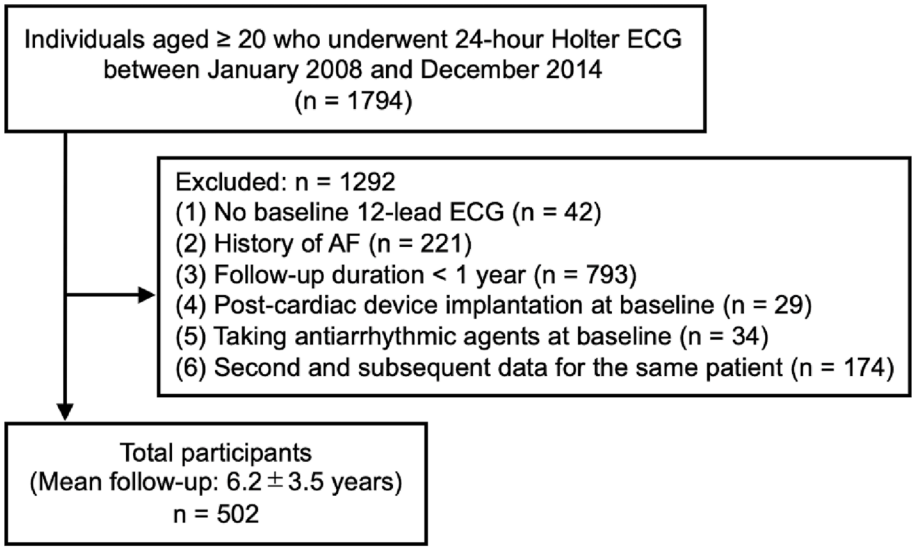

Fig. 1. Study population. ECG = electrocardiogram; AF = atrial fibrillation.

3. Results

3.1. Clinical characteristics

The mean age was 66.2 ± 14.2 years and 49.0% of the study participants were males. After a mean follow-up period of 6.2 ± 3.5 years, 66 of 502 patients (13.1%, 21.2 per 1000 patient-years) developed new-onset AF. Table 1 summarizes the baseline clinical characteristics. Patients who developed AF were significantly older ($p = 0.03$), more of them had a history of hypertension ($p = 0.03$), and they were more likely to be on antihypertensive medications ($p = 0.03$).

3.2. 24-hour Holter ECG and 12-lead ECG findings

On 24-hour Holter ECG, the mean total number of SVEs was 975 ± 3122 beats/day and the median 83 beats/day (range: 0–36440 beats/day, inter-quartile range: 25–346 beats/day). The total number of SVEs ($p < 0.001$) and SVE's longest run ($p < 0.01$) were significantly higher in patients with AF.

On 12-lead ECG, the PR interval ($p < 0.001$), amplitude of RV5 + SV1 ($p = 0.01$), and max P-wave duration ($p = 0.02$) were significantly higher in patients with AF. P-wave amplitude analyses revealed that significantly more P-wave amplitude reduction in the aVR lead ($p < 0.001$), P-wave amplitude increase in the V1 lead ($p = 0.02$), and amplitude ratio of P wave (aVR/V1) reduction ($p < 0.001$) in patients with AF.

3.3. Multivariate Cox regression analyses on the new-onset AF

The optimal cut-off points for the new-onset AF, determined from ROC curves, were total number of SVEs ≥ 100 beats/day (frequent SVEs), SVE's longest run ≥ 3 beats, PR intervals ≥ 185 ms, P-wave amplitude in lead aVR ≤ 0.04 mV, P-wave amplitude in lead V1 ≥ 0.10 mV, amplitude ratio of P wave (aVR/V1) < 1.0, amplitude of RV5 + SV1 ≥ 2.2 mV, and max P-wave duration ≥ 125 ms. As shown in Table 2, the multivariate analyses revealed that frequent SVEs (HR: 3.43; 95% CI: 1.70–6.91, $p < 0.001$), SVE's longest run ≥ 3 beats (HR: 3.01; 95% CI: 1.26–7.19, $p < 0.01$), PR interval ≥ 185 ms (HR: 2.50; 95% CI: 1.52–4.13, $p < 0.001$), amplitude ratio of P wave (aVR/V1) < 1.0 (HR: 2.67; 95% CI: 1.38–5.16, $p < 0.01$), and amplitude of RV5 + SV1 ≥ 2.2 mV (HR: 2.21; 95% CI: 1.19–4.08, $p < 0.01$) were independently associated with new-onset AF. The inclusion of clinical characteristics such as CHADS2, CHA2DS2-VASc, and CHARGE-AF score in the multivariate analysis did not change the number of significant risk factors.

3.4. The PAAFS score

The PAAFS score was constructed based on cutoff points identified as independent risk factors in the multivariate analysis. The mean PAAFS score was 2.5 ± 1.3. The annual incidence of AF for each PAAFS score were 0.0%, 0.2%, 0.7%, 1.9%, 5.6%, and 11.1%/year for scores 0 to 5, respectively (Fig. 2). For every one-point increase in the PAAFS score, the risk of developing AF increased with HR: 2.77 (95% CI: 2.19–3.56, $p < 0.001$). The ROC curve of the new-onset AF was depicted using the findings of this study (Fig. 3). The AUC for the 24-hour Holter ECG-only factors, including frequent SVEs and SVE's longest run ≥ 3 beats, was 0.73 ($p < 0.001$). The AUC for the 12-lead ECG-only factors, including PR interval ≥ 185 ms, P wave amplitude ratio (aVR/V1) < 1.0, and RV5 + SV1 amplitude ≥ 2.2 mV, was 0.72 ($p < 0.001$). Compared to the AUCs of 24-hour Holter ECG and 12-lead ECG, the AUC of the PAAFS score was 0.80 ($p < 0.001$), indicating an improvement in score. The AUC of the CHADS2 score was 0.60 ($p = 0.01$), the CHA2DS2-VASc score 0.58 ($p = 0.05$) and the CHARGE-AF score 0.61 ($p < 0.01$) with low predictive ability.

Table 1
Baseline characteristics of patients with and without new-onset AF.

Variable	All patients	New-onset AF		p-value
		No	Yes	
	(n = 502)	(n = 436)	(n = 66)	
Clinical characteristics				
Age, years	66.2 ± 14.2	65.6 ± 14.4	69.8 ± 11.7	0.03
Age ≥ 75, n (%)	164 (32.7)	137 (31.4)	27 (40.9)	0.13
Male sex, n (%)	246 (49.0)	210 (48.2)	36 (54.6)	0.33
Body mass index, kg/m^2	22.4 ± 4.0	22.4 ± 4.0	22.3 ± 4.1	0.82
Systolic blood pressure, mmHg	128.9 ± 17.8	128.9 ± 17.6	129.2 ± 19.0	0.87
Diastolic blood pressure, mmHg	73.6 ± 13.1	73.9 ± 13.1	71.9 ± 12.9	0.26
Hypertension, n (%)	279 (55.6)	234 (53.7)	45 (68.2)	0.03
Diabetes, n (%)	97 (19.3)	79 (18.1)	18 (27.3)	0.08
Congestive heart failure, n (%)	23 (4.6)	19 (4.4)	4 (6.1)	0.54
CAD / PAD, n (%)	82 (16.3)	74 (17.0)	8 (12.1)	0.32
Stroke / TIA, n (%)	23 (4.6)	20 (4.6)	3 (4.6)	0.99
Myocardial infarction, n (%)	35 (7.0)	32 (7.3)	3 (4.6)	0.41
Current smoker, n (%)	36 (7.2)	31 (7.1)	5 (7.6)	0.89
Antihypertensive medication, n (%)	289 (57.6)	243 (55.7)	46 (69.7)	0.03
Medication				
ACE-I/ARB, n (%)	189 (37.6)	155 (35.6)	34 (51.5)	0.01
Beta blocker, n (%)	103 (20.5)	84 (19.3)	19 (28.8)	0.07
Ca blocker (non-dihydrophyridine), n (%)	41 (8.2)	38 (8.7)	3 (4.6)	0.25
Ca blocker (dihydrophyridine), n (%)	168 (33.5)	146 (33.5)	22 (33.3)	0.98
Diuretic, n (%)	67 (13.3)	52 (11.9)	15 (22.7)	0.02
$CHADS_2$ score	1.2 ± 1.1	1.2 ± 1.0	1.5 ± 1.1	0.01
CHA_2DS_2-VASc score	2.5 ± 1.5	2.5 ± 1.5	2.9 ± 1.5	0.04
CHARGE-AF score	11.5 ± 1.5	11.5 ± 1.5	12.0 ± 1.3	< 0.01
24-hour Holter ECG parameters				
Minimum heart rate, beats	52.6 ± 8.6	52.7 ± 8.7	51.7 ± 8.5	0.39
Average heart rate, beats	73.3 ± 10.4	73.4 ± 10.5	72.4 ± 9.9	0.44
Maximum heart rate, beats	117.4 ± 19.1	117.4 ± 19.1	117.1 ± 19.7	0.90
Total number of SVEs, beats/day	975 ± 3122	762 ± 2783	2382 ± 4578	< 0.001
Total number of VESs, beats/day	1507 ± 4210	1452 ± 4007	1869 ± 5387	0.45
SVE's longest run, beats	11.3 ± 61.5	7.9 ± 47.5	33.6 ± 116.1	< 0.01
12-lead ECG parameters				
PR interval, ms	168.9 ± 31.1	167.1 ± 29.2	181.1 ± 39.6	< 0.001
QRS, ms	104.3 ± 23.0	103.9 ± 23.2	107.0 ± 21.2	0.32
Corrected QT Interval (QTc)	426.4 ± 30.6	425.4 ± 29.7	433.1 ± 36.0	0.06
Amplitude of RV5 + SV1, mV	2.7 ± 1.2	2.7 ± 1.1	3.1 ± 1.4	0.01
CRBBB, n (%)	46 (9.2)	38 (8.7)	8 (12.1)	0.37
CLBBB, n (%)	6 (1.2)	4 (0.9)	2 (3.0)	0.14
P-wave amplitude in lead aVR, 10^{-2}mV	6.8 ± 3.1	7.0 ± 3.1	5.5 ± 3.2	< 0.001
P-wave amplitude in lead V1, 10^{-2}mV	8.4 ± 5.0	8.2 ± 4.9	9.7 ± 5.2	0.02
Amplitude ratio of P wave (aVR / V1)	1.1 ± 1.0	1.2 ± 1.0	0.7 ± 0.5	< 0.001
Mean P-wave duration, ms	106.7 ± 14.5	106.2 ± 13.3	109.9 ± 20.6	0.05
Max P-wave duration, ms	119.2 ± 15.4	118.6 ± 14.2	123.3 ± 21.5	0.02
P-wave terminal force in lead V1, mV/ms	3.4 ± 4.3	3.3 ± 4.3	4.0 ± 4.2	0.24

AF = atrial fibrillation; CAD = coronary artery disease: PAD = peripheral artery disease; TIA = transient ischemic attack; ACE-I = angiotensin converting enzyme inhibitor; ARB = angiotensin II receptor blocker; ECG = electrocardiogram; SVE = supraventricular extrasystole; VES = ventricular extrasystole; CRBBB = complete right bundle branch block; CLBBB = complete left bundle branch block.

4. Discussion

The PAAFS score, combination of the ECG findings from 24-hour Holter ECG and 12-lead ECG, significantly improved the prediction accuracy of new-onset of AF compared to that of each ECG modality alone. Its predictive ability was superior to the clinical background represented by the CHADS2, CHA2DS2-VASc and CHARGE-AF score, respectively.

4.1. Each component of the PAAFS score and mechanisms of AF development

SVEs have long been considered a benign form of arrhythmia; however, they have recently been shown to be associated with AF. In a study by Inoue et al, SVEs ≥ 58 beats/day and SVE's longest run ≥ 5 beats were independent predictors of late recurrence after AF catheter ablation [13]. In our study, total number of SVEs ≥ 100 beats/day were found in 238 patients (47.4%) and SVE's longest run ≥ 3 beats in 310 patients (61.8%). These findings were independent risk factors in multivariate analyses, although the cut-off values were different. They are thought to reflect "triggers" for new-onset AF, and may contribute to the diagnosis of AF by providing an overall picture of SVE with 24-hour measurements, which has been difficult to obtain with short-time 12-lead ECG.

A *meta*-analysis reported an increased risk of AF (risk ratio: 1.45; 95% CI: 1.23–1.71, p < 0.01) in patients with prolonged PR (≥196–220 ms) [14], which was similar to our finding that PR interval ≥ 185 ms was associated with new-onset AF. Prolonged atrioventricular conduction time shortens left ventricular diastolic filling time, which can lead to increased left atrial pressure and inadequate mitral valve closure, and subsequent diastolic mitral regurgitation can lead to progressive left atrial remodeling [15,16]. Regarding the P-wave amplitude, Rader et al. reported that in patients with a sinus rhythm before cardiac surgery, a decrease in the P-wave amplitude in lead aVR and an increase in the positive or negative component of the P-wave amplitude in lead V1 of the preoperative 12-lead ECG were associated with the development of postoperative AF [10]. An increase in the positive component of the P-wave amplitude in the lead V1 is considered to reflect right atrial enlargement while an increase in the negative component reflects left atrial enlargement [10]. These suggest that the amplitude ratio of P wave (aVR/V1) reduction may reflect atrial enlargement due to atrial degeneration. Chrispin et al. reported that LVH findings in Sokolow-Lyon criteria [17] are associated with the new-onset AF, suggesting an association with left atrial volume, with high specificity but low sensitivity [11]. In the present study, a cutoff value of 2.2 mV was used, which may have resulted in a higher sensitivity for detecting left atrial remodeling. Overall, prolonged PR intervals, changes in the P wave-form, and increased amplitude of RV5 + SV1, calculated from the 12-lead ECG, accurately reflect atrial remodeling and may represent the "substrate" of AF.

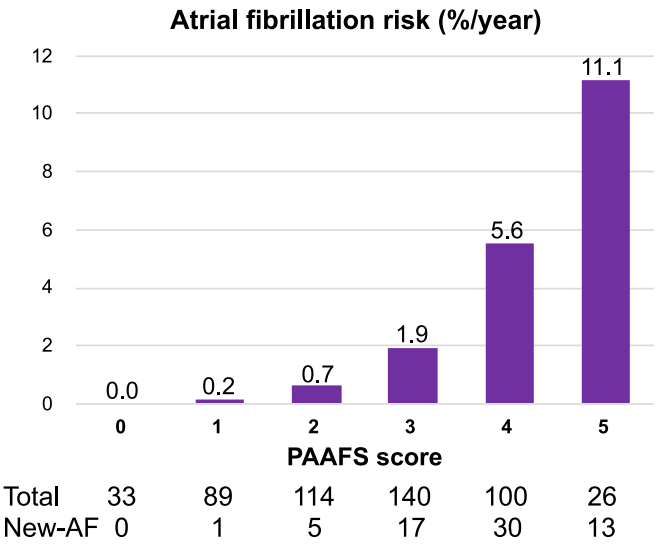

Fig. 2. The PAAFS score and annual incidence of AF. The upper part of the bar graph shows the annual incidence of AF by PAAFS score. The total number of patients and the number of AF cases for each score are shown below the graph. AF = atrial fibrillation.

4.2. Comparison of the PAAFS score with another predictive model

Christopoulos et al. conducted a population-based study using the Artificial Intelligence-Electrocardiography (AI-ECG) to compare the predictive ability of the AI-ECG and CHARGE-AF score for the prediction of new-onset AF [18,19]. AF model output and CHARGE-AF score independently predicted new-onset AF, with C-statistics of 0.69 for each alone, but increased to 0.72 for the combination. Of course, AI-ECG holds great promise in improving diagnostic accuracy, speeding up the diagnostic process, and enhancing patient care in the field of cardiology. However, clinical validation is crucial for the reliable deployment of AI-based systems. Unlike the AI-ECG based on deep learning, the PAAFS score has the advantage of being more easily socially implemented and explained. In our study, the AUC of CHARGE-AF score was 0.61 (p < 0.01), with low predictive ability, and consequently the CHARGE-AF score could not be an independent risk factor when included in a multivariate Cox regression analysis. The 24-hour Holter ECG detects SVE, which is long-duration information not available on the 12-lead

Table 2
Cox proportional hazard analysis.

Variable	Cox (Univariate)			Cox (Multivariate)		
	HR	95% CI	p-value	HR	95% CI	p-value
24-hour Holter ECG parameters						
Frequent SVEs (≥100 beats/day)	6.43	3.43–12.0	< 0.001	3.43	1.70–6.91	< 0.001
SVE's longest run ≥ 3 beats	5.92	2.70–13.0	< 0.001	3.01	1.26–7.19	< 0.01
12-lead ECG parameters						
PR interval ≥ 185 ms	2.57	1.57–4.21	< 0.001	2.50	1.52–4.13	< 0.001
Amplitude ratio of P wave (aVR / V1) < 1.0	4.25	2.22–8.12	< 0.001	2.67	1.38–5.16	< 0.01
Amplitude of RV5 + SV1 ≥ 2.2 mV	2.35	1.28–4.32	< 0.01	2.21	1.19–4.08	< 0.01
Max P-wave duration ≥ 125 ms	1.74	1.07–2.83	0.03			
P-wave amplitude in lead aVR ≤ 0.04 mV	3.16	1.94–5.17	< 0.001			
P-wave amplitude in lead V1 ≥ 0.10 mV	1.92	1.19–3.12	< 0.01			

HR = hazard ratio; CI = confidence interval; ECG = electrocardiogram; SVE = supraventricular extrasystole.

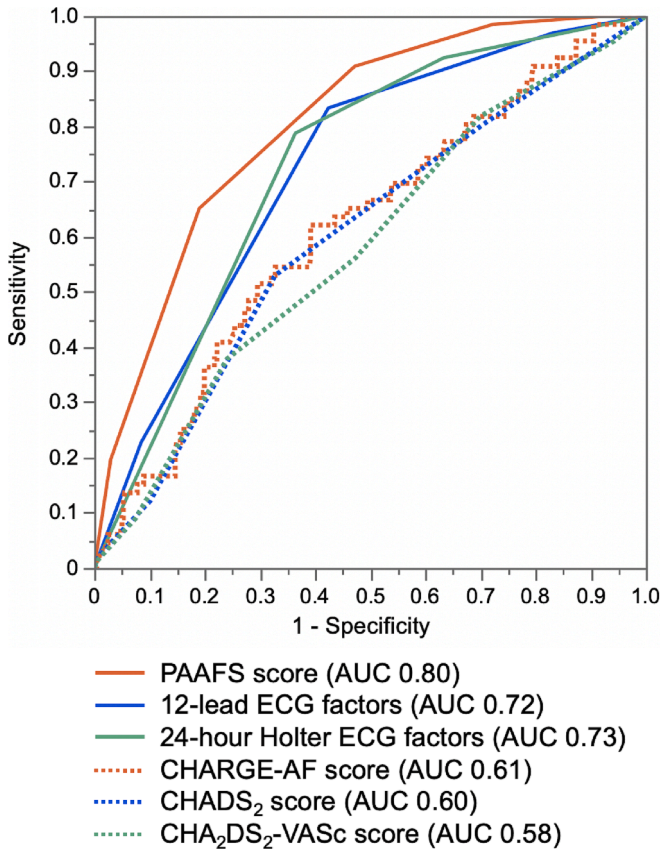

Fig. 3. ROC curve for new-onset AF. AUC = area under the curve, CHADS2 score = congestive heart failure, hypertension, age ≥ 75 years, type 2 diabetes, and previous stroke/transient ischemic attack [doubled], CHA2DS2-VASc score = congestive heart failure, hypertension, age ≥ 75 years [doubled], type 2 diabetes, previous stroke/transient ischemic attack [doubled], age 65 to 75 years, and sex category, CHARGE-AF score = 0.508 × age (5 years) + 0.248 × height (10 cm) + 0.115 × weight (15 kg) + 0.197 × systolic blood pressure (20 mmHg) − 0.101 × diastolic blood pressure (10 mmHg) + 0.359 × current smoker + 0.349 × antihypertensive medication + 0.237 × type 2 diabetes + 0.701 × congestive heart failure + 0.496 × myocardial infarction, ECG = electrocardiogram.

ECG, and both (24-hour Holter and 12-lead ECGs) are complementary in predicting AF. On the other hand, the CHARGE-AF score may be redundantly related to both "trigger" and "substrate".

The PAAFS score may be useful for stratifying patients who are more likely to develop AF and for determining the future course of treatment. For instance, patients in the low-risk group (score of 0–1) are considered to be at low risk of developing AF, and reassessments should be considered every few years. For middle-risk patients (score of 2–3), aggressive therapeutic interventions for AF risk factors such as hypertension, obesity, and sleep apnea [20] may be desirable. Patients in the high-risk group (score of 4–5) are more likely to develop AF, and frequent management with 24-hour Holter ECGs, external event loop recorder, portable ECG, and wearable ECG devices, in addition to interventions for risk factors, may lead to the early detection and prompt treatment of AF.

4.3. Study limitations

The present study is a retrospective analysis and follow-up ECG was not performed on specific dates, so that we tried to confirm the onset of AF by reviewing medical records and all available ECGs at the time of hospital visit or admission. Second, selection bias in the patient population may also have occurred because the patients in the study were those who underwent 24-hour Holter ECG screening to investigate symptoms and arrhythmias. Third, the time difference between the baseline 12-lead ECG and 24-hour Holter ECG examinations was set to be within 1 year. The median absolute value of the difference in examination dates was 12 days (interquartile range, 3–53 days), which was expected to have little effect on atrial degeneration. Finally, the study is a single-center retrospective study and an independent validation cohort is needed to validate the performance of the PAAFS score.

5. Conclusions

The PAAFS score, which combines 24-hour Holter ECG (total number of SVEs and SVE's longest run) and 12-lead ECG (PR interval, amplitude ratio of P wave (aVR/V1) and amplitude of RV5 + SV1), significantly improved the accuracy of predicting new-onset of AF compared to each ECG modality alone. The annual incidence of AF for each PAAFS score were 0.0%, 0.2%, 0.7%, 1.9%, 5.6%, and 11.1%/year for scores 0 to 5, respectively. For patients in the high-risk group, frequent ECG follow-up and interventions for AF risk factors should be recommended.

6. Author's contribution

TN and KS contributed to the conception and design of the work. MM, JM, NT, SS, HI and HS contributed to the acquisition and interpretation of data for the work. SM contributed to the interpretation of data for the work. TN analyzed the data and drafted the manuscript. The other authors critically revised the manuscript. All gave final approval and agree to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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IRB information

The present study was approved by the institutional Clinical Research Review Board of Kyoto Prefectural University of Medicine (approval registration no.: ERB-C-2409)

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